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Organizing Secretariat
Emilia Viaggi Congressi & Meeting S.r.l.
Via Porrettana, 76
40033 Casalecchio di Reno (BO)
tel. + 39 051 6194911 – fax + 39 051 6194900
e-mail: evcongressi@emiliaviaggi.it
web: www.emiliaviaggi.it

Catholic University of the Sacred Heart
Permanent Training Office
tel. + 39 06 30154886 – fax +39 06 3055397
e-mail: gchierchia@rm.unicatt.it
web: www.rm.unicatt.it

Italian Society of Uro-Oncology (SIUrO)
President: Giuseppe Martorana

Scientific Secretariat
Società Italiana di Urologia Oncologica (SIUrO)
c/o Clinica Urologica, Alma Mater Studiorum
Università di Bologna
Policlinico S. Orsola Malpighi
Padiglione Palagi, via P. Palagi, 9 – 40138 Bologna
tel. +39 051 6362421 – 051 302082 – fax +39 051 308037
e-mail: segreteria@siuro.it – web: www.siuro.it
1 LAPAROSCOPIC VERSUS OPEN RADICAL NEPHRO-URETERECTOMY FOR UPPER URINARY TRACT UROTHELIAL CANCER: ONCOLOGICAL OUTCOMES AND 5-YEAR FOLLOW-UP

Francesco Greco, Sigrid Wagner, Rashid M. Hoda, Amir Hamza and Paolo Fornara

Department of Urology and Kidney Transplantation, Martin Luther University, Halle/Saale, Germany

Laparoscopic surgery is increasingly accepted in the treatment of urological pathology. We compared the oncological outcomes of laparoscopic vs. open nephro-ureterectomy for upper urinary tract transitional cell carcinoma.

Patients and Methods: Between July 1999 and January 2003, 70 laparoscopic nephro-ureterectomies (LNU) and 70 open nephro-ureterectomies (ONU) for transitional cell carcinoma of the upper urinary tract (TCC) were performed. The open procedure was reserved for patients with previous abdominal surgery or with severe cardiac and/or pulmonary problems. Demographic data, perioperative and postoperative variables, tumour staging and histological grading and rates of metastasis were recorded and compared.

Results: For LNU and ONU, respectively, mean operative times were 240 min and 190 min; mean estimated blood loss was 70 ml in LNU and 120 ml in ONU. The definitive pathology showed a high incidence of tumour stage pT2 G2 in both LNU and ONU groups. The median follow-up period was 60 months. In the LNU group, the 5-year disease-free survival was 75%: 100% for pTa, 88% for pT1, 78% for pT2, and 35% for pT3 (p<0.0001). In the ONU group, the 5-year disease-free survival was 73% (LNU-ONU; p=0.037): 100% for pTa, 89% for pT1, 75% for pT2 and 31% for pT3 (p<0.0001).

Conclusion: The results of our long-term controlled study support the use of LNU as an effective alternative to an open procedure in the therapy of upper urinary tract urothelial cancer.

2 LAPAROSCOPIC VERSUS OPEN PARTIAL NEPHRECTOMY: ONCOLOGICAL AND FUNCTIONAL OUTCOMES OF A 5-YEAR PROSPECTIVE STUDY IN 250 PATIENTS

Francesco Greco, Sigrid Wagner, Raschid M. Hoda, Felix Kawan, Antonino Inferrera, Antonio Lupo and Paolo Fornara

Department of Urology and Kidney Transplantation, Martin Luther University, Halle/Saale, Germany

Objective: To evaluate the functional and oncological outcomes of laparoscopic partial nephrectomy (LPN) in comparison with open partial nephrectomy (OPN) for renal tumour.

Patients and Methods: Between July 1997 and January 2004, 125 LPN and 125 OPN were performed in our Clinic. Preoperatively, all the patients underwent intravenous pyelography and computed tomography (CT) for detailed information on tumour size, location, extent of parenchymal infiltration, and proximity to the pelvicaliceal system. Demographic data (age, gender), perioperative and postoperative parameters, including operating time, estimated blood loss, complications, length of hospital stay, renal function, histological tumour staging and grading, and metastasis rates were collected and analysed.

Results: The mean operative time for LPN and OPN was 135 min and 165 min, respectively. Mean warm ischemia time was 30 min (7-53 min) in the LPN and 28 min (6-50) in the OPN group. After 5 years from operation, the biochemical markers of glomerular filtration were completely normalized, demonstrating the absence of renal injury. The definitive pathological results showed an incidence of 68% for renal clear-cell tumour, 13% for chromophobe tumour, 17% for angiomyolipoma and 2% for benign complex cyst. The overall and cancer-specific survival rates at 5 years were 88% and 100%, respectively, in the LPN group and 86% and 98% in the OPN group.

Conclusion: Laparoscopic partial nephrectomy, if performed by a skilled laparoscopist in expert centres, can achieve oncological and functional outcomes that present no relevant differences in comparison with the open procedure.

3 THE EXTENDED 14-CORE PROSTATE BIOPSY SCHEME INCLUDING MIDLINE PERIPHERAL SAMPLING IS MANDATORY IN PATIENTS WITH LOW PSA DENSITY

Luigi Cormio, Fabrizio Lorusso, Oscar Selvaggio, Antonia Perrone, Giuseppe Di Fino, Mario De Slati, Pasquale Annese, Francesca Sanguedolce, Pantaleo Bufo and Giuseppe Carrieri

Ospedali Riuniti di Foggia, Italy

Aim: There is no general agreement on the ideal scheme for transrectal prostate biopsy (TPB) and whether the scheme should be adjusted to patient clinical parameters. This study aimed to evaluate the diagnostic yield of an extended 14-core TPB scheme in detecting prostate cancer (PCa) and to identify those patients who would benefit most from such a scheme.
**Patients and Methods:** Between December 2005 and September 2009, 922 consecutive men underwent an extended 14-core TPB because of serum PSA >4 ng/ml and/or abnormal digital rectal examination. The 14-core scheme included sextant biopsies, 2 biopsies (one basal and one apical) in each lateral peripheral zone and 2 biopsies (one basal and one apical) in each midline peripheral zone. Each core was numbered and analysed separately to determine the overall detection rate of 6-, 10-, and 14-core biopsy schemes, as well as the detection rate according to serum PSA and prostate volume. Complications occurring up to 20 days after the biopsy were also recorded.

**Results:** All procedures were carried out under local anaesthesia. PCA detection rate of 6-, 10-, and 14-core schemes was 30.9% (285/922), 35.5% (328/922), and 37.2% (343/922), respectively. When stratifying for clinical parameters, the increase in diagnostic yield of the 14-core scheme was greater in patients with low PSA levels (18.1%, 7.4%, and 0% for serum PSA levels <4 ng/ml, 4 to 10 ng/ml, and >10 ng/ml, respectively), with large prostate volumes (6.7%, 4.1% and 3% for prostate volume >55 cc, 35 to 55 cc, and <35 cc, respectively), and low PSA density (11% and 0.8% for PSA density <0.15 and ≥0.15, respectively). There was no major complication requiring hospitalization.

**Conclusion:** The present study confirms that the 10-core biopsy scheme provides better diagnostic yield than the sextant scheme and should replace it as the standard protocol for TPB. The extended 14-core scheme including midline peripheral sampling provides an overall increase in diagnostic yield of 4.5%; however, after stratifying for the evaluated clinical parameters (serum PSA, prostate volume and PSA density) it becomes clear that it should be considered only in patients with a serum PSA up to 10 ng/ml, and that it is most beneficial in patients with a low PSA density.

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**INTTEGRATED STAGING SYSTEMS FOR CONVENTIONAL RENAL CELL CARCINOMA: A COMPARISON OF TWO PROGNOSTIC MODELS**

Martella Oreste

Division of Urology, Giuseppe Mazzini Hospital, Teramo, Italy; Department of Health Sciences, L’Aquila University Medical School, L’Aquila, Italy

**Objective:** The objective of the current study was to compare, in a single centre experience, the discriminating accuracy of two prognostic models to predict the outcome of patients surgically treated for conventional renal cell carcinoma (RCC).

**Patients and Methods:** The clinical and pathological data of 100 patients surgically treated for RCC between 1998-2008 at our institution were retrospectively evaluated. For each patient, prognostic scores were calculated according to two models: the University of California Los Angeles Integrated Staging System (UISS) and the Stage, Size, Grade,
and Necrosis (SSIGN) developed at the Mayo Clinic. The prognostic predictive ability of models was evaluated using receiver operating characteristic (ROC) curves.

Results: The median follow-up was 62 (range 12-120) months. All clinical and pathological features that compound the algorithms were significantly associated with death from RCC in univariate and multivariate setting. The 5-year cancer-specific survival (CSS) according to the SSIGN score were 95% in the ‘0-2’ category, 88% in ‘3-4’, 60% in ‘5-6’, 37% in ‘7-9’ and 0% in the ‘≥10’ group (log-rank, p-value <0.001); according to the UISS the 5-year CSS probabilities in non-metastatic patients were 100% in low-, 80% in intermediate- and 54% in high-risk groups; in metastatic patients, the respectively CSS were 40% in low- and 25% in high-risk groups (log-rank, p-value <0.001). The area under the ROC curve was 0.815 for the SSIGN score and 0.843 for the UISS (p: 0.632).

Conclusion: In our series, the SSIGN and UISS discriminated well, without relevant differences. Currently both algorithms represent useful clinical tools that allow risk assessment after surgical treatment of RCC. We encourage uro-oncologist to begin to routinely rely on them in real-life practice.

7 ILEAL T POUCH CUTANEOUS CONTINENCY. FUNCTIONAL RESULT AFTER TEN YEARS

Gaetano Marino, Marco Pedalino, Otello Di Primio, Dorino Piras, Riccardo Vella, Enrico Vercesi and Marco Laudi

S.C. Urologia ASL T05, Torino, Italy

Aim: We report the functional results of 38 cases of urinary continent cutaneous diversion UCCD after ten years. The UCCD was developed with ileum using the serous lined extramural tunnel valve and Mitrofanoff procedure for continent mechanism in according to a personal modified T valve technique. The ureteral intestinal anastomosis is made by a split cuff nipple technique. In a few cases with ureteral dilatation, a double T pouch configuration was carried out using two single T valves for continent and antireflux mechanism.

Patients and Methods: From April 1999 to October 2009, 38 patients, on average aged 67 years, underwent radical cystectomy, pelvic lymphadenectomy and ileal continent cutaneous T pouch. Mean follow-up was 78 (range 5 to 128) months. Thirty-two patients were affected by invasive bladder cancer involving bladder neck, urethra or prostatic tract, and four patients were affected by cervical cancer. Two patients with other urinary diversion due to previous pelvic oncological surgical procedure (uretero cutaneostomy - uretero sigmodostomy) underwent urinary undiversion.

Results: At present, 22 patients are alive, showing a good continent mechanism and high capacity with low pressure, without urinary reflux. The evacuation intervals were about 4 (3.5-6) hours. Late complication directly related to the T pouch, were: 2 (5.2%) stone in to the pouch, (first case treated with holmium laser using flexible endoscopy by umbilical stoma, second case by open surgery), 4 (10.5%) stricture of uretero intestinal implant treated by balloon dilatation and stenting by percutaneous nephrostomical approach, 3 (7.9%) urinary incontinence treated by endoscopic procedure injecting silicon and autologous fat in the sub mucosa of the tunnel of T valve. One catheterization difficulty was reported and treated with balloon dilatation of tunnel of the T valve.

Conclusion: This ileal cutaneous continent diversion is indicated as an alternative to ileal conduit in selected patients that wish to maintain a good self image and who accept a periodical self catheterization by umbilical stoma. The modified T valve technique employed as a continent mechanism in a UCCD (created by J.P. Stein for antireflux procedure in a ileal T pouch neobladder) assures good continence and can be also performed in overweight patients. In all cases with hydronephrosis and dilated ureters, the T valve employed as antireflux procedure assures good upper urinary protection. In our experience after ten years, this ileal T pouch in relation to low early and late complications continues to be our choice of diversion technique.

8 SUNITINIB AND SORAFENIB THERAPY FOR PATIENTS WITH METASTATIC RENAL CELL CARCINOMA (mRCC): SAFETY PROFILE

Francesco Massari, Antonia Cricca, Francesca Sperandi and Andrea Angelo Martoni

A.O.U. Sant'Orsola-Malpighi, U.O. Oncologia Medica "Dott. Martoni", via Albertoni n.15, 40138 Bologna, Italy

Background: The incidence of renal cell carcinoma (RCC) is increasing worldwide. If detected early, RCC can be treated surgically, and 5-year survival rates approaching 85% can be achieved for patients with organ-confined disease (stages T1, T2, and N0). In reality, 40% to 50% of patients develop metastatic disease. Twenty to thirty percent of patients present with metastases, and 20% to 30% relapse distantly after curative nephrectomy (20%-30%). Treatment options for these patients are limited, and expected 5-year survival is approximately 10%. The outlook for patients with advanced RCC has improved due to the availability of targeted therapies, and with advances in the understanding of how to use these agents. Novel targeted agents that have shown
clinical efficacy in the treatment of metastatic RCC (mRCC) include the oral, multitargeted receptor tyrosine kinase inhibitors sunitinib malate and sorafenib tosylate. Their employment in clinical practice is increasing the familiarity with their safety profile and patient compliance. We have carried out a retrospective analysis on patients treated with these two agents at our Institution over the past 36 months.

Patients: A total of 35 consecutive patients with mRCC have been treated, 22 with sunitinib as first-line therapy and 13 with sorafenib as second-line treatment, for a median period of 10.0 (range: 0.4-33.3) months and 9.5 (range: 0.4-24.0) months respectively. Patient characteristics: median age: 55 (range: 42-74) years; median KPS 100% (range: 80-100%); histology was clear-cell carcinoma in all the patients.

Results: The most common drug-induced adverse events (% grade 3/4 in parenthesis) for sunitinib and sorafenib, respectively, were: asthenia 55% (14%) and 46% (8%); stomatitis 32% (9%) and 15% (0%); hand-foot syndrome 36% (5%) and 23% (8%); diarrhea 27% (9%) and 46% (23%); hypothyroidism 14% (0%) and 8% (0%); nausea/vomiting 9% (0%) and 8% (0%); hyperpyrexia (>38°C) 5% (0%) and 15% (0%). In addition, the following side-effects were observed only with sunitinib: hypertension 32% (0%), neutropenia 23% (5%); and only with sorafenib: rash/desquamation 31% (8%), alopecia 15% (0%). Sunitinib was temporally suspended (more than 14 days) in 7 patients (32%) for hypertension and stomatitis and sorafenib in 5 patients (38%) for diarrhea, asthenia and rash/desquamation. Sunitinib was suspended in 6 patients (27%) and sorafenib in 2 (15%) patients due to progressive disease. No patient refused to continue treatment.

Conclusion: Sunitinib and sorafenib have a partially superimposable side-effect profile and need to be accurately monitored. Hypertension and neutropenia, on the one hand, and cutaneous reactions on the other, are typical of sunitinib and sorafenib, respectively.

9 CONTEMPORARY IMPACT OF TRANSRECTAL ULTRASOUND IN PROSTATE CANCER DETECTION

Oreste Martella1, Giuseppe Paradiso Galatioto1, Guevar Maselli1, Paolo Galassi2 and Carlo Vicentini1

1Department of Health Sciences L'Aquila University Medical School, L'Aquila, Italy; 2Division of Urology, G Mazzini Hospital, Teramo, Italy

Aim: We evaluated the diagnostic accuracy of transrectal prostate ultrasonography (TRUS) in prostate cancer (PCa) diagnosis in a group of patients who underwent prostate biopsy in 2008.

Patients and Methods: A total of 100 patients (mean age, 65 years) underwent transrectal prostate biopsy at our centre. Indications for biopsy were: suspected malignancy at rectal examination or increase of total PSA and/or PSA velocity and/or PSA density and/or low percentage of free PSA. Ten to twelve biopsies, and additional ones in case of suspected echographic images, in every patient were carried out. Echographic aspects were classified as: highly suggestive of heteroplasia (focal or widespread hypoechoic area in the peripheral zone), weakly suggestive (small hypoechoic focal alterations), and isoechoic areas.

Results: At ultrasound examination, highly suggestive images were found in 20 patients, weakly suggestive images in 39 patients, and isoechoic images in 41 patients. PCa was diagnosed in 45 patients. 40% of tumours (18 patients) appeared as highly suggestive hypoechoic images, 31% (14 patients) as weakly suggestive, and 29% (13 patients) as isoechoic. The positive predictive value for isoechoic areas biopsies was 32%, 90% for highly suggestive hypoechoic images, and 36% for weakly suggestive images. In the latter, the diagnosis was often coincidental, i.e. in the opposite lobe, or in a different sextant of the same lobe (serendipity). The detection rate was 60% for prostate volumes ≤50 cc and 24% for volumes >50cc.

Discussion: The analysis of results allowed us to formulate the following considerations:
– 60% of currently diagnosed PCAs are not detectable by ultrasonography, or there are nonspecific echographic findings; 40% of tumours are detectable by ultrasonography with specific echographic findings;
– the clinical value of the hypoechoic focal alterations is similar to that of isoechoic ones;
– detection rate is positively influenced by prostate volume.

Conclusion: The study of hypoechoic and isoechoic biopsied areas shows a significant difference in TRUS accuracy in PCa diagnosis. In this set of patients, prostate volume and transrectal ultrasonographic findings proved to be the most informative variables for PCa risk at the moment of first biopsy at any age.

10 SINGLE-DOSE PRULIFLOXACIN CAN ENHANCE PATIENT COMPLIANCE WITH BCG INTRAVESICAL THERAPY FOR NON-MUSCLE-INVASIVE BLADDER CANCER

Vincenzo Serretta, Rosa Giamo, Dario Passalacqua, Antonina Ruggirello, Rosalinda Allegro and Darvinio Melloni

Section of Urology, Department of Internal Medicine, Cardiovascular and Nephro-Urological Diseases, University of Palermo, Italy
Aim: A relevant limit to Bacillus Calmette-Guérin (BCG) intravesical treatment is its local and systemic toxicity. Severe systemic toxicity, although rare, can be life-threatening. Topic and mild systemic toxicity, on the other hand, are frequent and responsible for the majority of treatment interruptions and low patient compliance. Preliminary reports suggest the activity of fluoroquinolones in reducing the toxicity of BCG (1, 2). A randomized pilot trial was designed to evaluate the protective activity of a single dose of prulifloxacin against BCG toxicity.

Patients and Methods: The protective action of prulifloxacin was evaluated in patients undergoing 6-week induction cycle of BCG after TUR of intermediate - high risk NMI-BC. The patients were randomized to receive BCG alone versus BCG plus prulifloxacin given as a single oral dose (600 mg) 6 hours after the instillation. BCG adverse events (AEs) were classified according to a four-class classification. EORTC QLQ - BLS24 was administered at baseline and a week after the 2nd, 4th and 6th instillation. Cystoscopy and cytology were performed 3-monthly. Recurrence and progression were recorded.

Results: Up to October 2009, the study included 258 instillations performed in 43 patients. The patients were randomized to BCG alone (Arm A) consisting of 132 instillations in 22 patients, versus BCG plus plurifloxacin (Arm B), 126 instillations in 21 patients. No significant difference was evident in baseline symptoms between the two groups. According to QLQ - BLS24, an advantage in favour of prulifloxacin emerged in overall incidence of nocturia (56% vs. 28.6%; \( p = 0.001 \)), insomnia (40% vs. 14.3%; \( p = 0.002 \)), urgency (70% vs. 42.6%; \( p = 0.05 \)), incontinence (44% vs. 12.7%; \( p = 0.01 \)) and inconvenience of intravesical therapy (84% vs. 63.5%; \( p = 0.02 \)). A higher benefit of prulifloxacin was evident after the 3rd-4th instillation. Prulifloxacin, although effective against local toxicity, does not seem able to prevent \( (p = 0.6) \) systemic class IIB and III AEs, occurring in 14.2% and 3.5% of patients respectively. No class IV AE was detected in our trial. Three patients of the prulifloxacin group and one patient of the control group definitively interrupted the treatment after the 3rd - 4th instillations. Anti-tuberculosis therapy was required for 3 months in one patient only. Three and two instillations were postponed for one-(two) week(s) in the prulifloxacin group and control group respectively. Prulifloxacin was generally well tolerated. It was suspended in one patient due to skin allergic reaction. Recurrence rates at 3-9 months did not significantly differ between the two groups.

Conclusion: Prulifloxacin improves patient compliance to BCG therapy, predominantly decreasing the incidence of local symptoms. No evidence emerges in our experience that it can prevent severe systemic adverse events.

References

II
pT2-3N0M0 PROSTATE CANCER WITH POSITIVE AND NEGATIVE MARGINS: CLINICAL OUTCOME AND TIME TO SALVAGE RADIOTHERAPY

Michele Lodde, Louis Lacombe and Yves Fradet

Department of Urology, Université Laval, CHUQ-Hôtel-Dieu de Québec, Québec, QC, Canada

Aim: To compare negative and positive margins of pT2-3N0M0 prostate tumours after radical prostatectomy (RP) in terms of percentage of biochemical recurrence (BR), salvage radiotherapy, androgen deprivation therapy (ADT), metastasis and cancer-specific mortality.

Patients and Methods: The cohort consisted of patients after RP with pT2-T3N0M0. Exclusion criteria were neoadjuvant and adjuvant ADT, adjuvant radiotherapy and a detectable PSA post RP. All patients were followed-up with 3 months PSA measurements. The BR was defined as a PSA>0.3 ng/ml (confirmed by a second measurement). At this point a 60 Gy salvage radiation therapy was proposed. In cases of a second biochemical progression, patients underwent ADT. The 5-year and 10-year biochemical-free (BFS), radiotherapy-free (RtFS), hormone therapy-free (HtFS), metastasis-free (metsFS) and cancer-specific survival (CSFS) were calculated using the Kaplan-Meier method.

Results: From our data base, we identified 1227 patients that met our inclusion criteria, 741 had no positive margins (Group A) and 486 had positive margins (Groups B). Median follow-up was 78 months (0.07-241 months) and the mean age was 63.4 years (SD 5.9 years). Groups A and B were comparable in term of PSA at prostatectomy (median 7 ng/ml vs. 8 ng/ml), cGleason score (GS=7: 25.9% vs. 25.1%) and clinical stage (pT2: 50.1% vs. 51.4%). However, group B had double the rate of T3 and extracapsular extension. At 5 years and 10 years, BFS rate was 89.8% and 77.4% for group A and 76.2% and 62.1% for group B (log-rank \( p = 0.0001 \)). RtFS rate at 5 and 10 years was 94.2% and 88% for group A and 81.3% and 75.2% for group B (log-rank \( p = 0.0001 \)). The HtFS rate was similar for both groups at 5 years (97.2% vs. 97.5%) but differed at 10 years (95.6% vs. 91%) (log-rank \( p = 0.02 \)). Nevertheless, no statistical difference was observed for the metsFS and CSFS rate at 5 years (99% for both groups). At 10 years, metsFS was 98.6% for group A (log-rank
p=0.28) and 96.2% for group B and CSFS 98% for Group a and 93.5% for group B (log-rank p=0.14).

Conclusion: In our study, 75% of patients with pT2-3N0M0 positive margins survive without the need for radiotherapy for 10 years. Patients with positive margins and delayed radiotherapy had similar rate of cancer-specific mortality and metastasis compared to the negative margin group at 5 years. At 10 years, CSFS was higher for the patients with negative margins compared to those with positive margins, but this difference did not reach statistical significance.

12 PROSTATE CANCER ANTIGEN 3 (PCA3) MOLECULAR URINE TEST CAN PREDICT UPGRADEING IN PATIENTS WITH LOW-RISK PROSTATE CANCER (PCA) UNDER ACTIVE SURVEILLANCE AND TREATMENT WITH 5 ALPHA REDUCTASE INHIBITORS (5-ARIs)

Jérôme Lévesque1, Michele Lodde1, Rabi Tiguert1, Louis Lacombe1, Jack Groskopf2, Harry Rittenhouse2 and Yves Fradet1

1Department of Urology, Laval University Québec, Québec, Canada;
2Gen-Probe, Inc., San Diego, California, U.S.A.

Background and Aim: The main risk of active surveillance for low-risk PCa patients is a missed high-grade prostate cancer (HG PCa), observed in around 20% of patients treated by surgery. Ongoing studies suggest that treating these patients with 5-ARIs could improve the detection of missed HG PCa at follow-up biopsy. PCA3 molecular urine test was previously shown to predict HG PCa at surgery. In this study, we assessed its utility to predict HG PCa on biopsy in patients with low-risk PCa under active surveillance and 5-ARIs treatment.

Patients and Methods: Patients with low-risk PCa (Gleason <6, PSA <10 ng/ml, <3/12 positive cores on TRUS biopsies) were offered treatment with 5-ARIs. They were followed up by repeated biopsies 6 to 12 months after treatment initiation and every 12 months thereafter. On the day of their follow-up biopsy, 25-35 ml of post digital rectal exam first catch urine was collected. Treated urine specimens were frozen within 4 hours of collection. PCA3 score was obtained from Gen-Probe laboratory by the APTIMA method. Specimens were collected from June 2006 to January 2009. PCA3 scores were compared to biopsy results to assess their predictability.

Results: Urine specimens were available for 59 patients, median age 65 (48-81) years. Median time of treatment before sample collection was 10 (3-28) months, median PSA at diagnosis was 4.9 (0.4-17.5) ng/ml and at collection, 3.3 (0.1-14.6) ng/ml. Median PSA density at diagnosis was 0.12 (0.03-0.39) ng/ml/cc and at collection, 0.08 (0.004-0.61) ng/ml/cc. The median PSA reduction from treatment initiation to specimen collection was 39% (-188 to 95%). At biopsy, 33 patients had a negative result, 17 had a Gleason 6 score, and 9 had an up-grading. The PCA3 score yielded an area under the curve for the receiver operating characteristic curve of 0.824 for cancer progression. At a cut-off value of 35, PCA3 score yielded a sensitivity and a specificity of 66.7% and 92%. Mean PCA3 score for HG PCa was 53±29 versus 25±22 (p=0.04) for persistent Gleason 6 and 22±21 (p=0.02) for negative biopsy.

Conclusion: PCA3 molecular urine test may be useful to identify early those patients with low-grade cancer that have undetected HG PCa that should be treated more aggressively.

13 SEX STEROIDS METABOLISM IN BENIGN AND MALIGNANT PROSTATE TISSUE: AN EX-VIVO MODEL TO CHARACTERIZE THE ROLE OF ENZYMATIC PROFILE IN BIOLOGICAL BEHAVIOUR

A.M. Isidori1, G. Franco2, M. Michetti2, N. Tartaglia2, D. Gianfrilli1, M. Cicciariello3, A. Lenzi1 and C. De Dominicis2

1Department of Medical Pathophysiology, 2Department of Urology, and 3Department of Radiology, Sapienza University of Rome, Italy

Background: In vitro studies revealed that androgens and estrogens play a crucial role in prostate homeostasis. However, human studies failed to correlate circulating sex hormones with prostate disease. We investigated whether local hormone metabolism accounts for this discrepancy.

Materials and Methods: Using an ex-vivo model of intact tissue cultures, we characterized the enzymatic profile of biopsy specimens from patients with benign prostatic hyperplasia (BPH) and cancer (PC), focusing on 17β-hydroxysteroid dehydrogenase (17βHSD) and aromatase activities.

Results: 13 BPH and 11 PC specimens were analysed. Tissue fragments were incubated with 3H-testosterone or 3H-androstenedione in serum-free medium. Conversion was evaluated by TLC separation and beta-scanning of organic extracted supernatants. We identified 3 different patterns for H3-androstenedione: 1) no conversion; 2) androstenedione to testosterone; and 3) androstenedione to estradiol. Interestingly, 64% of BPHs showed pattern 1 whereas 71% of PCs showed...
pattern 3. In PCs, androstenedione was metabolized at a rate of 5.99-7.5 fmol/h and estradiol accounted for 35% of total radioactivity. Enzymatic conversion correlated with histology and PSA, but not serum hormones. PCs with highest Gleason scores (9: 4+5) expressed pattern 2. Expression of 17βHSD isoenzymes-3/5 was associated with malignancy. No testosterone conversion occurred in 77% of BPHs (no 17βHSD/aromatase), whereas 10% of radioactivity was found in conjugated metabolites (BPH).

Conclusion: We found that 17βHSD and aromatase activity in prostate tissue cultures correlate with biological behaviour. Our study suggests that it is possible to estimate individual risk by characterizing individual enzymatic phenotype directly from biopsies. Increased production or clearance of potentially genotoxic metabolites could favour proliferation and transformation. These data also have implications on novel pharmacological targets.

14 TARDIVE INTRAVESICO-URETHRAL ANASTOMOSIS CLIP MIGRATION AFTER RETROPUBIC RADICAL PROSTATECTOMY

Stefano de Luca, Nicola Faraone, Paolo Caccia, Andrea Cavallini, Ernesto Giargia, Massimo Pasquale, Maria Sara Squeo and Donato Franco Randone

Divisione di Urologia, Ospedale Gradenigo, Torino, Italy

Background: Multiple modalities have been used for haemostasis during retropubic radical prostatectomy (RRP). We report a case of migration of a haemostatic clip into the vesico-urethral anastomosis 19 months after RRP.

Case Report: A 54-year-old man presented to our institution with a diagnosis of stage T1C prostate cancer. PSA was 8.71 ng/ml and a transperineal biopsy demonstrated Gleason score 5 (2+3) in 60% to 80% of cores from the left base and midgland. Past medical history was significant only for congenital haemocromatosis. The patient underwent RRP without complications. A combination of suture ligation, bipolar cautery and titanium clips (Ligaclip®Extra) were successfully used to achieve haemostasis at various stages of the procedure and during the regional lymphadenectomy. A monolateral nerve-sparing procedure was performed only on the right side owing to the high volume of tumour on the left. Three-four clips were used in the area of the right neurovascular bundle. The vesico-urethral anastomosis was achieved using knot 2-0 monocryl suture. Pathology showed Gleason 5 (2+3) with negative lymph nodes, negative margins, no seminal vesicle invasion and no angiolymphatic invasion. Postoperative recovery was unremarkable. A mild leak after removal of the bladder catheter was present for 1-2 months. PSA was undetectable within 3 weeks. Five months after surgery the patient complained of acute dysurea associated with persistent bladder spasms. The patient underwent endoscopic mono-incision of a severe vesico-urethral stenosis and no other abnormalities were observed in this region. At 17 months, the patient was without significant residual lower urinary tract symptoms. PSA remained undetectable. Following careful sexual counseling for residual erectile dysfunction he elected to undergo insertion of a semirigid penile prosthesis. Unsuccessful vesical catheterism before surgery was referred andsovrapubic-cystostomy was performed. Five days later, the patient underwent urethrocystoscopy and urethral bi-incision that demonstrated the presence of a clip firmly lodged in the region of the vesico-urethral anastomosis. We successfully removed the clip intact, using an alligator grasper. On retrospective re-evaluation of post-RRP urethro-cystogram, we noted the presence of the clip protruding into the anastomotic region. Sovrapubic-cystostomy was removed and an indwelling urethral catheter was left for 2 days. At 1 month, the patient was without residual urinary tract symptoms and underwent successful insertion of a semirigid penile prosthesis.

Discussion: Stenosis of the vesico-urethral anastomosis represents one of the commonest complications (19.2%) of radical prostatectomy. It generally occurs within 12 months after surgery. The most effective treatment is endoscopic mono-incision, which usually prevents recurrence without compromising continence. Several methods are used to ensure adequate haemostasis during radical prostatectomy. A commonly used device is the clip, which has been shown to be safe and reliable for vascular control in surgical procedures. To date, there have been very few reports of migration of these clips, usually occurring inside the bladder during a laparoscopic procedure and often causing subsequent calculus formation. Although these clips are useful, caution should be used in placement of the clips near the site of anastomosis during prostatectomy. To date, this is the first case reported in literature of clip migration into the vesico-urethral anastomosis after RRP. Retrospective re-evaluation of radiodiagnostic exams post-surgery is mandatory when these devices are used and in the presence of tardive persistent dysurea.

References
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TRANSITION ZONE CARCINOMA OF THE PROSTATE GLAND: EVALUATION OF THE INCIDENCE AND BIOLOGICAL BEHAVIOUR AFTER RADICAL PROSTATECTOMY

Stefano De Luca, Paolo Caccia, Andrea Cavallini, Nicola Faraone, Ernesto Giargia, Massimo Pasquale, Maria Sara Squeo and Donato Franco Randone

Div. Urologia Osp. Gradeno di Torino, Torino, Italy

Background: About 25% of all prostate tumours occur in the transition zone (TZ). TZ carcinoma are often well differentiated and considered clinically unimportant. We retrospectively analyzed 34 patients with TZ prostate carcinoma who underwent retropubic radical prostatectomy (RRP) in order to evaluate the incidence and the biological behaviour of this type of neoplasm.

Patients and Methods: Between 6/1994 and 6/2009, a total of 34 patients that underwent RRP at the Gradeno Hospital who had TURP/ADM (pT1b) or a biopsy positive for TZ carcinoma of the prostate gland (T1c-TZ) were identified. We perform routine TZ biopsy only in patients that required repeat biopsy. Patients were divided into two groups: pT1b (23 patients) and T1c-TZ (11 patients). The median follow-up was 57.5 months (6-86 months).

Results: The mean age was 67.3 years (51-73 years). Table I summarizes the pathological stage. Gleason score ≥7 was 30.4% in the pT1b group and 72.7% in the T1c-TZ group. We had no more surgical or post-operative complications in patients who had TURP/ADM at least 3 months before RRP. We found no difference in relapse-free survival between TZ and peripheral prostate carcinoma.

Conclusion: Routine TZ biopsy can be useful in patients that require repeat biopsy. TURP/ADM cannot be considered a curative treatment for TZ carcinoma, no pT0 was observed in our series. TZ carcinoma are often well differentiated and considered clinically unimportant. On the other hand, in our experience, a subset of these tumours, characterized by high tumour grade, has a significant risk of extraprostatic spread, margin positivity and possible biochemical failure, similar to peripheral prostate carcinoma.

### Table I. (abstract 15)

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<th>pT3aG2</th>
<th>pT3aG3</th>
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<th>pNx</th>
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<td>3</td>
<td>8</td>
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<tr>
<td>11 pts (T1c-TZ)</td>
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<td>2</td>
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References


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METABOLIC SYNDROME PREDICTS HIGH-GRADE PROSTATE CANCER: AN ITALIAN BIOPSY COHORT

Cosimo De Nunzio, Alberto Trucchi, Andrea Cantiani, Simone Albisinni, Cristina Avitabile, Francesco Iori and Andrea Tubaro

Department of Urology, Ospedale Sant'Andrea, University "La Sapienza", Rome, Italy

Background: The metabolic syndrome describes the combination of several metabolic abnormalities, including central obesity, dyslipidaemia, hypertension, insulin resistance and glucose intolerance (1). A possible relationship between prostate cancer and metabolic syndrome has been recently proposed (2). The aim of our study was to evaluate the association between metabolic syndrome and prostate cancer risk and grade among a consecutive series of men undergoing prostate biopsy.

Patients and Methods: From 2008 onwards, 100 consecutive men undergoing 12-core prostate biopsy at one centre in Italy were enrolled into a prospective database. Indications for a prostatic biopsy were a PSA value of 4 ng/ml or more and/or a positive digital rectal examination (DRE). Body mass index (BMI), as well as waist and hip circumferences were measured before the biopsy. Blood samples were collected before biopsy and tested for: total and free PSA levels, fasting glucose, triglycerides and HDLs.
Results: Of the 100 men, 40 (40%) had cancer on biopsy. Median age, PSA, and serum testosterone levels were 69 years, 5.8 ng/ml, and 3.3 ng/ml, respectively. Median BMI was 27 and 25 patients (25%) were classified as obese (BMI ≥30). A total of 54 patients (54%) presented metabolic syndrome according to ATPIII classification. Patients with metabolic syndrome presented a lower testosterone level when compared to patients without (p = 0.002). No significant differences for age, PSA value or prostatic volume were observed in patients with metabolic syndrome. Among the 40 patients with prostate cancer, 21 patients (52.5%) presented metabolic syndrome and 19 patients (47.5%) did not (p = 0.48). PSA was the only independent parameter associated with an higher risk of having cancer on biopsy (OR 1.12 per 1 unit PSA, p = 0.01). Among the 40 men with prostate cancer, 19 (47.5%) presented a Gleason score 6 and 21 (52.5%) a Gleason score ≥7. Among the 19 patients with a Gleason score 6, and the 21 patients with a Gleason score ≥7, 7 (36%) and 14 (66%), respectively, presented metabolic syndrome. The presence of metabolic syndrome was associated with an higher risk of high-grade disease and biopsy Gleason 7 or greater (OR: 4.1; p = 0.04).

Conclusion: Our study confirms patients with higher PSA values are at higher risk of prostate cancer and suggests the possible role played by the metabolic syndrome in the development of high-grade prostate tumours. Even though the molecular pathways are yet to be understood, abdominal obesity, hypertension, dyslipidaemia and impaired fasting glucose should be considered as important factors for prostate cancer differentiation and further investigations are needed.

References
Gleason score was 6±1, mean PSA value was 8.1±6.5 ng/ml, mean testosterone was 4.05±1.5 ng/ml, free testosterone was 8.4±3.6 ng/ml, mean SHBG was 35.9±12.3 nmol/l and mean CgA was 92±194 ng/ml. T2 stage was observed in 79 pts (65%), at least T3a was observed in 42 pts (T3a in 28 pts, T3b in 9 pts and T4 in 3 pts). Twenty-two (18%) patients presented positive surgical margins. Patients with high-stage prostate cancer presented an elevated PSA value and a lower serum level of SHBH (Table I). Multivariate analysis showed SHBG (OR: 0.95; CI: 0.92-0.99; p=0.004) as independent prognostic factor for high-stage disease. SHBH also significantly inverse correlated with pathological stage (r = -0.258; p=0.006). PSA also significantly correlated with pathological stage (r= 0.354; p< .001) and grade (r: 0.251; p=0.001) and is an independent prognostic factor for tumour grade (OR: 1.12; CI: 1.05-1.25; p=0.04)

Conclusion: Our data confirm that higher total PSA levels are associated with a high-stage after RRP. Serum level of SHBG seems to be reduced in patients with high stage and grade prostate cancer independently from serum testosterone and free testosterone levels. Further research into the relationship between hormonal status and prostate cancer is warranted, in particular to identify risk categories.

References

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SERUM ANDROGEN VALUE CANNOT PREDICT THE PRESENCE OF PROSTATE CANCER IN PATIENTS WITH HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA

Cosimo De Nunzio, Alberto Trucchi, Antonio Cicione, Alfonso Carlucchi, Andrea Cantiani, Francesco Iori, Cristina Avitabile and Andrea Tubaro

Department of Urology, Ospedale Sant’Andrea, University "La Sapienza", Rome, Italy

Background: High-grade prostatic intraepithelial neoplasia (HGPIN) has been reported in between 0.7 and 24% of biopsy samples, with a 23 to 79% risk of finding carcinoma on subsequent biopsy (1-2). The aim of our study was to evaluate the role of androgen status to predict the risk of prostate cancer in a group of patients with HGPIN.

Patients and Methods: From December 2003 to September 2009, patients referred to our prostate clinic with a PSA value more than 4 ng/ml or an abnormal digital rectal examination (DRE) were scheduled for TRUS prostatic biopsy with a 12 cores strategy. In patients with HGPIN, we proposed a second PSA evaluation and a new 12 cores biopsy after 6 independently from PSA value. We evaluated the association between pre-biopsy serum testosterone, sex hormone binding globulin (SHBG), free testosterone (serum samples were collected the day of each biopsy) and prostate cancer risk on a subsequent biopsy using the logistic regression analyses. Differences in cancer detection rate were also evaluated. Wilcoxon test was also used as appropriate for statistical analysis.

Results: A total of 650 patients underwent 12-core TRUS prostatic biopsy in the study period. Of 147 (22%) men with a diagnosis of HGPIN, 96 underwent a second prostatic biopsy after six months. The mean age was 65 ± 6 years, mean body max index (BMI) was 26.5, mean PSA value was 8.2 ± 5 ng/ml, with a mean prostatic volume of 61 ± 26 ml. Mean testosterone was 4.2 ± 1.5 ng/ml; mean free testosterone was 9.3±8.9 pg/ml, mean SHBG was 38.6 ±15 nmol/l, mean chromogranin was 112 ±196 ng/ml. At the time of the repeated biopsy the mean PSA value was 8.2 ± 7 ng/ml (p=0.65), mean testosterone was 4.37±1.67 ng/ml (p=0.199), mean free testosterone was 8.4±3.7 pg/ml (p=0.06), mean SHBG was 39±13 nmol/l (p=0.95), mean chromogranin 87±88 ng/ml (p=0.51). 18 patients (18.7%) presented prostate cancer (13 with a Gleason Score 6, 4 with a Gleason score 7 and 1 with a Gleason score 8); 62 (64.5%) showed isolated HGPIN, while 16 (12.8%) revealed chronic prostatitis. BMI, PSA and androgen status were not able to discriminate prostate cancer from benign disease on the second biopsy. On binary logistic regression analysis, the number of cores involved in HGPIN was the only independent parameter associated with the presence of cancer on a second biopsy (OR: 2.25, p=0.02)

Conclusion: HGPIN is a frequent lesion in biopsy samples. A new biopsy in this group of patients showed prostate cancer in about 20% of patients. Neither the androgen status, serum level of PSA, nor chromogranin were able to predict the presence of cancer. The number of cores involved by HGPIN seems to be useful in predicting the presence of cancer and in preventing unnecessary biopsies.

References
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OBESITY PREDICTS HIGH-GRADE PROSTATE CANCER IN AN ITALIAN BIOPSY COHORT

Cosimo De Nunzio1, Alberto Trucchi1, Andrea Tubaro1, Francesco Iori1 and Stephen J. Freedland2

1Department of Urology, Ospedale Sant’Andrea, University "La Sapienza", Rome, Italy;
2Duke Prostate Center, Duke University School of Medicine, Durham, North Carolina, U.S.A.

Prior work, mostly from series in the United States where PSA screening is commonplace, have found that among men undergoing prostate needle biopsy, obese men are more likely to have cancer and particularly high-grade cancer after adjusting for other clinical covariates (1). It has been hypothesized that this in part relates to delayed diagnosis among obese men due to lower PSA values from haemodilution (2). Whether similar associations would be present in an area where PSA screening was less prevalent and obesity rates were lower (i.e. Europe) is unknown.

Patients and Methods: From 2004 onwards, 562 consecutive men undergoing 12-core prostate biopsy at one centre in Italy were enrolled into a prospective database. We evaluated the association between body mass index (BMI; log-transformed, continuous variable) and prostate cancer risk and biopsy Gleason score using logistic regression analyses. All results were mutually adjusted for serum PSA, age, digital rectal examination findings, and transrectal ultrasound prostate volume.

Results: Of the 562 men, 242 (43%) had cancer on biopsy. Median age, PSA, and BMI were 67 years, 7.2 ng/ml, and 26.6 kg/m2, respectively. A total of 121 (22%) men had an abnormal rectal examination and a total of 101 men (18%) were obese. On univariate analysis, BMI was weakly and not significantly associated with reduced prostate cancer risk (p=0.10). After adjusting for multiple clinical variables and particularly the larger prostate size among obese men (Spearman, r=0.23, p<0.001 for prostate volume and BMI), BMI was not related to prostate cancer risk (p=0.43). Among men with cancer, higher BMI on univariate (p=0.006) and multivariate analysis (p=0.01) was associated with high-grade disease (Gleason 7 or higher).

Conclusion: Among men undergoing prostate biopsy in Italy, obesity is associated with high-grade disease. Although many of the men in this series were likely subjected to PSA screening as evidenced by the low rate of men with abnormal rectal examinations, the median PSA was higher than in prior biopsy series looking at obesity. Thus, even in a less aggressively screened cohort, obesity is associated with high-grade disease providing further evidence that obesity is associated with aggressive prostate cancer.

References

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LOW TESTOSTERONE PREDICTS OVERALL AND HIGH-GRADE PROSTATE CANCER IN AN ITALIAN BIOPSY COHORT

Stephen J. Freedland1, Cosimo De Nunzio2, Alberto Trucchi2, Erin Mcnamara1, Francesco Iori2 and Andrea Tubaro2

1Duke Prostate Center, Duke University School of Medicine, Durham, North Carolina, U.S.A.;
2Department of Urology, Ospedale Sant’Andrea, University "La Sapienza", Rome, Italy

Introduction: The role of androgens in prostate cancer development is highly debated (1). Recently, some studies have suggested men with low testosterone levels may be at an increased risk of high-grade disease (2). We sought to evaluate the association between serum testosterone and prostate cancer risk and grade among a consecutive series of men undergoing prostate biopsy.

Patients and Methods: From 2004 onwards, 562 consecutive men undergoing prostate biopsy at one center in Italy were enrolled into a prospective database. We evaluated the association between pre-biopsy serum testosterone and prostate cancer risk and biopsy Gleason score using logistic regression analyses. All results were mutually adjusted for serum PSA, age, body mass index, and digital rectal examination findings.

Results: Of the 562 men, 242 (43%) had cancer on biopsy. Median age, PSA, and serum testosterone levels were 67 years, 7.2 ng/ml, and 3.92 ng/ml, respectively. Higher testosterone levels were associated with a lower risk of high-grade disease whether defined as biopsy Gleason 7 or greater, (OR 0.89 per 1 unit testosterone, p=0.07), though this association was not statistically significant. Among the 242 men with cancer, higher testosterone levels were associated with a lower risk of high-grade disease whether defined as biopsy Gleason 7 or greater, (OR 0.88, p=0.25), 4+3 or greater (OR 0.83, p=0.09) or Gleason 8 or greater (OR 0.87, p=0.28), although none of these associations reached statistical significance. When high-grade disease was examined as high-grade vs. low-grade and/or no cancer, higher testosterone was associated with significantly fewer high-grade tumours when
high-grade was defined as Gleason 7 or greater (OR 0.85, p=0.03) or 4+3 or greater (OR 0.78, p=0.01). When testosterone was grouped into quartiles, the risk of high-grade disease was particularly pronounced among men in the lowest quartile. Men in the lowest quartile relative to the other quartiles were at increased risk of high-grade disease regardless of the definition of high-grade disease, though this only reached significance for a definition of Gleason 7 or greater (OR 2.24, 95% CI 1.05-4.75, p=0.04).

**Conclusion:** In this study of men undergoing prostate biopsy, lower testosterone levels were associated with increased risk of having cancer and increased risk of high-grade cancer among men with cancer. These data add to the growing literature suggesting that lower testosterone levels may be associated with more aggressive prostate cancer.

**References**


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**RADICAL PROSTATECTOMY DOES NOT INFLUENCE ANDROGEN LEVELS IN PATIENTS WITH PROSTATE CANCER**

Cosimo De Nunzio, Alberto Trucchi, Alfonso Carluccini, Antonio Cicione, Stefano Squillacciotti, Cristina Avitabile, Simone Albisinni, Francesco Iori and Andrea Tubaro

Department of Urology, Ospedale Sant'Andrea, University "La Sapienza", Rome, Italy

**Background:** No consensus has been reached yet as to the relation of androgens and prostate cancer. Several reports showed that patients with high-grade prostate cancer had significantly lower serum total testosterone levels than did those with low-grade tumours and radical prostatectomy seems to restore the hypoandrogenic state in these patients (1-2). The objective of this prospective study was to investigate the possible relation of androgens and prostate cancer in a patient cohort scheduled for radical prostatectomy.

**Patients and Methods:** A consecutive cohort of patients scheduled for radical prostatectomy in our outpatient clinic was enrolled in the study after informed consent was signed between January 2004 and August 2006. Indications for radical prostatectomy were T1-T3 prostate cancer. Blood samples were collected before radical prostatectomy and 12 months later and tested for: testosterone, free testosterone, sex hormone binding globulin (SHBG), and total and free PSA levels. Wilcoxon signed ranks test was used for statistical analysis.

**Results:** Forty-four patients were available for analysis. At the time of radical prostatectomy 15 patients (34%) had a Gleason Score 6, 24 patients a Gleason score 7 (54%), 1 patient (2%) Gleason score 8 and 4 patients with a Gleason score 9 (9%). Mean prostate cancer volume was 4.3 ± 7.3 cc. A total of 17 patients presented a tumour of pT2 stage, 22 patients pT3a, 3 patients pT3b and 1 patient pT4. Positive surgical margins were detected in 18 patients (40%). No significant changes of serum levels of testosterone, free testosterone and SHGB were observed after radical prostatectomy (Table I).

**Table I.**

<table>
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<th>Mean (SD)</th>
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<td>Free PSA (ng/ml)</td>
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<td>Testosterone (ng/ml)</td>
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<td>4.08 (1.48)</td>
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<td>Free Testosterone (pg/ml)</td>
<td>9.01 (3.64)</td>
<td>8.85 (3.04)</td>
<td>&lt;0.83</td>
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<tr>
<td>SHGB (nmol/l)</td>
<td>38 (14.39)</td>
<td>38.5 (17.3)</td>
<td>&lt;0.71</td>
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</tbody>
</table>

**Conclusion:** Our data do not support the hypothesis that prostate cancer impacts on the hypothalamic-pituitary-gonadal hormone axis. The cause and effect role of testosterone levels and Gleason score remains to be established.

**References**


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**25**

**ONCOLOGICAL AND FUNCTIONAL RESULTS IN SEMINAL VESICLES SPARING RADICAL PROSTATECTOMY: OUR EXPERIENCE**

Mauro Mari¹, Stefano Guercio¹, Alessandra Ambu¹, Francesco Mangione¹, Francesca Vacca¹, Massimo Di Lisa¹, Enrico Bollito² and Maurizio Bellina¹

¹Ospedale degli Infermi di Rivoli, UOC Urologia, Strada Rivalta 29, Rivoli, Torino, Italy;
²Az. Ospedaliera S. Luigi, Divisione di Anatomia Patologica, Regione Gonzole 10, Orbassano, Torino, Italy

**Background and Aim:** Seminal vesiculectomy is an integral part of the radical prostatectomy since its original description.
Dissection of seminal vesicles (SV) can damage the pelvic plexus, compromise trigonal, bladder neck, and cavernosal innervation, and contribute to delayed gain of continence and erectile function. Recently, however, a marked decrease in the percentage of the men with SV invasion has become evident. Radiotherapists are excluding the SV from their target volume in cases of low-risk prostate cancer. According to our preliminary experience and to recent reports, the seminal nerve-sparing radical prostatectomy (SSRP) technique improves functional postoperative results (earlier recovery of continence, better preservation of erectile function and quality of orgasm) without compromising oncological outcomes. In this study, we presented our experience using SSRP, evaluating oncological and functional results.

Patients and Methods: A total of 87 patients (pts), 71 with evaluable data, with clinically localized prostate cancer (cT1c-T2a, PSA< 10 ng/ml; Gleason score <7, percentage positive biopsy <33%) underwent neck-sparing SSRP (nerve-sparing unilateral or bilateral) from November 2001 to February 2008. All pts were continent, potent and able to achieve orgasm at baseline. They were all interested in recovery of postoperative sexual function and they provided an informed consent. Continence was defined as the use of no or one pad per day, men were considered potent if they engaged in sexual intercourse with or without the use of 5-phosphodiesterase inhibitors. Intraoperative histological examination on frozen section was performed to assess the absence of tumour invasion at the level of the junction between prostate and SV. One month after surgery all pts started sexual rehabilitation with 5-phosphodiesterase inhibitors.

Results: Neck-sparing SSRP was feasible in all patients. Medium follow-up was 37 (range 19-93) months. Pathological stage was pT0 in 1/71 pts (1%), pT2 in 58/71 pts (82%), pT3 in 12/71 pts (17%). A total of 10/71 pts (14%) had positive surgical margins (4 pT3, 6 pT2). Histological examination on frozen sections showed no cancer infiltration at the junction between prostate gland and SV. A total of 4/71 pts (5.6%) had PSA release (medium time 43.7 months), all pts received adjuvant radiotherapy and PSA decreased in all pts at <0.2 ng/ml. Of 71 pts, 60 (85%) maintained sexual function, 40/60 pts (67%) without use of 5-phosphodiesterase inhibitors. Median and average time of recovery of sexual function were 8.5 months. A total of 42/60 pts (70%) with normal sexual intercourse reported good ability to achieve orgasm. A total of 68/71 pts (96%) were continent after a median time of 3 months.

Conclusion: The SSRP showed good feasibility and improved early continence, erectile function and orgasm quality, without compromising cancer control. Leaving the SV in place did not increase the short-term PSA relapse rates.

26 THE RETROURETHRAL TRANS-OBTURATOR SLING IS AN EFFECTIVE AND ATTRACTIVE TREATMENT OPTION FOR MALE STRESS URINARY INCONTINENCE RESULTING FROM RADICAL PROSTATECTOMY (RP) AFTER 1 YEAR OF IMPLANTATION

Rossella Bertoloni, Michele Amenta, Giovanni Olivo, Luigi Motta, Alberto Laganà and Giuseppe Pecoraro

Ospedale Civile Isola della Scala, via Roma 64, Isola della Scala (VR), Italy

Background: Although surgical techniques for radical prostatectomy (RP) have been refined significantly, a significant number of patients still suffer from persisting post-prostatectomy stress urinary incontinence (SUI). Trans-obturateur male slings have been proposed to manage stress urinary incontinence (SUI) after prostatic surgery, but data are still lacking. The Advance male sling is a treatment option for post-prostatectomy incontinence (PPI), with the goal of eliminating urinary incontinence without affecting voiding parameters. The aim of the study was the prospective evaluation of the efficacy of the retrourethral transobturator sling for the functional treatment of male SUI after RP.

Patients and Methods: We conducted a prospective evaluation on 32 patients treated in a single center between 2007 and 2009 for mild to moderate SUI following prostatic surgery. In our study was included only patients with urethral closure during urethroscopy with external digital pressure of the perineum. All patients were comprehensively evaluated preoperatively and after 6 months and 1 year regarding daily pad use, 1-h and 24-h pad tests, residual urine, uroflowmetry. Seven patients were evaluated preoperatively and after 6 months with urodynamic testing. Cure was defined as no pad usage. Median follow-up was 13 (range: 6–26) months.

Results: A cure rate (no pads) is achieved of 84.38%, only 5 patients (15.62%) are using one pad for security reasons. No significant changes were seen in residual urine and flow rate. The Valsalva leak point pressure improved significantly (p=0.32), but the detrusor voiding pressure, postvoidal residual urine volume, and maximal and average flow rates remained relatively unchanged. Neither severe complication or postoperative urinary obstruction was noted during follow-up.

Conclusion: Placement of a transobturator sling is a safe and effective procedure, giving durable results after >1 year of follow-up. The cure of incontinence was accompanied without any changes in the other voiding parameters. Urethroscopy is an important diagnostic test to predict the success of the surgery.
PROSTATIC METASTASES OF RENAL CELL CARCINOMA

Rossella Bertoloni, Michele Amenta, Luigi Motta, Olivo Giovanni, Alberto Laganà and Giuseppe Pecoraro

Ospedale Civile Isola della Scala, via Roma 64, Isola della Scala (VR), Italy

Secondary tumours of the prostate originating from a distant primary neoplasm are rare. Usually, it is an incidental finding at autopsy, although it is found occasionally at surgery. Even rarer is the finding of metastatic renal cell carcinoma (RCC) to these organs when the patient is still alive. A review of the literature failed to disclose more than 5 cases of metastatic renal cell carcinoma to the prostate gland. We report a case of metachronous involvement of the prostate by RCC.

Case Report: An 82-year-old man underwent radical right nephrectomy (pT2N0M0 clear cell type, Fuhrman grade 2) and partial left nephrectomy (pT1N0M0 clear cell type, Fuhrman grade 2) of bilateral RCC. The man returned one month after surgery with urinary retention and, after catheterization and various attempts to treat the bladder outlet obstruction medically with alpha-blockers, the patient underwent transurethral resection of the prostate. The pathological examination demonstrated metastatic RCC, clear cell type. Staging evaluations included a chest radiography and bone scan, which were negative, and a computed tomography scan performed before the nephrectomy, which was also negative. At 6 months of follow-up, the patient had no evidence of the other disease recurrence. He has been scheduled for yearly follow-up with computed tomography of the abdomen and pelvis, and physical examination.

Discussion: The incidence of a solitary metastatic lesion in patients with renal cell carcinoma is 1.6% to 3.6% (1). Secondary neoplasms of the prostate are rare except for those that involve the gland by direct extension from adjacent structures. The most common expected sites of metastases are in the lungs, liver, bone, and brain. Before our patient, only 5 cases of metastatic RCC to the prostate had been reported (2-6). Of these, four were diagnosed before death. Of the 4 cases, 2 were early recurrences of RCC to the prostate (less than 1 year) and 2 were cases of a delayed (9 years) solitary metastasis. Several hypotheses have been proposed concerning the mode of dissemination of renal tumours to prostatic tissue. These include, in order of importance, direct arterial dissemination; retrograde venous dissemination; and lymphatic transmission. Direct arterial dissemination would explain the rarity of secondary prostatic tumours from the kidney and is supported by the theory of ‘cascade’ or multistep spread of renal cancer (2). However, Cihak et al. found intravenous metastatic renal carcinoma in the periprostatic veins, suggesting that retrograde venous spread does occur in rare cases. Our case calls attention to prostatic metastases of renal cell carcinoma, which clinically mimic benign prostatic hyperplasia, and illustrates the propensity of renal cell carcinoma for unpredictable presentation and unusual sites of metastasis.

References

ROBOTIC-ASSISTED LAPAROSCOPIC RADICAL CYSTECTOMY AND INTRACORPOREAL STUDER NEOBLADDERSURGICAL PROCEDURE AND SHORT-TERM CLINICAL OUTCOMES OF 9 PATIENTS

Roberto Nucciotti, Valerio Pizzuti, Fabio Massimo Costantini, Francesco Mengoni, Fabrizio Viggiani, Giandomenico Passavanti and Alessandro Bragaglia

U.O. Urologia-Grosseto, Italy

Aim: To describe our technique of robotic cystectomy and intracorporeal formation of Studer neobladder for treatment of carcinoma of the bladder.

Patients and Methods: We describe our surgical technique describing stepwise the surgical procedure and pathologic outcomes. After cystectomy the reconstruction phase starts from the anastomosis ileo-urethral about 40 cm from the ileocaecal valve. Then we proceed to section ileum through endoGIA. Detubularization of ileum neobladder occurs through cold robotic scissors. Studer reconfiguration is performed by pds running suture. To reduce urinary reflux, we prefer the Wallace type of anastomosis with a pro- peristaltic segment of nondetubularized ileum.

Results: We performed 9 robotic-assisted intracorporeal neobladder surgeries. Mean operating-room time of all patients was 6.3 h and mean surgical blood loss was 430 ml.
We prefer to stent the ureteral anastomosis for 2 weeks. There was only a major postoperative complication: an acute compartment syndrome of the lower leg of unknown cause.

**Conclusion:** The clinical and oncological follow-up of patients undergoing robotic-assisted intracorporeal urinary diversion appears to be favorable in the short term. As our follow-up increases, we should expect to continue to truly define the long-term clinical appropriateness and oncological success of this procedure.

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**OPTIMAL ACUTE TOXICITY PROFILE FOR CONCOMITANT PELVIC IRRADIATION IN 153 PROSTATE CANCER PATIENTS WITH TOMOTHERAPY**

Filippo Alongi1,2, Cesare Cozzarini1, Claudio Fiorino3, Barbara Longobardi3, Genoveffa Berardi1, Lucia Perna3, Riccardo Calandrino3 and Nadia Di Muzio1

1Radiotherapy, San Raffaele Institute, Milan, Italy; 2IBFM-CNR, Unità Operativa Supporto, Cefalù, Italy; 3Medical Physics, San Raffaele Institute, Milan, Italy

**Aim:** To assess toxicity profile after whole-pelvis irradiation (WPRT) image-guided tomotherapy with concomitant boosting of prostate/prostatic bed.

**Patients and Methods:** In the period March 2005-April 2009, 153 patients were treated with radical (RAD) or adjuvant/salvage (POST) intent with WPRT tomotherapy. According to internal guidelines, WPRT was always prescribed in: a) intermediate- and high-risk groups of patients in radical setting; b) node-positive patients and in node-negative patients submitted to limited lymphadenectomy (<8 removed nodes) and/or in the presence of adverse prognostic factors (Gleason Score >7 and/or pre-operative PSA > 10 ng/ml) in adjuvant or salvage setting. The median dose to the pelvic nodes was 51.8 Gy in 28 fractions, while concomitantly delivering 65.5-74.2 Gy to prostate/prostatic bed. All patients completed the minimum follow-up of 90 days after the end of the radiation treatment. Main clinical characteristics of the population were: median age: 71 (range 45–89) years; 19/153 patients suffered from hypertension; 65/153 patients had diabetes; 73/153 patients were submitted also to hormone therapy.

**Results:** Acute genitourinary (GU) toxicity ≥G2 according to RTOG scoring system was as follows: 25 (17 RAD+8 POST)/153 (16%) grade 2; 2 (2 RAD+0 POST)/153 (1%) Grade 3. Acute rectal toxicities were: 11 (3 RAD+8 POST)/153 (7%) grade 2; no grade 3. In total, only 13 (7 RAD+6 POST)/153 patients (8.5%) experienced grade 2 upper gastrointestinal toxicity; no patient experienced grade 3 toxicity, nor was there any treatment interruption due to uGI (or other) toxicity.

**Conclusion:** This study shows excellent results with regard to acute toxicity when pelvic irradiation was given concomitantly to that for the prostate region. Slightly increased (19 vs. 8 events of GU≥G2) acute toxicity was found in the RAD setting, probably caused by higher doses to the prostate region compared to the POST setting. However, further research is necessary to assess definitive late toxicity and tumour control outcome.

**30**

**INGUINAL METASTASIS FROM PENILE CARCINOMA IN SITU: A CASE REPORT**

Tullio Torelli1, Nicola Nicolai1, Mario Catanzaro1, Maurizio Colecchia2, Andrea Necchi1, Davide Biasoni1, Luigi Piva1, Angelo Milani1, Silvia Stagni1 and Roberto Salvioni1

1U.O. Urologia, and 2Dip. Anatomia Patologica, IRCCS Istituto Nazionale Tumori, Milano, Italy

**Background:** Penile carcinoma is uncommon, accounting for about 1% of malignancies. Carcinoma in situ may comprise about 10% of penile carcinoma. Unlike invasive carcinoma, node involvement is exceedingly rare in this setting and only three cases have been reported in international literature up to now. We report the fourth case.

**Case Report:** On the 11th March 2009, a 64-year-old man underwent a surgical circumcision and cold biopsies of the glans for several small, thickened and erythematous areas of penile prepuce and glans. Histology revealed squamous cell carcinoma in situ. On the 8th April 2009, a complete dioxide laser excision of glans mucosa was performed at our Institution, which confirmed plurifocal carcinoma in situ. Inguinal nodes were normal both at clinical examination and at ultrasound study. Follow-up was uneventful until October 2009, when a 3 cm left inguinal lymph-nodal enlargement was detected at ultrasound, which was confirmed by a CT scan of the abdomen and pelvis. Primary tumour did not recur, glans was completely resurfaced by normal epithelium and no further sites of disease were identified. On the 14th October 2009, a left inguino-iliaic lymphadenectomy was carried out by an inguinoabdominal access, which revealed metastatic squamous cells in 3 inguinal nodes with microscopic capsular spread. Other inguinal and iliac lymph-nodes were negative (3/11 nodes). We decided to perform contralateral lymphadenectomy due to the short interval between initial diagnosis and metastatic spread. On the 14th December 2009, a right inguino-iliaic dissection was performed and no disease was found (0/24 nodes).
This patient is currently undergoing adjuvant chemotherapy with taxotere-cisplatin-5-fluorouracil schedule q 21d.

Discussion: Invasive squamous cell carcinoma has a 20% rate of subclinical nodal metastasis in patients with nonpalpable inguinal nodes. It is recognized that carcinoma in situ can evolve in its invasive counterpart: Graham and Helwig analyzed 100 cases of carcinoma in situ and stated that approximately 10% of them developed invasive carcinoma, including 2 cases with metastasis (1). On the other hand, nodal metastasis associated with a penile carcinoma in situ is exceptional. Such an event has been reported in only 3 other cases (2). Biological explanations are lacking. One can simply hypothesize that a hidden area of invasive growth might be missed, due to the plurifocal (glans and prepuce) disease. To rule out this hypothesis, a full review of pathological specimens was performed, and no microfocal areas of invasive cancer were identified. Moreover, primary tumour did not recur. According to the ‘seed and soil’ theory revisited by Fidler (3), it might be that during the primary tumor’s natural history, neoplastic cells (seed) may invade the dermis, migrate and successfully proliferate in the lymph-nodes (soil) when host factors are favourable. Hence, the metastatic deposits progress and lead to further metastases without any further findings of local progression.

**Conclusion:** The prognosis of penile carcinoma in situ is excellent and it must be managed conservatively. An accurate follow-up schedule is necessary to monitor the risk of recurrent disease, as well as of new cancer arising. Metastatic disease from carcinoma in situ is very rare, but possible.

Special attention should be given to checking regional nodes during follow-up visits independently of local recurrence and type of tumour therapy.

**References**


**31 INTRATUBULAR GERM CELL NEOPLASIA IN PATIENTS WITH TESTICULAR CANCER: IMPLICATIONS IN TESTIS-SPARING SURGERY**

Gaetano Gulino1, Francesco Pierconti2, Alfonso D’onofrio1, Giuseppe Palermo1, Emilio Sacco1 and Pier Francesco Bassi1

1Dip. Urologia, and 2Istituto di Anatomia Patologica, Universita’ Cattolica del Sacro Cuore, Policlinico A. Gemelli, Roma, Italy

**Background:** Carcinoma in situ of the testis (intratubular germ cell neoplasia, ITGCN) is the preinvasive stage of germ cell tumours, whose main feature is the presence of neoplastic cells in seminiferous tubules. Although ITGCN has been described in testicular tissue adjacent to invasive cancer, no clear data have been reported on its prevalence, focality and on distance from the primary cancer focus. As far both multifocality and ITGCN are the major limitations to simple enucleation of germ cell testis tumours. This procedure is currently indicated in patients with bilateral tumours or single tumour in solitary testis and mass of diameter 2 cm or less. The aim of this study was to assess the prevalence and topographic localization of ITGCN in patients with testis germ cell tumours in order to detect any safety margin from primary cancer, that being the basis of such an organ-sparing surgery.

**Patients and Methods:** Forty-one orchiectomy specimens of patients with germ cell tumour of the testis were retrospectively analyzed by a single dedicated uropathologist. Multiple 5 mm sections were obtained along the major axis of the testis including the primary tumour and the ‘healthy’ tissue of the whole testis. Tissue sections were fixed in 10% formalin, embedded in paraffin and stained with haematoxylin-eosin. The mean diameter of the mass, the ratio between tumour and testis volume, the presence of foci of ITGCN and the distance of ITGCN from the primary mass were evaluated. Parameters of multifocality such as synchronous foci of cancer, vascular invasion or involvement of the rete testis were also sought.

**Results:** The mean age of patients was 32 years. Classic seminoma was found in 26 patients (19/26 stage I, 7/26 stage II or more), non seminomatous or mixed tumours in 15 (11/15 stage I, 4/15 stage II or more). The average diameter of the tumour masses was 23 mm, mean testicular diameter 45 mm and mean ratio between cancer mass and testis 0.51. In 18 specimens out of 41 (43%) ITGCN synchronous was documented, with single focus in 8 out of 41 (19.5%), with multiple foci in 10 out of 41 (24.3%). The average distance between ITGCN and the primary mass was 18 mm. In 3 specimens out of 41 (7.3%) evidence of multifocality was documented, with foci of synchronous invasive germ cell tumour size up to 8 mm.

**Conclusion:** Our preliminary data indicate that about half of patients with germ cell tumours, as well as the mass, histologically also present documented foci of malignancy in a pre-invasive stage (IGCTN) located up to 2 cm from the primary mass. A safety margin that allows such organ-sparing radical surgery has not been identified that is safe from the oncological standpoint.

**32 SEXUAL OUTCOMES AFTER ORGAN POTENCY-SPARING SURGERY AND GLANS RECONSTRUCTION IN PATIENTS WITH PENILE CARCINOMA**
Aim: Radical surgery, such as penile amputation, is still considered the ‘gold standard’ for treatment of invasive penile carcinoma T2-T3. However, despite good local control of disease, very poor anatomical, aesthetic, functional and psychological outcomes, such as chronic anxiety, depression and sexual disability, have been reported. The purpose of this study was to assess the impact of organ potency-sparing surgery and sexual disability, have been reported. The purpose of this psychological outcomes, such as chronic anxiety, depression and sexual disability, have been reported. The purpose of this study was to assess the impact of organ potency-sparing surgery in patients with locally confined carcinoma of the penis.

Patients and Methods: We evaluated retrospectively 42 patients (mean age 56 years) with penile cancer clinically confined (Ta, T1, T2), treated with diathermocoagulation in 6 cases with superficial lesions, glandulocoagulation and glanduloplasty with urethral mucosa and sparing of cavernosal apexes in 25 cases, glandulocoagulation and limited apical resection in 11 cases of stage T2. In all cases, T2 or G3 inguinal lymphadenectomy was performed according to Catalona’s technique. Sexual function, such as erection, ejaculation and libido were evaluated with IIEF-15 questionnaire related to the period preceding the macroscopic evidence of malignancy and 6 months after surgery. Quality of life was assessed by Bigelow-Young questionnaire, with questions related to unpleasant feelings, family and social relationships, quality of work. The scores related to the period of macroscopic evidence of the tumour have been compared to those obtained 6 months after surgery. Statistical analysis was conducted using t-Student for repeated measures and analysis of variance.

Results: Six months after surgery, 31/42 patients (73%) reported spontaneous rigid erections, 25/42 (60%) coital activity, while 19/25 (76%) of the group treated with glans reconstruction (urethral glanduloplasty) reported normal ejaculation and orgasm, regained an average of 35 days after surgery. The average IIEF-15 scores reported in the entire series in the domains of erection, libido and coital activity of the pre-cancer period were 22, 8 and 9, respectively, not statistically different (p> 0.05) than those (20, 7 and 8) recorded 6 months after surgery. In the group treated with glandular reconstruction (25 patients), pre-and post-operative IIEF-15 mean scores related to ejaculation and orgasm domains were not significantly different, at 8.9 and 6.7 respectively. Mean scores of Bigelow and Young questionnaires related to pleasant feelings, family, social and job relationships showed significant (p<0.01) improvement after surgery.

Conclusion: The sexual-sparing surgical treatments have a positive impact on a wide spectrum of patient's life including family relationships, social and working conditions. These treatments allow both oncological radicality and anatomopsychological integrity to be obtained, preserving body image and restoring complex functions such as erection and ejaculation.
Background and Aim: During robot-assisted radical prostatectomy (RALP) and extended pelvic lymph node dissection (ePLND) patients (pts) are in extreme Trendelenburg position. This might cause hypoperfusion of the lower extremities, pressure marks and skin damage. Therefore we investigated the creatinine kinase-concentration in blood (CK) during and after RALP and ePLND as an indicator of pressure damages due to the pts position.

Patients and Methods: In 60 consecutive pts undergoing RALP and ePLND, [CK], blood pH and base excess (BE) were measured during and after the procedure. The position damage was evaluated during the first 5 postoperative days and defined in 3 degrees (I: skin redness disappearing on finger pressure, II: skin redness not disappearing on finger pressure, III: skin lesion).

Results: The median age of the pts was 63 (43-73) years, median body mass index (BMI) was 26 (20-39), median operative time for RALP and ePLND was 317 (200-475) min and median time in the Trendelenburg position was 282 (170-470) min. The increase of [CK] became significant at 6 hours and maximal [CK] was reached 18 hours after the end of surgery. The [CK] values did not significantly influence the pH and BE values intraoperatively. There was no correlation between [CK] and BMI, operative time, length of the Trendelenburg position, age and perioperative creatinine values. The median [CK] value 6 hours postoperatively in the 39 pts without position damage was 491 (95-3863) IU; in the 16 pts with degree I position damage it was 1173 (186-5229) IU, and in the 5 pts with degree II + III position damage it was 4416 (457-15596) IU. The difference between the groups was statistically significant (Fisher Test \( p<0.05 \)).

Conclusion: [CK] increases to a maximum 18 hours after the end of surgery in patients after RALP and ePLND. [CK] elevation is not predictive of positioning damage. However, in the presence of skin lesion as a sign for pressure mark or damage, substantial [CK] elevation is probable. For pts with [CK] values higher than 5000 IU, whether a hypervolemic diuretic therapy for crush kidney prevention (as in trauma and burn injury) would be beneficial needs to be evaluated in further studies.

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SERUM TESTOSTERONE CAN AFFECT PREOPERATIVE URINARY CONTINENCE AND ERECTILE FUNCTION IN PATIENTS UNDERGOING RADICAL PROSTATECTOMY FOR CLINICALLY LOCALIZED PROSTATE CANCER

Mauro Gacci\(^1\), Giovanni Corona\(^2\), Nicola Tosi\(^1\), Lorenzo Masieri\(^1\), Michele Lanciotti\(^1\), Saverio Giancane\(^1\), Andrea Raugei\(^1\), Gianni Vittori\(^1\), Giovanni Apolone\(^3\), Annamaria Morelli\(^4\), Sandra Filippi\(^4\), Benedetta Fibbi\(^4\), Linda Vignozzi\(^4\), Gabriella Vannelli\(^4\), Alberto Lapini\(^1\), Sergio Serni\(^1\), Mario Maggi\(^4\) and Marco Carini\(^1\)

\(^1\)Department of Urology, University of Florence, Florence, Italy; \(^2\)Endocrinology Unit, Maggiore-Bellaria Hospital, Bologna, Italy; \(^3\)Center for the Evaluation and Research on Pain (CERP), Department of Oncology, Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy; \(^4\)Andrology Unit, Department of Clinical Physiopathology, University of Florence, Florence, Italy

The aim of present study was to evaluate the influence of serum testosterone (T) on urinary continence and sexual activity in patients undergoing radical prostatectomy for clinically localized prostate cancer.

Patients and Methods: A total of 257 patients were selected with the following inclusion criteria: radical prostatectomy (RP) for clinically localized PCa, preoperative filling out of QOL questionnaires (ULCA-PCI and IIEF), T and tPSA sampled the day before surgery. Exclusion criteria were neoadjuvant hormone or radiotherapy. We calculated the correlations between T and age, BMI, PSA, urinary function and bother(UF, UB) and sexual function and bother (SF, SB) and IIEF-5 in the whole population and in sub populations with normal (T\( \geq \)10.4 nmol/l) and low (T<10 ng/ml) T level with a Pearson and a Spearman correlation coefficient. We evaluated the differences in these parameters between patients with low and normal T with an unpaired samples t-test and a Mann-Whitney test. Finally, we evaluated the correlation between UF and SF, UB and SB, and between PSA and T in the overall population and separately in the patients with low and normal T with a Pearson correlation coefficient.

Results: Mean preoperative T was 13.5 nmol/l and 23.7% of patients presented a low T level. Mean age, mean BMI and mean preoperative tPSA at RP were 64.3 years, 25.9 and 9.0 ng/ml respectively. BMI resulted negatively correlated with T and normal T with a Pearson correlation coefficient.

Conclusion: The significant correlation between preoperative PSA and T exclusively in men with low T is in agreement with the ‘saturation’ model proposed by Morgentaler and Traish [Morgentaler A and Traish AM: Eur
Urol 55(2): 310-320, 2009]. The correlation between basal T and preoperative erectile function and urinary continence underlines the importance to assess T before RP.

36 IMPACT OF THE INvasion OF PERINEPHRIC AND RENAL SINUS FAT IN PATIENTS WITH RENAL CELL CARCINOMA AND VENOUS TUMOUR THROMBUS

Roberto Bertini

Istituto San Raffaele, Roma, Italy

Aim: To evaluate the impact of perinephric fat invasion (PFI) and renal sinus fat invasion (RSFI) on cancer specific mortality (CSM) in patients with renal cell carcinoma (RCC) with neoplastic thrombus.

Patients and Methods: From 1987 to 2008, 194 patients underwent radical nephrectomy for RCC with neoplastic thrombus. The microscopic slides from all tumour specimens were reviewed by a single experienced genitourinary pathologist. Ninety pts had either PFI (n=47) or RSFI (n=43). Of these, 60 pts had coexisting PFI and RSFI. Patient characteristics: median age 61 (range 24-91) years, pT3b/pT3c/pT4: 161/18/15, pN0/pN1/pN2/pNx: 119/13/43/19 (TNM 2002), G2/G3/G4: 41/102/51, M0/M+: 109/85. Associations with cancer-specific mortality (CSM) were evaluated by univariate analysis (Kaplan-Meier model) and univariate and multivariate Cox proportional hazards model, including Fuhrman grade, metastatic disease and nodal status and involvement of tumour fat invasion (TFI).

Results: Overall median follow-up was 20 (1-220) months, while median follow-up for alive patients was 36 months. The 3-year actuarial cancer-specific survival was significantly lower in pts with TFI (39%) than in pts without TFI (74%; \( p<0.001 \)). Kaplan-Meier survival analysis showed no difference between pts with PFI alone and pts with RSFI alone, while the presence of coexisting PFI and RSFI was associated with a higher risk of CSM (\( p<0.001 \)). Univariate Cox regression analysis confirmed that pts with PFI or RSFI had a poorer prognosis than pts without TFI (\( p<0.010 \)). Moreover, pts with coexistent PFI and SFI had a lower survival than patients with PFI or RSFI alone (\( p=0.026 \)). At multivariate analysis, the presence of synchronous metastases (\( p<0.001 \)), nodal involvement (\( p=0.002 \)) and TFI (\( p<0.001 \)) were associated with increased risk of dying from RCC. Specifically, coexisting PFI and RSFI had a significant poor prognosis (p=0.046, HR 1.78).

Conclusion: This study shows that pts affected by RCC with neoplastic thrombus and TFI have a significant worse prognosis compared with RCC with neoplastic thrombus alone. In particular, pts with coexistent PFI and RSFI have an increased mortality for RCC with neoplastic thrombus than pts with PFI or RSFI alone.

References

37 DIRECT INVASION OF THE ADRENAli GLAND IS A STRONG PREDICTOR OF CANCER-SPECIFIC MORTALITY IN pT3 PATIENTS WITH RCC: ANALYSIS FROM A SINGLE PATHOLOGIST

Marco Roscigno, Diego Angiolilli, Elena Strada, Francesco Sozzi, Giovanni Petralia, Rayan Matloob, Luigi Da Pozzo, Giorgio Guazzoni, Andrea Cestari, Massimo Freschi, Francesco Montorsi, Patrizio Rigatti and Roberto Bertini

Ospedale San Raffaele, Dip. Urologia, via Olgettina 60, 1132 Milano, Italy

Aim: To evaluate the effect of the direct invasion of the adrenal gland in patients with pT3 renal cell carcinoma (RCC) on cancer specific mortality (CSM).

Patients and Methods: From 1987 to 2007, 363 patients underwent radical nephrectomy for pT3-pT4 RCC (2002 TNM); 352 had pT3 disease and in 20 of them the adrenal gland was directly involved by the tumour. The microscopic slides from all tumour specimens were reviewed by a single experienced genitourinary pathologist (MF). Associations with cancer-specific mortality (CSM) were evaluated by univariate analysis (Kaplan-Meier model) and univariate and multivariate Cox regression analysis including T stage, metastatic disease and nodal involvement. A single uropathologist reviewed all the pathological slides.

Results: Median follow-up was 29 (2-252) months for the overall population and 65 (range 2-252) months for living patients. The 2-year cancer-specific survival in pT3 patients without direct adrenal involvement was 68% as compared to 12% of the patients with direct adrenal gland involvement (\( p<0.001 \)). At multivariable Cox regression analysis, the
direct adrenal gland involvement was an independent predictor of CSM (HR 3.03, p<0.001) together with pT stage (pT3a vs. pT3b vs. pT3c), presence of metastatic disease, and nodal status (pNx/pN0 vs. pN+) (all p<0.001). Kaplan-Meier survival analysis showed similar survival in pT3 patients with direct adrenal involvement and pT4 patients. Therefore, we performed subsequent analyses considering patients with adrenal gland involvement as pT4 patients. We found a statistically significant difference in 2-year estimate survival between reclassified pT3a-pT3b-pT3c and pT4 patients (78% vs. 57% vs. 58% vs. 22% p<0.001). The pT3-pT4 reclassification resulted an independent predictor of CSM at multivariable analysis (p<0.001), after adjusting for distant metastases and nodal status.

**Conclusion:** Renal cell carcinoma with direct extension into the adrenal gland predicts significantly worse survival and these patients have a prognosis similar to those with pT4 disease. Our data suggest that adrenal gland involvement should be considered a pT4 disease as proposed by the new TNM classification that will be effective from January 2010.

**References**
1 Moch H, Artibani W, Delahunt B et al: TNM classification that will be effective from January 2010. Should be considered a pT4 disease as proposed by the new TNM classification that will be effective from January 2010.


38 IMPACT OF TUMOUR THROMBUS CONSISTENCY (SOLID VERSUS FRIABLE) ON CANCER-SPECIFIC MORTALITY IN PATIENTS WITH RENAL CELL CARCINOMA AND VENOUS TUMOUR THROMBUS

**Roberto Bertini,** Marco Roscigno, Massimo Freschi, Umberto Capitanio, Diego Angiolilli, Elena Strada, Giovanni Petralia, Rayan Matloob, Francesco Sozzi, Alberto Briganti, Luigi Da Pozzo, Francesco Montorsi and Patrizio Rigatti

Ospedale San Raffaele, via Olgettina 60, Milano, Italy

**Aim:** We analyzed the effect of the consistency of a venous tumour thrombus (VTT) on cancer-specific mortality (CSM) in patients affected by renal cell carcinoma (RCC).

**Patients and Methods:** We retrospectively analyzed 174 patients with RCC and renal vein or inferior vena cava VTT who underwent radical nephrectomy and thrombectomy at our institute (1989-2007). All pathologic specimens were reviewed by a single uropathologist (MF), who had no knowledge of patient outcomes. Apart from traditional pathologic features, the morphologic aspect of a venous thrombus was evaluated to distinguish solid versus friable character. In a solid thrombus, tumour growth was compact and cohesive, with a rounded linear profile and, sometimes, a partial endothelial lining simulating a pseudocapsule. In a friable thrombus, tumour cells were intermingled with abundant necrosis and fibrin, and had a scalloped irregular profile and discohesive aspect, sometimes with thin papillary features. The prognostic role of thrombus consistency (solid vs. friable) on CSM was assessed by means of Cox regression models.

**Results:** The median follow-up was 24 months. The VTT was solid in 107 (61.5%) and friable in 67 (38.5%) patients. The presence of a friable VTT increased the risk of having synchronous nodal or distant metastases, higher tumour grade, higher pathologic stage, and simultaneous perinephric fat invasion (PFI) (all p<0.05). The median CSM-free survival was 33 months. The median CSM-free survival in patients with a friable or a solid VTT was 8 and 55 months, respectively (p<0.001). At multivariable analyses, the presence of a friable VTT was an independent predictor of CSM (p=0.02). The presence of a friable thrombus was the second most informative predictor (area under the curve [AUC]=62%) after the variable depicting the presence of a synchronous metastasis (AUC=68%). Moreover, inclusion of the variable ‘friable thrombus’ in a base model including ECOG PS, Fuhrman grade, and presence of nodal disease and metastatic disease significantly increased the accuracy in predicting CSM (+2.5%; p<0.001). On the contrary, extension of the tumour thrombus did not affect patient survival.

**Conclusion:** In patients with RCC and VTT, the presence of a friable thrombus is an independent predictor of CSM. We suggest that information about thrombus consistency be introduced into standard pathological reports. More research is needed to better clarify the prognostic role of thrombus consistency in patient outcomes.

**References**


41 TUMOUR NECROSIS AFFECTS PATIENT SURVIVAL IN NON-METASTATIC RENAL CELL CARCINOMA

Roberto Bertini, Marco Roscigno, Elena Strada, Giovanni Petralia, Rayan Matloob, Francesco Sozzi, Alberto Briganti, Andrea Gallina, Massimo Freschi, Luigi Da Pozzo, Francesco Montorsi and Patrizio Rigatti

Dip. Urologia, Ospedale San Raffaele, via Olgettina 60, 20132 Milano, Italy

**Aim:** The prognostic role of tumour necrosis in renal cell carcinoma (RCC) is still under debate. We aimed to evaluate whether tumour necrosis may affect cancer-specific mortality (CSM) in patients with RCC.

**Patients and Methods:** We retrospectively analyzed data of 1085 consecutive patients who underwent radical nephrectomy or nephron-sparing surgery for RCC, between 1987 and 2007. The Kaplan-Meier method and univariable and multivariable Cox regression analyses were used to determine the effect of predictors on CSM. Covariates consisted of TNM stage, Fuhrman grade, tumour size, symptom classification, and tumour necrosis. The analysis first addressed the entire patients population (n=1085) and then was repeated in patients with only non metastatic disease.

**Results:** Median follow-up was 60 months (2-254). Patient characteristics: median age 61 (range 24-91) years, pT1a/pT1b/pT2/pT3a/pT3b/pT3c/pT4 (TNM 2002): 362/253/134/157/149/16/14, pN0-pNx/pN+: 1004/81, G1/G2/G3/G4: 174/576/270/65, M0/M+: 908/177. Tumour necrosis was present in 401 patients (37.8%). In the overall population, tumour necrosis was associated with worse 5-year survival than patients without tumour necrosis (57% vs 90%; log-rank p=0.001). Nonetheless, tumour necrosis did not achieve the independent predictor status of CSM at multivariable Cox regression analysis, after adjusting for the above mentioned clinical and pathologic variables (p=0.22). In the subgroup of nonmetastatic (pNx-0 M0) patients, tumour necrosis was associated with worse 5-year survival (79% vs 95%; p<0.001) and was also independent predictor of higher risk of CSM at multivariable Cox regression analysis (p=0.44; HR: 1.7), together with pT stage (p<0.001) and tumour size (p=0.05).

**Conclusion:** Tumour necrosis seems to be associated with a higher risk of CSM in the nonmetastatic RCC population. In the presence of metastatic disease, tumour necrosis does not affect patient outcome.

42 THE NEW TNM STAGING SYSTEM FOR RENAL CELL CARCINOMA DOES NOT IMPROVE ACCURACY IN PREDICTING CANCER-SPECIFIC MORTALITY

Roberto Bertini, Marco Roscigno, Elena Strada, Giovanni Petralia, Rayan Matloob, Francesco Sozzi, Luigi Da Pozzo, Umberto Capitanio, Giorgio Guazzoni, Nazareno Suardi, Massimo Freschi, Francesco Montorsi and Patrizio Rigatti

Dip. Urologia, Ospedale San Raffaele, via Olgettina 60, 20132 Milano, Italy

**Aim:** The TNM staging system for renal cell carcinoma (RCC) has been recently updated and will be effective since January 2010: pT2 stage is split into pT2a (>7 cm) and pT2b (>10 cm); patients with tumour thrombus invading the renal vein are classified as pT3a; infiltration of the wall of the vena cava as pT3c; direct invasion of the adrenal gland is included in pT4 stage. Moreover, all nodal involvement is classified as pN1. We aimed to analyse whether the new TNM staging system is more accurate than the 2002 TNM classification in predicting the risk of cancer-specific mortality (CSM).

**Patients and Methods:** We retrospectively analysed data of 1,234 consecutive patients who underwent radical nephrectomy or nephron-sparing surgery for RCC, between 1987 and 2007. The Kaplan-Meier method and univariable and multivariable Cox regression analyses were used to determine the effect of the 2002 TNM and of the new TNM staging system on CSM. Finally, we compared the predictive accuracy of the 2002 TNM and of the new TNM staging system calculating the area under the ROC curve. Mantel-Haentzel test evaluated the differences in predictive accuracy between the two different classifications.

**Results:** Median follow-up was 60 (2-254) months. According to the 2002 TNM staging system, no difference was found in survival between pT2a and pT3c patients at univariable analyses. According to the new TNM staging system, no difference in survival was found between pT2a and pT2b stage; moreover, pT3a, pT3b and pT3c stage showed similar outcomes. At multivariable Cox regression analysis, both 2002 pT and the new pT classification resulted as independent predictors of the risk of CSM, after adjusting for distant metastases and nodal involvement. Finally, the model including 2002 TNM and the new TNM staging system showed similar accuracy in predicting CSM (AUC=88.2 vs. 87.7%; p=0.46)

**Conclusion:** In our population, the reclassification of disease into pT2a and pT2b failed to clearly distinguish two groups of patients with different prognoses. The same was observed in the case of pT3a, pT3b and pT3c subgroups of
patients. The new TNM staging system does not improve accuracy in predicting CSM with respect to the 2002 TNM staging system.

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DIFFERENT SURVIVAL OF HISTOLOGICAL SUBTYPE IN PATIENTS WITH RENAL CELL CARCINOMA

Roberto Bertini, Marco Roscigno, Diego Angiolilli, Elena Strada, Giovanni Petralia, Rayan Matloob, Francesco Sozzi, Luigi Da Pozzo, Nazareno Suardi, Firas Abdollah, Andrea Salonia, Massimo Freschi, Francesco Montorsi and Patrizio Rigatti

Dip. Urologia, Ospedale San Raffaele, via Olgettina 60, Milano, Italy

Aim: To evaluate the prognostic role of histological subtype in renal cell carcinoma (RCC). We aimed to specifically evaluate whether type I and type II papillary RCC behave differently from clear cell renal cell carcinoma.

Patients and Methods: We retrospectively analyzed data of 1216 consecutive patients who underwent radical nephrectomy or nephron-sparing surgery for RCC, between 1987 and 2007. The Kaplan-Meier method and univariable and multivariable Cox regression analyses were used to determine the effect of predictors on CSM. Covariates consisted of 2002 TNM stage tumour size, and histological subtypes, according to Heidelberg classification. Papillary RCC was subclassified in the basophil type I and eosinophil type II as defined by Delahunt and Eble. All the pathological slides were reviewed by a single uropathologist.

Results: Median follow-up was 60 (2-254) months. Patient characteristics: median age 63 (range 24-91) years, pT1a/pT1b/pT2/pT3a/pT3b/pT3c/pT4 (TNM 2002): 397/288/165/173/162/17/14, pN0/pN+/pNx: 547/89/580, M0/M+: 1018/198. Chromophobe, papillary type I, type II and clear cell RCC was diagnosed in 65, 82, 44 and 1025 patients, respectively. Five-year survival was 92%, 89%, 64% and 78%, respectively; (log-rank \( p < 0.001 \)). No difference in survival was found between chromophobe and type I papillary RCC (\( p = 0.524 \)). Multivariate Cox regression analysis confirmed histological subtype of RCC as an independent predictor of CSM, after adjusting for tumour size, pT stage, nodal status and presence of distant metastases (\( p = 0.019 \)). Specifically, chromophobe subtype and papillary type I had similar risk of CSM and had a better outcome than clear cell and papillary type II RCC. Moreover, papillary type II RCC was associated with higher risk of CSM with respect to clear cell RCC (\( p = 0.027; \) HR: 1.96).

Conclusion: Chromophobe and papillary type I RCC had similar survival rates, which were better than those for clear cell and papillary type II histology. Papillary type II RCC seems to be independently associated with a worse prognosis than clear cell RCC.

References

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PERCUTANEOUS CRYOABLATION (PCA) FOR RENAL MASSES: IS SOMETHING GOING TO CHANGE?

Nicola Nicolai, Carlo Sprefico, Mario Catanzaro, Tullio Torelli, Silvia Stagni, Davide Biasoni, Luigi Piva, Andrea Necchi, Angelo Milani, Paolo Girotti, Alfonso Marchianò and Roberto Salvioni

Istituto Nazionale dei Tumori, via Venezian 1, Milano, Italy

Background: Detection of small renal masses is increasing due to increasing occurrence of renal cell cancer (RCC) and to the wide use of abdominal ultrasound in general practice. Many of these patients are elderly or affected by morbidities which may contraindicate surgery. Moreover, biology of small renal masses is not perfectly understood.

Patients and Methods: In October 2007, we started PCA which was initially planned for patients who were unfit for standard surgical treatment and having anterior lesions of the kidney. An argon-based cryosurgery unit (Endocare, Irvine, CA, 1.7-2.4 mm cryoprobes) was used. In order to evaluate probe positioning and ice ball size, a standard scan is carried out every 5 minutes until obtaining target temperature (–20°/–40°) in the targeted volume. Ice-ball would exceed tumour margins by at least 5 mm through 2 freezing cycles of 13-15 minutes separated by a passive warming cycle of 12-15 minutes. Immediate postoperative monitoring provided clinical examination, haemochromate examination and CT scans without contrast medium at 24 hours. Follow-up protocol provided a multi-slice spiral CT examination with contrast medium at 1, 3, 6, 9 and 12 months after PCA and afterwards every 6 months. A...
complete lack of enhancement of a previously enhancing mass was considered as a surrogate of a complete response.

Results: Between October 2007 and September 2009, 29 patients (median age: 73, range 52-82 years; M/F: 19/10) underwent a total of 30 CT-guided PCA procedures performed by one interventional radiologist (CS). Six underwent PCA due to recurrent disease following previous surgery for RCC and 23 were new patients. Out of the latter a PC biopsy revealed RCC in 17, oncocytoma in 2 and was not diagnostic in 2 patients. Median diameter was 30 (range 12-70) mm. Six patients had a solitary kidney due to previous surgery. ASA score was ≥3 in 14 patients. General anaesthesia was indicated in 15 cases. One patient underwent contextual PCA of a bone metastasis. PCA was completed in all cases without intraoperative complications. All patients complained of mild pain on day one. CT scans at 24 hours revealed a hematoma in 17 (58.6%) patients: 2 of them (6.9%) had a significant anemia, one needing a transarterial embolization of a small intra-renal arterial branch. In 27 patients, no contrast enhancement was found during follow-up. Two patients showed recurrent disease: one had an initial 30 mm RCC still having a thin peripheral enhancement 1 month after PCA; one with a history of bilateral RCC, had a 24 mm left renal recurrence (initially 28 mm) 9 months later. Both patients were successfully re-treated with PCA. All patients are alive and disease free after a median follow-up of 12 (range 3-24) months. Serum creatinine remained unchanged both immediately and during follow-up.

Conclusion: Asymptomatic detected renal masses are an emerging issue. Although surgical excision still represents the gold standard, indications to surgery require an evaluation of co-morbidities, surgical risks, life expectancy and clinical relevance of the disease. Our data show that PCA: 1) is a feasible and safe technique in unfit patients; 2) is active in local control of renal cancers, also larger than 30 mm; 3) can be repeated in case of persistent or recurrent renal enhancing areas; 4) can be considered in multimodality approach (contextual PCA of renal and bone masses). Limitations consist of: 1) short follow-up period, unable to evaluate oncological efficacy; 2) unsolved problem of which is the best way to assess local efficacy, as lack of enhancing area is just a surrogate; 3) imperfect accuracy of pre-treatment biopsy, which was not diagnostic in less than 10% of patients; 4) possible overtreatment for benign lesions as oncocytomas.

References

48 RENAL CELL CARCINOMA WITH SYNCHRONOUS BLADDER METASTASES: CASE REPORT AND REVIEW OF THE LITERATURE

Fabiano Palmieri, Michele Malizia, Giorgio Bruno and Salvatore Voce
Santa Maria delle Croci Hospital, Ravenna, Italy

Background: Renal cell carcinoma rarely presents with distant metastasis and the diagnosis is frequently performed when the neoplasm is localized inside the kidney. Moreover, involvement of the urinary bladder is rarely diagnosed and only few cases are reported in literature. We present a case of synchronous metastases to the urinary bladder in a patient affected by right renal cell carcinoma with pulmonary metastases.

Patients and Methods: A 60-year-old women presented at our Department with gross hematuria, right flank pain and an increase in serum creatinine (i.e. 3.5 mg/dl). The computed tomography revealed a voluminous right renal mass (16 cm in longest diameter) with neoplastic thrombus extending through the vena cava, pulmonary metastases and a solid lesion of the posterior wall of the urinary bladder. The patient underwent transurethral resection of bladder and the histological examination revealed a clear cell carcinoma metastases. Two weeks later we performed a right radical nephrectomy, resection of the vena cava thrombus and an extendend lymphnode dissection. The pathologic examination revealed a grade 3, pT4, N0 renal cell carcinoma. Bone scans resulted negative for metastases.

Results: One month past surgery, the patient underwent medical therapy with sorafenib. At present (12 months past surgery), the patient is alive and the last computed tomography revealed a reduction of the pulmonary metastases.

Conclusion: Urinary bladder metastasis from renal cell carcinoma is extremely rare. At present, only 29 cases are reported in literature. The 3-year survival rate was 80% in the presence of a solitary bladder metastasis and 20% in the presence of multiple metastases. There are many hypotheses concerning the mechanism of spread to the urinary bladder. Direct implantation, venous embolism and lymphatic spread are the mechanisms advocated.

References

49 SINGLE-DOSE VERSUS 5-DAY ANTIBIOTIC THERAPY IN PATIENTS UNDERGOING TRANSRECTAL PROSTATE BIOPSY: OUR PRELIMINARY EXPERIENCE

Fabiano Palmieri, Michele Malizia, Giorgio Bruno and Salvatore Voce
Santa Maria delle Croci Hospital, Ravenna, Italy

Background: The prostate biopsy represents the method of choice in the diagnosis of prostate cancer, being one of the urological procedures more frequently performed in the clinical daily practice. The most frequent complications are surely that of hemorrhagic type such as haematuria, haematospermia and rectal bleeding, but also acute retention of urine and infections of the lower urinary tract. The incidence of these events reported in literature ranges from 2.8% to 70%. The bacteria involved in lower urinary tract contamination in the course of prostate biopsy are gram negative. We compared the incidence of infective events between a single-dose and a 5-day antibiotic prophylaxis of prulifloxacina.

Patients and Methods: In the course of 2009, 257 patients were submitted to transrectal echo-guided prostate biopsies. Of these patients, 60 were randomized in two groups: group A (30 patients) received a single dose of prulifloxacin whilst the patients of group B (30 patients) had a 5-day course of prulifloxacina.

Results: The mean age of patients was 64 (range 80-49) years. The incidence of hyperpyrexia was comparable in the two groups: 3 cases in group A (10%) and 2 cases in group B (6.6%). In all cases, fever was associated with positive urine cultures.

Conclusion: Our experience suggests that a single dose of antimicrobial prophylaxis is reasonable in selected patients undergoing prostate biopsy.

References


50 PRIMARY TESTICULAR LYMPHOMA AND CONTROLATERAL CRYPTORCHIDISM

Giacomo Perugia1, Giuseppe Di Natale1, Domenico Di Viccaro1, Simone Teodonio1, Gino Bova1, Alessandro Chinazzi2, Antonio De Cillis1, Valerio Olivieri1, Giuseppe Borgoni1 and Marcello Liberti1

1Dipartimento di Scienze Urologiche "U. Bracci", Viale del Policlinico 155, 00161 Roma, Italy;
2Dipartimento di Scienze Biochimiche "A. Rossi Fanelli", Piazzale Aldo Moro 5, 00185 Roma, Italy

Background: Testicular lymphoma accounts for 1%–9% of all testicular neoplasm and 1%-2% of all non-Hodgkin lymphomas, with an estimated incidence of 0.26/100,000 per year. Although uncommon in general, lymphomas of the testis are the most common testicular malignancy in men 60 years of age and older, and may be the primary and only manifestation of malignant lymphoma, that is the initial sign of a systemic disease. Secondary involvement of the testis in patients with lymphoma is far more common than primary testicular lymphoma. Various reports have advocated prior trauma, cronic orchitis, cryptorchidism, and filarisis of the spermatic cord, as potential risk factors, but predisposing causes for the development of testicular lymphoma are still unclear. We describe a case of diffuse large B-cell testicular lymphoma associated with controlateral cryptorchidism.

Case Report: A 63-year-old man, apparently in good health, came to our attention for left testicular/scrotal swelling of several months duration, associated with rare scrotal pain during sexual intercourse, previously treated with different courses of antibiotics. Scrotal examination demonstrated a firm, painless, palpable testicular mass within the left hemiscrotum. Ultrasound scan showed the left testicle to be enlarged, with two hypoechoic 3.4 and 2.7 cm heterogeneous vascular masses with no involvement of the adjacent epididymis, and an hypoplastic controlateral testis with an hypechoic streak (microlithiasis) within an homogeneous hecotexture. Normal blood flow was found on Doppler ultrasound. Medical history revealed a previous surgical treatment for right cryptorchidism and the results of an accurate physical examination and blood test,
including testicular cancer markers, were no contributory. The patient underwent left orchidectomy and pathological features, according to the WHO classification system, showed the presence of diffuse large B-cell lymphoma (CD45+, CD20+, vimentin+), with no involvement of the epididymis, tunica albuginea or spermatic cord. Complete haematological and biochemical examinations, total-body computerized tomography, and bone marrow aspirate and biopsy did not show extratesticular involvement of the disease, and the case was classified according to the modified Ann Arbor Staging system as a stage I-E disease. The patient is receiving chemotherapy by means of R-CHOP (cyclophosphamide, doxorubicin, vincristine and radiation therapy).

**Conclusion:** Primary non-Hodgkin lymphoma of the testis is a rare disease associated with a high incidence of recurrence, even years after complete response, and a poor prognosis. Diffuse large-B cell testicular lymphoma is the most common histotype in primary forms, and has a high incidence of bilateral involvement and shows propensity for extranodal spread to the skin, subcutaneous tissue, central nervous system, lung and Waldeyer’s ring. Stage and pathological grading are the most important predictive factors for outcome, and further optimal treatment following orchidectomy is still unclear because the rarity of this disease, and because of the lack of prospective or randomized studies. Concerning the risk factors, there are no well-documented predisposing causes for primary testicular lymphoma, and anectodal reports associated with trauma, chronic orchitis, and cryptorchidism have been published. It is interesting to note how the case described is associated with contralateral cryptorchidism and testicular microlithiasis, both considered predisposing factors for testicular cancer; therefore the patient should have short- and long-term follow-up due to the increased risk of contralateral recurrence of lymphoma.

**References**

### 51 MINI-INVASIVE OPEN TUMOUR ENucleATION VS. PERCUTANEOUS RADIOFREQUENCY ABLATION (PRA) OF SMALL RENAL MASSES <3 CM IN ELDERLY PATIENTS: LONG-TERM RESULTS OF A PROSPECTIVE FOLLOW-UP STUDY

Maurizio Brausi, Giuseppe De Luca, Mirko Gavioli, Giorgio Verrini, Gianluca Simonini, Alberto Romano, Giancarlo Peracchia, Massimo Viola and Giovanni Luca Giliberto

Department of Urology, AUSL Modena, via Molinari 1, Carpi, Italy

**Background and Aim:** The objectives of this study were to evaluate and compare the oncological outcomes of old pts with renal tumours who received open surgery or PRA and to observe side-effects.

**Patients and Methods:** From 2002 to 2006, 53 pts with small renal masses <3 cm diagnosed with US+CT were included in this prospective study. The first and standard treatment offered to our pts is surgery (open or laparoscopic). When pts are at high risk or refuse surgery, a PRA approach or Active surveillance is offered. A total 27 pts, mean age 72.3 years (Group A), received open surgery: tumour enucleation through a mininvasive procedure. We adopted a small flank incision (6-7 cm) with *in situ* enucleation of the tumour. Flow seal was used in 9 pts for haemostasis while interrupted sutures were used in 16. Twenty pts., with a mean age 73.3 years (Group B), received PRA. The male to female ratio was 23/4 in Group A vs. 20/6 in Group B. Mean tumour diameter was 2.1 cm and 2.5 cm in Group A and B, respectively. Tumour location was left side 14/11, right side 13/15. General anaesthesia was always used in Group A, while local anesthesia along the needle tract was used in 23/26 pts receiving PRA. One pt. had general anaesthesia; 2 pts were not treated because of the difficult tumour location.

**Results:** Mean follow-up in Group A and Group B was 60 (34-81) and 55.4 (38-81) months, respectively. Group A: histology: 23/27=renal cell carcinoma, 1 angiomyolipoma and 3 oncocytomas (11.1%); grade: G1=6, G2= 12; chromophobe=2, papillary=3. Mean blood loss was 127.6 cc (50-400 cc). Intra-operative margins were always negative (3-6 fragments). Mean hospital stay was 5.4 days. Complications: 3/27 pts (11.1%) had 2 units of blood transfused postoperatively. A total of 2/27 pts (7.4%) died of pulmonary embolism and cardiac failure 2 and 3 years from surgery, while 25/27 (92.6%) pts had no evidence of disease without local or distant recurrence. Renal function is normal (mean serum creatinine: 1.02mg/dl) in all the pts. Group B: No histology. Mean blood loss=0. Mean hospital stay: 1 day. Complications: 1 pt had nausea. A total of 4/24pts (16.6%) died of cardiovascular diseases after 3-7-24-36 months from PRA; 2 pts. were not followed up. 2/22 pts (9.1%) had a complete CT response, 3/22 (13.6%) had an increase in tumour diameter of 5 mm (PR) after 56, 59 and 72 months, and 17/22 pts (77.3%) had stable disease on CT.

**Conclusion:** Open surgery (mininvasive tumour enucleation) remains the best therapeutic option for elderly patients with small renal tumours. The oncological outcome is excellent and the complication rate low. PRA can be offered to pts. at high risk or refusing surgery.
RADICAL CYSTECTOMY AND ORTHOTOPIC NEOBLADDER IN WOMEN: LONG-TERM EVALUATION

Maurizio Brausi, Alberto Romano, Giancarlo Peracchia and Giuseppe De Luca

Department of Urology, AUSL Modena, Italy

Aim: The objectives of this multicentre study were to evaluate the long-term function, morbidity and outcome of orthotopic bladder replacement in women receiving radical cystectomy.

Patients and Methods: From 1982 to 2004, 60 women underwent radical cystectomy and orthotopic neobladder in 4 urological centres. The mean age was 60.2 (range 32-74) years; 57/60 presented with bladder carcinoma, while 3/60 had contracted bladder. Pathological staging was: T2-T3 in 52/60, T1 in 5. A total of 7/60 patients had positives nodes. The grade was G3 in 49/60 and G2 in 8/60. In the last 47 patients, the preservation of the hypogastric plexus without resecting the pubourethral legaments and the preservation of the autonomic fibers reaching the urethra was attempted. Ileum was used in 59/60 cases; 44/60 patients had a modified Studer procedure, 9 had a Padua ileo-bladder, and 6 had Camey II; 1/60 underwent colon conduit and 6/44 patients received adjuvant chemotherapy. Continence was determined before and after treatment in 42 patients with urodinamic studies. 3 patients had pre-op stress incontinence.

Results: Perioperative mortality was zero. Two patients were lost to follow-up and were excluded from this analysis. The mean follow-up for 58 patients was 72 (range 3-252) months. The mean hospital stay was 16.8 (range 7-22) days. Major early complications (first 30 days) were 3/60 (5.0%); a bowel obstruction requiring surgery, 1 pulmonary embolus and 1 metabolic acidosis, treated with medical therapy. Major late complications were 8/58 (13.8%): 3 cases of stenosis of ureteral anastomosis, 3 vesico-vaginal fistula and 2 with pouch prolapse. There were 6/58 (10.3%) minor late complications: 3 patients had stones in the pouch, 2 had recurrent UTI, 1 had laparocoele. Disease progression was 13.7% (8/58): 3 patients had local progression (pelvis) and 3 had distant metastasis, 2 had local+distant in a mean time of 18 months. Overall, 7/58 (12.2%) patients died of their disease after a mean time of 13.4 months. The long-term continence (no/1 small pad) rate (mean time 62.2 months) was 72.4% (42/58). A total of 9/58 (15.5%) patients had chronic urinary retention requiring intermittent catheterization; 7/58 patients (12.1%) had incontinence (>3 pads/day) which was treated in 3 patients with collagen injection to the bladder neck: both improved from 3-5 pads to 1-2 pads/day. Three patients had an indwelling catheter, 1 no therapy.

Conclusion: The results of our study show that orthotopic bladder replacement in women is indicated. The long-term function is good and the late complication rate is tolerable. The incontinence rate can be improved with pouch suspension, careful preparation of the urethral stump and minimal dissection in the region between vagina and urethra.

AGE >70 YEARS IS AN ABSOLUTE CONTRAINDICATION TO ORTHOTOPIC BLADDER REPLACEMENT AFTER RADICAL CYSTECTOMY (RC) IN WOMEN: A MULTI-INSTITUTIONAL STUDY

Maurizio Brausi1, Giuseppe De Luca1, Alberto Romano1, Giancarlo Peracchia1, Carlo Daniele2, Pietro Cortellini3 and Alberto Reggiani4

Departments of Urology, AUSL 1Modena, 2Ferrara, 3Parma and 4Bologna, Italy

Aim: To evaluate the morbidity, outcome and function of orthotopic neoabladder replacement in women >70 years of age receiving RC and compare them to a female population <70 years operated on in the same period of time.

Patients and Methods: From 1982 to 2007, 69 women underwent RC and orthotopic neobladder in 4 centres. The surgical technique used was previously described and was similar in all the centres. A total of 15/69 patients (21.7%) were >70 years (Group A); mean age 77.6 (range 72-83) years; 54/69 pts. (78.3%) were <70 years (Group B): mean age 59.2 years (range 46-70 years). Patients A: p stage T1=2/15, T2=6/15, T3=6/15, T4=1/15; N+=1/15 (6.6%); Grade: 15/15=G3. These elderly patients strongly refused the concept of wearing an external urinary appliance and consented to RC only if an orthotopic neobladder was performed. Group B: 3/54 had a contracted bladder; pStage: recurrent CIS=3, T1=6/51, T2=19/51, T3=22/51, T4=1/51; N+=8/51 pts. (15.7%). Grade: G2=9/51, G3=42/51.

Results: The mean follow-up was 64.2 months. Three pts in Group A and two pts in Group B were lost to long term follow-up. Group A: Overall survival (OS) =7/15 (46.6%), disease-specific survival (DSS)=8/15 (53.4%). A total of 7/15 pts (46.6%) progressed in a mean time of 15.7 months. Early complications were: vesico-vaginal fistula=6/15 pts (40%); 3/6 pts had Foley catheter stripping during the post-operative period because of delirium. Late complications (12 pts): incontinence rate (severe-moderate)=5/12 (41.6%). Continence rate (0-1 pad)=3/12 (25%). Hypercontinence=1/12 (8.3%) (int.catheter), indwelling catheter=3/12 (25%), pouch prolapse=1/12 (8.3%). Group B: OS=41/54 (75.9%), DSS=42/54 (77.7%), progression=13.7%. Early complications: 1
bowel obstruction requiring surgery, 1 pulmonary embolus and 1 metabolic acidosis treated with medical therapy. Late complications: 3/54 ureteral anastomosis (5.55%), 2/54 vesicovaginal fistula (3.7%), 2/54 pouch prolapse (3.7%). Continen ce rate (0-1 pad)=39/54 pts (72.2%). A total of 9/54 pts (16.6%) had incontinence (severe, moderate); 7/54 pts had chronic urinary retention (12.9%).

Conclusion: Orthotopic neobladder in women older than 70 determines a very high complication rate (50%) and a high incontinence rate (41.6%). Some complications are due to delirium developed in the postoperative period which causes catheter stripping with bladder neck lesions. In these patients orthotopic neobladder is an absolute contraindication.

55 PERCUTANEOUS RADIOFREQUENCY ABLATION (PRA) VS. WATCHFUL WAITING (WW) FOR SMALL RENAL TUMOURS (<3 CM): FIRST RESULTS OF A PROSPECTIVE STUDY

Maurizio Brausi, Giuseppe De Luca, Mirko Gavioli, Giorgio Verrini, Gianluca Simonini, Alberto Romano, Giancarlo Peracchia, Massimo Viola and Giovanni Luca Giliberto

Department of Urology, AUSL Modena, Italy

Aim: PRA and WW are 2 possible options for selected pts with small renal masses. The objective of this study was to evaluate and compare the results of PRA and WW on renal tumours (<3 cm) in terms of tumour progression diagnosed and controlled at CT during the same period of time.

Patients and Methods: From May 2004 to July 2006, 30 pts with renal masses <3 cm diagnosed by ultrasound (US) and CT were recruited, after signed informed consent, in this prospective, not randomised study. Overall, 15/30 pts were followed up (WW) (Group A) and 15/30 pts received PRA of the tumours (Group B). After diagnosis, pts were offered the standard treatment of the centre: open surgery. When this was not possible or refused, PRA and WW were proposed. In Group A, 7/15 pts were ASA IV (4>83 years), 8/15 refused any treatment. In Group B, 12/15 were ASA IV (6>83 years) and 3/15 refused surgery. The mean age in Group A was 66.25 vs. 68.2 years in Group B. The mean tumour diameter was 2.0 cm in Group A and 2.5 cm in Group B. PRA was performed using a 9 tines needle under US control in local anesthesia (lidocaine along the needle tract) in the OR. The duration of the treatment was 18-20 minutes. Pts in both groups were followed up with CT every 3-4 months for the first year and every 6 months thereafter.

Results: The mean follow-up was 14.9 (range: 3-29) months. In Group A, 3 pts. were lost to follow-up vs. 0 in Group B. In Group A, 10/12 pts had stable disease (SD) at CT (86.4%). In 2/12 pts, the diameter of the lesion increased from 2 to 4 cm and from 1.5 to 2 cm, in 6 and 3 months respectively. Progression rate was 16.7%. In Group B, 15/15 pts (100%) had SD at CT (no enhancement). Side-effects: 1/14 pts had nausea and lumbar pain after PRA, which were controlled by medical therapy.

Conclusion: PRA was a safe and reliable procedure in patients with small renal masses. SD was observed in 100% of pts. WW policy for these patients was less reliable. A total of 17% of pts had progression in tumour diameter in 3-6 months and needed surgery.

56 RADICAL CYSTECTOMY (RC) FOR INVASIVE BLADDER CANCER IN PATIENTS OCTOGENARIANS: LONG-TERM FOLLOW-UP

Maurizio Brausi, Mirko Gavioli, Giorgio Verrini, Gianluca Simonini, Alberto Romano, Giancarlo Peracchia, Giuseppe De Luca, Massimo Viola and Giovanni Luca Giliberto

Department of Urology, AUSL Modena, Italy

Aim: The objectives of the study were to evaluate morbidity, overall survival (OS) and disease-specific survival (DSS) after radical cystectomy (RC) in octogenarians in the long term.

Patients and Methods: From 2000 to 2007, 420 pts with infiltrative or recurrent high grade T1 TCC of the bladder received RC and urinary diversion at a single institution: 105/420 patients (25%) were 80 years old or older. The mean age was 83.2 years and 73 men and 32 women were included. A total of 88/105 (83.9%) pts had one or more comorbidities. ASA score was used for classifying preoperative risk: 21/105 (20%) were ASA 2, 55/105 (52.4%) ASA 3 and 29/105 (27.6%) ASA 4. Overall, 40/105 pts (38%) received RC+lymphadenectomy through a peritoneal approach, while 65/105 pts (62%) had an extraperitoneal RC. A total of 53/105 (50.5%) had ureterocutaneostomy (UCS) as a diversion, while 38/105 (36.2%) had Bricker, 14/105 pts (13.3%) had an orthotopic neobladder. Pathological stage was: Tis+T1 in 11/105 pts (10.4); T2b in 15/105 (14.3%); T3a in 24/105 (22.8%); T3b in 37/105 (35.2%); T4 in 18/105 (17.1%); 23/105 patients (21.9%) were N+ (pT3-T4). A total of 81/105 patients (77.2%) were in the intensive care unit for 1-6 days. Overall, 51/105 patients (48.6%) were transfused; the average number of blood units received was 3.5 U.

Results: The mean follow-up was 46.5 (24-96) months. Perioperative mortality was 8.5% (9/105). Mean hospital stay was 14.5 (7-35) days. The complication rate (medical and surgical) was 36%; 8.3% of patients required a second
operation. Medical and surgical complications by ASA were: ASA2=11.8%, ASA 3=(50%) and ASA4=38% respectively. The medical complication rate by surgical approach was: extraperitoneal 40.4%, peritoneal 27%. The surgical complication rate was: 12.8% with the extraperitoneal route, 29.7% with the peritoneal approach. A total of 82 pts had regular long-term follow-up. After 1-, 2- and 3-year OS was 60%, 43.6% and 39.9%, respectively. DSS was 63.3% after 1-year, 51.2% after 2 years and 50% after 3 years.

**Conclusion:** The results of our study support the use of RC in octogenarians. Mortality and complications were acceptable. Major complications were correlated with high ASA score (3-4), urinary diversion (Bricker) and surgical approach (peritoneal route).

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**57 MINI-INVASIVE ANATOMICAL EXTRAPERITONEAL RADICAL CYSTECTOMY (RC): A SIMPLE, SAFE AND EFFECTIVE TECHNIQUE FOR PATIENTS WITH BLADDER CANCER (BC)**

**Maurizio Brausi, Mirko Gavioli, Giorgio Verrini, Gianluca Simonini, Alberto Romano and Giancarlo Peracchia**

Department of Urology, AUSL Modena, Italy

**Background and Aim:** RC is considered the standard treatment of muscle-invasive or high-grade, recurrent BCG refractory Ta-T1. Usually RC is performed with a long supra-umbilical incision, the peritoneum is entered and the abdominal viscera are exposed for many hours, with great fluid loss from the patient. In addition, positioning a neobladder or an ileal conduit inside the peritoneum may increase the risk of life-threatening complications (peritonitis) as in the case of urinary leakage. The objectives of this study were to evaluate and compare the immediate surgical results of a minimvasive, anatomical, extraperitoneal RC in terms of operating time, complication rate, blood loss, local recurrence and continence (for orthotopic neobladder) vs standard RC.

**Patients and Methods:** From 2000 and 2005 303 RCs were performed at our Institution (Group A). They were: orthotopic neobladder 116/303 (38.2%), Bricker=80/303 (26.4%), ureterocutaneostomy (UCS)=86/303, prostate and gynecological-sparing RCs=21/303 (6.9%). A total of 84/303 RCs were performed in the elderly (>80 years) (27.7%). In January 2006, we changed our technique. In 2 years (2006-2007), 90 mini-invasive, anatomical RCs were performed through an extraperitoneal route (Group B): orthotopic neobladder=60/90 (66.6%), Bricker=10/90 (11%), UCS=12/90 (13%), prostate and gynecological-sparing RCs=8/90 (8.8%). Surgical technique: 1. Small sub-umbilical skin incision (7-8 cm). 2. Retzius space penetration. 3. Bilary extended LAD (obturator, internal external, common iliac and presacral nodes). 4. Early ligation of obliterated umbilical artery, meticulous dissection and ligation of the superior and inferior bladder pedicles. 5. Santorini plexus ligation. 6. Retrograde cystectomy leaving the peritoneum intact. 7. Intra-operative frozen sections of nodes, urethral and ureteral stumps and definitive lateral bladder margins. 8. Small peritoneal incision and selection of the ileum, 20 cm from the ileal cecal valve. 9. Whale-tail shaped neobladder (2 chimneys) in case of orthotopic neobladder.

**Results:** Mortality: Group A=1% vs. 0 in Group B. Mean blood loss: 780 cc vs. 423 cc. Mean operating time: 280’ vs. 272’. Mean hospital stay: 17 vs. 16 days. Re-operation rate: 5/303(1.6%) in Group A: 3 pts for urinary leakage, 2 for bowel occlusion vs. 0/90 in Group B. Local recurrence (mean follow-up 30.2 months): 4.3% vs. 2%. In pts receiving orthotopic neobladder: daily continence rate was 96% vs. 95%, and nightly continence rate was 48% vs. 44%.

**Conclusion:** Mini-invasive, anatomical retrograde RC performed through the extraperitoneal approach is simple, safe and very well accepted by patients. A significant reduction in blood loss vs. the standard technique was observed. The complication rate (re-operation) was zero. Local recurrence was significantly reduced compared to the standard technique. Elderly patients are ideal candidates.

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**59 PRIMARY CORD LEIOMYOSARCOMA: A CASE REPORT AND A REVIEW OF THE LITERATURE**

**Tarcisio Paniccia1, Aldo Bove2, Giuseppe Bongarzoni2, Enrico Maria Casilesi2, Paolo Pompa3, Donato Dente4 and Luciano Corbellini2**

1 Dipartimento di Urologia and 2 Dipartimento di Chirurgia, Università G. D’Annunzio, Chieti, Italy; 3 Dipartimento di Urologia, Ospedale SS. Annunziata, Chieti, Italy; 4 Dipatimento di Urologia, Policlinico U. Primo, Roma, Italy

**Case Report:** A 78-year-old patient was referred to our hospital for a nonpainful groin mass. During his hospitalization, the following tests were carried out: routine blood test, tumoural markers (all negative) and groin ultrasound scan. The patient underwent a left orchiectomy. The histology revealed epithelioid leiomyiosarcoma of the spermatic cord. After the surgery, total-body CT with contrast revealed the presence of multiple bilateral lung metastases. Leiomyiosarcoma is a rare tumour for which the surgical therapy is still the gold standard; if the procedure has been radical, good disease-free follow-up is possible, otherwise even if for palliative therapy only, in the
The non-steroidal anti-androgen bicalutamide

**Background:**

Benzi 10, 16132 Genova, Italy

Biologia e Genetica, Università di Genova, Largo Rosanna per la Ricerca sul Cancro e Dipartimento di Oncologia,

expressed by this cell line are common to PCa.

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and TAM, we investigated if NM proteins are modulated by the combination effect of BIC and/or TAM on LNCaP cells. This cell line is a good model to study the role of NM proteins in the prostate carcinogenesis process because more than 70% of the proteins their expression was correlated with the level of tumour hormone. NM proteins specific for PCa were found; in some cases their expression was correlated with the level of tumour differentiation and with the risk of biochemical progression (2). We have identified one of these proteins as heterogeneous ribonucleoprotein K (hnRNP K) (3). In order to clarify the basic molecular mechanisms of the combination effect of BIC and TAM, we investigated if NM proteins are modulated by BIC and/or TAM on LNCaP cells. This cell line is a good model to study the role of NM proteins in the prostate carcinogenesis process because more than 70% of the proteins expressed by this cell line are common to PCas.

**Results:**

Proteomic study revealed that exist a similarity in the changes of the NM proteins elicited by drugs alone but that their combination does not result in a simple additive effect. HnRNP K was remarkably down-regulated after treatment for 72 h both with 10 μM BIC and with 10 nM TAM, whereas the co-administration of two drugs did not affect the protein expression. When the localization of the hnRNP K and the androgen receptor (AR) in the different cellular compartment was invesigated, more interesting results arose. Both proteins were found predominantly in the nucleus, with a small amount present in the cytoplasm After BIC treatment, hnRNP K underwent a significant decrease within the NM, concomitant with a lowering of AR in the nucleus. Analogous but less intense effects were observed after TAM treatment. When the cells were simultaneously exposed to two drugs, a significant increase in the nuclear level of both hnRNP K and AR occurred. Images obtained by confocal microscopy were in complete agreement with the Western blot results.

**Conclusion:**

These findings demonstrate that, at least in vitro, BIC and TAM interfere with AR modulation. In our opinion, the combined used of these drugs in the clinical setting calls for further investigations. Moreover, these results confirm a key role of the hnRNP K in prostate carcinogenesis.

**References**


**Materials and Methods:**

LNCaP cells were cultured in monolayer in the presence of 0.1 nM 5α-dihydrotestosterone and incubated either with BIC or 4-hydroxytamoxifen (TAM) or the combination of the two drugs. NM proteins were analyzed by two-dimensional gel electrophoresis. PDQuest image analysis software was used to generate a comparative NM proteoma analysis. Modulation and compartmentalization of AR and hnRNP K were studied by Western blot in whole cell lysate, cytoplasm, nucleus and NM. The nucleoplasm localization of the two proteins was also evaluated by confocal laser scanning microscopy.

**Results:**

Preliminary studies showed a significant reduction of the troublesome effects when tamoxifen (TAM) was concomitantly administered with BIC. However, the results reported in the literature seem to be preliminary and possible interferences between BIC and TAM could be present; some concern about the use of antioestrogens in PCa still exist. It is known that one of the modulators of hormone action is the nuclear matrix (NM): the subnuclear structure that plays a pivotal role in the spatial and temporal coordination of gene activation events. In 1980, Barrack and Coffey (1) first demonstrated specific binding of oestrogens and androgens to the NM and reported that the interaction between steroid receptors and the NM correlate with the physiological response of tissue to steroid hormone. NM proteins specific for PCas were found; in some cases their expression was correlated with the level of tumour differentiation and with the risk of biochemical progression (2). We have identified one of these proteins as heterogeneous ribonucleoprotein K (hnRNP K) (3). In order to clarify the basic molecular mechanisms of the combination effect of BIC and TAM, we investigated if NM proteins are modulated by BIC and/or TAM on LNCaP cells. This cell line is a good model to study the role of NM proteins in the prostate carcinogenesis process because more than 70% of the proteins expressed by this cell line are common to PCAs.
Estimated the late genitourinary (GU) morbidity by measuring the changes from baseline (pre-radiotherapy) to month 28 in PPBC, voiding symptoms, IPSS-QoL, NIF (Qmax and PVR) and LENT/SOMA urinary function domain. The percentage of men with abnormal NIF at 12 and 28 months after radiotherapy was also quantified. GU morbidity resolution was defined as the return to within 20% of the pre-radiotherapy urinary symptoms.

**Patients and Methods:** Patients with intermediate risk factors according to D’Amico criteria were selected. All patients received 6 months of hormonal therapy (HT) with a LHRH agonist and a non-steroidal antiandrogen. All patients were treated by the same hypofractionated schedule to a total dose of 54.3 Gy in 15 fractions of 3.62 Gy delivered 3 times/week. Patients were assessed at baseline and weekly during radiotherapy. Subsequently, patients were assessed at 4 and 12 weeks after radiotherapy, and every 3 months thereafter. An alpha value threshold of 0.05 was used. Normally distributed variables were presented as means and confidence interval at 95% (95% CI) and was analysed by the one way-ANOVA test for repeated measures with Tukey HSD post hoc test. Continuous variables not normally distributed were presented as medians and 95% CI and was analysed by the Friedman test with Tukey HSD post hoc test. For matched pair-wise multiple comparisons, dichotomous variables were compared with Cochran’s Q test. For matched pair-wise comparisons the McNemar test was used.

**Results:** Subjective perception of storage symptoms: The PPBC changes at baseline and 12 and 28 months after radiotherapy showed no significant worsening following treatment. The mean value of PPBC was 2.67 (2.39 to 2.94) at baseline, 2.95 (2.72 to 3.18) at 12 months and 2.86 (2.66 to 3.05) at 28 months (p=0.077).

Subjective perception of voiding symptoms: The assessment of voiding symptoms showed that there was no significant difference in the perception of incomplete emptying [baseline: 1.74 (1.52 to 1.96); month 12: 1.95 (1.76 to 2.15); month 28: 1.93 (1.78 to 2.07); p=0.208], intermittency [baseline: 1.81 (1.60 to 2.03); month 12: 2.05 (1.88 to 2.21); month 28: 1.95 (1.73 to 2.17); p=0.245], weak urinary stream [baseline: 2.43 (2.14 to 2.71); month 12: 2.71 (2.52 to 2.91); month 28: 2.64 (2.41 to 2.88); p=0.219] and hesitancy [baseline: 2.62 (2.38 to 2.86); month 12: 2.79 (2.60 to 2.97); month 28: 2.69 (2.50 to 2.87); p=0.513].

LENT/SOMA urinary function: The median urinary function score for the entire study group was 0.42 (0.23 to 0.31) at baseline, with a significant worsening at 12 months [0.54 (0.35 to 0.44) (p<0.0001)] and subsequent improvement at 28 months [0.45 (0.25 to 0.36) (p=0.094)].

Objective measures of voiding difficulties: The assessment of Qmax showed no significant worsening with respect to baseline [13.7 ml/s (12.9 to 14.5)] was observed at 12 [13.3 ml/s (12.6 to 14.0)] and 28 [13.8 ml/s (13.0 to 14.5)] months (p=0.687). For PVR, a transient increase at 12 months [90.1 ml (72.1 to 108.1)] with respect to baseline [60.8 ml (49.5 to 72.1)] was observed (p=0.021) with subsequent decrease at 28 months [84.0 ml (67.7 to 100.4)] (p=0.086). No significant increase in the percentage of men with pathological NIF at 12 (78.4%) (p=0.063) and 28 months (62.7%) (p=0.50) was observed.

IPSS quality-of-life: The score of IPSS-QoL remained unchanged after radiotherapy. At baseline, the mean score was 3.36 (3.09 to 3.62), whereas at 12 and 28 months following radiotherapy, the mean score was 3.55 (3.34 to 3.76) and 3.50 (3.25 to 3.75) (p=0.103).

**Conclusion:** Our study seems to suggest that a hypofractionated radiotherapy schedule for the treatment of prostate cancer is safe in terms of late urinary morbidity. Further study will be required to confirm our results.

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**AZACITIDINE TREATMENT SENSITIZES AGAINST BICALUTAMIDE AND RADIOTHERAPY IN ANDROGEN INDEPENDENT PROSTATE CANCER CELLS**

**Giovanni Luca Gravina**<sup>1,2</sup>, Claudio Festuccia<sup>2</sup>, Stefania Di Sante<sup>3</sup>, Francesco Marampon<sup>1,2</sup>, Amato Fratticci<sup>1</sup>, Eleonora Carosa<sup>3</sup>, Alessandra Castrì<sup>3</sup>, Luca Ventura<sup>4</sup>, Emmanuele A. Jannini<sup>4</sup> and Vincenzo Tombolini<sup>1</sup>

**Department of Experimental Medicine, Division of Radiotherapy and**<sup>2</sup>**Radiobiology, and**<sup>3</sup>**Department of Experimental Medicine, Course of Endocrinology and Medical Sexology, University of L’Aquila, Italy;**

**Division of Anatomo-Pathology, San Salvatore Hospital, L’Aquila, Italy**

**Background:** The terminal stages of metastatic prostate cancer are characterized by androgen independence, which represents a significant therapeutic problem. Hyper-methylation of the androgen receptor (AR) promoter down-regulates AR expression and is thought to be one mechanism for development of hormone-refractory prostate cancer (HRPC). Here, we investigated the effect of Aza-CR...
FIBROMYXOID SARCOMA OF THE KIDNEY

Matteo Arancio, Stefania Ranzoni, Nicola Maffei, Alessandro Delsignore, Giuseppe Landi, Maurizio Marcato, Alessandro Mina and Carlo Martinengo

S.C. Urologia, ASL “NO”, Presidi Ospedalieri di Borgomanero e Arona, Italy

Background: Low-grade fibromyxoid sarcoma, defined by Evans in 1987, is a rare soft tissue tumour characterized by apparently benign histological features and an indolent and malignant progression, with late local relapses and distant metastases. It affects young adults, with a slight preference for males. The most common locations are the thigh, the inguinal region, and the shoulder. A kidney location is exceptional. The treatment of choice is surgery.

Case Report: An 83-year-old woman presented with right flank pain, asthenia, and weight loss. She had no haematuria or urinary symptoms. The physical examination revealed a large right-sided abdominal mass. Laboratory tests (complete blood count, blood and urine biochemistry, and coagulation) were within normal ranges. Thoracoabdominal computerized tomography (CT) showed a large mass on the right kidney measuring 14 cm in its maximum diameter that compressed and displaced abdominal structures, including the right renal vein and the vena cava, which were permeable. Thrombosis of bilateral femoral veins was also found. The other examinations were normal. A right radical nephrectomy with exeresis of the renal mass was performed.

Conclusion: Low-grade fibromyxoid sarcoma has a slow progression, but is often intractable due to its metastasizing potential and the eventual development of local relapses. Despite this, cases have been described with a survival of 50 years after initial diagnosis. According to the literature, the first-choice treatment is surgery, which can change the natural progression of the disease; the role of chemotherapy and radiation therapy is uncertain. The surgical margins are the most important independent factor in local control. Re-intervention is justified in order to obtain disease-free surgical margins. In cases of low-grade STS with adequate surgical resection margins, complementary treatments are not indicated.
Background: It is impossible to identify patients who will require prostatic repeat biopsies (false negative at initial biopsy), while not exposing the low-risk population (probable true negative at initial biopsy) to additional invasive procedures. Some studies show that the prostate cancer antigen 3 (PCA3) assay may aid in deciding which patients need a repeat biopsy. PCA3 encodes a prostate-specific mRNA that serves as the target for a novel urinary molecular assay for prostate cancer detection. An increasing PCA3 score corresponds with an increasing probability of a positive repeat biopsy. In these studies, the PCA3 score had greater diagnostic accuracy than PSA or %fPSA for predicting repeat prostate biopsy outcome, even at a sensitivity of 80-90%. The objective of the study was to evaluate the ability of PCA3, added to measurements of PSA, to predict cancer detection after a first negative biopsy.

Patients and Methods: Men with more than one previous negative prostate biopsy scheduled for repeat biopsy were enrolled in ten Regione Piemonte clinical centres. Prospectively, data of 241 patients were analysed; the patients were enrolled between 06-10-2008 and 31-03-2009. PSA and %fPSA were assessed simultaneously for each participating patient. First-catch urine samples were collected following an extended DRE (three strokes per lobe). The urine sample was processed and tested to quantify PCA3 and PSA mRNA concentrations using the PROGENSA PCA3 assay. The PCA3 score was calculated as PCA3 mRNA/PSA mRNA × 1000. At least 10 standardized peripheral zone biopsy cores were taken by experienced physicians. The specimens were evaluated by experienced pathologist for each centre. Patient characteristics were tested using the Fisher’s exact test for qualitative variables and the Mann-Whitney test for quantitative ones. Bivariate correlations were used to describe the degree of linear relationship between continuous variables, such as PSA, %fPSA and PCA3 score values. The status at final biopsy was used as a dependent variable in different univariate and multivariate binary logistic regression models, testing age, PSA and %fPSA 1-Bx, PSA and %fPSA 2-Bx, PSA and %fPSA 3-Bx, PCA3 score, digital rectal exam (suspicious vs. unsuspicious) and prostate cancer familiarity (any vs. none) as predictors of positive final biopsy. All reported p-values are two-sided at the conventional 5% significance level. Data were analysed as of September 2009 by SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

Results: Among 241 patients, a total of 227 urine samples (94.1%) had adequate concentrations of PCA3 and PSA mRNA to elaborate the PCA3 score. The positive repeat biopsy rate was 30.8% (70/227). The 70 patients with a positive biopsy did not have total PSA values statistically significant higher than those with a negative biopsy. Patients with a cancer-positive biopsy had clinical stage T1c, T2 and T3, in 71%, 15% and 9% of cases respectively. Using PCA3 score of 35 as a cut-off value, the test had 70.3% sensitivity for the detection of PCa, 81.6% specificity and a negative predictive value of 86.3%. The only statistical significant risk factor was PCA3 (Table I).

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR</th>
<th>95% CI</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA ratio (median-range)</td>
<td>0.94</td>
<td>0.88-1.01</td>
<td>0.058</td>
</tr>
<tr>
<td>PCA3 PSA score (median-range)</td>
<td>1.05</td>
<td>1.03-1.08</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Dependent variable: positive final biopsy

Conclusion: In our experience the only statistical significant risk factor was PCA3, the diagnostic role of %fPSA being borderline. We confirm that the use of PCA3 in a clinical setting, after one ore more negative biopsy, may help to stratify patients according to their risk for biopsy and cancer detection, although a large-scale validation study will be needed to address assay standardization, optimal cutoff values, and appropriate patient populations.

References
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PCA3 SCORE AND PROSTATE CANCER: IS 35 REALLY THE BEST CUT-OFF?


Background: New biomarkers are required in order to avoid unnecessary prostatic biopsies. The PCA3 gene product is specifically overexpressed in prostate tumour cells, and modern molecular biology techniques allow us to use a specific test for this gene in order to select patients who have a high risk of having prostate cancer. The test has a specificity of over 80%, while the specificity of PSA testing is 25%. The PSA test is not at all selective for aggressive cancer, while the tumours PCA3 detects are aggressive in 85% of cases. The cut-off suggested by PROGENSA PCA3 assay is 35. The objective of this study was to verify if this score is the best cut-off value for the exam in patients with more than one previous negative prostate biopsy scheduled for repeat biopsy.

Patients and Methods: Prospectively, data of 227 patients with one or more previous negative prostate biopsies scheduled for repeat biopsy in ten Regione Piemonte clinical centres between 06-10-2008 and 31-03-2009, were analyzed. The urine sample following an extended DRE was processed and tested to quantify PCA3 and PSA mRNA concentrations using the PROGENSA PCA3 assay. The PCA3 score was calculated as PCA3 mRNA/PSA mRNA × 1000. The cut-off point for PCA3 score (ideal for accuracy, sensitivity and specificity) was identified by a receiver operating characteristic (ROC) analysis. The chosen cut-off of 40 and another three cut-off values (35, 50 and 70) were used to determine the association between PCA3 score and prostate cancer. Patient characteristics were tested using the Fisher’s exact test for qualitative variables and the Mann-Whitney test for quantitative ones. The status at final biopsy was used as a dependent variable in different univariate and multivariate binary logistic regression models. All reported p-values are two-sided at the conventional 5% significance level.

Results: Overall, 70 of 227 repeat biopsies (30.8%) were positive for cancer. The performance characteristics at different PCA3 score cut-off points are shown in Table I:

<table>
<thead>
<tr>
<th>PCA3 score</th>
<th>Negative re-biopsy</th>
<th>Positive re-biopsy</th>
<th>p-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 35</td>
<td>122 (87.1%)</td>
<td>18 (12.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 35</td>
<td>35 (40.2%)</td>
<td>52 (59.8%)</td>
<td></td>
</tr>
<tr>
<td>≤ 40</td>
<td>136 (88.3%)</td>
<td>18 (11.7%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 40</td>
<td>21 (28.8%)</td>
<td>52 (71.2%)</td>
<td></td>
</tr>
<tr>
<td>≤ 50</td>
<td>148 (86.0%)</td>
<td>24 (14.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>9 (16.4%)</td>
<td>46 (83.6%)</td>
<td></td>
</tr>
<tr>
<td>≤ 70</td>
<td>151 (80.7%)</td>
<td>36 (19.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt; 70</td>
<td>6 (15.0%)</td>
<td>34 (85.0%)</td>
<td></td>
</tr>
</tbody>
</table>

*Fisher’s exact test.

Using a PCA3 score of 40 as a cut-off value, the test had 74.3% sensitivity for the detection of PCa, 86.6% specificity and a negative predictive value of 88.3%.

Conclusion: PCA3 urine tests improve the specificity in prostate cancer diagnosis and have thus the potential to reduce the number of unnecessary prostate biopsies and to predict repeat biopsy outcomes. Recently, it was demonstrated that the highest increment in predictive accuracy resulted from a PCA3 assay cut-off threshold of 17, where a 5% gain in PA (from 0.68 to 0.73, p=0.04) was recorded. On the contrary, in our experience, a PCA3 score cut-off of 40 provided the optimal balance between sensitivity and specificity, with a negative predictive value of 88.3%. A large-scale validation study will be needed to address optimal cut-off values.

References
IS PCA3 ASSAY ALSO OVEREXPRESSED IN HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA AND ATYPICAL SMALL ACINAR PROLIFERATION? THE PIEMONTE EXPERIENCE OF 227 CASES


Background: High-grade prostatic intraepithelial neoplasia (HG-PIN) and atypical small acinar proliferation (ASAP) in the setting of prostatic needle biopsies are considered premalignant although questions still remain. Several studies observed higher rates of cancer for the ASAP. Urine PCA3/PSA mRNA ratio score is known to be useful for determining the risk of prostate cancer in patients undergoing repeat prostate biopsy. The objective of the current study was to evaluate the ability of PCA3 to predict HG-PIN and ASAP detection after a first negative biopsy.

Patients and Methods: Prospectively, data of 227 patients, scheduled for repeat biopsy in ten Regione Piemonte clinical centres between 06-10-2008 and 31-03-2009, were analysed. Men with HG-PIN (55/227, 24.2%) or ASAP (45/227, 19.8%) at prior biopsy were included in the study. Patient characteristics by repeat biopsy are reported in Table I:

<table>
<thead>
<tr>
<th>HG-PIN</th>
<th>Negative</th>
<th>Positive</th>
<th>p-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA</td>
<td>7.49 ng/ml (median-range) (1.32-26.00)</td>
<td>7.20 ng/ml (1.59-23.00)</td>
<td>0.728</td>
</tr>
<tr>
<td>%PSA</td>
<td>15.00 (median-range) (0.13-42.00)</td>
<td>19.00 (0.16-87.00)</td>
<td>0.003</td>
</tr>
<tr>
<td>PCA3 score</td>
<td>26.00 (median-range) (1.00-254.00)</td>
<td>31.00 (3.00-220.00)</td>
<td>0.560</td>
</tr>
<tr>
<td>ASAP</td>
<td>7.56 ng/ml (median-range) (1.32-26.00)</td>
<td>6.56 ng/ml (2.00-17.00)</td>
<td>0.037</td>
</tr>
<tr>
<td>%PSA</td>
<td>16.00 (median-range) (0.13-38.35)</td>
<td>15.00 (0.50-87.00)</td>
<td>0.466</td>
</tr>
<tr>
<td>PCA3 score</td>
<td>25.00 (median-range) (1.00-254.00)</td>
<td>33.00 (8.00-221.00)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Patient characteristics were tested using the Fisher’s exact test for qualitative variables and the Mann-Whitney test for quantitative ones. All reported p-values are two-sided at the conventional 5% significance level.

Results: Total PSA, %PSA and PCA3 values were compared in HG-PIN- or ASAP-positive patients at repeat biopsy versus negative ones (Tables II and III).

Conclusions: The detection of HGPIN in a prostate biopsy is actually controversial in terms of deciding if repeat biopsy should be done. A recent study suggested that multifocal HGPIN is highly associated with prostate cancer, whereas unifocal HGPIN does not differ from the normal population. On the contrary the finding of ASAP is an indication for re-biopsy because of the higher rates of cancer. Recents studies demonstrated that PCA3 score was higher in men with HGPIN than in those without. In our experience we did not observe any significant correlation between PCA3 score and the presence of multi- or unifocal HGPIN. In contrast, we observed that the median PCA3 score was higher in men with ASAP (p=0.011): 33 (range 1-254) versus 25 (8-221).
References

67 TUMOUR ENUCLEATION FOR RENAL CELL CARCINOMA: DETAILED ANALYSIS OF COMPLICATIONS AT A SINGLE CENTRE PROSPECTIVE STUDY

Gianni Vittori, Andrea Minervini, Alberto Lapini, Saverio Giancane, Agostino Tuccio, Giampaolo Siena, Sergio Serni and Marco Carini

Department of Urology, University of Study of Florence, Florence, Italy

Aim: The technique of tumour enucleation (TE) showed excellent oncological results, and cancer-specific and disease-free survival similar to those reported after standard partial nephrectomy. The aim of the present study was to assess the incidence of intra- and postoperative complications of TE.

Patients and Methods: In July 2006, a prospective database was created to evaluate the efficacy and safety of TE. From July 2006 to February 2009, 167 patients with a mean age of 63 (range 14-85) years underwent TE for renal cell carcinoma (RCC), by blunt dissection using the natural cleavage plane between the pseudocapsule and the normal parenchyma. Haemostasis was achieved with the apposition of running sutures on the surgical bed, hemostatic agents and horizontal interrupted sutures. All the intra- and postoperative complications were registered and stratified for severity according to the 5-level scale NCI-CTC v2.0 (National Cancer Institute Common Toxicity Criteria versione 2.0; available at http://ctep.cancer.gov/guidelines/). Other variables assessed were BMI, clinical diameter, warm ischemia time, operative time, conventional pathologic prognostic factors, intra- and postoperative blood loss, and time to discharge.

Results: Mean (range) BMI was 25.6 (19.1-37.6). The mean clinical diameter (range) of the tumour was 3.3 (1-10) cm. Mean operative time (median, range) was 109 (110; 65-195) minutes. In 154 cases (92%), the TE was performed during warm ischaemia, while in 13 patients (8%), no vascular clamp was used. Mean ischemia time (median, range) was 16.1 (15, 5-31) minutes. Pathological tumour diameter was (range) 3.1 (0.5-12.5) cm. The histotype analysis showed clear cell carcinoma in 76.7% of cases, papillary in 16.3%, and chromophobe in 7%. Benign tumour was diagnosed in 14% of cases. Pathological TNM stage was pT1a in 111 cases (77.1%), pT1b in 24 (16.6%), pT2 in 4 (2.8%), pT3a in 4 (2.8%) and pT3b in 1 (0.7%). Intraoperative blood loss (median, range) was 175 (120; 25-650) cc. The mean (median, range) reduction of Hb (Δ) (preoperative vs III postoperative) was 2.5 (2.4; 0.3-5.7) g/dl. Intra- and postoperative complications occurred in 3.6% and 16.2% of patients, respectively. In accordance with the NCI-CTC v2.0 system, the severity of postoperative complications was grade I in 29.6% of cases, grade II in 55.5% and grade III in 14.8% (Table I). Complications of severity grade IV and V, such as chronic functional deprivation or exitus never occurred. Mean (mean, range) length of hospital stay was 6 (4-24) days.

Conclusion: Our study demonstrates that TE is a safe technique, with a low rate of bleeding and a very low incidence of major complications (grade III) with need for reoperation.

Table I. Incidence of surgical complications stratified for severity according to the NCI-CTC v2.0 system.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Events</th>
<th>Patients</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>8</td>
<td>4.8%</td>
<td>29.6%</td>
</tr>
<tr>
<td>II</td>
<td>15</td>
<td>9%</td>
<td>55.5%</td>
</tr>
<tr>
<td>III</td>
<td>4</td>
<td>2.4%</td>
<td>14.8%</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>V</td>
<td>0</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>16.2%</td>
<td>100%</td>
</tr>
</tbody>
</table>

68 POSTOPERATIVE COMPLICATIONS OF TUMOUR ENUCLEATION FOR RENAL CELL CARCINOMA: RISK FACTORS ANALYSIS OF A SINGLE-CENTRE PROSPECTIVE STUDY

Gianni Vittori, Andrea Minervini, Alberto Lapini, Agostino Tuccio, Giampaolo Siena, Saverio Giancane, Sergio Serni and Marco Carini

Department of Urology, University of Study of Florence, Italy

Aim: The tumour enucleation (TE) technique showed excellent oncological results, similar to those after standard
partial nephrectomy. The aim of the present study was to analyse the potential contribution of several preoperative and intraoperative variables to the development of postoperative surgical complications, in a prospective and homogeneous cohort of patients who underwent NSS by TE.

Patients and Methods: In July 2006, a prospective database was created to evaluate the efficacy and safety of TE. From July 2006 to February 2009, 167 patients with a mean age of 63 (range 14-85) years underwent NSS by TE for renal cell carcinoma (RCC). All the postoperative complications were registered and included in the study. The variables considered were classified into two groups. Preoperative variables included age, gender, ECOG grade, BMI, ASA, surgical indication (imperative vs. elective), clinical diameter, blood count and serum creatinine. Intraoperative variables included operative time, warm ischemia time, hemostatic agents used in the surgical bed (floseal vs. tachosil), time to achieve haemostasis (as the time elapsed between haemostatic agent apposition and achievement of haemostasis) and intraoperative blood loss. Chi-square test and t-test were used for univariate analysis; multivariate analysis was used for significant variables at univariate analysis.

Results: Postoperative complications occurred in 16.2% of patients (27 cases). The most common event was postoperative bleeding which occurred in 18 patients (10.8%). Blood transfusions were the sole treatment in 16 cases, while super-selective embolization of renal artery branch was necessary in one case, and re-intervention in one. Prolonged leakage from the drainage occurred in 6 cases, with no need for JJ stent positioning. Medical cardiovascular and thromboembolic complications were reported in 9 patients (5.4%). ECOG performance status ≥2 (p=0.07), clinical tumour diameter (p=0.055), preoperative haematocrit (p=0.027), and intraoperative blood loss (p=0.0001) were significantly associated with the risk of postoperative complications. At the multivariate analysis of the preoperative variables, only clinical tumour diameter was confirmed as an independent risk factor for postoperative complications development.

Conclusion: Our study demonstrates that TE is a safe technique which can guarantee a low incidence of postoperative complications. Clinical tumour diameter is an independent risk factor for the development of surgical complications. Among intraoperative variables, only blood loss was a significant risk factor at the univariate analysis.

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TC-GUIDED PERCUTANEOUS RADIOFREQUENCY ABLATION OF RENAL CELL CARCINOMA, A GOOD THERAPEUTIC CHOICE

Donato Dente1, Paolo Pompa2, Dino Petrone2, Renzo Rossetti2, Concezio Tucci2, Giuseppe Gaspari2 and Tarcisio Paniccia3

1Dipartimento di Urologia, Polic. U. Primo, Università Sapienza, Roma, Italy; 2Dipartimento di Urologia, Ospedale SS. Annunziata, Chieti, Italy; 3Dipartimento di Urologia, Università G. D'Annunzio, Chieti, Italy

Background: Radical nephrectomy and nephron-sparing surgery are the gold standard in treatment of renal cancer; however, radiofrequency ablation is attractive as a minimally invasive treatment option in select patients. The aim of our study is to report our experience in use of radiofrequency ablation of renal cell carcinoma.

Patients and Methods: Between 2007 and August 2009, 32 lesions (25 exophytic, 7 intraparenchymal and one central) in 28 pts (mean age 75 years) were treated with TC-guided percutaneous radiofrequency ablation. Four pts had 2 lesions; 3 pts had only one kidney due to progressed nephrectomy because of RCC, and 4 also had oncological comorbidity; the remaining patients refused the surgical option. The average size of the mass was 3.8 cm. All the lesions were diagnosed first by ultrasound and then with CT. Successful ablation was regarded as any lesion showing less than 10 H of contrast enhancement on CT.

Results: The technical success of the procedure was obtained in all cases. No postoperative complication occurred in any patient. After one month of follow-up, the TC control showed no enhancement in 26/28 patients and in 2/28 the ablation was incomplete. For this reason the 4 patients underwent a second treatment.

Conclusion: These results with RFA of RCC are encouraging for the future. This kind of treatment can be useful for patients who for many reasons are not able to undergo a surgical procedure. This procedure is also not associated with perioperative side-effects. However, further follow-up is necessary to evaluate the long-term efficacy of this technique.

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TRANSPERITONEAL RESECTION OF MUCINOUS ADENOCARCINOMA OF THE URACHUS USING ULTRACISION

Mario Falsaperla, Marco Puglisi, Gianluca Salerno, Alberto Saita, Giuseppe Morgia and Mario Motta

Azienda Ospedaliero-Universitaria, Policlinico-Vittorio Emanuele, via S. Sofia 78, 95123 Catania, Italy

We treated a rare case of urachal neoplasm communicating with the dome of the bladder, documented by TC and, anatomopathologically, a mucinous adenocarcinoma, in a patient who has tank of penis prosthesis located in the Retzius space. After cystoscopy, documenting the communication point with the
dome of the bladder, we started laparoscopic transperitoneal surgery. We inserted the optical trocar using the open technique under the xiphoid, about 15 cm above the umbilicus, then we placed three operative trocars in direct view, of 5, 12 and 15 mm. Once the neoplasm was encountered, we removed the omentum from the lower part using a hand-controlled ultracision and bipolar system. This showed the large volume of the neoplasm, that we separated in the upper side from the adjacent tissues and from the fascia through a harmonic system. We proceeded cranio-caudally until the bladder limit was shown, paying attention to separating the neoplasm from adjacent tissues. Bladder was separated from its prepubic side where we evidenced the penis prosthesis that was not affected. In this phase, laterally, we have found the umbilical arteries bilaterally which they went isolated, clipped with HEM-O-LOK and cutted. We then separated the neoplasy from the bladder wall, both from the anterior and posterior side, evidencing the limits of the tumour. Laparoscopic manoeuvres were not easy because of the large volume of the tumour. We then used an EndoGia 60mm stapler with parenchymal clips of 4.8 mm using double recharge which allowed us to completely isolate the neoplasm, avoiding cutting the bladder or the neoplasm itself. Finally, we removed the tumour using a 15 mm endobag and we made accurate haemostasis. We controlled the seal of the bladder, filling it with 180 ml until it was certain that no fluid was leaking outside. A drain was finally placed in the pelvis. A postoperative evaluation of the neoplasm showed evidence of a perfect suture line, along the limit between the neoplasm and the healthy tissue.

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INFLAMMATORY MYOFIBROBLASTIC TUMOUR OF TESTICLE: A CASE REPORT AND REVIEW OF THE LITERATURE

Tommaso Brancato¹, Pietro Nupieri¹, Roberto D’Ascenzo¹, Gianni Paulis¹, Giuseppe Orsolini¹, Rosaria Alvaro³ and Luca Turrini²

¹Department of Urology, and ²Department of Pathology, Regina Apostolorum Hospital Rome, ³Tor Vergata University of Rome, Italy

Background: Inflammatory myofibroblastic tumour (IMT) is a distinctive lesion composed of myofibroblastic spindle cells with an inflammatory infiltrate of plasma cells, lymphocytes and eosinophils. This concept is relatively new, since this cell type was defined less than 30 years ago, and there is as yet no firm consensus as to how a myofibroblast should be defined either morphologically or phenotypically (1). The disease primarily involves visceral and soft tissue of children and young adults, and sometimes in adulthood, and has a female predominance and overall is frequent in the first two decades of life. The most common sites are the lung, mesentery and omentum, but also gastrointestinal tract, pancreas, skin, breast, bone, central nervous system and genitourinary tract. Testicular IMT is rarest and only three cases are reported in the literature (2). The aetiology of IMT is not well understood; it has been postulated that these lesions are the result of a reaction to trauma, surgery, infection or local irritation, although in many cases an underlying cause is never found.

Case Report: A 42-year-old healthy Caucasian male noticed a swelling and a palpable mass in the left scrotum, detected occasionally. The patient denied any history of fever, urethral discharge and previous history of urinary tract or sexually transmitted infections and tuberculosis. Physical examination revealed a indurate solid mass about 2 cm in the upper pole of the left testicle. Scrotal ultrasound demonstrated a solid heterogeneous mass, 1.5 cm, involving the upper pole of the left testicle with moderate peripheral vascular vessels. Haematological markers and CT abdominal scan excluded a seminoma or non-seminomatous testicular cancer. The patient underwent an open biopsy with a histology report of “mesenchimal neoplasm likely benign” on frozen sections, and successive orchietomy. The histological findings macro-scopically demonstrated a single 1.5 cm, well-delimited, yellow-white lesion of testicular tissue. The tumour had spindle fusiform cells, with vesiculuous nuclei between fibrocollagenous stroma, macrophage and lymphocyte infiltrations. Seminal ducts were displaced or surrounded and atrophic. Immuno-histochemically, fusiform cells were strongly positive for vimentin, weakly positive for CK-MNF116 and actin, and negative for CD34, inhibin-alpha subunit, desmin, calretinin and PLAP. Mitotic activity was low and typical. The diagnosis was of inflammatory myofibroblastic testicular tumour (Figure 1).

Conclusion: Limited data are available on the clinical outcomes of solitary visceral lesions such as that in the present case. Our patient, while sharing some of the morphological findings common to myofibromas, to our knowledge, and based on a Medline search, represents the fourth case of gonadal inflammatory myofibroblastic tumour ever reported (2, 3). Such a histological appearance can, however, mimic a wide variety of other tumours and tumour-like lesions, among which mesenchymal sarcoma, spindle cell carcinoma, follicular dendritic cell tumour, and inflammatory pseudotumour are the main differential diagnoses. The diagnosis of IMT is based on the histological features of spindle myoepithelial cell proliferation, lymphocytic and inflammatory infiltration, absence of atypical nuclei nor mitosis, Immunomarkers could substantiate the diagnosis of IMT. In our patient, the spindle cells stained positively for vimentin, had low positivity for CK-MNF116 and actin, but were negative for CD34, desmin, calretinin and PLAP. CK positivity and prominent inflammatory infiltrate help to differentiate IMT from myofibroma, of which only 8 cases are described in the literature to date. Surgical
excision is definitive to exclude malignant aetiology for scrotal masses. Our patient and most patients described in the literature had orchidectomy as a final treatment (4, 5). Radiological studies are unable to differentiate benign from malignant nature and definitive diagnosis is established on surgical exploration. Depending on the gross characteristics and frozen section of clinically distinct masses, either a local excision or radical orchidectomy is offered. Thus, even though the disease has benign nature and course, it is crucial to counsel patients for orchidectomy as definitive diagnosis is established on surgical exploration and definitive histological examination.

References
1 Classification of Tumours – Pathology and Genetics of Tumours of Soft Tissue and Bone. Fletcher CDM, KrisHnan UK and Merteens F. Lyon: World Health Organisation, 2002.

Figure 1. High power view of vimentin positivity of spindle cells mixed with abundant inflammatory cells (CD45+).

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LAPAROSCOPIC MANAGEMENT OF INTEARORTOCVAL TESTIS TUMOUR METASTASIS

Mario Falsaperla, Marco Puglisi, Gianluca Salerno, Alberto Saita, Giuseppe Morgia and Mario Motta

Azienda Ospedaliero-Universitaria, Policlinico-Vittorio Emanuele, via S. Sofia 78, 95123 Catania, Italy

Case Report: We treated a paracaval right lymph node metastasis of immature testicular teratoma in a patient who underwent adjuvant chemotherapy. The lesion, documented by TC and PET during the oncological follow-up was treated using a transperitoneal approach. The lesion, which was oval (3x3.5 cm), was carefully separated by the caval vein and the anterior side of aorta with high risk of parietal injury. We used cold forceps, bipolar and endo-peanut to find the correct cleavage plane and sunder the lesion. The tenacious adherences, due to the chemotherapy, made the surgery particularly complex, with high haemorrhagic risk. The anatormopathological evaluation confirmed the presence of a lymphonodal metastasis of immature testis teratoma, compatible with the primary testicular lesion.

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PROGNOSTIC VALUE OF KARYOTYPE ANALYSIS IN CLEAR CELL RENAL CARCINOMA: A STUDY OF 131 PATIENTS WITH LONG-TERM FOLLOW-UP

A. Antonelli1, N. Arrighi1, R. Tardanico2, P. Balzarini2, T. Zanotelli1, L. Perucchini1, A. Cozzoli1, D. Zani1, S. Cosciani Cunico 1 and C. Simeone 1

1Division of Urology and 2Department of Pathology, Spedali Civili Hospital, University of Brescia, Brescia, Italy

Aim: Analysis of karyotype in renal cell carcinoma has a diagnostic role, but most of the published studies failed to prove its prognostic value due to their small number of cases or short follow-up time. We evaluate our experience after a long-term follow-up.

Patients and Methods: Between 1997 and 2002 at our Departments, the tumoral karyotype of surgically treated patients for renal tumour was studied by a classic cytogenetic analysis. Specimens were evaluated only by an experienced uropathologist (RT) and genetist (PB). Clinical, surgical, cytogenetical and postoperative controls data were collected in a prospective fashion. For this study, cases with clear cell renal carcinoma were selected to analyse the possible relationship between karyotype abnormalities and disease-free survival, adjusting the results for tumour diameter, Fuhrman's grading, staging according to TNM 2002, microvascular embolization, tumoural necrosis and sarcomatous differentiation.

Results: A total of 131 cases were analysed (74 males, 57 females, average age 62.9 years, range 27-85 years) with an available and pathological (not 46 XX or XY) karyotype, followed-up for a mean time of 67 months (range 12-136 months). In fact, 22 patients (16.8%) died from their disease and 10 (7.6%) are alive with progression. The chromosomes most frequently altered were 3 (75.6% of the cases), Y (40.6% of males), 7 (29.8%), 14 (25.2 %), 6 (22.1%) and 20 (20.6%).
We found a statistically significant relationship between disease-free survival and the loss of chromosome 19 (log-rank test \(p=0.0002\)), chromosome 20 (\(p=0.0063\)), and chromosome 22 (\(p=0.0067\)), independently of all the other pathological factors analysed for the loss of 22 at multivariate analysis.

**Conclusion:** The pattern of alterations of the karyotype of clear cell renal carcinoma is typical, and mainly regards chromosome 3. Our analysis shows a prognostic role for the loss of chromosome 19, 20 and, moreover, of 22. Even if these results must be considered as preliminary, it should be noted that three genes involved in the progression of CRCC are found on these chromosomes: r AGPTL4, FKBP12 and PDGFB, and this evidence may provide a biological basis for our findings.

**74 CLINICAL FEATURES AND PROGNOSIS OF PATIENTS WITH RENAL CANCER AND A SECOND MALIGNANCY**

Alessandro Antonelli, Nicola Arrighi, Danilo Zani, Laura Perucchini, Alberto Cozzoli, Tiziano Zanotelli, Sergio Coscianni Cunico and Claudio Simeone

Chair of Urology, University of Brescia, Italy

**Aim:** To evaluate the epidemiological aspects, the clinical features and the prognosis of patients with renal cancer affected by a second malignancy.

**Patients and Methods:** Since 1983, our institution has prospectively compiled a database concerning all the patients who underwent surgery for renal neoplasia in our centre. In the present study, we compared patients with a second primary malignancy diagnosed before, at the same time or the present study, we compared patients with a second malignancy. The follow-up lasted on average 71 months after the treatment of the renal neoplasia. The second neoplasia was antecedent in 115 patients (average latency period 4.4 years), synchronous in 97 patients and subsequent in 103 patients (average latency period 4.4 years).

In most of the cases, the renal tumour was associated with (in descending order) prostate, bladder and bowel cancer for men and breast, gynaecological organs, thyroid and bladder cancer for women. With respect to the patients who were not affected by a second neoplasm, those with multiple malignancies were on average older and had smaller, low-grade and low-stage incidental renal tumours. After a match-paired comparison adjusted by sex, mode of diagnosis, dimension, grade, stage and histological subtype of the cancer, no significant differences were noticed in the cause-specific survival of patients with multiple malignancies compared to those affected by renal neoplasia. The contemporaneous diagnosis of renal and secondary neoplasia had an independent negative impact on the cause-specific survival of patients with multiple malignancies.

**Conclusion:** The association between renal cancer and other malignancies is a relatively frequent event without any impact on the patient’s’ prognosis. Therefore, this factor should not be taken into account when treating renal tumour. In cases of contemporaneous diagnosis of the two malignancies, a close follow-up is advisable since the prognosis is less favourable.

**75 LAPARO-ENDOSCOPIC SINGLE-SITE PARTIAL NEPHRECTOMY WITHOUT ISCHEMIA**

Luca Cindolo1, Francesco Berardinelli1, Stefano Gidaro1,2, Fabio Neri1, Fabiola R. Tamburro1 and Luigi Schips1

1Urology Unit, S. Pio da Pietrelcina Hospital, Vasto (CH), Italy; 2Department of Surgical and Experimental Sciences, Chieti-Pescara University, Chieti, Italy

**Background:** Nephron-sparing surgery (NSS) ensures excellent oncological and functional outcomes in treating small renal masses. Laparo-endoscopic single-site surgery (LESS) is one of the major advances in the evolution of minimally invasive surgery. We describe our initial surgical experience and assess the feasibility of LESS unclamp NSS.

**Patients and Methods:** From April to September 2009, evaluation of patients undergoing LESS unclamped NSS at our institutions was performed. Patients with solitary, exophytic, enhancing, small (≤ 4.0 cm) renal masses and normal contralateral kidney were selected. An open Hasson transperitoneal pararectal or transumbilical approach was utilised. A single multichannel port (TriportTM) provided infra-abdominal access. Rigid and 5 mm articulable instruments were used for dissection, tumour exposure and excision under normal renal perfusion. The hemostasis was achieved by means of haemostatic glue, oxidized-cellulose bolster, and stitches. Perioperative, pathological, hematological data together with a subjective evaluation of the pain (VAS) and the scars were entered prospectively into a database and assessed.

**Results:** Six patients underwent LESS unclamped NSS (mean operative time: 167 min; mean blood loss: 210 ml). One patient with a left posterior mass required conversion to standard laparoscopy due to intraoperative bleeding. One patient developed a cerebrovascular accident. No transfusion was required. Pathology revealed 2 RCC, 1 AML, 3 benign cysts (mean tumour size 2.1 cm). Only one specimen (AML) was focally positive on final histopathology. A mean difference of 2.7 g/dl in haemoglobin was recorded with a minimal pain in POD1 (V AP: 2.3). Mean length of stay was 6 days.
Conclusion: LESS unclamped NSS in selected renal masses is feasible, provides postoperative outcomes overlapping the standard counterpart and ensures subjective satisfaction. The use of additional trocars should be considered for the haemostasis by stitches and for liver retraction. A wider experience and longer follow-up are necessary to establish the role of this technique.

References

Results: The OCTO™ LESS nephrectomy was successfully completed. The mean operative time was 150 min (estimated blood loss 170 ml). No perioperative complications were recorded. Pathology examination confirmed a T1b clear cell carcinoma.

Conclusion: The OCTO™ in LESS tumour nephrectomy seems to be feasible and safe, not requiring articulable instruments resulting in a more comfortable operation without external clashing. In our experience, due to the easy driving of the instruments, this device seems to be more close to a standard laparoscopy than a pure LESS approach. Prospective studies on wide surgical series are needed for any further conclusion.

References

NEW ADVANCES IN LAPARO-ENDOSCOPIC SINGLE-SITE SURGERY: FIRST TUMOUR NEPHRECTOMY BY OCTO™ LESS

Luca Cindolo¹, Stefano Gidaro¹,², Francesco Berardinelli¹, Fabio Neri¹, Fabiola R. Tamburro¹ and Luigi Schips¹

¹Urology Unit, S. Pio da Pietrelcina Hospital, Vasto (CH), Italy;
²Department of Surgical and Experimental Sciences, Chieti-Pescara University, Chieti, Italy

Background: LESS is one of the latest surgical advances; it is based on new devices that allow, with a single incision, access to the operative field. To improve this approach, different techniques and instruments appeared in the last years on the surgical panorama. The OCTO™ trocar is one of the last access devices, and provides the capability for multi-tasking by using multiple ‘tentacles’ and the flexibility for rapidly changing surgery. We describe the use of this new device during a left tumour nephrectomy for RCC.

Patients and Methods: A 72-year-old woman with a left upper pole renal tumour (tumour size 6 cm) was selected for this intervention. Prior to surgery, the patient was informed that the procedure would be attempted via a single port and she gave consent to additional incision if necessary. Demographics, perioperative and pathological records were collected, together with postoperative data. OCTO™ was used through a 4-cm pararectal incision with 5 mm 30°optic and two standard 5 mm instruments, the specimens being extracted via a 10 mm bag.

Results: The OCTO™ LESS nephrectomy was successfully completed. The mean operative time was 150 min (estimated blood loss 170 ml). No perioperative complications were recorded. Pathology examination confirmed a T1b clear cell carcinoma.

Conclusion: The OCTO™ in LESS tumour nephrectomy seems to be feasible and safe, not requiring articulable instruments resulting in a more comfortable operation without external clashing. In our experience, due to the easy driving of the instruments, this device seems to be more close to a standard laparoscopy than a pure LESS approach. Prospective studies on wide surgical series are needed for any further conclusion.

References
Patients and Methods: We retrospectively analysed our institutional RP databases and included all consecutive patients with high-risk localized PCAs. All patients underwent a wide radical prostatectomy with pelvic LND. Clinical data, including patient age, preoperative PSA, clinical stage and biopsy Gleason score, were collected, together with histopathology data on specimen Gleason score, pathological stage, section margins and lymph node invasion. Kaplan-Meier analysis with log-rank test was used to estimate the impact of age on CSS and OS. Cox multivariate models were used to assess the predictive value of age on CSS and OS, corrected for PSA, specimen Gleason score, lymph node invasion. We used the predictive value of age on CSS and OS, corrected for PSA, specimen Gleason score, lymph node invasion, pathological stage and section margins.

Results: Between April 1987 and April 2009, 1584 patients with cT3-4 or PSA >20 ng/ml or biopsy Gleason score >8 underwent an RP at seven European institutions. Mean age was 65.4 years (SD +/- 6.8). Median PSA was 22.8 ng/ml (IQR 10.7-36.6). Of the patients, 669 (42.2%) presented with <cT3 and 915 (57.8%) with cT3 disease. Biopsy Gleason score was <8 in 1179 (74.4%) and ≥8 in 403 (25.6%). PSA was <20 in 657 (41.5%) and ≥20 in 927 (58.5%). In total, 1098 (69.4%) patients were <70 years, 483 (30.6%) were ≥70 years old. Adjuvant treatment was administered in 67.0% of patients. Mean follow up was 67.1 months (SD +/- 43.6). Age <70 years was not a predictor for CSS (p = NS). While age was significantly related to overall survival (p = 0.0001), the median overall survival of patients aged ≥70 was 161 months, and in patients aged ≥75 years (7%, n=11) median survival was 137 months. In the Cox multivariate analysis, age <70 years was not significantly related to CSS; however, age >70 years was an independent predictor of OS (p < 0.0001, HR 1.68, 95% CI 1.28-2.19), besides lymph node invasion, specimen Gleason score and surgical margin status.

Conclusion: The oncological outcome of senior adults with high-risk localized prostate cancer undergoing surgery, appears to be highly satisfactory. Even though age >70 was significantly correlated to overall mortality, median overall survival time in this age group was well over 10 years, mirroring correct patient selection. Senior adults who have few comorbidities may still be candidates for surgical management of high-risk prostate cancer.

78 CONTEMPORARY MANAGEMENT OF NON-MUSCLE INVASIVE BLADDER CANCER AT ITALIAN REFERRAL CENTRES ADOPTING EAU GUIDELINES

Paolo Gontero1, Marco Oderda1, Vincenzo Altiéri2, Riccardo Bartoletti1, Tommaso Cai1, Renzo Colombo4, Antonio Curotto1, Francesco Marson1, Savino Di Stasi6, Massimo Maffezzini7, Vincenzo Serretta8, Filippo Sogni9, Carlo Terrone9, Vincenzo Mirone2 and Giorgio Carmignani5

1Urologia 1, Università degli Studi di Torino, Torino, Italy; 2Clinica Urologica, Università Federico II di Napoli, Napoli, Italy; 3Clinica Urologica, Università Federico II di Napoli, Napoli, Italy; 4Clinica Urologica, Università di Firenze, Firenze, Italy; 5Clinica Urologica, Università di Tor Vergata, Roma, Italy; 6Urologia, Ospedale Galliera, Genova, Italy; 7Urologia, Università di Palermo, Palermo, Italy; 8Clinica Urologica, Università del Piemonte Orientale, Novara, Italy

Background: Previously reported pattern of care surveys for non muscle-invasive bladder cancer (NMIBC) employing mailed questionnaires to urologists or random patient samples resulted in conflicting degrees of agreement with existing reference guidelines. In the current study, contemporary information on the management of NMIBC was generated from a sample of Italian referral centres declaring adoption of EAU guidelines.

Patients and Methods: In April 2009, eight Italian referral centres for the management of NMIBC were asked to compile a database of all pathological and prognostic characteristics relative to all consecutive patients with a NMIBC who had undergone a TUR between January 1st and March 31st. In September, they were asked to complete additional fields of the database concerning treatment and short-term follow-up information. Descriptive analysis on disease management was carried out.

Results: Out of a total of 410 available patients, 66 were excluded for violation of inclusion criteria (35 for being T2 and 31 for being T0 at entry TUR) thus 344 were evaluable. Response rate for both questionnaires was 100%. Data on focality and size of the tumour were provided in 34% and 90% respectively, and EAU risk stratification in 100%. A total of 40/57 (70%) of T1G3 underwent a repeat TUR. Overall, 23% received intravesical chemotherapy, 15% as first-line and 8% as second-line treatment. An early single induction course. T1G3 received BCG and chemotherapy as first-line therapy in 43/57 (75%) and 5/57 (9%) respectively. Three months’ cystoscopy was reported for 82% of patients with a recurrence rate of 16%.

Conclusion: Clinical management of NMIBC at Italian Institutions declaring conformity to EAU guidelines showed variable degrees of agreement with the guidelines. Discrepancies may partly reflect the low level of evidence of some of the recommendations.
IS THERE A PSA UPPER LIMIT FOR RADICAL PROSTATECTOMY?

Paolo Gontero1, Marco Oderda1, Francesco Marson1, Arianna Gillo1, Martin Spahn2, Giansilvio Marchioro3, Alessandro Tizzani1, Hendrik Van Poppel4 and Steven Joniau4

1Department of Urology, University of Turin, Turin, Italy; 2Department of Urology, Julius Maximilians Universität Würzburg, Würzburg, Germany; 3Department of Urology, University of Eastern Piedmont, Novara, Italy; 4Department of Urology, University Hospitals Leuven, Leuven, Belgium

Background and Aim: While radical prostatectomy is increasingly being recommended in high-risk prostate cancer (PC) with a PSA above 20 ng/ml, there is little knowledge about its feasibility at higher cut-off levels. We aimed to assess the feasibility of radical prostatectomy (RP) in a series of PC patients with very high PSA by comparing the clinical outcomes of different PSA thresholds (20.1-50 ng/ml, 50.1-100 ng/ml and >100 ng/ml respectively).

Patients and Methods: Within a multicentre European retrospective database of 712 RP in patients with a baseline PSA over 20 ng/ml, we identified 48 PCs with a preoperative PSA above 100 ng/ml, 137 with a PSA between 50.1 and 100 ng/ml and 527 with PSA values between 20.1 and 50 ng/ml. Comparisons between groups were performed using Chi-square test, ANOVA and Kaplan-Meier analysis with log-rank test.

Results: Pathological characteristics significantly worsened with increasing PSA thresholds. A significantly higher proportion of patients underwent adjuvant or salvage hormone therapy in the higher PSA intervals as compared to the lower ones. The ten-year projected cancer-specific survival (CSS) (79.8% in the PSA over 100 ng/ml group vs. 85.4% in the PSA 50.1-99 ng/ml group vs. 90.9% in the PSA 20.1-50 ng/ml group; p=0.037) but not overall survival (OS) (59.6% in the PSA over 100 ng/ml group vs. 71.8% in the PSA 50.1-99 ng/ml group vs. 75.3% in the PSA 20.1-50 ng/ml group; p=0.087) appeared significantly affected by the different PSA thresholds. Overall, treatment failure and clinical failure occurred significantly more often in the higher PSA groups (both p=0.007 respectively). At a median follow-up of 78.7 months, 25.8%, 6.6% and 8.3% in the 20.1-50 ng/ml and 50.1-100 ng/ml groups and in the PSA >100 ng/ml threshold respectively were cured by surgery alone. When including adjuvant radiotherapy and/or hormonal therapy, 62.8%, 50.3% and 37.5% of patients in the different PSA subgroups, respectively, were free from treatment failure.

Conclusion: Increasing PSA cut-off values above the 20 ng/ml threshold are associated with significantly worse postoperative pathological features, suggesting that the prognostic utility of PSA is maintained above this threshold. Ten-year CSS, while showing significant reduction with increasing PSA values intervals, remains relatively high even for PSA above 100 ng/ml. RP as part of a multimodal treatment strategy may thus be an option, even in selected PC patients with a PSA above 100 ng/ml.

PHARMACOKINETICS, PHARMACOLOGICAL STABILITY AND SAFETY OF MMC ADMINISTERED WITH A NEW HYPERTERMIA DEVICE

Paolo Gontero1, Paola Milla2, Nicoletta Serra1, Fiorito Chiara1, Francesco Marson1, Luigi Cattel1 and Alessandro Tizzani1

1Urologia 1, Università degli Studi di Torino, Italy; 2Istituto di Farmacologia, Università degli Studi di Torino, Italy

Background: Hyperthermic administration of MMC with the Synergo has proved effective with acceptable tolerability profile in high risk non muscle invasive bladder cancer. The major drawback is the high costs of both the device and disposable catheters. We report data on drug stability and safety of Unithermia, a new hyperthermia device for intravesical administration of MMC.

Patients and Methods: Ten patients with a BCG recurrent intermediate risk NMIBC were enrolled in the phase I part of the study and received 6 weekly instillations of MMC Unithermia. In all, 20 mg MMC diluted in 50 ml were administered via the Unithermia device for 45 minutes at a temperature of 42°C. A fresh drug solution was replaced at 23 minutes of every cycle. Pharmacological stability was tested by HPLC analysis of residual MMC on the drug solutions retrieved at mid and end of each instillation. Blood samples were taken at 0, 12, 23, 34 and 45 minute time intervals for the evaluation of plasmatic pharmacokinetic of MMC. Adverse events were graded according to the CTCAEv6. Cystoscopy was planned every 3 months for the first year.

Results: MMC stability was evaluated for 39 cycles: the median recovery of MMC was 66% and 99% in the drug solution retrieved at mid and end of each instillation. Blood samples were taken at 0, 12, 23, 34 and 45 minute time intervals for the evaluation of plasmatic pharmacokinetic of MMC. Adverse events were graded according to the CTCAEv6. Cystoscopy was planned every 3 months for the first year.

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Urinary side-effects did not go beyond grade

Cystoscopy was planned every 3 months for the first year.

Urinary side-effects did not go beyond grade

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2, 1 patient developed grade 3 systemic skin reaction and 3 patients discontinued the treatment at the 4th, 5th and 5th instillation respectively. Necrotic area on the posterior bladder wall was observed in 1/10 at cystoscopy.

**Conclusion:** The analysis of drug solutions retrieved at mid and end of instillation demonstrates that MMC stability was not affected by Unithermia administration, and that absorption of drug occurs mainly during the first 23 minutes. The almost negligible plasmatic levels of MMC agree with the absence of systemic adverse events.

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**5-AZACITIDINE RESTORES AND AMPLIFIES THE BICALUTAMIDE RESPONSE OF PROSTATE CANCER CELLS**

Claudio Festuccia1, Giovanni Luca Gravina1,2, Francesco Marampon1,2,4, Emmanuele A. Jannini3, Richard G. Pestell4 and Vincenzo Tombolini1,2

1Department of Experimental Medicine, Laboratory of Radiobiology, 2Department of Experimental Medicine, Division of Radiotherapy, and 3Department of Experimental Medicine, Chair of Sexual Medicine, University of L'Aquila, L'Aquila, Italy; 4Department of Cancer Biology and Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, U.S.A.

**Background:** Epigenetic modifications play a key role in the in prostate cancer (Pca) progression to a hormone refractory state (HRPC) and the current use of agents targeting epigenetic changes has become a topic of intense interest in cancer research. In this regard, 5-azacitine (5-Aza) represents a promising epigenetic modulator. This study tested the re-activation of hormonal response of AR-negative PC3 cell line was partially due to the AR re-expression mediated by 5-Aza treatment. In contrast, the increase in the response to anti-androgenic therapy in 22rv1 did not correlate with AR expression levels. Furthermore xenograft studies revealed that the combined treatment of 5-Aza with AR-antagonist BCLT had additive/synergistic effects in repressing tumour growth in vivo and the underlying mechanisms responsible for these effects seem to be in part mediated by induction of apoptosis.

**Conclusion:** This study strongly suggests a therapeutic potential of 5-Aza in combination with anti-androgen therapy in patients with both AR-expressing and AR-deficient HRPC.

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**TUMOUR ENUCLEATION TECHNIQUE FOR THE TREATMENT OF RENAL TUMOURS**

Andrea Minervini, Agostino Tuccio, Sergio Serni, Nicola Tosi, Giampaolo Siena, Federico Lanzì, Mario Alberto Rossetti, Gianni Vittori, Alessandro Ierardi, Lorenzo Masieri, Michele Lanciotti, Saverio Giancane, Annalisa Mantella, Saba Khorrami, Alberto Lapini and Marco Carini

Department of Urology, University of Florence, Careggi Hospital, Florence, Italy

**Objectives:** Nephron-sparing surgery (NSS) performed as enucleoresection is the gold standard for the treatment of RCC ≤4 cm in greatest dimension. Recently, the indication for NSS has been extended to tumours up to 7 cm. The aim of the study is to report our experience in renal tumours treated by the enucleation technique.

**Patients and Methods:** From January 1995 to December 2007, 722 patients underwent kidney surgery for the treatment of single, sporadic neoplasm. None of the patients included in the study had pre- or intra-operative suspicion of positive nodes and were free from distant metastasis before surgery (M0). Of these, 432 patients (59.8%) had NSS performed as tumour enucleation (TE), while 290 patients (40.2%) had radical nephrectomy. Of the 432 patients, 67 (15.5%) benign tumours were excluded from the retrospective analysis. The study consists of 365 patients with single, sporadic pathologically confirmed RCC. Kaplan-Meier method was used to evaluate the survival probability and the log-rank test to estimate the difference between the analysed variables.

**Results:** According to the 2002 TNM classification, 275 tumours were pT1a (75.3%), 57 pT1b (15.6%), 10 pT2 (2.7%), 21 pT3a (5.8%) and 2 (0.6%) pT3b. On the basis of Fuhrman nuclear grading, 81 (22.2%) tumours were G1, 234 (64.1%) G2 and 50 (13.7%) G3/G4. The mean (SD, range) tumour greatest dimension was 3.5 (1.7; 0.6-14) cm. The histopathologic review according to the WHO 2004 classification revealed 287 clear cell (78.6%), 43 papillary (11.8%), 30 chromophobe (8.2%) RCCs and 5 (1.4%) others. One patient died in the immediate postoperative period due to vascular complications. The mean (median, range) follow-up was 57 (45; 1-174) months. The 5- and 10-year overall survival were 81.7% and 70%, respectively. The 5- and 10-years cancer-specific survival
TUMOUR ENUCLEATION VERSUS RADICAL NEPHRECTOMY IN THE TREATMENT OF INTRACAPSULAR RENAL CELL CARCINOMA UP TO 7 CM

Andrea Minervini, Sergio Serni, Giampaolo Siena, Nicola Tosi, Agostino Tuccio, Mario Alberto Rossetti, Gianni Vittori, Alessandro Ierardi, Saverio Giancane, Federico Lanzi, Lorenzo Masieri, Michele Lanciotti, Annalisa Mantella, Saba Khorrami, Alberto Lapini and Marco Carini

Department of Urology, University of Florence, Careggi Hospital, Florence, Italy

Aim: To compare the oncological outcomes of tumour enucleation (TE) versus radical nephrectomy (RN) in pT1 renal cell carcinomas.

Patients and Methods: From January 1995 to December 2007, 722 patients underwent kidney surgery for the treatment of single, sporadic RCC. None of the patients included in the study had pre- or intra-operative suspicion of positive nodules and were free from distant metastasis before surgery (M0). Of these, 475 patients (65.8%) were pT1 at the pathological examination and were included in the study analysis. Kaplan-Meier method was used to evaluate the survival probability and the log-rank test to estimate the difference among the analyzed variables.

Results: Of the 475 patients, 332 had TE (69.9%), while 143 patients (30.1%) had RN. According to the 2002 TNM classification, 326 tumours were pT1a (68.6%) and 149 were pT1b (31.4%). The incidence of G1-2 and G3-4 nuclear grade was not significantly different between pT1a tumours treated with RN and TE while it was statistically significant for pT1b tumours (p=0.038). The incidence of conventional clear cell RCC was not significantly different for both pT1a and pT1b treated with either RN or TE. Mean pathological tumour size was significantly different in patients who had either RN or TE for pT1a (3.3 cm vs. 2.8 cm) and pT1b (5.6 cm vs. 5.0 cm) tumours (p<0.0001). The mean (median, range) follow up was 62 (48, 1-174) months. There were no significant differences in cancer-specific survival (CSS) between patients undergoing TE or RN for either pT1a (p=0.46) or pT1b (p=0.44) tumours. The 10-year CSS for pT1a treated with RN and TE was 92.6% and 94.9%, respectively. The 10-years CSS for pT1b treated with RN and TE was 87.5% and 90.4%, respectively. There were also no significant differences in overall survival (OS) between patients with pT1 RCC treated either with RN or TE; indeed, the 10-year OS was 71.5% and 71.9%, respectively. Overall, 3 patients with pT1a RCC developed isolated renal recurrence during the study period and this was always elsewhere in the kidney.

Conclusion: NSS is the gold standard for pT1 tumours. Our retrospective analysis shows that TE can achieve oncological results similar to those of RN for the treatment of intracapsular tumours up to 7 cm in greatest dimensions, provided tumours are carefully selected based on their safe and complete resectability. Our results clearly represent further evidence for adopting the TE technique as the standard procedure for the excision of pT1a and pT1b RCCs.

RADIOSENSITIZING EFFECTS OF THE PAN ENDOTHELIN RECEPTOR ANTAGONIST, MACITENTAN, IN PRECLINICAL MODELS OF PROSTATE CANCER

Claudio Festuccia1, Giovanni Luca Gravina1,2, Sandra D’Ascenzo1, Vincenza Dolo3, Enrico Ricevuto5 and Vincenzo Tombolini12

1Radiobiology Laboratory, 2Radiotherapy Division and 4Clinical Oncology Division, Department of Experimental Medicine, 3Clinical Pathology Chair, Department of Health Sciences, and Department of Experimental Medicine, University of L’Aquila, 67100 L’Aquila, Italy

Endothelin-1 (ET-1) and endothelin receptor A (ETRA) are overexpressed in prostate cancer tissues. In addition, ET-1 plays a major role in tumour angiogenesis acting through both ETRA and ETRB. Macitentan, also called Actelion-1 or ACT-064992, is a new dual ETRA/ETRB antagonist. In this report, we demonstrate that ACT064992 reduced tumour cell proliferation of a wide range of prostate cancer cell lines. In addition, suboptimal doses of this drug were able to sensitize PC3 and 22rv1 cell lines to radiotherapy both in vitro and in vivo. The effects of this combinatory treatment were higher in vivo suggesting the presence of both direct and indirect effects on tumour cells of ACT064992. The immunohistochemical analyses performed on 22rv1 and PC3 xenograft tissues demonstrated that ACT064992 reduced significantly the...
neoadjuvant therapy (lower micro vessel densities) both when administered alone and in association with radiotherapy. This selectivity was additionally supported by the higher expression of the ETRB in tumour vessels when compared to those observed in tumour cells. Conversely, prostate cancer cells were stained with antibodies recognizing ETRA. Therefore, we analysed the effects of ACT064992 on proliferation and differentiation of human endothelial cells in vitro. We observed that ACT064992 treatment reduced cell proliferation and cord formation of human microendothelial cells. Previously, it had been demonstrated that (i) the block of tumour-selective increase in the vascular endothelin 1/ETRA pathway led us to unravel an important reserve of vasorelaxation that can be exploited to selectively increase tumour response to radiotherapy; and (ii) hypoxia-inducible factor-1alpha (HIF-1alpha) has emerged as the key regulator of the cellular response to radiotherapy-induced hypoxia, an event often associated to tumour progression, neoangiogenesis and metastases. Therefore we analysed the effects of ACT064992 on HIF1alpha expression. We demonstrated that although the levels of HIF1alpha were not significantly influenced by ACT064992 alone, the induction of HIF1alpha in radiotherapy-treated tumours was significantly reduced. Conversely, VEGF expression was significantly lower in ACT064992 treated tumours. Our results indicate that angiogenic responses to radiotherapy can be significantly reduced by the block of both ETRA and ETRB. Dual ETR blockade antagonizes both tumour associated ETRA and endothelial cells-associated ETRA and ETRB. Treatment with ACT064992 is able to ameliorate sensitively the effects of radiotherapy in preclinical models of prostate cancer.

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**OZARELIX, A FOURTH GENERATION GnRH ANTAGONIST, INDUCES APOPTOSIS IN HORMONE REFRACTORY ANDROGEN RECEPTOR NEGATIVE PROSTATE CANCER CELLS**

Claudio Festuccia1, Donatella Dondi2, Margherita Piccolella2, Alessia Locatelli2, Giovanni Luca Gravina1,3, Vincenzo Tombolini1,3 and Marcella Motta2

1Experimental Medicine Department, Radiobiology Laboratory, and 2Experimental Medicine Department, Division of Radiotherapy, University of L’Aquila, Italy; 3Endocrinology Department, Center of Endocrinological Oncology, University of Milano, Italy

Background and Aim: Antagonistic or agonistic analogues of gonadotropin-releasing hormone (GnRH) are extensively used for the treatment of prostate cancer through the inhibition of secretion of gonad steroids. However, the majority of recurrent prostate tumours are androgen independent. This study explored the in vitro effects on DU145 and PC3 cell lines, representing useful two models of aggressive androgen-independent prostate cancer, of a fourth generation GnRH antagonist, Ozarelix.

Materials and Methods: Ozarelix was added to cultures and toxicity and cell cycle modifications were investigated by tests on cell viability, caspase activity and FACScan.

Results: Ozarelix showed antiproliferative effects and produced an accumulation of cells in G2/M cell-cycle phase. Apoptosis was linked with caspase-8-dependent caspase-3 activation with down-regulation of c-FLIP (L) and a sensitization to TRAIL-induced apoptosis linked also to increased expression and activity of death receptors DR4/5 and Fas.

Conclusion: TRAIL-resistant cancer cells can be sensitized to TRAIL by combination therapy and agents able to activate this apoptotic pathway, which may improve therapeutic effects in advanced hormone- and chemoresistant prostate cancer. Considering that literature data show that the last generation GnRH antagonists, such as Ozarelix, possess lower in vivo side-effects and higher pharmacological effects of previous GnRH agonists or antagonists, our results provide the biologic basis for the development of clinical strategies based on these drugs in advanced castration resistant prostate cancer.

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**ROBOT-ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY AND SEXUAL – RELATIONAL SATISFACTION. A PSYCHOEDUCATIONAL GROUP INTERVENTION’S EFFICACY EVALUATION**

Raffaella Balestrieri1, Carlo Ambrosi2, Luca Barlascini3, Serena Detti2, Elena Vegni3 and Ottavio De Cobelli2

1Servizio di Psicologia, AO- San Paolo, via di Rudini 8, Milano, Italy; 2Divisione di Urologia, Istituto Europeo di Oncologia, via Ripamonti 435, Milano, Italy; 3Cattedra di Psicologia Medica San Paolo- Polo Universitario, via di Rudini 8, Milano, Italy

Background: Prostate cancer is the most frequent neoplasy in male population. Surgical approach by nerve-sparing technique causes a minor damage in cavernous nerves without assuring erectile function (1). Pharmacological therapy can treat this dysfunction, but only 30%-50% of patients use it one year after post surgical intervention (2). We observed that patients experience sexual disorder as a threat to their male identity (3). Patient’s problems connected to sexual recovery could be related to psycho-emotional difficulties.
Aim: The aim of this study is to evaluate the efficacy of a psycho educational group intervention for patient treated by radical laparoscopic robot-assisted prostatectomy nerve sparing by considering two levels: quality of life and sexual satisfaction.

Patients and Methods: The intervention was conducted by a multidisciplinary team and consisted in ten sessions. A special focus was on psychological and sexual aspects connected to surgical intervention’s consequences. Participant’s quality of life (QLQ-C30) and sexual satisfaction (SESAMO) was explored before and after the psycho educational intervention. A multidimensional scale for assessment of erectile dysfunction (IIEF) was filled in by participants before and after surgery (3 months and 6 months follow up). The Wilcoxon test was used for the QLQ-C30, a descriptive analysis about SESAMO was conducted. Because an opportunistic control group was feasible for the QLQ-C30, a descriptive analysis about SESAMO was conducted. Observation of the data shows the size effect.

Results: This study enrolled 30 patients: 17 participated in the psycho-educational group, 13 in the control group; 13 participants at the psycho-educational group completed QLQ-C30 pre and post tests; 17 participants completed SESAMO pre and post tests; 13 participants and 13 patients of control group completed IIEF. Observation of the data shows the following. QLQ-C30 rates revealed an improvement post intervention on physical, emotional and social dimensions. SESAMO questionnaire showed a general decrease of sexual-relational difficulties; an increase of body image awareness was also detected in the post test, and the necessity to improve communication on sexual themes with the partner emerged. The Desire scores of the IIEF seems to decrease in both groups at the 3-month follow-up, but at 6 months, the scores of the psycho educational group increased to values similar to those before surgery. Statistical analysis is still ongoing.

Conclusion: Data showed that this psycho-educational group intervention has a global effect on both socio-relational and sexual aspects. A greater awareness of the ‘bodily experience’ is underlined and a higher sexual desire compared to the control group.

References
approximately 8 cm in diameter, adjacent to the lower pole of the right kidney. The nephrectomy specimen showed a pale yellow colored, uncircumcised solid lesion (maximum diameter 11 cm) confined to the lower pole of the right kidney and infiltrating the renal capsule and perirenal adipose tissue. Multiple surgical margins were not involved and the tumour was histologically diagnosed as malignant fibrous histiocytoma. Postoperative course was uneventful. After surgery, radiotherapy was delivered with a maximum dose of 14 Gy and a median dose of 11 Gy to the contralateral kidney. Although the mean dose to the kidney did not exceed tolerance, a total dose of 50 Gy was administered to not exceed the dose constraints. No acute and late toxicities and no postirradiation complications have occurred except for a G1 (RTOG toxicity criteria) acute cutaneous toxicity. Eighteen months after surgery the patient is alive without local recurrence and metastases.

Conclusion: Primary renal MFH is a rare tumour and the common presenting symptoms are similar to other renal mass lesions. Radical nephrectomy is the most important chance of cure although adjuvant treatment is required due to high risk of local recurrence and distant metastasis. Management of MFH has not been standardized and the role of adjuvant radiotherapy is still unclear but this case has showed good tolerance and good outcome with adjuvant radiation therapy. Further studies are necessary to improve survival of patients and to better evaluate the most appropriate adjuvant treatment for this rare neoplasm.

References
Conclusion: Patients with adrenocortical carcinoma have a poor prognosis and surgery is the most important chance of cure for them. Despite a complete tumour resection most patients will eventually develop local recurrence or distant metastases. Thus adjuvant treatment options need to be evaluated in high-risk patients (e.g., radiation therapy of the tumour bed and/or chemotherapy). Our case has showed good tolerance and good outcome with a compete resection and adjuvant radiochemotherapy but the standard treatment for this kind of tumour is still debated. Only large prospective multicentre trials comparing different treatment options will allow to make progress in the management of this rare neoplasm.

References

90 SINGLE PREOPERATIVE INTRAVESICAL INSTILLATION OF ELECTROMOTIVE MITOMYCIN-C FOR PRIMARY NON-MUSCLE INVASIVE BLADDER CANCER: A PROSPECTIVE RANDOMIZED TRIAL

Emanuele Liberati1, Cristian Verri1, Marco Casilio1, Maurizio Brausi2, Gioia Leprini1, Germano Zampa3, Marco Valenti4 and Savino Mauro Di Stasi1

1Department of Surgery/Urology, Tor Vergata University, V.le Oxford 81, 00133, Rome, Italy;
2O.U. of Urology, AUSL Modena, via G. Molinari 2, 41012 Carpi, Italy;
3O.U. of Oncology, Nuovo Regina Margherita Hospital, V.le di Trastevere 72, 00153, Rome, Italy;
4Section of Medical Statistics and Epidemiology, University of L’Aquila, L’Aquila, Italy

Background: Early single instillation of chemotherapy after TUR is recommended in the European Association of Urology Guidelines. Nevertheless, the procedure is suboptimal for patients with multiple tumours, sometimes is not tolerated and it can result in severe complications. In both laboratory and clinical studies, intravesical electromotive drug administration (EMDA) increased mitomycin-C (MMC) bladder uptake, resulting in an improved clinical efficacy in non-muscle invasive bladder cancer (NMIBC). We compared the effects of one immediate pre-TUR intravesical EMDA/MMC instillation with one immediate post-TUR intravesical passive diffusion MMC (PD/MMC) instillation and TUR alone in patients with NMIBC.

Patients and Methods: From 1994 to 2003, 352 eligible patients with primary NMIBC were randomized into 3 groups who underwent transurethral resection alone (TUR/alone; n=116); TUR plus single immediate postoperative instillation (immediately after TUR) of 40 mg PD/MMC with a dwell time of 60 minutes (n=119); or single immediate preoperative instillation (immediately before TUR) of 40 mg EMDA/MMC with 20 mA electric current for 30 minutes (n=117). Patients with intermediate and high-risk NMIBC underwent adjuvant intravesical therapy. The primary end points were the recurrence rate and disease-free interval. All clinical analyses were performed on an intent to treat basis.

Results: During a median follow-up of 85.4 months, there was recurrence in 188/352 patients (53.4%), including 74/116 (63.8%) TUR/alone group, 70/119 (58.8%) in PD/MMC post-TUR group and 44/117 (37.6%) in EMDA/MMC pre-TUR group (p≤0.001). In 30/352 patients (8.5%) with low risk disease, only 1 (3.3%), in EMDA/MMC pre-TUR group, had recurrence (p=0.409). In 225/352 patients (63.9%) with intermediate risk disease, 119 (52.9%) had recurrence, 47/75 (62.7%) in TUR/alone group, 46/77 (59.7%) in PD/MMC post-TUR group and 26/73 (35.6%) in EMDA/MMC pre-TUR group (p=0.001). In 97/352 patients (27.6%) with high disease, 68 (70.1%) had recurrence, 27/33 (84.4%) in TUR/alone group, 24/32 (75.0%) in PD/MMC post-TUR group and 17/33 (51.5%) in EMDA/MMC pre-TUR group (p=0.012). Overall median disease-free interval was 12.9 months for TUR/alone group, 16.4 months for PD/MMC post-TUR group and 56.9 for EMDA/MMC pre-TUR group (p≤0.001). In the PD/MMC post-TUR group, 43 patients (36.1%) had bladder symptoms and 28 (23.5%) had treatment discontinued because of pain or bladder spasms. No side-effects were observed in EMDA/MMC pre-TUR group.

Conclusion: In patients with intermediate and high-risk NMIBC one immediate pre-TUR intravesical EMDA/MMC instillation decreases the risk of recurrence and enhances the disease-free interval, compared with one immediate post-TUR intravesical PD/MMC instillation and TUR alone.

*Robert (Bob) L. Stephen leaves us with the memory of an inspiring teacher, scientist, colleague and friend. We sorely miss him.

91 SUCCESSFUL RESECTION OF POST-CHEMOTHERAPY METASTASES FROM NON-SEMINOMATOUS GERM CELL TESTICULAR CANCER

Franco Morelli, Anna Maria Capotorto, Lucia Lombardi, Pasquale Setolta, Nicola Sebastio, Antonio Cisternino and Evaristo Maiello
Casa Sollievo della Sofferenza, S. Giovanni Rotondo, Foggia, Italy

Background: Radical surgery of residual mass after frontline chemotherapy is a basis of the treatment for patients with poor risk germ cell tumours (GCT).

Case Report: A 22-year-old man was referred to our hospital in March 2009 for treatment of advanced testicular GCT. Whole body computed tomography (CT) showed lung, liver, mediastinal and bulky retroperitoneal metastases (stage III C). He underwent left orchiectomy followed by cisplatin based combination chemotherapy achieving serum tumour markers normalization. A CT performed after four courses of BEP demonstrated a complete remission of lung, liver and mediastinal metastases and a partial remission of retroperitoneal disease. After six weeks, a new CT confirmed the same results. Considering this stable response, we resected the residual disease. Postoperative pathologic examination disclosed the presence of fibrosis/necrosis.

Conclusion: After technically possible, resection of residual disease after a favourable response to chemotherapy for non seminomatous germ cell tumour, can provide pathologic assessment of the response and offer patients a chance of long term survival.

References

92 PRIMARY METASTATIC RENAL CARCINOID IN HORSESHOE KIDNEY

Ettore De Berardinis, Antonio Gatto, Gabriele Antonini, Domenico Di Viccaro and Costantino Cerulli

Dipartimento di Urologia, Università Sapienza di Roma, Policlinico Umberto I, viale del Policlinico 155, 00161 Roma, Italy

Background: Primary carcinoid is a neuroendocrine tumour of low degree of malignancy. It is very common in the gastrointestinal tract, lungs and in other body regions. Renal carcinoid, frequently associated with horseshoe kidney, is very rare (in the literature only 56 cases are described). The natural history of the disease has better prognosis when associated with horseshoe kidney than in normo-functional ones. The history of a patient suffering from a renal carcinoid in a horseshoe kidney, who had liver metastasis after six years from the first surgery, was reviewed.

Case Report: A 56-year-old male patient, who underwent abdomino-pelvic ultrasound and total body CT scan, showed a horseshoe kidney and a bulky solid mass of 6x6 cm at the lower pole of right kidney. The patient underwent partial nephrectomy with resection of the lower half of the affected kidney and the isthmus; the excision margin was 2 cm of normal renal parenchyma on either side of the mass. Microscopic examination of the lesion gives evidence of renal carcinoid. The immunohistochemical test showed that the tumour tissue was strongly positive for cytokeratin, chromogranin-A and synaptophysin. After a follow-up of 24 months, he was still negative for recurrence or distant metastasis. In March 2008, the patient had the first metastasis of the liver. He underwent a second surgery to remove the lesion. At the microscopic evaluation the diagnosis of well-differentiated neuroendocrine carcinoma was confirmed. The later instrumental tests demonstrated presence of several metastatic lymph node recurrences.

Results: Primary carcinoid of the kidney has a slow clinical course. Young adults (+/- 50 years old) without distinction of sex are most affected. On average, 50% of patients report flank/abdominal pain and/or hematuria and 7% present a carcinoid syndrome at the time of diagnosis; the remaining cases are asymptomatic.

Conclusion: Renal carcinoid has better prognosis in the horseshoe kidney than in kidney with normal compliance. Recurrences are not excluded and the treatment of choice remains the full or partial nephrectomy.

93 SMALL CELL CARCINOMA OF THE URINARY BLADDER: REVIEW OF THE LITERATURE AND PRESENTATION OF A CASE REPORT

Ettore De Berardinis, Antonio Gatto, Gian Maria Busetto, Mariarosaria Di Placido and Costantino Cerulli

Dipartimento di Urologia, Policlinico Umberto I, Università Sapienza di Roma, Italy

Background: Small cell carcinoma of the urinary bladder (SCCUB) is a neuroendocrine tumour. It occurs frequently in the respiratory and gastrointestinal tracts while in the urogenital tract is very uncommon. Generally the risk factors for this neoplasm are smoking and chronic disease of the bladder. We report the case of a patient with SCCUB that was treated only with neoadjuvant chemotherapy.

Case Report: A 60-year-old male patient, smoker, suffering from macroscopic hematuria and lumbar pain was submitted for abdomino-pelvic ultrasound which showed a bladder wall...
sessile formation. The tumour was treated with TURB (trans urethral resection of bladder). During histological examination a small cell cancer of the bladder was diagnosed. Total-body CT scan detected many lesions (right adrenal, liver, vegetans neoplasm of the bladder trigone, lymph node swelling). The patient underwent neoadjuvant chemotherapy with cisplatin plus vinblinblin. The disease progressed and at a second total-body CT scan new liver and lungs lesions were observed; lymph node involvement and bone metastases were reported. Topotecan, chosen as second-line therapy, was unsuccessful. The patient was treated with palliative therapy.

Results: SCCUB is a rare and aggressive tumour that especially affects males in 60-70 years of age. The incidence among bladder tumours is 0.5-1.0%. The immunohistochemical tests with chromogranin-A and synaptophysin appear to be highly specific for this type of cancer. Five-year cancer-specific survival is estimated at approximately 8%.

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A NEW MOLECULAR CHEMOSENSITIVITY TEST TO DETECT THE EFFICACY OF INTRAVESICAL ADJUVANT THERAPY IN THE TREATMENT OF NON-MUSCLE INVASIVE BLADDER CANCER

Ettore De Berardinis1, Gian Maria Busetto1, Gabriele Antonini1, Mariarosaria Di Placido1, Arianna Petracca2, Chiara Nicolazzo2, Vincenzo Gentile1 and Paola Gazzaniga2

1Dipartimento di Urologia e 2Dipartimento di Medicina Sperimentale, Policlinico Umberto I, Università Sapienza di Roma, Italy

Background and Aim: The treatment of choice for high-risk NMIBC is still controversial, and no markers are still available to guide the urologist in the individualization of therapy. Although intravesical chemotherapeutic and immunotherapies represent the gold standard in adjuvant setting after TURB, the percentage of recurrence and progression under treatment is still high. We describe the design of a chemosensitivity assay based on the expression of genes involved in the resistance to standard intravesical regimens.

Patients and Methods: Sixty-four patients with high-risk NMIBC were enrolled, all candidates for TUR-B followed by intravesical treatment. All patients were evaluated by cystoscopy 3 and 6 months after TUR-B. One mg of tumoural tissue from each patient was kept for molecular assay subjected to RNA extraction and RT-PCR amplifications with primers specific for MRP1, MRP2, hENT1, dCK, α5β1 integrin, used to trace a specific chemosensitivity profile to drugs commonly used in intravesical regimen: anthracyclines, mitomycin-C, gemcitabine and BCG. On the basis of densitometric analysis of the amplification bands obtained by normalization with the GAPDH internal controls, a chemosensitivity molecular profile was obtained for each patient. High, intermediate and low sensitivity to mitomycin-C, epirubicin, and doxorubicin were considered at a ratio MRP/GAPDH <1, =1, >1 respectively. For gemcitabine resistance, sensitivity, intermediate sensitivity and resistance were considered at a ratio hENT-dCK/GAPDH >1, =1 and <1 respectively. Sensitivity to BCG was evaluated as follows: high, intermediate, low sensitivity in the presence of α5β1/GAPDH >1; =1 ; <1 respectively. We then compared both molecular profiles of chemosensitivity to the clinical response to the intravesical regimen adopted in the first 6 months of follow-up.

Results: This chemosensitivity test was able to predict response to treatment in 93% of patients. The assay is easy to perform, at a low cost and with rapid time of execution.

Conclusion: Our results are encouraging in view of an individualized therapeutic approach in order to provide a higher treatment success rate while sparing patients unnecessary toxicity from drugs that are not suited for their tumours.

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DETECTION OF CIRCULATING TUMOUR CELLS AS PROGNOSTIC FACTOR IN INTRAVESICAL ADJUVANT THERAPY IN NON-MUSCLE INVASIVE BLADDER CANCER

Ettore De Berardinis1, Gian Maria Busetto1, Gabriele Antonini1, Mariarosaria Di Placido1, Arianna Petracca2, Chiara Nicolazzo2, Vincenzo Gentile1 and Paola Gazzaniga2

1Dipartimento di Urologia e 2Dipartimento di Medicina Sperimentale, Policlinico Umberto I, Università Sapienza di Roma, Italy

Background and Aim: The prognosis of T1G3 bladder cancer is highly variable and not predictable basing upon clinical and pathological prognostic factors. There is need for improvement in risk stratification in this population; understanding the molecular profile of individual patients could provide a more personalized and tailored treatment. Main objective was to evaluate the prognostic significance of Survivin in tumour tissues and that of Survivin-expressing circulating tumour cells (CTCs) in T1G3 tumours.

Patients and Methods: Fifty-four patients with T1G3 non muscle invasive bladder cancer (NMIBC) were enrolled. Additional inclusion criteria were: tumour size<3 cm; absence of CIS and multifocality. Planned follow-up was 24 months. Survivin was evaluated by RT-PCR in tumoural tissues. CTCs were isolated from blood by CELLlection™ Dynabeads coated with the monoclonal antibody towards the human epithelial cell adhesion molecule. Cells were lysed and Dynabeads Oligo(dT) was used to capture poly A+ mRNA.
cDNA was synthesised and analysed for the expression of CD45, CK8 and Survivin. The primary end point was disease-free survival (DFS); the favourable group at 24 months was defined as that without any clinical evidence of disease (NED); the unfavourable group was that with evidence of recurrent (RD) or progressive disease (PD). Tumoural Survivin expression and presence of CTCs were tested for correlation to DFS. Multivariate analysis was used to investigate whether CTC presence was an independent indicator of DFS.

**Results:** Survivin was found in 50% of tumours. Survivin-negative patients had a longer DFS than Survivin-positive ones ($\chi^2: 4.572; p=0.029$). CTCs were found in 24/54 patients (44%); 92% of CTCs expressed Survivin. The difference in DFS between CTC-negative and CTC-positive patients was statistically significant ($\chi^2: 28.098; p<0.001$). CTC presence was found to be an independent prognostic factor of DFS ($p<0.001$).

**Conclusion:** CTC presence is an independent prognostic factor in high-risk NMIBC patients.

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**96 THE PREDICTIVE ROLE OF RE-TURB IN THE EVALUATION OF T1HG BLADDER NEOPLASM PROGRESSION RATE**

Roberto Giulianelli, Luca Albanesi, Francesco Attisani, Barbara Gentile, Stefano Brunori, Luca Mavilla, Francesco Pisanti, Giorgio Vincenti and Stefano Nardoni

Casa Di Cura Villa Tiberia, via Emilio Praga 26, Roma, Italy

**Background:** High-grade bladder neoplasia (T1HG TCC) represents a true therapeutic challenge, with a 20% risk of progression. The use of BCG immunotherapy reduces the risk but sometimes a restaging TURB better predicts early-stage progression.

**Patients and Methods:** A cohort of 285 patients presenting primitive cancer of the bladder underwent TURBt from 01/2004 to 12/2008; of these, 92 (30.8%) were T1HG. After a month, all these HG cancer patients underwent a reTURB by the same surgeon to evaluate recurrence and progression-free survival. ReTURB consisted of a wide resection of the margins and depth of each tumour size as well as complete resection and fulguration of all suspected residual tumours. The follow-up results included a cystoscopy every 3 months, associated with carcinoma in situ. The remaining 22 patients with T1HG are still progression free. The multivariate analysis showed that the mean variable of early progression was the histopathological findings of the reTURB ($p=0.01$), followed by the results of the first cystoscopy ($p=0.002$) and the presence of CIS ($p=0.02$).

**Conclusion:** ReTURB in patients affected by HG superficial disease identify those with a high rate of early progression, allowing the selection of patients who need an immediate radical surgical treatment (early cystectomy) in order to have a better follow-up and survival.

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**98 BULKAMIDE HYDROGEL: LIMITS OF A NEW BULKING AGENT IN THE MINI-INVASIVE THERAPY OF INCONTINENCE AFTER PROSTATECTOMY**

F. Mantovani, S. Maruccia, G. Cozzi, E. Tondelli and F. Rocco

Fondazione IRCCS Ca’ Granda - Ospedale Maggiore Policlinico, via Francesco Sforza 35, Milano, Italy

**Background and Aim:** Bulkamide cross-linked polyacrylamide hydrogel is a new bulking agent, less expensive and more effective than other injectables because less quantity is needed and it is not re-adsorbable. It can improve results in the treatment of female incontinence, where it is has been well tested, but also in new fields such as post-prostatectomy incontinence and vescico-uretheral reflux.

**Patients and Methods:** Here we present a procedure for restoring contience in males by prostate reconstruction in anastomotic area injecting a syringe of bulkamide in position 3 and one in position 9 by the help of a McGuire injector. The procedure is performed under local anaesthesia by urethral irrigation with 20 ml bupivacaine. The procedure used is the following. We cross the sphincter, look at the bladder and then perform the double injection. The result is checked by a stop.
test filling the bladder with 200 ml of saline solution. In severe or relapsed incontinence, a 3-injection procedure is recommended, adding a third injection in position 6, improving occlusive function. Last but not least, in extreme cases where incontinence is still present after pharmacological therapy, urorehabilitation and ProAct implant, 3 syringes are distributed from the anastomotic area to the bulbomembranous urethra by specular occlusive injections.

Results: A total of 12 patients, operated on between January 2008 and December 2009 and of mean age 68 years, were assessed with a follow-up period of one year. The patients reported a significant improvement of continence: use of pads was reduced from an average of 5.4/day to 2.7/day. In a questionnaire given to patients before surgery, the perception of disorder linked to loss of urine, on a scale from 0 to 10, was an average of 8.8; after surgery the average was of 7.2.

Interpretation of results: Time to improved continence due to training of the sphincter externus muscle cannot be shortened, but the quality of life during this time can be improved. In the case of a severe lesion of the sphincteric muscle, continence cannot be improved for a longer period and the results are poor. In these cases, procedures such as implantation of an artificial urinary sphincter may be required

Conclusion: Bulkamid cannot promise more than ensuring that quality of life can be improved significantly, reducing urine leakage without complete recovery but also with no worsening.

References

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125I BRACHYTHERAPY FOR EARLY-STAGE PROSTATE CANCER AT SAN FILIPPO NERI HOSPITAL IN ROME: PRELIMINARY RESULTS

Tiziana Palloni1, Francesco Pio Mangiacotti2, Assunta Petrucci2, Giorgio Maria Giacomini3, Georgy Bakaev3, Marco Martini1, Vincenzo Ciccone1, Alfredo Siniscalchi1, Francesco Vidiri1, Antonella Ciabattoni1, Rita Consorti2, Patrizia Soldini1, Manuel De Maio3 and Maria Alessandra Mirri1

1UOC Radioterapia, 2UOSD Fisica Sanitaria, e 3UOSD Urologia Oncologica, Azienda Complesso Ospedaliero San Filippo Neri, via G. Martinotti 20, 00135 Roma, Italy

Background: Ultrasound-guided prostate brachytherapy (USBT) is now a widely used modality in the treatment of prostate cancer with a 10-year biochemical progression-free survival (bPFS) of 80-90% for low-risk patients. The results of long-term follow-up have shown better bPFS after brachytherapy than after conventional external-beam radiotherapy (EBRT) and similar survival after radical prostatectomy (1). San Filippo Neri Hospital is currently the only Hospital in central Italy to offer USBT. The aim of this paper is to present our one-year experience.

Patients and Methods: In our Hospital, all prostatic cancer patients are managed from diagnosis to the cure by a multidisciplinary team (urologist, oncologist, radiation oncologist, medical physicist, anaeasthetist) who is able to offer them all the current treatment options. Patients were selected for brachytherapy according to ABS recommendations (PSA ≤ 10 ng/ml, Gleason score ≤ 6, T1-T2a) (2), good urinary functionality and prostate volume ≤ 50 g. The USBT was performed with 18-gauge needles loaded with customized strand seeds created using the QuickLink® system (BARD). The prescription dose was 145 Gy. The attempted pre-implant dosimetric goals (2) were prostate V100 (the percentage of prostate volume that received the prescribed dose) (3), D90 (the dose that covers 90% of the prostate volume) ≥ 145 Gy, urethra D1 (the maximum dose allowed to the 1% of the urethra) < 210 Gy and rectum D2cc (the dose allowed to 2cc of the rectum wall) < 145 Gy (3). One month after USBT, CT scan was performed for post-implant dosimetric planning: a prostate D90 value ≥ 140 Gy was considered a measure of a good implant quality. All patients underwent regular three-month clinical multidisciplinary follow-up, including digital rectal examination and PSA determination. The pre- and post-implant dosimetric parameters, the number of seeds and needles used, the time needed to perform the procedure, the acute and late genitourinary (GU) and gastrointestinal (GI) toxicity using EORTC/RTOG criteria, erectile function preservation and post-USBT PSA levels were reported.

Results: Between January 2009 and January 2010, 11 men with early low-risk disease received 125I prostate USBT without androgen deprivation or supplemental external radiotherapy. Mean age was 56 years (range 50-73) and mean pre-treatment PSA value was 57 ng/ml (r.: 3.87-8.75). The mean pre-USBT prostate volume (cc) was 36.35 (r.: 24.21-58.16). The average number of seeds and needles implanted were 73 (r.: 58-91) and 23 (r.: 17-29) respectively. Our pre-implant dosimetric results were: mean prostate V100 99.51% (r.: 98.61-100), mean prostate D90 183.61 Gy (r. 178-192.46), mean rectum D2cc 107.46 Gy (r.: 81.24-125.85) and mean urethra D1 were 203.78 Gy (r.: 193.45-220.68). At the one-month post-planning, mean prostate D90 was 142.15 Gy (r.: 123.55-166.64). As a result of the learning curve, the time needed to perform the procedure decreased in one year from 4 h 30 mins to 2 h 20 mins. With a median follow-up of 7.5 months, 3/11 (28 %) and 1/11 (9%) of patients presented grade 1 and grade 2 GU toxicity respectively; 2/11 (18%) of patients developed grade 1 GI toxicity; one patient reported...
transient left leg paresthesia and weakness, probably due to the position requested for the implant. Erectile function was preserved in the whole group. Three months after USBT, the mean reduction of the PSA values was 75.32% (r.: 49.58-90.70%).

**Conclusion:** Our experience, although limited, confirms that USBT is a safe and effective curative modality for men with low-risk organ-confined prostate cancer, strongly motivated to maintain erectile function, urinary continence and have a rapid return to normal activity.

**References**

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**PROPOSAL FOR A NEW STRATEGY FOR ACTIVE SURVEILLANCE IN LOW-RISK PROSTATE CANCER: PIMAS**

**Andrea B. Galosi**¹, Vito Lacetera¹, Rodolfo Montironi², Luciano Burattini³, Massimo Cardinali⁴ and Giovanni Muzzonigro³

¹Clinica Urologica, ²Istituto di Anatomia Patologica, ³Clinica di Oncologia, e ⁴U.O di Radioterapia, Università Politecnica delle Marche, Azienda Ospedali Riuniti, Ancona, Italy

**Background:** In accordance with guidelines, an alternative choice for patients with very low-risk prostate cancer (PCA) is active surveillance (AS) in order to avoid overtreatment. PRIAS-Italy (Prostate Cancer Research International Active Surveillance) is the only protocol available in Italy. This protocol presents some risks: for example, the risk of understaging and undergrading is 30% and 20-40% of patients, respectively, since it is based on an initial 10-12 core biopsy. Our research offers proposals for an alternative AS protocol based on early repeated saturation biopsy using transperineal template-guided mapping biopsy. Furthermore, last generation MRI and PCA3 are included as optional instruments for active monitoring.

**Patients and Methods:** A multidisciplinary approach involving urologists, oncologists, radiotherapists and pathologists has been developed based on critical analysis of available European and American protocols for AS. We identified criteria for inclusion, follow-up strategy and triggers for treatment in patients carefully selected for active surveillance.

**Results:** Inclusion criteria:

a) Pathological assessment: histologically proven PCA (reviewed by expert uro-pathologist), initial biopsy Gleason score ≤3+3, < 3 positive cores, < 50% any core involvement, absence of tumour perineural infiltration. These features must be confirmed by repeat saturation biopsy (template transperineal biopsy) (1).

b) Patient assessment: age >65 years or life expectancy <15-20 years (using life expectancy tables and Charlson Score Index). Initial evaluation of lower urinary tract symptoms (LUTS): no bladder outlet obstruction or urinary symptom score >16. Psycho-social evaluation (anxiety, depression) and informed consent. Patients must be willing to attend the follow-up.

c) Clinical tumour evaluation: clinical stage T1-T2a based on digital rectal examination (DRE), transrectal ultrasound (TRUS); magnetic resonance (MR) (spectroscopy imaging, 3-Tesla) is an optional tool.

d) Laboratory: PSA total <15; PSA density <0.2; PSA velocity <0.75; PSA doubling time >3 ng/cc/year; normal testosterone value; urinary PCA-3 test is an optional tool.

e) Nomograms: <10% of tT3 probability and 10 years-PFS >95% based on Kattan et al. (2) nomogram and >90% probability of indolent PCA based on Steyerberg nomogram (3).

Follow-up strategy: Every 3 months, serum PSA. Every 6 months: DRE, TRUS, LUTS assessment. Every 12 months: testosterone, PCA-3 and MRI are optional. Standard biopsy is suggested every 18 months up to 5 years, then every 2 years. Saturation biopsy after 5 years and 12 years using transperineal template-guided mapping biopsy. After 12 years, follow-up based on a re-evaluation of life expectancy.

Triggers to repeat biopsy before schedule: Clinical progression (detected by DRE, TRUS, MRI), biochemical progression (PSA >15, PSAD >0.2, PSA velocity >0.4, PSADT <10 years, PCA-3 turns positive or increases), testosterone below the normal value.

Triggers for treatment: Histological progression (any Gleason pattern 4-5, >2 positive cores, >50% core involvement, perineural infiltration, >2 small cancer foci in other zones of the prostate), PSADT <3 years, clinical progression (cT3/cT2b-c), patient’s motivation.

**Conclusion:** We believe that PIMAS is the safest approach possible. The risk of missing the window of curability of PCA is possible but very limited. Adequate initial assessment using saturation transperineal template-guided biopsy is the
best method to evaluate grade, tumour extension within the gland. MR and PCA3 could be evaluated as new methods to detect early progression of PCA.

References

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HAEMOSTATIC SPONGE APPLICATION ON DENONVILLIER FASCIA AFTER OPEN NERVE-SPARING PROSTATECTOMY
Andrea B. Galosi, Vito Lacetera, Marco Tiroli, Alessandro Conti and Giovanni Muzzonigro
Clinica Urologica, Università Politecnica delle Marche, Azienda Ospedali Riuniti, Ancona, Italy

Background: Recently, the application of haemostatic devices (TachoSil) in the surgical field after nerve-sparing radical retropubic prostatectomy (NS-RRP) has been suggested. Energy-free haemostasis should be carried out to avoid heat damage to small nerve fibres as well as stitches that may lead to nerve entrapment. Haemostatic sponges have the advantages to avoid any nerve or vascular damage. However, application of this device is difficult since the sponge easily slips away from the soft tissue (Denovillier fascia) or is accidentally displaced during tying of anastomotic sutures. We describe our technique of Tachosil application to the posterior surgical field after NS-RRP.

Materials and Methods: After NS-RRP, haemostatic sponge application in the posterior surgical field is performed after accurate control of active bleeding vessels using clip and/or stitches. TachoSil covers Denovillier fascia in order to include neurovascular bundles (NVBs). a surgical glove is then placed over the sponge and compressed by a small towel. The surgical glove avoids adhesions between the sponge and towel. After 10 minutes, the towel and surgical glove are removed. We have always verified the complete adhesion between sponge and Denovillier fascia including the NVBs. If there is bleeding or clots between tissues and sponge, the adhesion will be incomplete, hence the sponge is removed and the manoeuvre repeated.

Results: The technique is safe and useful in obtaining haemostasis in NVBs. We treated 20 cases using this procedure when haemostasis was considered non optimal using the standard technique (clip and stitches).The time lost to place the sponge is limited (5 min.). About 10 min., it is the time necessary to reach complete sponge adhesion to tissue.

Conclusion: The technique allows effective and safe application of haemostatic sponge on NVBs and Denonvillier fascia.TachoSil sponges help to reach haemostasis avoiding neural damage in the NVBs when haemostasis is considered inadequate using conventional technique.

References

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SOLITARY FIBROUS TUMOURS OF THE GENITOURINARY TRACT: TWO CASE REPORTS WITH LITERATURE REVIEW
Vito Lacetera1, Andrea B. Galosi1, Rodolfo Montironi2, Valerio Beatrici3, Antonio Cicetti3, Giuliana Gabrielloni3, Alfonso Cristalli3 and Giovanni Muzzonigro1
1Clinica Urologica, and 2Istituto di Anatomia Patologica, Università Politecnica delle Marche, Azienda Ospedali Riuniti, Ancona, Italy; 3U.O. di Urologia, Ospedale S. Croce, Fano, Italy

Background: Solitary fibrous tumours (SFTs) are rare neoplasms, frequently arising from the pleural cavity, but extrapleural SFTs have been increasingly described in various locations, including the genitourinary tract. We report two cases of SFT, the first arising from the kidney and the other from the prostate. We discuss the clinicopathological features, the differential diagnosis and prognosis of SFTs with a literature review.

Case Reports: #1: A 49-year-old man had a left renal mass incidentally discovered by an abdominal US-examination. CT examination confirmed a well-delineated, homogeneous mass
measuring 4.5 cm that exhibited enhancement with contrast medium suggestive of renal cell carcinoma (RCC). The patient underwent radical nephrectomy.

#2: A 60-year-old man with lower urinary tract symptoms, PSA 0.6 ng/ml, was found to have an enlarged and hard left lobe of the prostate on DRE; TRUS and MRI showed a solid, circumscribed mass in the left transitional zone. TRUS-guided needle biopsies was performed. The diagnosis of SFT of the prostate was made based on histopathological and immunohistochemical findings. The patient underwent retropubic radical prostatectomy.

Results: Case #1: The cut section of the resected kidney revealed a nodular, well-circumscribed, grayish to white, firm tumour of 4x4 cm without invasion of the renal capsule. Microscopically, the tumour showed variable cellularity consisting of a mixture of short fascicular arrangements of spindle cells and dense collagenous bands. Case #2: The pathology report described a well-circumscribed, rubbery mass measuring 8x7 cm with tan-yellow to white cut surface, in the left transitional zone compressing the normal prostatic tissue. Microscopically, the tumour consisted of short spindle cells separated from dense collagenous bands with a pseudoangiomatous appearance. On immunohistochemistry, cells from both tumour stained diffusely for CD 34, vimentin, BCL-2 and collagen IV but were negative for desmin, S-100, C-KIT and cytokeratins. The findings were more consistent with SFT. The patients are alive with no evidence of recurrent disease 18 and 12 months after surgery.

Conclusion: We reported these two cases because SFTs of the genitourinary system are very rare: Around 20 and 30 cases of SFTs arising from the kidney and the prostate respectively are reported in the literature and in all the reported cases, the diagnosis was made by a pathologist (immunohistochemical study is the key to diagnosis). The differential diagnosis includes other benign and malignant spindle cell tumours of the kidney (fibroma, histiocytoma, sarcoma, leiomyosarcoma, GIST) and renal cell carcinoma; prostatic SFTs should be distinguished mainly from stromal tumours of uncertain malignant potential (STUMPs) and GIST. Clinical behaviour is difficult to predict, most SFTs are benign lesions but about 10% can be aggressive; completeness resection of the tumour is the main prognostic factor. A long-term follow-up is mandatory. Urologists should be aware of this entity that is more frequently observed nowadays than in the past.

References

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DIAGNOSIS OF BLADDER CANCER WITH HEXYLAMINOLEVULINATE (HEXVIX) ‘BLUE LIGHT’ FLUORESCENCE CYSTOSCOPY: INITIAL SINGLE-CENTRE EXPERIENCE.

Valerio Beatrici, Antonio Cicetti, Giuliana Gabrielloni, Alfonso Cristalli and Vito Lacetera
U.O. di Urologia, Ospedale S. Croce, Fano, Italy

Background: Several studies have shown that blue-light cystoscopy with hexaminolevulinate (HAL-BLC) is superior to standard white-light cystoscopy (WLC) in diagnosing bladder tumours, with a clinically relevant impact on patient management. We aimed to compare HAL-BLC with WLC in the diagnosis of non-invasive bladder tumours (NIBC).

Patients and Methods: Between January 2009 and January 2010, a total of 27 patients with suspected bladder cancer (positive urine cytology or history of CIS or high grade non-invasive bladder cancer with WLC negative) were investigated with HAL-BLC, using Hexvix (PhotoCure, Oslo, Norway, 50 ml 8 mM 1 hour before cystoscopy) and the D-light system (Karl Storz, Tuttlingen, Germany) to detect fluorescence.

The bladder was mapped initially under white light and then under blue light. Biopsies were taken from abnormal urothelium detected by white light and by fluorescence. All cytological and histological specimens were reviewed by a pathologist unaware of the result of the light system used.

Results: A total of 27 cystoscopies were performed (23 men/4 women; median age 75 years, range 56-88 years). of the 27 patients, 2 (7.5%) were previously untreated for NIBC, and 25 (92.5%) were under surveillance for previous NIBC. 14 patients (51%) have received instillation stopped at least 6 months before HAL-BLC. In 10/27 (37%) patients the indication was positive urine cytology and 17/27 (63%) had previous history of CIS or high grade NIBC with WLC negative. On average, 1 lesion was detected by WLC (range 1 to 4) and 2.2 lesions by HAL-BLC (range 1 to 5). NIBC (Ta/T1) or preneoplastic lesion (high grade dysplasia) of the bladder was diagnosed in 17/27 patients (62%) and 12 of 17 (47%) of these patients had at least 1 additional lesion detected by HAL-FC (p=0.002); in addition, NIBC was diagnosed only by HAL-FC in 8 of them. Improvement in CIS detection 10 vs 1. False-positive rates were 27% with HAL-BLC and 25% with WLC. Comparing the patients...
with NIBC who completed 9 months of follow-up after TURB, no tumour recurrence was seen.

**Conclusion:** Additional pathologies were detected by HAL-BLC in 44% of the sample. We conclude that HAL-BLC is a key step in the management of patients with suspected bladder cancer, and particularly useful for patients with positive urinary cytology or CIS history and WLC negative.

**References**


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DELAYED ANDROGEN DEPRIVATION THERAPY AT TIME OF BIOCHEMICAL RECURRENCE IN PATIENTS WITH POSITIVE LYMPH NODES AFTER RADICAL PROSTATECTOMY

Michele Lodde1, Michael Mian1, Angelo Naselli2, Paolo Puppo2, Louis Lacombe1 and Yves Fradet1

1Université Laval, CHUQ-Hotel-Dieu de Québec, Québec, QC, Canada;
2Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy

**Background:** To determine the biochemical recurrence-free survival (BRFS) and the potential prognostic factors for biochemical recurrence (BR) in patients that underwent radical prostatectomy and an extended lymphadenectomy in the prostate-specific antigen era.

**Patients and Methods:** Included patients had node-positive prostate cancer after RP and extended lymphadenectomy. Exclusion criteria were neoadjuvant and adjuvant ADT, adjuvant radiotherapy and detectable PSA three months after surgery. Follow-up consisted in 3-monthly serum PSA, digital rectal examination for the first 2 years and monthly thereafter. BR-free survival (time from surgery to PSA≥0.3ng/ml or adjuvant radiotherapy) or ADT-free survival (time from surgery to first castration, chemical or surgical) were analysed with the Kaplan-Meier methods. The Cox proportional hazards model was used to identify independent prognostic factors for all two end points.

**Results:** Between January 1991 and April 2008, 70 patients that responded to our inclusion criteria were found. Patient’s age was ≤65 in 41.7% of the cases. PSA was in ≥10 in 47.1% of the patients and in 50 cases the cancer was extraprostatic. The median of nodes extracted was 17 (range, 3 to 38) and the median of positive nodes 1 (range, 1-12). Median follow-up was 78 months (range, 15-197). Overall, 40 patients had BR. The median for BR was reached at 57.3 months (95% CI 47.7-67.4). BR-free survival rate at 2 years was 77.9% and 41.9% at 5 years. The ADT-free survival rate at 2 years was 78% and at 5 years 59.5%. The median time to ADT was 72.9 months (95% CI 49.9-95.9). Gleason score favoured patients with better differentiated tumours, with 67.1 months median time to BR for patients with GS≤6 and 27.7 months for those with GS=8-10. In the Cox regression analysis, the number of positive nodes remained an independent predictor for BR.

**Conclusion:** At 5 years, 42% of the patients after RP with positive nodes and delayed ADT are still free from BR and 60% free from ADT. GS and number of positive nodes are prognostic factors for such events. Delayed ADT at BR in patients with low burden of metastatic node disease and low GS could avoid immediate ADT to reduce the side-effects.

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PROSPECTIVE TRIAL WITH RADICAL PROSTATECTOMY AND INTRAOPERATIVE RADIATION THERAPY FOR CLINICALLY LOCALY ADVANCED PROSTATE CANCER: CLINICAL ASPETCS AND RESULTS AFTER 5 YEARS EXPERIENCE

Giansilvio Marchioro1, Marco Krengli2, Matteo Vidali3, Alessandro Volpe1, Roberto Tarabuzzi1, Stefano Zaramella1, Michele Billia1, Monica Zaccero1, Andrea Ballarè3, Pina Apicella2, Bruno Fre4 and Carlo Terrone1

1Department of Urology, and 2Department of Radiotherapy Medicine, Maggiore della Carità Hospital, University of Eastern Piedmont, Novara, Italy; 3Clinical Chemistry Unit, University of Eastern Piedmont, Novara, Italy; 4Department of Urology, Santa Maria della Misericordia Hospital, University of Udine, Udine, Italy

**Background:** Intraoperative radiation therapy (IORT) is a new radiotherapeutic technique that can deliver high doses of radiation during surgical treatment. Four years ago, we started a prospective feasibility study of IORT during radical prostatectomy (RP) for locally advanced prostate cancer (PCa). We report data on functional outcome, morbidity, toxicity (RTOG Scoring Criteria) and oncological follow-up.
Patients and Methods: From September 2005, 52 patients with locally advanced PCa were treated. A total of 44 had a minimum follow-up of 6 months. Inclusion criteria were: Age <75 years, clinical stage T3-4, N0-1, M0, probability of extracapsular disease >25% (Kattan’s nomograms), no inflammatory bowel disease. During surgery, the prostate was exposed with dissection of endopelvic fascia and puboprostatic ligaments. The distance between prostate and rectum was measured with ultrasound. A collimator (Mobetron, Intraop, California, USA) with diameter of 5.0-6.0 cm and an angle ‘bevel’ of 15-30° was introduced in the surgical field and delivered a dose of 10-12 Gy with 9-12 MeV. The dose was prescribed to the isodose of 90%. The volume treated included prostate, seminal vesicles and periprostatic area. RP was then completed and an extended lymphadenectomy was performed. Mean IORT time was 30 minutes. Postoperative RT treatment 3 months after IORT was planned for 38/44 patients. A box technique (Foton X 6-15 MV) was used and a dose of 50 Gy, in fractions of 2 Gy/day, was delivered. Hormonal therapy (HT) was prescribed when indicated.

Results: The median patient age was (IQR, range) 67.2 years (62.3-73.0, 56-75) and the median PSA (IQR, range) 12.7 ng/ml (6.6-31.1, 2.0-63.9). Biopsy Gleason Score ranged from 4 to 9; 11 patients (25%) received a neoadjuvant treatment. The majority of the patients had clinically locally advanced PCa (75%). We observed no intra- or perioperative complications; the highest doses absorbed from the rectum were 0.1-2 Gy. The pathological stage was: 11 pts T2, 30 pts T3, 3 pts T4; positive lymph nodes were found in 9 (20.5%) and positive surgical margins were found in 26 patients (59%). A total of 38 patients underwent postoperative RT treatment, with a median follow-up of 24 months (6-46). Rectal and urinary RT toxicity was low (G0-G2). Minor surgical complications were observed in nine patients (20.4%), including five lymphoceles (11.4%), two pelvic anastomotic strictures (Table I). Group B had a higher number of extracapsular disease >25% (Kattan’s nomograms), no inflammatory bowel disease. During surgery, the prostate was exposed with dissection of endopelvic fascia and puboprostatic ligaments. The distance between prostate and rectum was measured with ultrasound. A collimator (Mobetron, Intraop, California, USA) with diameter of 5.0-6.0 cm and an angle ‘bevel’ of 15-30° was introduced in the surgical field and delivered a dose of 10-12 Gy with 9-12 MeV. The dose was prescribed to the isodose of 90%. The volume treated included prostate, seminal vesicles and periprostatic area. RP was then completed and an extended lymphadenectomy was performed. Mean IORT time was 30 minutes. Postoperative RT treatment 3 months after IORT was planned for 38/44 patients. A box technique (Foton X 6-15 MV) was used and a dose of 50 Gy, in fractions of 2 Gy/day, was delivered. Hormonal therapy (HT) was prescribed when indicated.

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Conclusion: The IORT procedure during RP represents a safe procedure, with acceptable surgical time and minimal toxicity for patients with locally advanced PCa. A larger number of cases and a longer follow-up is needed to confirm these findings and to assess long-term side-effects and biochemical control.

References

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IS INTRAOPERATIVE RADIATION THERAPY AND RADICAL PROSTATECTOMY BETTER THAN ADJUVANT RADIATION THERAPY AFTER RADICAL PROSTATECTOMY FOR CLINICALLY LOCALLY ADVANCED PROSTATE CANCER?

Giansilvio Marchioro1, Marco Krengli2, Matteo Vidalì3, Alessandro Volpe1, Roberto Tarabuzzi1, Michele Billia1, Stefano Zaramella1, Andrea Ballarè2, Pina Apicella2, Simone Crivellaro4, Bruno Frei4 and Carlo Terrone1

1Department of Urology, and 2Department of Radiotherapy Medicine, Maggiore della Carità Hospital, University of Eastern Piedmont, Novara, Italy; 3Clinical Chemistry Unit, University of Eastern Piedmont, Novara, Italy; 4Department of Urology, Santa Maria della Misericordia Hospital, University of Udine, Udine, Italy

Background: Radical prostatectomy (RP) for locally advanced prostate cancer (PCa) is frequently combined with adjuvant radiotherapy (ART) and hormonal therapy (HT) in a multimodal approach. Intraoperative radiotherapy (IORT) is also under assessment for locally advanced PCa. We retrospectively analysed our experience with RP and IORT for locally advanced PCa and compared the results with a similar group of patients who underwent RP and ART in the 5 years before the introduction of IORT at our centre.

Patients and Methods: Between November 2005 and November 2008, 45 patients with locally advanced PCa underwent RP+IORT (Group A). After exposure of the anterior face of the prostate, a dose of 12 Gy was given by a dedicated linear accelerator (MOBETRON) and then RP was completed. If definitive pathology confirmed advanced disease, postoperative RT (45 Gy) was prescribed. Group A was compared with 50 patients who underwent RP and ART (Group B) before November 2005.

Results: Significant differences between Group a and B were observed only for mean operating time (IORT adds 30 minutes on average to the procedure) and incidence of anastomotic strictures (Table I). Group B had a higher number of pT3a tumours and a lower number of pT2 tumours compared to Group A. Lymphocele occurred in 4/45 patients (8%) in Group a and in 5/50 (10%) in Group B; one pelvic haematoma occurred in both groups. No significant differences were observed for hospital stay and catheterization time. In
Group A, 3 patients experienced grade 0-2 rectal toxicity (diarrhoea and tenesmus), while 4 patients in Group B experienced these symptoms. For both groups, grade 2 urinary toxicity occurred in one patient. No significant differences have been observed for complications or recovery of urinary continence.

**Conclusion:** IORT during RP is a feasible and safe procedure, with a similar complication rate compared to RP and ART. Therefore IORT can be proposed as a treatment choice for patients with locally advanced PCa. Longer follow-up is needed to assess long-term toxicity and local tumour control with IORT.

### Table I.

<table>
<thead>
<tr>
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<th>Group a (N: 45)</th>
<th>Group B (N: 50)</th>
<th>p-Value</th>
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<tr>
<td>Neoadjuvant therapy</td>
<td>6/45 (13%)</td>
<td>6/50 (12%)</td>
<td>ns</td>
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<tr>
<td>Mean age (years)</td>
<td>67.4 (56-75)</td>
<td>66.8 (48-75)</td>
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<tr>
<td>Clinical stage</td>
<td>3T1c–1T2b–2T2c–</td>
<td>3T2a–6T2b–5T2c–</td>
<td>ns</td>
</tr>
<tr>
<td>Mean PSA at diagnosis</td>
<td>27.26 ng/ml</td>
<td>27.5 ng/ml</td>
<td>ns</td>
</tr>
<tr>
<td>Biopct GS</td>
<td>7.73 (4-9)</td>
<td>7.8 (5-9)</td>
<td>ns</td>
</tr>
<tr>
<td>Mean operative time</td>
<td>237 (min)</td>
<td>185</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean hospital stay (days)</td>
<td>4.5</td>
<td>4.5</td>
<td>ns</td>
</tr>
<tr>
<td>pT2</td>
<td>3pT2a–3pT2b–2pT2c</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>pT3a</td>
<td>5/45 (11%)</td>
<td>21/50</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>pT3b</td>
<td>20/45</td>
<td>19/50</td>
<td>ns</td>
</tr>
<tr>
<td>pT4</td>
<td>5/45</td>
<td>8/50</td>
<td>ns</td>
</tr>
<tr>
<td>Mean GS</td>
<td>8.1 (6-10)</td>
<td>7.64 (5-10)</td>
<td>ns</td>
</tr>
<tr>
<td>Positive margins</td>
<td>26/45 (57 %)</td>
<td>30/50 (60%)</td>
<td>ns</td>
</tr>
<tr>
<td>Anastomosis structure</td>
<td>4/45 (8%)</td>
<td>8/50 (16%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**References**


**107 RADICAL PROSTATECTOMY FOR PATIENTS WITH CLINICALLY LOCALLY ADVANCED PROSTATE CANCER: SURVIVAL ANALYSIS AND ONCOLOGICAL OUTCOME**

Giansilvio Marchioro¹, Alessandro Volpe¹, Matteo Vidalib, Gloria Maso¹, Stefano Zaramella¹ Roberto Tarabuzzi¹, Francesco Varvellov, Monica Zaccheroil, Elisa De Lorenzis¹, Bruno Frea³ and Carlo Terrone¹

¹Department of Urology, Maggiore della Carità Hospital, University of Eastern Piedmont, Novara, Italy; ²Clinical Chemistry Unit, University of Eastern Piedmont, Novara, Italy; ³Department of Urology, Santa Maria della Misericordia Hospital, University of Udine, Udine, Italy

**Aim:** To report the outcomes of a single institutional study on 98 patients with clinically locally advanced prostate cancer (Pca) and prostate-specific antigen (PSA) ≥20 ng/ml who underwent radical prostatectomy (RP) and pelvic lymphadenectomy (PNLD).

**Patients and Methods:** We performed a retrospective review of PCA patients who had initial PSA values above 20 ng/ml and were treated with RP between 1999 and 2005. Biochemical recurrence was defined as a double rise in PSA levels over 0.2 ng/ml after RP. Adjuvant or salvage radiotherapy (RT) or hormonal therapy (HT) were indicated according to institutional protocols. Overall (OS), cancer-specific (CSS), clinical progression-free (CPFS), and biochemical progression-free survival (BRFS) were calculated for the entire cohort and select subgroups using the Kaplan-Meier method with log-rank test and Cox multivariate analysis.

**Results:** The mean patient age was 66 (range IQR 61.8-71) years. Mean PSA was 30.4 (range IQR 24.4-45) ng/ml. PCa was clinically locally advanced in 59% of cases. At pathology, locally advanced disease was found in 72.4% of cases (27.6% pT3a, 30.6% pT3b, and 14.3% pT4). Positive surgical margins and lymph node involvement were observed in 68% and 23% of cases respectively. Mean follow-up was 65.3 (range IQR 46.0-96.5) months. Adjuvant RT and HT were administered in 51% and 69% of patients. OS, CSS and BRFS at 5 and 10 years were 85% (55%), 93% (71%) and 53% (36%), respectively. We did not find any significant predictor for OS, CSS and CPFS. Gleason score at biopsy, but not PSA, was strongly associated with a worse CSS. Interestingly, we observed that only pathological stage, seminal vesicle invasion and PSA at diagnosis were independent predictors of BRFS.

**Conclusion:** RP is an effective first step in a multimodality approach for locally advanced PCa, with
convincing cancer-related outcomes. Patients with PSA ≥20 ng/ml should be considered for an aggressive approach, starting with radical surgery. Most patients need adjuvant HT or RT. This study confirms that RP should be considered as the first step in a multimodality approach for clinically locally advanced PCa.

References

108
DO PATIENTS TREATED WITH RADICAL PROSTATECTOMY FOR LOCALLY ADVANCED PROSTATE CANCER AND PSA >50 ng/ml HAVE A WORSE PROGNOSIS THAN PATIENTS WITH PSA>20 ng/ml?

Giansilvio Marchioro1, Gloria Maso1, Matteo Vidalii2, Alessandro Volpe1, Roberto Tarabuzzi1, Stefano Zaramella1, Monica Zucchero1, Elisa De Lorenzis1, Simone Crivellaro3, Bruno Frea3 and Carlo Terrone1

1Department of Urology, Maggiore della Carità Hospital, University of Eastern Piedmont, Novara, Italy; 2Clinical Chemistry Unit, University of Eastern Piedmont, Novara, Italy; 3Department of Urology, Santa Maria della Misericordia Hospital, University of Udine, Udine, Italy

Aim: To report the outcomes of a single institutional study on 98 pts with clinically locally advanced prostate cancer (PCA) and prostate-specific antigen (PSA) ≥20 ng/ml who underwent radical prostatectomy (RP) and pelvic lymphadenectomy (PNLD).

Patients and Methods: We performed a retrospective review of PCA patients who had initial PSA values above 20 ng/ml (Group A), treated with RP between 1999 and 2005. Overall (OS), cancer specific (CSS), clinical progression free (CPFS), and biochemical recurrence free survival (BRFS) of these patients were compared with those of other patients who had initial PSA values above 50 ng/ml (Group B). Biochemical recurrence was defined as a double rise in PSA levels over 0.2 ng/ml after RP. Adjuvant or salvage radiotherapy (RT) or hormonal therapy (HT) were indicated according to institutional protocols. OS, CSS, CPFS and BRFS were calculated for the entire cohort and select subGroups using the Kaplan-Meier method with log-rank test and Cox multivariate analysis.

Results: The mean age was 66 (range IQR 61.8-71) years, with no significant differences between Group A and B. Mean PSA was 30.4 (range IQR 24.4-45) ng/ml. No differences between the two groups were observed for pathological stage, positive surgical margins and lymph node involvement. Mean pathological Gleason score was significantly higher for Group B (p=0.005). Mean follow-up was 65.3 (range IQR 46.0-96.5) months. Table I describes OS, CSS and BRFS at 5 and 10 years for Group A and B. Only BRFS was significantly higher for Group a vs. Group B.

Table I.

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-Year survival</td>
<td>10-Year survival</td>
<td>5-Year survival</td>
<td>10-Year survival</td>
</tr>
<tr>
<td>OS</td>
<td>86%</td>
<td>71%</td>
<td>83%</td>
</tr>
<tr>
<td>CSS</td>
<td>92%</td>
<td>92%</td>
<td>89%</td>
</tr>
<tr>
<td>BRFS</td>
<td>63%</td>
<td>58%</td>
<td>20%</td>
</tr>
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</table>

OS, overall survival; CSS, cancer specific survival; BRFS, biochemical recurrence-free survival.

Conclusion: RP provided good results in cT3-4 disease. PSA value at diagnosis in our series could not discriminate OSS and CSS, while BRFS was lower for patients with a PSA above 50 ng/ml. This study confirms that RP should be considered as the first step in a multimodality approach for locally advanced PC independently on PSA value at diagnosis.

References
GILBERT'S SYNDROME, UGT1A1 *28 AND BLADDER CANCER

Background: UDP-glucuronosyltransferases 1A (UGT1A) are detoxifying enzymes which convert endogenous substrates, dietary constituents and potential carcinogens to inactive hydrophilic glucuronides. UGT1A may be important to protect cells from cancer in organs naturally exposed to potential carcinogens such as smoking and diet derivatives. Recent study showed that UGTs were highly expressed on the surfaces of normal bladder and a general protein down-regulation associated with neoplastic cells. Gilbert's syndrome causes mild, unconjugated hyperbilirubinemia. The basis of the disorder is a 70% reduction in bilirubin glucuronidation catalyzed by UGT1A, which is the result of a homozygous TA insertion (TA7) into the promoter region of the UGT1A gene (UGT1A1*28).

Patients and Methods: UGT1A1 genotypes were determined from the peripheral venous blood of 92 patients with bladder cancer (TCC) and 109 healthy controls (benign prostatic hyperplasia, urolithiasis). The mean age of the cases was 72 (range 36-92) years, the mean age of healthy controls was 68 (range 55-85) years. Of the 92 patients with bladder cancer, 73 patients (80%) have been diagnosed with non-muscle-invasive bladder cancer, 19 patients (20%) with muscle-invasive bladder cancer; 32 patients (35%) had low-grade disease and 60 patients (65%) high-grade disease.

Results: There were no associations between TA genotype and the risk of bladder cancer (TA6/TA6 vs. 43; TA6/TA7 39 vs. 48; TA7/TA7 14 vs. 17, patients vs. controls). No differences were observed when smoking patients were considered.

Conclusion: There were no relevant associations between the UGT1A*28 genotype and increased bladder cancer risk.

References

STEREOTACTIC HYPOFRACTIONATED BODY RADIOTHERAPY: AN EMERGING TREATMENT APPROACH FOR CLINICALLY LOCALIZED PROSTATE CANCER

Background: The low alpha/beta ratio for prostate cancer suggests a good response to hypofractionation. Experimental data, high-dose rate (HDR) brachytherapy, and some experiences of hypofractionated EBRT have already shown high tumour control rates while maintaining an equivalent dose to normal tissues for late effects and reducing acute effects. Cyberknife is currently being used as a monotherapy treatment for early-stage prostate cancer, and because of similar conformity and dose fractionation to HDR brachytherapy, local control and toxicity rates are expected to be similar. We tested this hypothesis in men with clinically localized prostate cancer.

Patients and Methods: Between July 2007 to December 2009, 51 patients aged 60-83 years, with low and selected intermediate risk prostate cancer were treated with Cyberknife stereotactic radiosurgery as primary therapy at our institution. The treatment regimen consists of a total dose of 38 Gy delivered at 9.5 Gy per fraction, with > 95% of the planning treatment volume (PTV) encompassed within the prescription isodose volume. Three gold fiducial markers were placed in the prostate gland by the treating urologist using transrectal ultrasound guidance, and to allow fiducial stabilization and resolution of swelling, prostate planning study was performed one week after fiducial implantation. Axial CT images and MRI T1-T2 sequences were acquired and fused to accurately differentiate the prostate and the organ at risk. The PTV included the GTV expanded by 3 mm posteriorly and 5 mm in all other directions. Patients were seen in follow up by the radiation oncologists or urologist 10 days post-treatment, 1 month later and every 3 months for 2 years with PSA levels assessed at each follow-up. Self-administered questionnaire, such as the International prostatic Symptom Score and the International Index of Erectile Function, was used to better
define urinary function and sexual activities. Toxicity analysis was performed using the Radiation therapy oncology Group/European Organization for Research and Treatment of Cancer (RTOG-EORTC) acute and late radiation morbidity scoring system.

Results: All patients were placed on 3-blockade medication at the initiation of their Cyberknife treatment. IPSS scores increased over the first month of treatment but return to baseline by four months. Acute side effects were generally mild and resolved shortly after treatment. No patients experienced urinary retention or developed urethral stricture to date. One patients, with prior TURP, experienced incontinence. Rectal bleeding was observed in 2 patients.

The patterns of PSA response, show a gradual decline with a psa nadir below 1.0 ng.ml after 12 months. To date all patients are alive, no patients, except one who developed distant metastases, has experienced a PSA failure.

Conclusion: Early clinical results are encouraging and we conclude that Cyberknife robotic radiosurgery is a feasible and an emerging non invasive treatment approach to deliver Hypofractionated radiotherapy for localized prostate cancer. Additional follow up is required to better evaluated potential late toxicity and long-term PSA outcomes.

References

112 RARE CASE OF ISOLATED BLADDER NEUROFIBROMA

Roberto Giulianelli, Luca Mavilla, Luca Albanesi, Francesco Attisani, Stefano Brunori, Barbara Cristina Gentile, Stefano Nardoni, Francesco Pisanti and Giorgio Vincenti

Casa di Cura Villa Tiberia, via Emilio Praga 26, Roma, Italy

Neoplastic cells were spindle-shaped, with pyknotic irregular nucleus, eosinophilic cytoplasm and ill-defined cellular border. Intercellular matrix was clear, loose and included sporadic inflammatory cells (mastcells, foamy histiocytes, mature lymphocytes, etc.). There were no deposits of myxoid substance (PAS -). Neoplastic cells showed strong positive reaction for immunohistochemistry staining with S-100 protein and negative reaction with smooth muscle actin and with CD68. Moreover, the lesion showed low proliferation rate as evaluated by Ki-67 (~5% of neoplastic cells).

Results: These pathological findings refer to a neurofibroma of the bladder wall, being histiocytic, myxoid and/or smooth muscle origin of the lesion were excluded regarding the immunohistochemical data. No malignant transformation, nor recurrence, nor other organ involvement were observed during a follow-up of 1 year.

Conclusion: Neurofibromatosis is a rare systemic disease, and bladder involvement is rarer. The final diagnosis is pathological and immunohistochemical, and the treatment is usually conservative.

113 THE ROLE OF POSITIVE SECTION MARGINS IN PATIENTS WITH HIGH RISK PROSTATE CANCER TREATED BY RADICAL PROSTATECTOMY – PROSPECTIVE ANALYSIS OF 566 PATIENTS


Aim: To evaluate the extent of positive surgical margins (PSM) and their influence on progression and survival in high-risk prostate cancer (PCa).

Patients and Methods: Prospective single-centre (4) evaluation of 566 consecutive men with high risk PCa (PSA>20, cT3-4, GS>8) who underwent wide RP+pLA. Localization and number of PSMs were evaluated prospectively. The number of PSMs were coded into 4 groups (none, 1, 2 and >3 PSM). Kaplan-Meier method with log-rank test and the multivariate Cox regression analysis were used for the outcome analysis.

Results: The overall rate of PSM was 52.1% in Cox multivariate analysis, surgical margin status was an independent prognostic factor in cancer-related death (HR 1.40 (95% CI 1.0633 to 1.8555) and in overall survival (HR 1.22 (95% CI 1.0110 to 1.4730). It lost its significant as independent prognostic factor in biochemical (HR 1.14 (95% CI 0.9654 to 1.3544) and clinical recurrence (HR 1.18 (95% CI 0.9620 to 1.4689).

Table. (abstract 113)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No SM</th>
<th>1 PSM</th>
<th>2 PSM</th>
<th>3 PSM</th>
</tr>
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<tbody>
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<td>No. of patients</td>
<td>265</td>
<td>166</td>
<td>50</td>
<td>85</td>
</tr>
<tr>
<td>Ø Age, years (+/–SD)</td>
<td>67 (6.2)</td>
<td>67 (6.3)</td>
<td>68 (5.9)</td>
<td>66 (6.3)</td>
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<td>Ø PSA (ng/ml) (+/–SD)</td>
<td>&lt;0.05</td>
<td>27.06 (26.2)</td>
<td>35.5 (54.0)</td>
<td>40.4 (34.5)</td>
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<td>4.3%</td>
<td>8%</td>
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<td>8%</td>
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<td>pT3a</td>
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<td>42.8%</td>
<td>28%</td>
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<td>40.9%</td>
<td>48%</td>
<td>41.2%</td>
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<tr>
<td>pT4</td>
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<td>12.0%</td>
<td>16%</td>
<td>49.4%</td>
</tr>
<tr>
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<td>13.9%</td>
<td>33.7%</td>
<td>46%</td>
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<td>Adjuvant RT</td>
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<td>3.4%</td>
<td>10.2%</td>
<td>12%</td>
</tr>
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<td>Adjuvant HT</td>
<td>&lt;0.0001</td>
<td>63%</td>
<td>89.7%</td>
<td>92%</td>
</tr>
<tr>
<td>Projected survival (years)</td>
<td>5</td>
<td>10</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Freedom from biochemical recurrence</td>
<td>0.0912</td>
<td>81%</td>
<td>72%</td>
<td>68%</td>
</tr>
<tr>
<td>Freedom from clinical recurrence</td>
<td>&lt;0.0001</td>
<td>92%</td>
<td>89%</td>
<td>86%</td>
</tr>
<tr>
<td>Cancer-specific survival</td>
<td>&lt;0.0001</td>
<td>98%</td>
<td>96%</td>
<td>98%</td>
</tr>
<tr>
<td>Overall survival</td>
<td>0.0331</td>
<td>89%</td>
<td>80%</td>
<td>86%</td>
</tr>
</tbody>
</table>
Conclusion: Patients with high-risk localized prostate cancer have a significant risk for PSM after RP. PSM enhances the risk of death and is an independent predictor of cancer-related death and death from other causes.

References

114 PREDICTING PROSTATE CANCER-SPECIFIC OUTCOME AMONG MEN WITH PSA ≥20 ng/ml AND MULTIPLE UNFAVOURABLE RISK FACTORS: A MULTI-INSTITUTIONAL OUTCOME STUDY OF 712 PATIENTS


1Department of Urology and Pediatric Urology, University Hospital Würzburg, Germany;
2Department of Urology, University of Turin, Turin, Italy;
3Department of Urology, and 4Institute for Biostatistics and Statistical Bioinformatics, University Hospitals Leuven, Leuven, Belgium;
4Department of Urology, University of Piemonte Orientale, Novara, Italy;
5Department of Urology, Université Catholique De Louvain, Brussels, Belgium;
6Department of Urology, Community Hospital Karlsruhe, Karlsruhe, Germany

Background and Aim: The value of radical prostatectomy (RP) as an approach for high-risk prostate cancer (PCa) patients is highly controversial. We aimed to distinguish outcome among patients with high-risk PCa based on PSA >20 ng/ml treated by RP using a system that takes into account the number of high risk factors. Analysis was carried out of data for 712 patients from 6 European centres.

Patients and Methods: We retrospectively analysed our institutional radical prostatectomy databases and included all consecutive patients with a preoperative PSA >20 ng/ml and a negative bone scan. Clinical node positive disease in the pelvic area was not considered an exclusion criterion. All patients underwent a wide radical prostaticectomy with pelvic lymph node dissection. Adjuvant or salvage treatment was administered according to institutional protocols. Patients were followed-up at regular time intervals with PSA testing. Imaging studies were performed at the time of biochemical failure or at symptoms. The entire cohort and subgroups were analysed to determine whether an increasing number of unfavourable high risk factors (PSA >20 ng/ml, clinical stage >T3, Gleason score >8) was associated with the histopathological outcome, biochemical progression (BP), clinical failure (CF), cancer-related death (CRD) and overall survival (OS) using the Cox multivariable analysis and Kaplan-Meier method.

Results: Between 1987 and 2005, 712 patients with PSA >20 ng/ml underwent a wide RP and bilateral pelvic lymphadenectomy at 6 European centres. Mean follow-up was 78.7 years. Of the study cohort, 48.5% had isolated PSA>20, 31.9% PSA>20 and clinical stage >T2, 7.3% PSA>20 and Gleason score >7; 12.4% had all three high-risk factors. The number of high risk factors was found to be significantly associated with histopathological outcome (isolated PSA>20/20 ng/ml: 33% pT2, 85% pN0; all three high-risk factors: 4.5% pT2, 49%pN0, p<0.001). The biopsy Gleason score (bGS) was the strongest predictor of outcome in Cox multivariable analysis for clinical progression (HR 1.345 (95% CI 1.147-1.577)) and cancer-related death (HR 1.666 (95% CI 1.292-2.147)). Men with GS <7 were unlikely to die from prostate CRD (<9% at 10-years) while GS >8 was associated with significantly higher CRD (35% at 10-years).

Conclusion: PCa with PSA >20 ng/ml represents a heterogeneous group. Men with Gleason score <7 are at minimal risk of dying from tumour-related causes. Patients with high-grade tumours or all three high-risk parameters are at an increased risk of CRD and should be considered for clinical trials to assess whether survival is prolonged with the addition of novel agents to current standard of care.

References
115
NEW PERINEAL TENSIVE TRANSOBTURATOR TAPE (T-TOT) FOR POST-PROSTATECTOMY URINARY INCONTINENCE

Andrea Ceresoli, Davide Abed El Rahman, Alberto Cazzaniga, Gaetano Grasso Macola and Andrea Guarneri

Istituto di Urologia, Ospedale San Giuseppe, Gruppo Multimedica, via San Vittore 12, Milano (Università Degli Studi Di Milano), Italy

Bulbourethral transobturator sling data from other investigators report a success rate from 53% to 85%. Since the degree of sling tension and its adjustment seems to be important for achieving complete urinary continence, we present results on our first consecutive 12 patients, with mild post prostatectomy stress urinary incontinence (defined as less than 500 ml) who underwent a new perineal tensive transobturator polypropylene tape (T-TOT) procedure at our institution.

Results: Pre-operative mean ALPP was 23 cmH2O (SD +/- 10), RLPP was 24 cmH2O (SD +/- 6) and the mean pad test was 324 g (SD +/- 176). The overall success rate was 58.3% (7 patients) complete responders (CR), 33.3% (4 patients) partial responders (PR) and 8.33% (1 patient) failure. No significant urodynamic outlet obstruction nor urethral erosion had occurred at 9-months’ follow-up. Postoperative ICIQ-SF questionnaire score significantly dropped from 11 to 3 (p<0.01).

Conclusion: Perineal T-TOT showed safe and effective results similar to conventional bulbourethral transobturator male slings without obstructive symptoms despite maximal tension being used. Longer prospective follow-up is needed to determine the long-term efficacy of this procedure and the effective preservation from urethral erosion.

116
URINARY PROTEOMICS IN RENAL CELL CANCER BY MALDI-TOF MASS SPECTROMETRY: A PRELIMINARY CONTROLLED STUDY

Mario Gardi1, Matteo Vittori1, Rosanna Inzitari2, Chiara Fanali2, Federica Iavarone2, Andrea Volpe1, Emilio Sacco1, Francesco Pinto1, Salvatore Recupero1, Antonio Destito1, Massimo Castagnola2 and Pierfrancesco Bassi1

1Urology Department, University Hospital 'A. Gemelli', Catholic University, Rome, Italy; 2Institute of Biochemistry and Clinical Biochemistry, Catholic University, Rome, Italy

Background: Renal cell cancer (RCC) substantially lacks biomarkers to assist clinicians in diagnosis, prognosis and response to therapy. Moreover, recent studies have demonstrated that the urinary proteome or peptidome is more complex than expected. The aim of this study was to compare the proteomic profile of urine from RCC patients and healthy controls defined by mass spectrometry (MS) analysis focused on small and medium size peptides (1000-10000 Da).

Patients and Methods: Urine from 36 RCC patients and 26 healthy controls matched by age and sex were collected between June 2008 and May 2009. People with chronic renal failure or abnormal urination or diagnosis of any other active tumour or a history of any other tumour treated during the last three years were excluded. All samples were purified with the ClinProt® method by functionalized magnetic beads (MB-HIC, magnetic beads based hydrophobic interaction chromatography) and then analyzed by matrix assisted laser desorption ionization – time of flight (MALDI-TOF) MS. Samples from each group were randomly divided into two sub-groups: A training set consisting of 20 controls and 20 RCC patients, for pattern recognition and cross validation, and a test set of 6 healthy controls and 16 RCC patients for pattern validation. Statistical analysis and pattern recognition were performed using the ClinProt Tools® 2.0 software, performing detection of significant peaks, spectra comparison and multivariate algorithms to generate patterns.

Results: Using the training set, we detected about 80 differentially expressed peaks. Sixteen were found to be significantly differentially expressed. Through two multivariate algorithms and interactive analysis, we selected a pattern of three signals able to distinguish RCC patients from controls: peak A= 1913.01 +/- 5 Da, found to be underexpressed in RCC patients, peak B= 2041.22 +/- 5 Da and peak C= 3725.91 +/- 8 Da, found to be overexpressed in RCC patients. The combination of the three peaks allowed to separate the two populations of the test set with a sensibility value of 93.4% and a specificity value of 71.4%.

Conclusion: RCC patients have a different urinary subproteome in the range of the small peptides compared to healthy controls. The identified molecular masses represent potential RCC urinary biomarkers and need in-depth analysis in order to define their amino acid sequences.

117
LOCAL RECURRENCE AFTER SIMPLE TUMOUR ENucleATION FOR RENAL CELL CARCINOMA: RESULTS OF A PROSPECTIVE SINGLE-CENTRE STUDY

Andrea Minervini1, Agostino Tuccio1, Giampaolo Siena1, Gianni Vittori1, Maria Rosaria Raspolli2, Claudio di Cristofano3, Alberto Lapini1, Sergio Serni1 and Marco Carini1

Departments of 1Urology and 2Pathology, University of Florence, Careggi Hospital, Florence, Italy;
Case Report: A 67-year-old woman was referred to the Department of Urology for left flank pain developed seven days after hysterectomy for uterine leiomyomatosis. The patient had no history of previous flank trauma, renal stone or upper urinary tract infections. Physical examination was unremarkable, with only minimal flank pain at Giordano manoeuvre; body temperature was 37°C, blood pressure was 120/75 mmHg, white cell count was within the limits (9×10⁹ white blood cells/l); renal and liver functions were normal (serum creatinine 0.9 mg/dl, total bilirubin 0.8 mg/dl).

After ultrasound and plain abdomen film and, a severe left hydronephrosis was documented, with no sign of ureteral stones or pelvic masses. The diagnosis was hyalogenic (post-surgical) obstruction of the distal portion of the ureter. The plain abdomen film incidentally discovered a 3 cm calcified ring on the left renal shadow (Figure 1 left). Percutaneous pyelography confirmed the hydronephrosis, and showed no relationship between the calcified mass and the collecting system (Figure 1 right). A 3-dimensional CT scan revealed a 3 cm round hollow mass with calcified walls located in front of the anterior renal surface. The lesion had no connection with the renal pelvis (Figure 2 left) but was firmly related to the renal artery, and was compatible with calcified renal artery aneurysm (RAA) (Figure 2 right). The patient was treated with ureteral reimplantation, with an open access performed on the suture of the previous surgical approach. A direct ureteral reimplantation on the upper bladder wall was carried out, with psoas hitch and double J urethral stenting. At the 1 month follow-up visit, there was a complete recovery of the obstruction. The vascular surgeon suggested a watchful waiting by monitoring blood pressure, renal function, and imaging every 6 months.

RAA are rare, with an estimated incidence below 1%. Hypertension and fibro-muscular disease of the renal artery are the leading classes of risk (1). There is no significant difference in side presentation (right side in 43%, left in 36% and 21% bilateral). Aneurysm usually involves the main renal artery or the primary branches. Mean size at diagnosis ranges from 0.5 to 8 cm, with a mean diameter of 2.1 cm. Degenerative (arteriosclerosis, fibrodysplasia), inflammatory (arteritis) or traumatic diseases, including iatrogenic damages after kidney puncture (1), may cause RAA. RAA can be classified into 4 categories: 1) true macroaneurysm; 2) aneurysmal dissections; 3) fusiform microaneurysmal dilations; and 4) microaneurysm resulting from arteritis (2). They are usually asymptomatic, and serum creatinine levels are mostly within normal range at diagnosis. Complications, including renovascular hypertension, renal embolization...
with infarction, thrombosis or dissection, and arteriovenous fistula, (1) are rarely reported. The diagnosis has been recently increased by the spreading use of imaging techniques (3). Conventional renal angiography represents the gold standard in the detection of renal aneurysms, although spiral CT renal angiography with three-dimensional reconstruction (3D-CT) adds the benefits of being quicker, more cost-effective, and non-invasive. Moreover, the use of a 3D-CT workstation allows accurate treatment planning, especially for endovascular procedures (4). Management options include observation, trans-catheter-occlusion or surgical intervention. The indications for surgery include: symptomatic or enlarging aneurysms, renal embolization, aneurysms in pregnant females or those considering pregnancy, renovascular hypertension, aneurysms >2.5 cm (5).

References

Figure 1. Left: Plain abdomen film showing a left 3 cm calcified ring on the left renal shadow. Right: Pyelography demonstrating no relationships of the calcified mass with the collecting system.

Figure 2. Left: CT scan showing a calcified round mass facing anterior renal surface. Right: 3-Dimensional CT reconstruction showing the relationship with renal artery, compatible with calcified renal artery aneurysm.

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CO₂ LASER EXCISION OF SUPERFICIAL CANCER OF THE PENIS: TWO YEARS’ EXPERIENCE

Tullio Torelli, Mario Catanzaro, Nicola Nicolai, Luigi Piva, Davide Biasoni, Angelo Milani, Andrea Necchi, Silvia Stagni and Roberto Salvioni

U.O. Urologia, Fondazione IRCCS Istituto Nazionale Tumori, via Venezian 1, 20133 Milano, Italy

Background: Partial or total penile amputation for localized cancer has excellent local tumour control but heavily affects psychosexual function. Laser treatment has been shown to have the same cure rates (1) but superior cosmetic and functional results (2). In this report, we present our results obtained with dioxide laser (CO₂) ablation of superficial penis cancer from July 2007 to October 2009.

Patients and Methods: From July 2007 to October 2009, we treated patient with spinocellular cancer ≤pT1 with CO₂ laser ablation. If we observed a bulky, exophytic and well-differentiated cancer, neoadjuvant vinblastine, bleomicine and methotrexate treatment was prescribed (VBM; up to 12 weekly treatments) for tumour downsizing. Mean age was 58.7 (range 33-81) years. Under local anesthesia, we performed laser resection of lateral and deep margins (with excision depth 2-2.5 mm in lamina propria) and a adjunctive vaporization of the wound bed to seal small blood and lymphatic vessels. The wound bed was always healed by second intention. In accordance to disease size, its location and mono or plurifocality, we performed small laser ablation up to complete glans decortication. If needed, circumcision was performed.

Results: In 36 patients, 6 neoadjuvant VBM were performed and there were 5 recurrences: overall there were 27 simple laser ablations (single and small lesions), 6 wide ablations (large or plurifocal lesions), 8 circumcisions (prepuce). After treatment, no major adverse events were recorded. On the average, there was local pain for three weeks, but after five weeks no clinical problems were claimed and the mucosal recovery was quite
complete. Histological reports in 30 previously untreated patients were 24 CIS, 5 pT1G1, 1pT2G2. Six VBM-pretreated patients had, before therapy, well-differentiated (4 pts) and moderately differentiated tumours (2 pts). After therapy, their histology was: 4 NED, 1 CIS and 1 pT2G1. In 5 relapsed patients, the same histological pattern (3 pT1G1 and 2 CIS) was confirmed. Mean follow-up was 11.6 (range 2-27) months and the mean relapse time was 7.8 (range 5-12) months. Only 2 patients needed a partial penectomy (pT2), 1 after CO2 laser ablation (pT2 G2 at the initial diagnosis) and 1 after an insufficient VBM response. Only one patient, with previous plurifocal CIS, underwent bilateral inguinal node dissections for metastatic disease at left 3 inguinal lymph nodes. Up today, all the patients are alive with no evidence of disease.

Conclusion: Our experience in the treatment of superficial penile cancer with the dioxide laser treatment shows that we had a good patient selection and an effective disease control with low relapse rate (13.9%, 5/36), 2 partial penectomy (5.6%, 2/36) and 1 metastatic disease (2.7%, 1/36) with no major adverse events and good functional results. The good results may be amplified by neoadjuvant VBM chemotherapy, in large, exophytic tumours. To avoid failures, appropriate patient selection and a close follow-up are mandatory because invasive cancer is not treated successfully by laser as confirmed by other authors (3) and the mean relapse time is less than one year.

References

ARE THE EAU GUIDELINES ON PROSTATE CANCER FOLLOWED BY ITALIAN UROLOGISTS? RESULTS FROM THE M.I.R.R.O.R. (MULTICENTRE ITALIAN REPORT ON RADICAL PROSTATECTOMY OUTCOMES AND RESEARCH) GROUP

Alchiede Simonato1, Virginia Varca1, Mauro Gacci2, Marco Carini3, Giulio Nicita4, Andrea Decensi5, Aldo Franco De Rose1, Massimo Maffezzini3, Ottavio de Corbelli4, Roberto Salvioni5 Andrea Briganti6, Vincenzo Mirone2 and Giogio Carmignani3

1Urology Clinic, “L. Giuliani”, Genova, Italy;
2Department of Urology, University of Florence, Italy;
3Department of Oncology, Ospedali Galliera Genova, Italy;
4Department of Urology, IEO Milano, Italy;
5Department of Urology, Istituto Tumori Milano, Italy;
6Department of Urology, HSR Milano, Italy;
7Department of Urology, University Federico II, Napoli, Italy

Aim: The European Association of Urology (EAU) Guideline Group for prostate cancer (PCa) prepared guidelines to help urologists assess the evidence-based management of PCa and to incorporate the guideline recommendations into their clinical practice. In the present study, we tried to evaluate if these recommendations are still complied with or not.

Patients and Methods: From October 2007 to December 2008, a large amount of data related to radical prostatectomies were prospectively recorded into the “M.I.R.R.O.R.” project (Multicentric Italian Report on Radical Prostatectomy: Outcome and Research). This study involved 136 Italian centres and gathered the data of 2425 patients. Among these patients, we took into account all examinations for preoperative staging: we correlated them with data from PSA and prostate biopsy and we then compared these data with the recommendations of the guidelines.

Results: According to the EAU guidelines, patients with PSA<20 and Gleason score<6 can avoid preoperative staging. Among the 1063 patients matching these characteristics, 53.34% underwent examinations for T-staging, 51.27% for N-staging and 71.21% for M-staging. In addition, patients with PSA <10 and Gleason score <6 could avoid lymphadenectomy. Among these 876 patients, 74.09% underwent a lymphadenectomy and about 2% were pN+.

Conclusion: The M.I.R.R.O.R. project data seem to show that the EAU guidelines are only partially followed by Italian urologists at present.

121 THERMO-CHEMOTHERAPY FOR INTERMEDIATE OR HIGH-RISK RECURRENT NON MUSCLE-INVASIVE BLADDER CANCER PATIENTS AFTER FIRST-LINE THERAPY FAILURE


Urology, Catholic University Medical School, Rome, Italy

Background: In the case of refractory urinary bladder neoplasm, cystectomy is the treatment of choice and the gold standard. Combining thermal energy and chemotherapy instillation offers ancancer advantages over chemotherapy instillation alone to prevent or delay tumour recurrence or progression. Clear synergistic effect of
mitomycin-C (MMC) and hyperthermia was demonstrated in four human bladder cancer cell lines. Cytostatic agent uptake by malignant cells and its intracellular distribution are improved by increased cellular permeability. Furthermore, drug metabolism and reaction with DNA is increased and DNA repair is inhibited. The Synergo unit SB-TS101 has been devised to deliver local bladder hyperthermia with concomitant intravesical chemotherapy as a prophylactic or ablative therapy for STCCB. Thermochemotherapy (MMC/hyperthermia) has proven to be more effective than MMC alone for patients with Ta-1 G1-3 in comparative studies with ablative as well as prophylactic intent.

**Patients and Methods:** Between January 2006 and December 2009, 24 patients (mean age: 62.6 years) were enrolled in our department. Patients had recurrent stage carcinoma in situ (CIS), Ta and T1, grade G1 to G3 non muscle invasive bladder cancer (NMIBC) and were non responders, previously treated with chemotherapeutic or immunotherapeutic drugs; 5 were treated with MMC and 19 were treated with bacillus Calmette-Guerin (BCG). All patients were required to have intermediate or high-risk SB-TCC according to the European Association of Urology (EAU) criteria. Based on the goal of treatment, patients were divided into two therapeutic groups: prophylactic and ablative. The prophylactic protocol included six weekly sessions followed by four to six monthly sessions to complete a total of 12 sessions. The ablative protocol consisted of 8 weekly sessions followed by 6 monthly sessions. A cystoscopy was recommended after the sixth weekly session to assess tumour response. If an inadequate response was observed (<50% reduction of initial tumour size), the patient was classified as a non-responder and was referred to other forms of therapy. Patients that completed treatment and became tumour free underwent 6 additional monthly sessions.

**Results:** Twenty (16 males and 4 females) out of twenty-three patients enrolled were evaluable. Eight were treated with a prophylactic protocol and twelve with ablative. In the ablative group, five patients (42%) were disease free, with a follow-up of 14.2 months, and six (50%) had recurrence or persistence of disease. One patient was lost at follow-up. In the prophylactic group, four (50%) patients were disease free with follow-up of 14.7 months and four (50%) had recurrence. Overall, nine patients (47%) were disease free with a follow-up of 14.7 months, while ten (53%) had recurrence or persistence of disease. Only in one patient (5%) was progression to muscle-invasive disease observed.

**Conclusion:** Intravesical thermochemotherapy may be used as an alternative treatment in patients non responders to conventional chemo-immunotherapy and in some cases could be a valid option before radical cystectomy.

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**122 PRELIMINARY RESULTS OF NEOADJUVANT APPROACH WITH INTENSIVE INTRAVESICAL MITOMYCIN C IN NON-MUSCLE-INVASIVE BLADDER CANCER**


**Background:** Intravesical chemotherapy is a universally accepted therapy in the prophylaxis of non muscle-invasive bladder cancer recurrence. The aim of this work is to verify the tolerability and the preliminary clinical results of intensive intravesical instillations of mitomycin C (MMC) as a neoadjuvant regimen.

**Patients and Methods:** From November 2007 to May 2009, 26 consecutive patients with a history of low-stage/grade tumour and a long recurrence-free time, with endoscopic diagnosis of single or multiple papillary neoplasm with maximum diameter below 1 cm at the time of engagement were enrolled. Five patients were not evaluable and 1 patients was lost at follow-up. The mean age of the patients was 66.8 years. Forty mg of MMC were instilled in the bladder three times a week for two weeks as an outpatient regimen. The evaluable patients completed the treatment. The mean follow-up was 5.5 months. Toxicity was evaluated according to WHO Common Toxicity Criteria, Version 3.0. Endoscopic examination was carried out before the scheduled transurethral resection at the end of treatment, with voiding and washing cytological examination and biopsy of all suspicious lesions.

**Results:** The adverse events seen were negligible. Nine out of 20 patients (42.8%) were negative at endoscopy, with normal spontaneous and washing cytological examinations. No inflammatory lesions were found as a result of intensive intravesical treatment. Eleven patients (57.2%) showed persistence of disease and therefore underwent scheduled transurethral resection.

**Conclusion:** MMC is a well-known chemotherapeutical agent for intravesical therapy of superficial bladder cancer. In view of testing its activity directly on this type of neoplasm, we have begun a neoadjuvant program. No toxicity was reported. Intensive neoadjuvant intravesical instillations of MMC has shown promising activity in patients with a history of low-stage/grade and a long recurrence-free time: 9 out of 20 patients with a complete response avoided transurethral resection, while in the case of persistent disease, reduction of the number of neoplasms or maximum diameter of the largest lesion was obtained.
NEWER THERAPEUTICAL APPROACH FOR NON-MUSCLE-INVASIVE BLADDER CANCER: INTENSIVE MITOMYCIN C THERAPY


Urology, Catholic University Medical School, Rome, Italy

Background: Intravesical chemotherapy is a universally accepted therapy in the prophylaxis of non muscle-invasive bladder cancer recurrences. However, adjuvant chemotherapy has no apparent long term impact on progression and survival. The aim of this work was to verify the tolerability and the preliminary clinical results of intensive intravesical instillations of mitomycin C.

Patients and Methods: From September 2007 to September 2008, 20 consecutive patients with pathologically confirmed intermediate-risk superficial bladder cancer were enrolled after complete transurethral resection of all visible tumours. The mean age of the patients was 64.6 years. Forty mg of MMC were instilled in the bladder three times a week for two weeks as an outpatient regimen. All patients completed the treatment. Mean follow-up was 8.1 months. Local and systemic toxicity was evaluated according to WHO Common Toxicity Criteria Version 3.0. Endoscopy was scheduled 3 and 6 months from the end of treatment, with voiding and washing cytological examination, biopsy of all suspicious lesions and resection of any papillary lesion.

Results: The local adverse events seen were negligible, while no significative deviation from normal values were seen in blood counts for each patient before and after intravesical treatment. Endoscopy findings of 18 (90%) and 16 out of 20 (88.9%) patients were negative at three and six months, respectively, with normal spontaneous and washing cytological examinations. Overall, 80% of patients enrolled were disease free after at least 6 months of follow-up. No inflammatory lesions were found as a result of intensive intravesical treatment.

Conclusion: MMC is a well-known chemotherapeutical agent for intravesical therapy of non muscle-invasive bladder cancer. In view of improving its results, we intensified the cadence of instillations. No significant local or systemic toxicity were reported. Intensive intravesical instillations of MMC might also be employed as neoadjuvant treatment before transurethral resection.

NPC – A NEWER REVOLUTIONARY TEST FOR EVALUATION OF CLINICAL SERIES. BLADDER CANCER


1 Urology, Catholic University Medical School, Rome, Italy; 2 Department of Statistics and 3 Department of Electronic Engineering, University of Padua, Italy

Aim: To identify the predictive variables affecting the outcome after radical surgery for bladder cancer by newer non-parametric combination (NPC) of dependent permutation methodology.

Patients and Methods: A retrospective analysis of the anamnestic, diagnostic, pathological and postoperative variables of 1312 patients who had undergone radical cystectomy for bladder cancer in 11 Italian oncological centres was carried out using the newer NPC test. This methodology allowed any type of variable (categorical and quantitative) to be handled and takes into account the multivariate relation among variables.

Results: We found a significant prognostic predictive value (p<0.01) for tumour clinical staging, hydronephrosis, tumour pathological staging, grading, presence of carcinoma in situ, regional lymph node involvement, metastasis, corpora cavernosa invasion, vascular invasion, lymphatic invasion and prostatic invasion. Moreover, concerning the postoperative status, the disease and therapy after cystectomy and the recourse to adjuvant chemotherapy were also of prognostic significance. P-values were corrected for the multiplicity, using a closed testing procedure.

Conclusion: Using the NPC test, we detected more prognostic factors involved in the outcome of patients undergone radical surgery for bladder cancer. As a corollary, we think that this newer methodology can make a significant contribution to successful research in biomedical studies with several endpoints and we recommend it when using non-normally distributed data, missing values, high-dimensional data and small sample sizes.

MULTILOCULAR CYSTIC NEPHROMA: LAPAROSCOPIC TREATMENT

Roberto D’Ascenzo, Pietro Nupieri, Gianni Paulis, Giuseppe Orsolini, Rosaria Alvaro, Anna Crescenzi and Tommaso Brancato

1 Department of Urology, 2 Department of Pathology, Regina Apostolorum Hospital Roma, Italy; 3 Tor Vergata University of Rome, Italy
Background: Multilocular cystic nephroma is a rare benign renal tumour, which usually presents a clinical picture and radiological features not distinguishable from those of malignant renal neoplasm. Several names have been used to describe this kidney lesion, including benign multilocular cyst, multilocular renal cyst and cystic nephroma. Presenting symptoms vary with the patient’s age. The most common presenting feature in children and adults is an abdominal mass. Other symptoms include diarrhoea, fever, haematuria and anorexia. Less frequent symptoms are pain, hypertension and urinary tract infections. We report a case of unilateral cystic nephroma for which the treatment consisted of percutaneous fine-needle aspiration and cytological analysis followed by radical nephrectomy due to an uncertain cytological pattern mimicking renal cell carcinoma.

Case Report: A 44-year-old female complaining of mild gross flank pain and microhaematuria. An abdominal ultrasound showed a multilocular renal cyst with thick septa and small wall calcifications. The diagnosis was confirmed by abdominal computed tomography (8 cm middle right renal multilocular cyst with multiple septa). A needle percutaneous echo-guided aspiration was then performed. The cytological morphological analysis showed red blood cells, macrophages and epithelial cells in papillary architecture, indicative of a malignant papillary neoplasm. Because of the cyst localization and dimensions, and the results of needle aspiration, we excluded a partial nephrectomy procedure and a laparoscopic nephrectomy was performed after patient informed consent. The procedure was without complication and the patient was discharged three days later. The definitive tissue analysis integrated with immunohistochemical assays excluded the diagnosis of a malignant neoplasm, showing patterns of cystic nephroma. Multilocular cystic nephroma can occur both in children and adults. Most paediatric cases are seen in both sexes in the first 4 years of life. In adults, it occurs with a female predominance and incidence peak in the second, fifth and sixth decades. Symptoms and signs include abdominal mass with or without abdominal pain, haematuria and hypertension. Haematuria is often associated with herniation of the tumour into the renal pelvis, resulting in pressing necrosis of the overlying transitional epithelium with consequent ulceration and bleeding. In 1989, Joshi and Beckwith (1, 2) further reformulated the criteria for the diagnosis of a multilocular cyst, specifying that: (a) tumour is composed entirely of a cyst and their septa; (b) cystic nephroma is a discrete well-demarcated mass; (c) septa form the solid component and form the outlines of the cyst without expansive nodules; (d) cysts are lined by flattened, cubical, or hobnail epithelium and septa contain fibrous tissue in which well-differentiated tubules may be present. Differential diagnosis ranges from polycystic kidney, hydronephrotic kidney, nephroblastomas, Wilms’ tumour, mesoblastic nephroma to cystic renal cell carcinoma (RCC) (3). Ultrasound, dynamic computed tomography and dynamic magnetic resonance imaging cannot reliably distinguish between malignant and benign cystic tumours. Surgical intervention is the only effective method to differentiate cystic nephroma from a malignant lesion of the kidney. The diffusion of laparoscopic techniques enhances the pitfalls of the decision-making due to the uncertain pattern of imaging techniques and the evaluation of risk/benefit ratio of fine-needle aspiration and cytology to confirm the presence of a malignant lesion having evident legal consequences (4).

References

126 USE OF 3D T2-WEIGHTED MR SEQUENCES FOR THE ASSESSMENT OF NEUROVASCULAR BUNDLE CHANGES AFTER NERVE-SPARING RADICAL RETROPUBIC PROSTATECTOMY (RRP): A POTENTIAL DIAGNOSTIC TOOL FOR OPTIMAL MANAGEMENT OF ERECTILE DYSFUNCTION AFTER RRP

Alessandro Sciarr1, Valeria Panebianco2, Stefano Saliccia1, Andrea Alfarone1, Alessandro Gentilucci1, Danilo Lisi2, Susanna Cattarino1, Silvia Bernardo2, Roberto Passariello2 and Vincenzo Gentile1

1Department of Urology and 2Department of Radiology, Sapienza University, Rome, Italy

Background: Erectile dysfunction is one of the complications after radical retropubic prostatectomy, and recovery of erectile function is quantitatively related to the preservation of the neurovascular bundles. The aim of our study was to assess, in patients submitted to a nerve-sparing radical retropubic prostatectomy, the capability of a dedicated 3D isotropic
magnetic resonance imaging MRI T2-weighted sequence in the depiction of postoperative changes of neuro-vascular bundle formation.

Patients and Methods: A total of 53 consecutive patients underwent a bilateral nerve-sparing radical retropubic prostatectomy. Two postoperative MRI examinations and International Index of Erectile Function five-item questionnaire were carried out at 6 and 12 months. Morphological imaging of the post-prostatectomy fossa was performed, first acquiring turbo spin-echo T2- weighted sequences in the axial and coronal planes and then with 3D T2-weighted isotropic sequence on the axial plane. Image findings were scored using a relative five-point classification (0=normal; I=mild; II=mild to moderate; III=moderate; IV=severe alterations) and correlated with postoperative International Index of Erectile Function five-item score questionnaire.

Results: Image interpretation was performed by two radiologists scoring MRI alterations by the use of axial and multiplanar reconstruction 3D T2 isotropic sequence. The radiologists placed 43.30% of patients in class 0 (23/53 normal or quite normal), 32.00% in class I (17/53 mild), 11.40% in class II (6/53 mild to moderate), 7.50% in class III (4/53 moderate), and 5.70% in class IV (3/53 severe). In all cases, the correlation and regression analysis between the 3D T2 isotropic sequence and International Index of Erectile Function five-item score, resulted in higher coefficients values of rho=0.45; p=0.0010.

Conclusion: The MRI protocol and neurovascular bundle change classification score proposed in this study would represent an additional tool in the postoperative phase of patients with erectile dysfunction.

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VALUE OF MAGNETIC RESONANCE SPECTROSCOPY (MRS) AND DYNAMIC CONTRAST-ENHANCED MAGNETIC RESONANCE (DCEMR) IMAGING FOR THE CHARACTERIZATION OF HIGH-GRADE PROSTATIC INTRAEPITHELIAL NEOPLASIA (HGPIN) FOCI

Alessandro Sciarrà1, Valeria Panebianco2, Stefano Salciccia1, Andrea Alfarone1, Alessandro Gentilucci1, Danilo Lisi2, Susanna Cattarino1, Silvia Bernardo2, Roberto Passariello2 and Vincenzo Gentile1

1Department of Urology and 2Department of Radiology, Sapienza University, Rome, Italy

Background: Despite an increasing interest in HGPIN, the clinically suspicious aspect of this premalignant lesion remains poorly characterized. The aim of this study was to analyse the MRS and DCEMR imaging features of isolated HGPIN lesions.

Patients and Methods: From January 2007 to November 2008, 330 cases were included in a protocol that involves the use of MRSI and DCEMR for the diagnosis of prostate diseases. Of these, 27 patients with isolated (no prostate cancer diagnosis) HGPIN histological diagnosis at the first prostate biopsy were included in the present study. All cases were previously submitted to MRSI/DCEMR (1.5 T scanner) and, no later than 10 days to a random 12-core biopsy scheme. Biopsy targeting was carried out in zones corresponding to those analysed with MRSI and DCEMR.

Results: A total of 30 HGPIN foci in 27 patients with a diameter of 6 mm or greater were analysed and compared to 24 peripheral zone areas of normal prostate tissue. At MRSI, HGPIN foci were characterized by a significantly higher (p<0.05) absolute value of choline and choline plus creatine/citrate ratio when compared to normal tissue. At DCEMR, HGPIN foci were characterized by lower values of all dynamic parameters but differences did not reach statistical significance (p>0.05).

Conclusion: In our experience, HGPIN lesions can be metabolically characterized by MRSI through the absolute value of choline and choline plus creatine/citrate ratio.

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TSH ELEVATION AS MARKER OF EFFICACY IN SUNITINIB RECEIVING PATIENTS WITH METASTATIC RENAL CELL CARCINOMA

Valentina Baldazzi1, Renato Tassi1, Alberto Lapini2, Salvatore Caruso1, Greta Cipriani1, Sara Diacciati1, Carmine Cerullo1, Lorenzo Brogi1, Carmine Santomaggio1, Marco Carini2 and Roberto Mazzanti1

1Oncologia Medica 2 e 2Urologia 1, AOU Careggi, Italy

Background: Since 2006, a thyroid dysfunction has been described in patients undergoing sunitinib therapy with an unexpected high incidence (from 30% to 85% of patients). An association between hypothyroid state and improved outcomes has been suggested in cancer patients. We present the results of our prospective evaluation of newly onset hypothyroidism and its relationship with patient outcome in a cohort of front-line sunitinib-receiving patients affected by metastatic renal cell carcinoma (mRCC).

Patients and Methods: Between July 2007 and June 2009, 23 patients affected by mRCC were referred to our institution. The median age was 61 (range 50-75) years. All patients received first-line sunitinib, with a daily administration according to the following 6-week schedule: 4-week daily administration (ON) and 2-week withdrawal (OFF). Drug interruption and dose adjustment to 37.5 mg daily or other 6-week schedule were performed. All patients had normal
thyroid function at baseline. Thyroid function tests, inclusive of serum TSH, free triiodothyronine (fT3) and free thyroxine (fT4), were evaluated at the beginning and at the end of every cycle. Antibodies against thyroid peroxidase (TPO-Ab), thyroglobulin (Tg-Ab), and the TSH receptor (TR-Ab) were analysed for each patient before the beginning of the treatment and every 12 weeks. Before the beginning of treatment, median TSH concentration resulted in 1.7 mUI/l (range 0.55-3.4 mUI/l). Antibodies against thyroid (as TPO-Ab, Tg-Ab and TR-Ab) were absent or within the normal range for all patients.

Results: During sunitinib administration, 14 patients (60.9%) showed at least one elevated TSH level. The remaining 9 patients did not develop any biochemical alteration of thyroid function during the treatment. TSH levels up to 46 mUI/l were observed, and the highest levels of TSH were reported in patients receiving sunitinib for a longer time. During a complete cycle of treatment, an alternate course of TSH concentration was detected, with higher levels on the last day of sunitinib administration, while during the OFF period, TSH levels usually fell to normal or at least to lower levels, suggesting a direct relationship between sunitinib administration and thyroid function abnormalities. In our cohort of patients, fT3 and fT4 were always within a normal range. We observed a progressive reduction in mean fT4 levels during the treatment (on average from 14.0 mUI/l at baseline to levels between 12.4 and 11 mUI/l after three cycles of treatment). Progression-free survival (PFS) was evaluated in our cohort of patients according to thyroid function. Median PFS was 9.6 months in all patients, but was significantly longer (11.4 months vs. 6.6 months) in those who showed a significant reduction in thyroid function, as compared to those who remained euthyroidic. Survival analysis, (Figure 1) according to Kaplan-Meier method for survival showed a slight but statistically significant survival advantage in hypothyroid patients (p=0.03).

Conclusion: A direct correlation between sunitinib-induced thyroid dysfunction and clinical outcome was observed. Understanding the biology and aetiology of sunitinib-induced thyroid dysfunction and assessing its correlation with treatment outcome will help to define the role of thyroid dysfunction as a surrogate marker for efficacy of sunitinib in patients with advanced RCC. Further analysis in larger cohort of patients will help in defining the exact role of TSH elevation and hypothyroidism as possible surrogate markers of treatment efficacy.

References

129 ROBOTIC HIFU IN THE TREATMENT OF PROSTATE CANCER: FOCUS ON EARLY COMPLICATIONS

Francesco Pisanti, Francesco Attisani, Stefano Brunori, Luca Mavilla, Luca Albanesi, Barbara Cristina Gentile, Giorgio Vincenti, Teuta Shestani and Roberto Giulianelli

Villa Tiberia, Roma, Italy

Aim: To evaluate early complications of robotic high-intensity focused ultrasound (HIFU) treatment in patients with prostate cancer. Initial experience with short-term results is presented.

Patients and Methods: From October 2008 to October 2009, 55 patients were included in a therapy protocol with robotic HIFU. Patients were fully informed and consented to the procedure. Data were prospectively collected and retrospectively analysed. The endpoint of the study was to evaluate early complications: registration of any somatic side-effect, complication and discomfort was updated at every patient’s follow-up. Functional outcomes in terms of urinary status and continence were assessed. Sexual function was not included in the analysis. Patients underwent HIFU with the second-generation Ablatherm device (Technomed SA, Vaux en Velin France). Treatment was performed by two skilled urologists all over the prostate gland under spinal anaesthesia. Transurethral resection of the prostate (TURP) was indicated in all the patients (performed at least one month earlier) in order to reduce the risk of post-procedure acute urinary
retention (AUR). Follow-up: clinical evaluation including digital rectal examination, transrectal ultrasound (TRUS) and uroflowmetry after 14, 30, 90 days and every 3 months thereafter. Urinary status (IPSS score) and continence were evaluated. Sextant biopsy was conducted at 3 months and serum prostate-specific antigen (PSA) was measured every 3 months after HIFU treatment. Treatment failure was defined as any positive biopsy.

Results: All the 55 enrolled patients were considered evaluable for the actual analysis. Just one patient underwent salvage treatment after 6 months previous robotic HIFU (positive follow-up biopsy and increasing PSA value). The mean follow-up was 9 (range 3-15) months. Median catheter time was 10 days and the most common adverse event reported was acute AUR. Postoperative sloughing of necrotic tissue in the prostatic fossa (evaluated by TRUS) presented in 2 cases (4%) and resolved with catheter wash out; pelvic perineal pain reported in 1 patient (2%), rectal bleeding in 1 patient (2%) and scrotal oedema in 1 case (2%). Late complication (1-3 months) included bladder-neck stenosis in 3 patients (6%) and pre-sphincteral stenosis in 2 patients (4%). Moreover, grade 1 urinary incontinence reported in 10 patients (20%), grade 3 in 1 patients (2%) and OAB (due to TURP performed 1-2 mo. before) in 15 patients (30%). Major complications like rectovesical fistula just in the salvage robotic HIFU patient because of a rectal wall cancer invasion associated with an anatomical pathological reassessment (CT scan evidence). No urinary tract infection was reported. Intra/perioperative death, thrombosis/pulmonary embolism never occurred nor was there any necessity for blood transfusion, emergency operation or intensive care.

Conclusion: These results indicate that robotic HIFU is associated with low morbidity. The second-generation prototypes dramatically reduced serious adverse events; however, a few complications and side-effects are reported and they tend to increase with the number of local pre-treatments.

130 SUNITINIB AND ALTERED PARATHYROID FUNCTION

Valentina Baldazzi1, Renato Tassi1, Alberto Lapini2, Salvatore Caruso1, Greta Cipriani1, Sara Diacciati1, Carmine Cerullo1, Carmine Santomaggio1, Marco Carini2 and Roberto Mazzanti1

1Oncologia Medica 2 e 2Urologia 1, AOU Careggi, Italy

Background: Sunitinib malate is an orally bioavailable tyrosine kinase inhibitor, with a known activity against many tyrosine kinase receptors (RTK) involved in tumour growth and angiogenesis, such as the vascular endothelial growth factor receptors (VEGFR1,2,3), C-KIT receptor and the platelet-derived growth factor receptors α and β (PDGFR). As sunitinib activity involves many pathways both in healthy and malignant tissues and its use in clinical practice is quite recent, many of its possible side-effects are not well described. Here we report the incidence of newly onset hyperparathyroidism in a cohort of sunitinib-receiving patients affected by metastatic renal cell carcinoma (mRCC).

Patients and Methods: Between July 2007 and December 2009, 25 patients affected by mRCC were referred to our institution. The median patient age was 61 (range 48-79) years. All these patients received a first-line sunitinib according to the following 6-week classic schedule: 4-week 50 mg sunitinib daily administration (ON) followed by 2-weeks withdrawal (OFF). Drug interruptions and dose adjustment were performed, if required, depending on reported toxicities and according to the manufacturer’s recommendations. Since first reports showed elevated serum parathyroid hormone (PTH) in some of these patients, we begun a prospective evaluation of parathyroid function tests, and calcium metabolism in patients receiving sunitinib. Therefore, 17 patients were eligible for a parathyroid function assessment, complete plasma levels of intact PTH, serum levels of total calcium, and phosphorus, serum 25-hydroxyvitamin D and 1,25-dihydrovitamin D, urine analysis and urinary calcium and phosphorus. All biochemical evaluations were performed at the end of each sunitinib ON period as routine biochemical evaluations. Before the beginning of treatment, PTH, serum and urinary calcium and phosphates levels were within a normal range in every patient (on average 4.91 pmol/l; normal range 1.3-7.6 pmol/l).

Results: On average, patients received a sunitinib administration for 6.4 cycles and ranged from 2 to 20 6-week cycles. During sunitinib administration, 11 patients (64.75%) developed elevated PTH levels, with low-to-normal serum calcium and phosphate levels. In some patients, elevation of PTH was detectable from the first cycle of sunitinib and rose up to 68.1 pmol/l in one case. On average, patients presented an elevation of PTH after 3 sunitinib administration cycles (range 1-5 cycles). Serum calcium and phosphate and vitamin D levels were always within the normal range. Patients presenting elevated PTH also showed low or undetectable urinary calcium levels. Such abnormalities usually persist, but do not progress, during long-term therapy with sunitinib.

Conclusion: In our cohort of patients, hyperparathyroidism, with associated changes in mineral metabolism develops in an elevated proportion of patients undergoing sunitinib, suggesting that this drug may affect mineral and bone remodelling. This observation was first reported in patients receiving imatinib for chronic myelogenous leukaemia or other malignancies. It has been suggested that imatinib may
interfere with osteoclast function directly inhibiting PDGF receptor B on osteoclasts, and indirectly by inhibiting PDGF receptor A on osteoblasts. These events result in decreased bone re-absorption and decreased serum ionized calcium that induces compensatory hyperparathyroidism, with decreased renal calcium excretion and, ultimately, a correction of serum calcium levels. As sunitinib also inhibits PDGF receptors, we can hypothesize similar events occur as suggested for imatinib. This observation suggests that abnormalities in bone metabolism may be a side-effect common to tyrosine kinases that inhibit the PDGF receptor family. If such data were to be confirmed in larger analysis, routine monitoring of bone metabolism during sunitinib administration would be recommended, to recognise in vivo effects on bone mass and attempt a treatment of this side-effect, especially during longer duration therapy.

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1H-MRI IN VIVO PROSTATE SPECTROSCOPY (1H-MRSI) AT 1.5 T AND EX-VIVO HIGH RESOLUTION MAGIC ANGLE 1H-NMR SPECTROSCOPY AT 11 T AFTER RADICAL RETROPUBIC PROSTATECTOMY (RRP): COMPARISON AND CORRELATION OF NEW METABOLITE LEVELS IN PROSTATE CANCER

Eleonora Santucci1, Valeria Panebianco1, Alessandro Sciarra2, Stefano Salciccia2, Maria Cristina Valerio3, Andrea Alfarone2, Alessandro Gentilucci2, Danilo Lisi1, Susanna Cattarino2, Silvia Bernardo1, Roberto Passariello1 and Franco Di Silverio2

1Department of Radiology, 2Department of Urology and 3Department of Chemistry, Sapienza University, Rome, Italy

Aim: To assess if an ex vivo metabolomic approach can be used to discover metabolic biomarkers that are distinct in prostate cancer and healthy glands and whether there is any correlation with metabolites obtained by standard in vivo 1H-MRSI.

Patients and Methods: We retrospectively reviewed a total of 51 prostate MRI examinations, including morphological imaging, 1H-MRSI and DCE-MRI protocols, carried out from June 2009 to December 2009. All patients underwent 1H-MRSI at 1.5T. After the RRP, a high resolution 11 T spectroscopy was performed on surgical samples. The compounds of samples were identified and quantified by comparing the spectrum to a collection of reference spectra of pure compounds. Multivariate analysis was applied on 1H-NMR metabolites curve and correlated with those of in vivo MRSI. This is used to discern significant patterns in complex data sets and is particularly appropriate in situations where there are more variables than samples in the data set and to classify metabolites in classes.

Results: This approach, applied to 1H-MRSI/DCE-MRI results, allowed us to differentiate among the various prostatic diseases in a non-invasive way with a 100% accuracy. These findings suggest that multivariate analysis of 1H-MRSI/DCE-MRI can significantly improve the diagnostic accuracy for these pathological entities.

Conclusion: This work may provide the basis for further development of new in vivo MRSI acquisition modalities and may improve diagnostic accuracy to identify biochemical changes and also metabolic markers for cancer diagnosis.

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SEQUENTIAL TARGET THERAPY FOR METASTATIC RENAL CELL CARCINOMA: WHICH CHOICE? A CASE REPORT

Renato Tassi1, Valentina Baldazzi1, Alberto Lapini2, Salvatore Caruso1, Greta Cipriani1, Sara Diacciati1, Carmine Cerullo1, Carmine Santomaggio1, Marco Carini2 and Roberto Mazzanti1

1Oncologia Medica 2 e 2Urologia 1, AOU Careggi, Italy

Background: Molecular anticancer drugs represent a standard of treatment for metastatic renal cell carcinoma (mRCC). In fact, an increasing number of such agents are being approved for the treatment of this disease. However, the correct sequence of drugs which result in better patient outcome has not yet been well established. Therefore, clinicians have to choose between different agents depending on patient and disease characteristics. Here we present a case of sequential target therapy administration leading to a complete disease response in a patient referred to our institution.

Case Report: In January 2009, a 74-year-old woman was referred to our institution with the diagnosis of liver metastasis from renal clear cell carcinoma. She suffered from hypertension, with good cardiac function. In May 2002, the patient underwent a right radical nephrectomy for a renal clear cell carcinoma (pT3N0Mx, Furhman G1). In November 2008, an abdominal CT scan showed a single nodular hepatic lesion characterized by a high arterial contrast enhancement (diameter 2 cm) and three pancreatic lesions with the same contrast characteristics.
Background: Prostate cancer (PCa) is the most common malignancy of solid organs affecting men in the Western world. Currently, serum prostate-specific antigen (PSA) is the screening test widely used in the diagnosis and management of patients with PCa. In relation to the poor sensitivity and specificity of PSA, there is an urgent need for additional markers. To improve the diagnostic accuracy, proteomic profiling of serum represents a valuable tool for biomarker discovery in prostate cancer. Our study aimed to describe and compare the serum proteome pattern in PCa patients and in a matching control group. In order to enhance the detection of the low abundance protein fraction (LAP), the most probable source of biomarkers, the performance of three different strategies: ProteoMiner (Bio-Rad), MARS Human-7HPLC column immunofinity depletion (Agilent) and Dynabeads SCX (Invitrogen), in combination with 2-D electrophoresis (2-DE) analysis, were evaluated. Advantages and disadvantages of these approaches are discussed and results are compared.

Patients and Methods: Donors: serum samples were from patients with PCa and PSA>4 ng/ml (group A); benign prostate hyperplasia (BPH) and PSA<4 ng/ml (group B); BPH and PSA<4 ng/ml (group C); and healthy donors (group D). Sera from each group (20 patients/group) were pooled. Sera from donors were matched for age and dietary and smoking habits.

ProteoMiner: 1 ml of each pooled serum sample was loaded on the ProteoMiner column. Two different elution methods were tested: i) single-step elution protocol (elution reagent: 4 M urea, 1% CHAPS, 5% acetic acid), compatible with the following 2-DE; ii) sequential elution procedure [elution reagents: a) 1 M sodium chloride, 20 mM HEPES, pH 7.4; b) 200 mM glycine, pH 2.4; c) 60% ethylene glycol; d) 33.3% 2-propanol, 16.7% acetonitrile, 0.1% trifluoroacetic acid]. Protein precipitation step with acetone was set-up prior to 2-DE.

MARS Human-7HPLC: The 7 most abundant proteins (HSA, IgG, IgA, transferrin, haptoglobin, α1-antitrypsin, fibrinogen) were depleted using a System Gold HPLC apparatus (Beckman). To remove salts from elution buffers and concentrate depleted sera, a protein precipitation was carried out using 7.5% TCA for 1 h at -20°C, followed by 4 washes in 90% acetonitrile.

Dynabeads SCX: Sera pools were diluted 1: 50 in 20 mM citric acid pH 3 and 10 mM sodium chloride, which represents the absorption buffer required for the prefractionation tool. Sequential elution by increasing pH was carried out.

Gel image analysis: for spot detection, images of gels captured with ProXPRESS 2D System (Perkin-Elmer) were analysed by Progenesis SameSpots software (Nonlinear Dynamics Ltd).

Results: ProteoMiner: single-step elution protocol was chosen for further experiments, as it exhibited a better...
reproducibility of spots detected in 2-DE compared with the sequential elution procedure. Reproducibility of protein yield was evaluated for sera pool of groups A and D (mean ± SD): 1468±35 μg (CV%=2.4) and 1340±33 μg (CV%=2.6), (n=3), respectively. MARS Human-7: referring yield, reproducibility of the amount of proteins quantified in flow-through fractions were (mean ± SD) 195 ± 35 μg, CV% 4 (n=8). The number of spots detected in 2-DE, evaluated for triplicate samples, always showed good reproducibility with CV% lower than 10% both for ProteoMiner and MARS. Dynabeads: SCX fractionation was not satisfactory, as high abundance proteins compete with LAP for absorption to the solid phase on the beads, resulting in almost the same protein composition in the different fractions, as verified by nLC-MS/MS analysis. In addition, this approach had a high variability, so it was abandoned. Comparison of 2-DE images of serum of group D showed that complementary results are provided by ProteoMiner and MARS techniques.

**Conclusion:** In this study, the experimental procedures for ProteoMiner, MARS and Dynabeads SCX strategies were set up including sample preparation and 2-DE protocols. Our findings suggest that immunodepletion and ProteoMiner approaches are complementary and can be readily integrated into an analytical strategy for biomarker discovery. Future investigations will be focused on describing the proteomic profile of different groups of patients utilizing both these procedures.

**134 DOES THE DEFINITION OF “MICROFOCUS” AS A SINGLE POSITIVE CORE WITH 5% OR LESS TUMOUR INVOLVEMENT HAVE CLINICAL VALUE IN PREDICTING NON ORGAN-CONFINED PROSTATE CANCER AT RADICAL PROSTATECTOMY?**

Vincenzo Scattoni1, Firas Abdollah1, Luca Villa1, Renzo Colombo1, Marco Roscigno1, Diego Angiolilli1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitano1, Massimo Freschia1, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, Hsan Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

**Aim:** To verify whether the definition of “microfocus” as 5% or less tumour involvement within a single core in patients with clinically low-risk prostate cancer (PCa) is an independent predictor of non organ-confined PCa at radical prostatectomy (RP).

Patients and Methods: We analysed a cohort of 234 patients with a single positive core of PCa at PBx who were subsequently submitted to RP between May 2001 and April 2009, at a single tertiary referral centre. Only patients with a clinically low-risk tumour (defined as PSA≤10 ng/ml, clinical stage T1c and Gleason score ≤6 at biopsy) were included. These criteria yielded 144 eligible patients. Non organ-confined disease was defined as the presence of extraprostatic extension, seminal vesicle invasion and/or lymph node invasion. Patients were divided according to the extent of cancer invasion in the single core: ≤5% (group 1) vs. >5% (group 2). The correlation between % of tumour involvement within the core and adverse pathological outcomes was evaluated using univariate and multivariate logistic regression analyses after adjusting for patient age and total PSA at diagnosis, prostate volume (PV) and the extent of biopsy scheme (<12 cores vs. ≥12 cores).

**Results:** Mean and median patient age at surgery were 62.9 and 63 years, respectively. Mean and median PSA at diagnosis were 5.8 and 5.8 ng/ml, respectively. The mean number of cores at biopsy was 17.3 (median: 17.5, range: 6-24). The number of cores taken at PBx was <12 in 20.8% (n=30), and ≥12 in 79.2% (n=114) of patients. The percentage of tumour involvement within the core was ≤5% in 80.6% (116) and >5% in 19.4% (28) of men. The rate of patients with non organ-confined disease at RP was 9.7% (14). There was no significant difference in the rate of non organ-confined PCa between group 1 and group 2 (9% and 14.2%, respectively, p=0.7). At multivariate analysis, the percentage of tumour involvement within the core (≤5% vs. >5%) was not a significant predictor of non organ-confined disease at RP (OR=0.82, p=0.8). Total PSA at diagnosis was the only independent predictor of adverse pathological outcome at RP (OR=1.44, p=0.02).

**Conclusion:** We report one of the largest series focusing on patients with low-risk prostate cancer and a single positive core. Our results seem to suggest that the definition of “microfocus” as a single core tumour involvement of 5% or less has dismal value in predicting the presence of non organ-confined disease at RP.

**135 ROLE OF DUAL SOURCE CT CYSTOGRAPHY AND VIRTUAL CYSTOSCOPY IN DETECTION OF BLADDER CANCER: COMPARISON WITH PHOTODYNAMIC DIAGNOSIS (PDD) METHOD**

Luisa Di Mare1, Valeria Panebianco1, Silvia Bernardo1, Susanna Cattarino2, Ettore De Berardinis2, Gian Maria Busetto2 and Franco Di Silverio2

1Department of Radiology and 2Department of Urology, Sapienza University, Rome, Italy
Aim: To evaluate the role of CT cystography (CTC) and virtual cystoscopy (VC) with dual source technique in detection of bladder lesions using cystoscopy with photodynamic diagnosis (PDD) as reference standard.

Patients and Methods: Thirty haematuric patients suspicious for bladder cancer, and fourteen patients who had undergone transurethral resection of the bladder were studied by CTC and VC, included post-contrast scan. The patient population was divided into three groups based on lesion size at PDD cystoscopy. Results of the CT study were compared with those of conventional cystoscopy and PDD cystoscopy.

Results: PDD cystoscopy depicted 92 bladder lesions in the 44 patients examined. Sensitivity and specificity values of CTC and VC alone were constantly lower than those of the combined-approach (group 1: 93.25% and 92.54%; group 2: 100% and 100%; group 3: 100% and 100%, respectively). With regard to lesion size, it has been also demonstrated that multidetector-row CT performed with thin-slice reconstructions (1 mm) allows a good sensitivity in the detection of lesion larger than 1 mm. Receiver operating characteristic curve analysis showed that the combined approach decreases the lower dimensional threshold for lesion detection (1.4 mm).

Conclusion: CTC with dual source technique and VC are promising diagnostic approaches for bladder tumours measuring in the range of 1–5 mm. This technique is less invasive than conventional cystoscopy and can be used to evaluate areas difficult to assess with cystoscopy such as the anterior bladder neck. The main disadvantage of CTC and VC is the low sensitivity in depicting flat lesions, as demonstrated on cystoscopy with the PDD method.

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PREDICTORS OF GLEASON SUM SIGNIFICANT UPGRADE IN PATIENTS WITH LOW-RISK PROSTATE CANCER AND A SINGLE POSITIVE CORE AT PROSTATE BIOPSY: CLINICAL IMPLICATIONS

Vincenzo Scattoni1, Firas Abdollah1, Luca Villa1, Renzo Colombo1, Marco Raber1, Marco Roscigno1, Diego Angiolilli1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi1, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, H San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

Aim: To identify independent predictors of biopsy Gleason sum significant upgrading in patients with low-risk prostate cancer (PCa) and a single positive core at prostate biopsy (PBx).

Patients and Methods: We evaluated a cohort of 234 patients who had a single positive core of PCa at PBx, subsequently submitted to radical prostatectomy (RP) between May 2001 and April 2009 at a single tertiary referral centre. Only patients with a clinically low-risk tumour (defined as PSA≤10 ng/ml, clinical stage T1c and biopsy Gleason score ≤6) were included. These criteria yielded 144 eligible patients. Significant Gleason score upgrading was defined as a shift to Gleason score ≥7 at RP. Univariate and multivariate logistic regression analyses were used to test the association between age, total PSA, prostate volume (PV), biopsy scheme (<12 cores vs. ≥12 cores), percentage of tumour involvement within the core (≤5% vs. >5%) and significant Gleason score upgrading at RP.

Results: Mean and median patient age at surgery was 62.9 and 63 years, respectively. Mean and median PSA at diagnosis was 5.8 and 5.8 ng/ml, respectively. Mean PV was 62.2 cc (median: 59 cc). The number of cores taken at PBx was <12 in 20.8% (30), and ≥12 in 79.2% (114) of patients. The percentage of tumour involvement within the core was ≤5% in 80.6% (116) and >5% in 19.4% (28) of men. At univariate analysis, PV was the only predictor of Gleason sum significant upgrading at RP (p=0.02; OR: 0.97). At multivariate analysis, total PV (OR: 0.96, p=0.009) and the percentage of tumour involvement within the core (>5% vs. ≤5%; OR: 2.81, p=0.04) were independent predictors of Gleason sum significant upgrading at RP.

Conclusion: We report one large series of patients with low-risk PCa and a single positive core. In this patient category, total prostate volume and the percentage of tumour involvement within the core represent independent predictors of Gleason sum significant upgrading. These data should be taken into account when biopsy data are considered as parameters for selecting patients for conservative treatments or active surveillance protocols.

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SINGLE MINUTE FOCUS OF PROSTATE CANCER ON NEEDLE BIOPSY: PREDICTING FACTORS FOR LOCALLY ADVANCED PROSTATE CANCER ON RADICAL PROSTATECTOMY

Vincenzo Scattoni1, Luca Villa1, Renzo Colombo1, Marco Raber1, Firas Abdollah1, Marco Roscigno1, Diego Angiolilli1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, H San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy
**Aim:** To identify factors predicting the presence of locally advanced prostate cancer at radical prostatectomy (RP) in patients with a single minute focus on needle biopsy.

**Patients and Methods:** In our series of 6,658 consecutive needle biopsies performed from November 1992 to April 2009, we analysed 432 patients (6.4%) with single microfocus of prostate cancer (one single neoplastic lesion ≤ 5% in one biopsy core or ≤ 0.5 mm in length). Out of 432 patients, 234 were treated with RP. Univariate and multivariate analyses were used to identify independent predictors on biopsy, including age, total PSA, clinical stage, Gleason score on biopsy, prostate volume (PV) and number of cores of locally advanced disease (extracapsular tumour and/or lymph node invasion) on RP. The multivariate model was used to develop and internally validate a nomogram.

**Results:** The mean age and PSA were 63.7 years (median: 64 years) and 7.22 (median: 6.2) ng/ml, respectively. Clinical stage was T1c in 93.1% and T2a in 6.9% of men. Gleason score on biopsy was ≤ 6 in 92.3%, 7 in 5.9% and ≥ 8 in 1.8% of patients. At univariate analysis, only Gleason score (≤ 6 OR=0.98, p=0.02) and PV (OR=0.98, p=0.03) were significantly correlated to the presence of locally advanced disease. Gleason score (≤ 6 vs. 7 OR=3.5, ≤ 6 vs. ≥ 8 OR=8.8, p=0.02) and PV (OR=0.98, p=0.03) remained independent predictors of locally advanced disease on multivariate analysis. We used these predictors to develop a nomogram which had an accuracy of 68% on the 200 bootstrap internal validations.

**Conclusion:** The risk of diagnosing a single microfocus of prostate cancer on needle biopsy is quite low (6.4%). The risk of finding locally advanced prostate cancer is about 10%. Our nomogram permits the prediction of locally advanced disease in patients with a microfocus of prostate cancer on biopsy.

**CT PERFUSION OF PROSTATE USING A 64MD CT SCANNER: INITIAL EXPERIENCE HAVING RADICAL PROSTATECTOMY AND WHOLE MOUNT PATHOLOGY AS STANDARD OF REFERENCE**

**A.L. Pastore**1, G. Pulleschi1, P. Paolantonio2, A. Ripoli1, L. Silvestri1, D. Autieri1, D. Bellini2, A. Laghi2, V. Petrozza3 and A. Carbone1

1Urology Unit, Sapienza University of Rome Polo Pontino, Terracina (LT), Italy; 2Radiology Unit Polo Pontino, Sapienza University of Rome, Latina, Italy; 3Histopathology Unit Polo Pontino, Sapienza University of Rome, Latina, Italy

**Aim:** To assess the feasibility of CT perfusion of prostate gland in patients with prostatic carcinoma using a 64-raw-MDCT scanner.

**Patients and Methods:** From November 2008 to March 2009, ten consecutive male patients (mean age 69.3 years, range, 59-76 years) with proven prostatic carcinoma scheduled for radical prostatectomy were enrolled in our study. Patients underwent CT perfusion of the prostate gland, then they were submitted to radical prostatectomy within two weeks of the CT study. Whole mount pathology was available in all cases. Two radiologists performed image analysis as well as perfusion measurements using automatic software for perfusion analysis based on deconvolution methods. Image analysis was performed in consensus with a pathologist by comparing CT image with whole mount specimens. CT perfusion parameters were measured using regions of interest in foci of prostate carcinoma as well as in tumour-free peripheral zones. These data were compared by means of Wilcoxon test (Z<0.001).

**Results:** Blood volume and blood flow values were increased in neoplastic tissue while mean transit time values were shorter in neoplastic tissue compared to the normal peripheral zone. Mean values of blood volume and blood flow in prostatic carcinoma and normal peripheral zone, respectively, were 4.3 and 0.7 ml/100 g of wet tissue, 155.6 and 13.3 ml/100g of wet tissue per minute, 27.5 and 5.3 ml/100 g of wet tissue per minute. Mean values of mean transit time in prostatic carcinoma were 23.5 seconds versus 103.2 seconds of normal peripheral prostatic zone. Statistical analysis showed a significant difference in blood volume, blood flow, mean transit time and permeability surface area product between normal gland and prostate cancer.

**Conclusion:** CT perfusion of prostate is a feasible technique in patients with prostatic carcinoma. In our series, prostatic cancer had higher values for blood volume and blood flow, and lower values for mean transit time. These data may reflect tumour vascularization. CT perfusion of prostate glands seems to be a promising tool for in vivo quantification of prostate tumour angiogenesis.

**BODY MASS INDEX IS SIGNIFICANTLY ASSOCIATED WITH TUMOUR VOLUME IN PROSTATE CANCER**

Vincenzo Scattoni1, Luca Villa1, Renzo Colombo1, Marco Raber1, Firas Abdollah1, Marco Roscigno1, Andrea Salonia1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, Vita-Salute University, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy
Background: Body mass index (BMI) has been shown to be related to benign prostatic hyperplasia and prostate cancer pathophysiology. Altered hormonal milieu in overweight and obese men may influence androgen-dependent prostate cancer growth. However, no study has yet focused on the association between BMI and prostate tumour volume (TV) at radical prostatectomy (RP).

Patients and Methods: We analysed 1275 patients with prostate cancer who underwent an RP at a single tertiary care institution between January 2003 and December 2008. All patients had clinical and pathological characteristics available, including data on BMI and tumour volume, which was assessed using a planimetry-based methodology. One-way analysis of variance (ANOVA) was used to evaluate the mean tumour volume according to BMI World Health Organization categories (normal weight, <25 kg/m² vs. overweight, 25-30 kg/m² vs. obesity 30-35 kg/m² vs. severe obesity, >35 kg/m²). Univariable linear regression analyses targeted the association between BMI and tumour volume at RP. Multivariable linear regression analyses were adjusted for age, PSA level, biopsy Gleason sum, clinical stage and prostate volume.

Results: Mean age at surgery was 64.7 years (median 65, range: 39-85 years). Mean PSA value was 10.3 ng/ml (median 6.6, range: 0.3-327 ng/ml). Mean BMI was 26.3 kg/m² (median 26, range 16.7-42.0 kg/m²). Overall, 468 (36.7%), 657 (51.5%), 135 (10.6) and 15 (1.2%) were normal weight, overweight, obese and severely obese, respectively. Mean TV in the overall population was 5.6 cc (median 3.3, range 0.1-61.2 cc). When segregated according to BMI, mean TV was 5.0, 5.8, 6.3, 9.2 cc in normal, overweight, obese and severely obese patients, respectively (p=0.03). At univariable analysis, BMI was significantly associated with TV at RP (p<0.001). At multivariable analysis, BMI reached independent predictor status after adjusting for patient age at surgery, pre-operative PSA, biopsy Gleason sum, clinical stage and prostate volume (p=0.03).

Conclusion: We demonstrated that BMI is independently associated with prostate cancer volume at RP. The current results seem to indirectly suggest that hormonal metabolism may play a key role in prostate cancer stage and aggressiveness.

CAN WE PREDICT LYMPHORRHOEA AND CLINICALLY SIGNIFICANT LYMPHOCELE AFTER RADICAL PROSTATECTOMY AND PELVIC LYMPH NODE DISSECTION?

Vincenzo Scattoni1, Umberto Capitanio1, Nazareno Suardi1, Renzo Colombo2, Marco Raber1, Firas Abdollah1, Luca Villa3, Diego Angiolilli3, Carmen Maccagnano1, Andrea Gallina1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, University Vita-Salute, San Raffaele Scientific Institut, via Olgettina 60, 20132 Milano, Italy

Background: Lymphorrhoea and lymphoceles are reported complications after radical prostatectomy (RP) and pelvic lymph node dissection (PLND). However, to date, no study focused on the clinical and pathological variables that may help clinicians in predicting and preventing this surgical sequela. We aimed at identifying the predictors of lymphorrhoea and clinically significant lymphocele (CSL) in prostate cancer (PCa) patients treated with RP and PLND.

Patients and Methods: We prospectively analysed 501 cases of patients with PCa treated with RP and PLND between January 2006 and December 2008 at a single tertiary referral centre. All patients had detailed clinical and pathological data collected in a prospectively recorded database. The inclusion criteria of this prospective study were a successful bladder neck preservation and a watertight urethrovescical anastomosis at the end of the procedure. Patients were excluded when anastomotic leakage was evidenced in the postoperative period. Drains were removed when the amount of lymph was less than 20 cc during the previous 24 hours. Lymphorrhoea was defined as the total amount of lymph drained by the drains until their removal. CSL was defined as the presence of a symptomatic lymphocele requiring treatment. Univariable and multivariable linear regression models tested the association between the available predictors (age, body mass index, ASA score, prostate volume, clinical stage, number of removed nodes, surgeon, pathological T and N stage) and lymphorrhoea. Univariable and multivariable logistic regression models tested the association between all the predictors and the presence of CSL.

Results: The mean and median number of nodes removed was 21 and 20 (range 3-63), respectively. Both linear and logistic multivariable regression analysis showed that the number of removed nodes and age (both p<0.01) were the only two statistically significant predictors of total amount of lymphorrhoea and CSL after RP and PLND. Specifically, every additional node removed increased the risk of having CSL by 5%. In the same fashion, every additional year of age increases the risk of having CSL by 5%. No other clinical, pathological or surgical variables were associated with the total amount of lymphorrhoea nor CSL after RP (all p>0.2).

Conclusion: The number of lymph nodes removed and age at surgery showed a positive association with the amount of lymphorrhoea and the risk of developing a CSL. Our results may assist clinicians in selecting the most suitable individual treatment modality, in choosing the most appropriate surgical technique and the most proper management in the postoperative period, when surgery is performed.
NO RESIDUAL TUMOR (PT0) AT RADICAL PROSTATECTOMY IN CLINICAL T1A-B PROSTATE CANCER. DEVELOPMENT OF A NOVEL AND USER-FRIENDLY PREDICTING TOOL: STAGE (CT1A VS. CT1B) DOES NOT IMPROVE THE ABILITY TO PREDICT PT0

Vincenzo Scattoni1, Luca Villa1, Renzo Colombo1, Marco Raber1, Firas Abdollah1, Marco Roscigno1, Diego Angiolilli1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology, and 2Department of Pathology, Vita-Salute University, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

Introduction: The Absence of residual tumor at radical prostatectomy (pT0) is a non-negligible issue in patients with incidental prostate cancer (cT1a-cT1b) after surgery for benign prostatic hyperplasia (SxBPH). However, no tool predicting the absence of residual tumor at pathological assessment is currently available. Therefore, we aimed to develop a user-friendly tool predicting the presence of pT0 disease at radical prostatectomy (RP).

Patients and Methods: The study included 158 consecutive cT1a-b prostate cancer patients treated with RP between January 1996 and January 2009 at a single European tertiary referral center. All patients had complete clinical and pathological data. In particular, PSA values before and after SxBPH were available in all cases. A novel risk stratification tool was developed applying the non-parametric tree modeling technique of classification and regression tree analysis (CART). The tool automatically selected the most informative predictors among all the obtainable variables (namely: age and PSA at SxBPH, PSA after SxBPH before RP, cT1a-b stage, prostate volume before and after surgery for BPH, Gleason sum at SxBPH). The area under the receiver characteristic curve (AUC) method was used to quantify the predictive accuracy (PA) of the model which was internally validated with 200 bootstrap resamples.

Results: The mean and median age at prostate cancer diagnosis was 66 years. Overall, 95 (60.1%) patients were staged cT1a while the remaining 63 (39.9%) had cT1b prostate cancer. Mean and median PSA before SxBPH was 5.7 and 4.2 ng/ml, while mean and median PSA after SxBPH was 1.7 and 1.1 ng/ml, respectively. Mean and median prostate volume before and after SxBPH was 65.8 and 58 cc, and 31.9 and 30.5 cc, respectively. Overall, 21 patients (13.9%) showed no residual tumor (pT0) at RP. Three risk groups of having pT0 disease at RP were identified: a) low risk (n=54): PSA after SxBPH < 1.0 ng/ml and PSA before SxBPH > 2.0 ng/ml (risk of pT0: 14.8%); c) high risk (n=78): PSA after SxBPH < 1.0 ng/ml and PSA before SxBPH < 2.0 ng/ml (high risk group, 42.3%). The bootstrap-corrected accuracy of the proposed model was 77.1%.

Conclusion: No residual tumor (pT0) at RP in patients with cT1a-T1b prostate cancer is a non-negligible entity. However, the rate if pT0 is significantly associated with the levels of PSA before and after surgical treatment for BPH. Stage (cT1a vs. cT1b) does not improve the ability to predict pT0. We provided a user-friendly, accurate and clinically useful flow chart to predict the absence of residual tumor at RP after the diagnosis of incidental prostate cancer.

*Probability not to find residual tumor (pT0) at RP in patients with cT1a-T1b prostate cancer.

A PROPOSAL FOR THE IDEAL SAMPLING SCHEME IN PROSTATE REPEATED BIOPSIES: A RECURSIVE PARTITIONING ANALYSIS BASED ON 24-CORE SYSTEMATIC BIOPSY

Vincenzo Scattoni1, Nazareno Suardi1, Renzo Colombo1, Marco Raber1, Firas Abdollah1, Marco Roscigno1, Diego Angiolilli1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, Vita-Salute University, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

Aim: To identify the optimal combination of sampling sites (number and location) to detect prostate cancer in patients already submitted to an initial negative prostatic biopsy.

Patients and Methods: A transrectal ultrasound-guided systematic 24-core biopsy (24PBx) was prospectively performed with local anaesthesia in the outpatient setting in 354 consecutive patients after a first extended (10- to 14-core) negative biopsy. The 24PBx was obtained by the overlapping
of medial sextant, lateral sextant, octant subcapsular, and quadrant transition cores. Before fixation, each single core was individually inked with different colors according to the prostatic location sampled. We set the cancer-positive rate of the 24PBx at 100% and calculated the percentage of the tumour detected for 255 possible combinations of sampling sites. Using a 10-fold cross-validated recursive partitioning analysis, we selected the optimal biopsy scheme that detected 95% of the tumours with the minimum number of cores.

Results: The mean PSA value was 9.0±15.2 ng/ml and DRE was positive in 9.0% of the patients. The 24PBx detected prostate cancer in 91 patients (25.7%) in the entire population. The cancer detection rate was 22.5%, 27.3%, 42.2% and 60% in patient with a initial negative biopsy, initial biopsy positive for HGPIN, for ASAP, and for ASAP and HGPIN, respectively. The mean cancer detection rates of 8-, 10-, 12-, 14-, 16-, 18-, and 20-core schemes was 18.0%, 19.5%, 20.9%, 22.1%, 23.1%, 24.1%, and 24.1% according to the various combinations, respectively. An 8-, 10-, 12-, 14, 16-, 18-, and 20-core scheme detected (95% CI) 67-72%, 74-77%, 80-82%, 85-86%, 89-91%, 92-94% and 92-95% of all tumours according to the various combinations, respectively. Recursive partitioning analysis selected a specific combination of 16 cores as the optimal biopsy scheme for the entire population.

Conclusion: Both the number and the location of biopsy cores taken affect cancer detection rates in a repeated setting. We propose an optimal combination of 16 cores as the minimum number of sampling sites that is able to detect the 95% of the tumours detected with a saturation scheme.

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THE ROLE OF SALVAGE LYMPH NODE DISSECTION IN PATIENTS WITH LYMPH NODAL RECURRENCE OF PROSTATE CANCER AFTER RADICAL PROSTATECTOMY

Vincenzo Scattoni1, Nazareno Suardi1, Manuela Tutolo1, Alberto Briganti1, Luigi F. Da Pozzo1, Roberto Bertini1, Renzo Colombo1, Firas Abdollah1, Marco Roscigno1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, Vita-Salute University, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

Background and Aim: The management of patients with biochemical recurrence after radical prostatectomy remains controversial. We tested the role of salvage lymph node dissection (LND) in prostate cancer patients treated with radical prostatectomy and with biochemical recurrence associated with PET/CT scan lymph node pathological uptake, identifying the predictors of response to surgery.

Patients and Methods: Between 2002 and 2009, 49 prostate cancer patients, treated with radical prostatectomy, and with biochemical recurrence and with PET/CT scan pathological lymph node uptake were submitted to salvage LND. Local and systemic recurrence were previously excluded with transrectal biopsy and bone scan, respectively. We evaluated the PSA outcome of these patients after surgery, as well as the follow-up in terms of biochemical recurrence. Logistic regression and Cox regression analyses were used to identify the predictors of complete PSA response to surgery and predictors of recurrence after surgery, respectively.

Results: The mean and median age at surgery were 64.1 and 64.0 years, respectively. Mean and median time to biochemical recurrence after radical prostatectomy were 38.8 and 33.5 months, respectively. Mean and median PSA at surgery were 4.3 and 2.3 ng/ml respectively. All patients underwent pelvic LND and 35 (71.4%) patients underwent retroperitoneal LND. The mean and median number of removed and of positive nodes were 27.7 and 21 and 7.76 and 2, respectively. One month after LND, PSA was <0.2 ng/ml in 30 patients (61.2%). At multivariable logistic regression analysis, after adjusting for pathological characteristics at radical prostatectomy, PSA at surgery and time to biochemical recurrence represented independent predictors of PSA response to surgery (p=0.007 and p=0.01 respectively). The mean and median follow-up after LND were 30.6 and 27 months, respectively. One- and two-year biochemical recurrence-free survival in patients with complete PSA response were 81.8 and 41.7%, respectively. At multivariable Cox regression analysis, after adjusting for time to biochemical recurrence after radical prostatectomy, for the number of nodes removed and for pre-operative PSA, only the number of positive nodes represented an independent predictor of PA recurrence (HR=1.09; p=0.01).

Conclusion: Salvage LND represents a valid therapeutic option only for a minority of patients with biochemical recurrence and with PET/CT scan pathological lymph node uptake. Roughly, 60% of patients can achieve complete PSA response. Of these, roughly 40% will experience significant biochemical recurrence-free survival. These results need to be confirmed with longer follow-up.

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COMPARISON OF PROSTATIC SCHEMES IN PATIENTS SUBMITTED TO AN INITIAL 24-CORE SYSTEMATIC BIOPSY IN DETECTING SIGNIFICANT AND INSIGNIFICANT PROSTATE TUMOURS

Vincenzo Scattoni1, Nazareno Suardi1, Renzo Colombo1, Marco Raber1, Firas Abdollah1, Marco Roscigno1, Diego
Angiolilli1, Carmen Maccagnano1, Andrea Gallina1, Umberto Capitanio1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, Vita-Salute University, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

Aim: To evaluate how many significant and insignificant (IPca) prostate tumours can be detected with a saturation 24-core biopsy scheme (24PBx) compared with an extended scheme in the initial setting.

Patients and Methods: A total of 785 patients were consecutively and prospectively submitted to transrectal (TRUS) 24-core ultrasound-guided biopsy in the office. The scheme consisted of the overlapping of the classical sextant scheme of Hodge (6H), the more lateral sextant scheme of Stamey (6S), eight more lateral and subcapsular cores (8L), and four cores from the transition zone (4TZ). We first calculated the detection rates of the Hodge sextant scheme (6HPBx) and Stamey sextant scheme (6SPBx) and 8 lateral cores scheme (8PBx) of all the patients ignoring the results from the other cores as if they had not been taken. Furthermore, we calculated the detection rates of different schemes which were obtained combining 6S+6H PBx (12-core scheme) (12PBx), and 6S+8L PBx (14-core scheme)(14PBx). The 18-core scheme was obtained combining 6S+6H+8L without the two more medial basal cores (18PBx) and the 20-core scheme adding the 6S+6H+8L (20PBx). The 24-core (24PBx) scheme resulted from adding all cores (6S+6H+8L+4TZ). Afterwards, we compared the overall detection rate and the detection rate of IPCa by means of 6-, 12-, 14-, 18-, 20-core schemes with 24PBx. We also calculated the percentage of improvement in cancer detection rate. IPCa was defined according to Epstein criteria.

Results: The 24PBx yielded a diagnosis of prostate cancer in 45.4% of the patients compared with 31.2%, 32.6%, 38.6%, 39.0%, 42.7%, 44.6% and 44.8% of patients on the basis of 6HPBx, 6SPBx, 8PBx, 12PBx, 14PBX, 18PBx and 20PBx, respectively. The overall cancer detection rate of the 24PBx was significantly higher than that of the 6HPBx, 6SPBx, 8PBx, 12PBx, but was not significantly higher than 14PBx, 18PBx or 20PBx. The 24PBx procedure improved the diagnosis yield by 31.1%, 28.0%, 14.8%, 14.0%, 5.8%, 1.6% and 1.1% compared with 6HPBx, 6SPBx, 8PBx, 12PBx, 14PBx, 18PBx and 20PBx, respectively. The 24PBx detected 51 (14.3%), 49 (13.9%), 47 (13.4%), 40 (11.9%), 23 (7.5%), 26 (8.6%), 14 (5.5%) and 9 (3.7%) insignificant prostate tumours, respectively. The IPCa detection rate of the 24PBx was significantly higher than that of the 6HPBx, 6SPBx, 8PBx and 12PBx, but not significantly higher than 14PBx, 18PBx, nor 20PBx.

Conclusion: Our initial 24PBx detected significantly more tumours than an extended approach with 12PBx (an ~14% improvement in cancer detection rate), but also detected significantly more insignificant prostate tumours.

BIOCHEMICAL RECURRENCE IN PATIENTS SUITABLE FOR ACTIVE SURVEILLANCE WHO WERE TREATED WITH RADICAL PROSTATECTOMY

Vincenzo Scattoni1, Nazareno Suardi1, Alberto Briganti1, Andrea Gallina1, Umberto Capitanio1, Marco Bianchi1, Manuela Tutolo1, Andrea Salonia1, Manuela Tutolo1, Roberto Bertini1, Renzo Colombo1, Massimo Freschi2, Claudio Doglioni2, Patrizio Rigatti1 and Francesco Montorsi1

1Department of Urology and 2Department of Pathology, Vita-Salute University, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milano, Italy

Aim: Active surveillance represents a commonly proposed therapeutic option for low-risk prostate cancer patients. However, no data regarding long-term biochemical recurrence are available in patients treated with radical prostatectomy after an active surveillance program fails. Such data will need to be compared to the real outcome of patients who are suitable for active surveillance and who are now treated with radical therapies. We addressed the biochemical recurrence rates in patients suitable for active surveillance who were treated with radical prostatectomy.

Patients and Methods: The study relied on a population of 1,283 patients, treated with radical prostatectomy in a single institution between 2000 and 2009, with complete biopsy and pathological parameters available. We selected patients suitable for active surveillance according to the criteria proposed by Van den Bergh et al. (Eur Urol 2008), resulting in 199 (15.5%) patients selected for the analyses. Kaplan-Meier analyses addressed the biochemical recurrence-free survival in the overall population as well as in the population of patients who could have been considered eligible for active surveillance.

Results: The mean and median age were 64.6 and 65.5 years, respectively. Mean and median PSA were 5.8 and 5.9 ng/ml, respectively. The median number of biopsy cores taken was 18. At radical prostatectomy, 94.0% of patients had organ-confined disease, 4.5% had extracapsular extension, 1.5% had seminal vesicle invasion and 1.0% had lymph node involvement. A significant Gleason score upgrading between biopsy and RP was recorded in 51 (25.6%) of patients. Mean and median follow-up were 32.5 and 26.5 months, respectively. In the
population of patients suitable for active surveillance, only one patient developed biochemical recurrence, thus resulting in a 5-year recurrence-free survival of 100%.

**Conclusion:** Roughly 15% of patients treated with radical prostatectomy may be selected for the active surveillance protocols according to the criteria proposed by Van den Bergh et al. Patients suitable for active surveillance and treated with radical prostatectomy show an excellent prognosis. Active surveillance protocols will need to be compared to RP series results in order to represent a safe alternative for patients with low-risk prostate cancer.

### 146 PROSTATE GLAND MAPPING BEFORE FIRST BIOPSY IN PATIENTS WITH ELEVATED PROSTATE-SPECIFIC ANTIGEN (PSA) LEVELS: ROLE OF MAGNETIC RESONANCE SPECTROSCOPY IMAGING (MRSI) AND MAGNETIC RESONANCE PERFUSION (MRP) AT 3 TESLA PRELIMINARY EXPERIENCE

Valeria Panebianco¹, Silvia Bernardo¹, Alessandro Sciarrà², Stefano Salciccia², Andrea Alfarone², Alessandro Gentilucci², Danilo Lisi¹, Susanna Cattarino², Roberto Passariello¹ and Vincenzo Gentile²

¹Department of Radiology and ²Department of Urology, Sapienza University, Rome, Italy

**Aim:** To prospectively evaluate the role of MRSI and MRP in the detection of prostate tumour foci in patients with persistently elevated PSA levels and prior negative random transrectal ultrasounds (TRUS).

**Patients and Methods:** We recruited in the study 30 consecutive patients, aged between 49 and 68 years old (mean 60.3 years old) and a first negative TRUS, elevated PSA (range: 4.1-20 ng/ml) ratio (free PSA/total PSA) <20 % and negative digital rectal examination. Exclusion criteria for the study were: previous hormonal, surgical or radiation therapies and familiarity for prostate cancer. Prostate mapping with MRSI at 3 T permits to evaluate small tissue volumes by small isotropic voxels (up to 2 mm³). All patients underwent TRUS-guided biopsy (12-core laterally directed TRUS-guided prostate biopsy) on the basis of MRSI and MRP results. All first biopsies were homogeneously performed in our Department by the same physician, as part of the patients’ urological work-up.

**Results:** On a patient by patient basis, MRSI had a sensitivity of 93%, specificity of 89% and accuracy of 90%; MRP had a sensitivity of 88%, specificity of 85% and accuracy of 84% and the combination of MRSI plus MRP asensitivity of 94%, specificity of 90%, and accuracy of 93%, for predicting prostate cancer detection.

**Conclusion:** The combination of MRSI and MRP at 3T showed the potential to guide biopsy to histologically confirmed cancer foci in patients with previously negative TRUS and may be the basis for further investigations of small focus tumours.

### 147 METRONOMIC CYCLOPHOSPHAMIDE IN HORMONE-REFRACTORY PROSTATE CANCER

Valentina Baldazzi¹, Renato Tassi¹, Alberto Lapini², Alice Lunghi², Marco Carini² and Roberto Mazzanti²

¹Oncologia Medica 2 e ²Urologia 1, AOU Careggi, Italy

**Background:** The use of small doses of drugs without extended rest periods, called ‘metronomic’ or ‘high time’ chemotherapy, is an effective regimen characterized by an increasing interest in recent years. Cyclophosphamide (Ctx) is a bi-functional alkylating agent which has been used to treat a variety of malignancies. It has been shown that a continuous low dose of Ctx can cause enhanced immune responses against a variety of antigens, and inhibition of angiogenesis. Both dexamethasone (Dex) and Ctx have been used to treat hormone-refractory prostate cancer (HRPC). Here we present our experience on the use of low-dose Ctx-Dex in the treatment of HRPC.

**Patients and Methods:** From February 2003 to October 2009, we evaluated 63 patients affected by HRPC. Median patients age was 72.5 (range: 50-80) years. The mean Gleason score was 6.8 (range: 3-9). Forty patients (65.5%) presented only biochemical disease; 23 (34.5%) patients had a metastatic disease (the majority of patients had node or bone metastases) and only 7 (11.1%) of these patients received a prior chemotherapy. Ongoing androgen deprivation was required to maintain castration status. The mean PSA level at the beginning of chemotherapy was 54.35 ng/ml (range: 5.5-560 ng/ml). Only 7 (8.75%) patients presented a PSA ≥100 ng/ml. Eligibility criteria for treatment were: histological diagnosis of prostate adenocarcinoma; hormone-refractory state as evidenced by two consecutive increases in PSA after antiandrogen withdrawal; life expectancy of at least 6 months; ECOG P.S: ≤2; bone marrow, renal and liver function within a normal range. Patients received low-dose Ctx of 50 mg in the morning, and Dex 0.5 mg in the evening, without any breaks in a metronomic manner. Treatment was continued until disease progression or intolerable side-effects. Response to treatment was evaluated every 4 weeks by PSA measurement and every 3 months by CT scan and bone scan. The decline of PSA was considered to assess the response consistent with the response guidelines from Prostate-Specific Antigen Working Group.
Results: After 2 months of treatment 56 (88.8%) patients had a PSA response. This response was maintained in 47 patients (74.6%) after 6 months of therapy. In these patients, we established an intermittent treatment, interrupting drug administration when PSA level was lower and restarting when PSA was back at the same level that it was at the beginning. A total of 27 patients showed a response to the therapy after 12 month of treatment; 10 patients (12.5%) presented a PSA response after 24 months, and 5 (6.25%) patients for more than 36 months. No G3-G4 toxicities were recorded.

Conclusion: HRPC remains an incurable disease. The median survival of these patients was approximately 12 months. First-line chemotherapy in metastatic HRPC is docetaxel, but it has a limited efficacy in terms of improving survival. Moreover, this treatment is burdened with adverse events such as neutropenia, anaemia, allergic reaction, fluid retention, fatigue, diarrhoea, nausea or vomiting, and sensory neuropathy. Whether a chemotherapeutic treatment is useful in patients with only biochemical disease is unclear. For this reason, we often need less toxic chemotherapeutic regimens without a negative impact on quality of life. Ctx-Dex is an effective and well-tolerated therapy. Therefore, it can also be used in unfit patients. Based on our experience, this therapy could be indicated in patients with low PSA level and with long doubling time.

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THE ONCOGENIC POTENTIAL OF HUMAN POLYOMAVIRUS BK IN PROSTATE CANCER

Saliccia Stefano1, Alfaroni Andrea1, Cattarino Susanna1, Mischitelli Monica2, Fioriti Daniela3, Bellizzi Anna2, Anzivino Elena2, Barucca Valentini2, Colosimo Maria Teresa2, Sciarra Alessandro3, Di Silverio Franco1, Chiarini Fernanda2 and Pietropaolo Valeria2

1Department of Urology, and 2Department of Public Health Sciences, University “La Sapienza”, Rome, Italy; 3National Institute for Infectious Diseases “Lazzaro Spallanzani”, Rome, Italy

Background: Prostate cancer (PC) remains the most commonly diagnosed malignancy and the second leading cause of cancer-related death in men of Western countries. Screening programs have been implemented to diagnose men with PC in its early stages and although only a subset of men diagnosed with localized PC will experience metastasis, more specific biological criteria should be addressed to better clinically differentiate patients with more aggressive versus indolent PC. Moreover, the molecular pathology of PC is complex and in its relative infancy. Multiple factors contribute to the development and progression of PC: Infectious agents, host immune response and tumour host cytokines might play a role in its pathogenesis and/or progression. Human polyomavirus BK (BKV) is also a good candidate because it naturally infects humans, it is usually acquired early in life, and almost 90% of adults are seroconvert. BKV resides in the kidneys in a latent or persistent state, but it can be reactivated upon immunosuppression of the host. Its oncogenic potential is linked especially to large T-Antigen (TAg). TAg displays multiple functions that alter the normal physiological metabolism of cells, leading to immortalization and neoplastic transformation, and both binds and blocks the functions of tumour suppressor proteins, in particular p53 (1). Moreover, preparing the cellular metabolism to support optimal viral replication, it deregulates cell-cycle control pathways, inducing cell proliferation. BKV has been reported to be detected in a number of human tumours, in particular, those of the urinary tract, since BKV is an uredeliotropic virus (2). Finally, the BKV genome contains a transcriptional control region (TCR) that binds transcriptional cell factors (i.e. p53 oncosuppressor) and undergoes deletion and enhancement processes. This generates variants that might impair the replication ability of the virus, leading to an increased transformation potential.

Patients and Methods: On this basis, data regarding 36 patients (median age of 63 years) with biopsy-proven clinically T2-T3N0M0 prostate adenocarcinoma were analysed. Tumour grade was described at radical prostatectomy according to the Gleason grading system. BKV sequences were sought in urine, blood, and fresh and paraffin-embedded prostate cancer samples by means of quantitative assay. In addition, BKV-TAg and tumour suppressor p53 localization in neoplastic cells was examined by immunohistochemistry with antibodies specific to TAg or p53. Finally, the sequencing analysis of p53-specific DNA-binding exons (exons 5-9) was carried out to determine if p53 mutations might be correlated with viral infection and/or progression of the cancer. As controls, 15 patients (median age of 67 years) with histological diagnosis of benign prostatic hyperplasia were examined.

Results: Results showed that BKV-DNA was found in urine (62%), plasma (33%), and in fresh prostate cancer
specimens (80%). No controls were found to be positive. The analysis of p53 gene showed several mutations in patients with high Gleason score, according to tumour advanced stage. In particular, it was found that codons 249 (exon 7) and 273 (exon 8) were more susceptible to mutation for all examined patients. Immunohistochemical analysis showed the localization of p53 and TAg in the cytoplasm, whereas in TAg-negative tumours, p53 expression was nuclear.

**Conclusion:** Results obtained allowed us to conclude that BKV acts as a cofactor in the pathogenesis of PC. However, more investigations are required to elucidate the pathways by which BKV could trigger neoplastic transformation.

**References**


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### 149 TISSUE PHARMACOKINETICS OF MITOMYCIN-C IN THE HUMAN BLADDER WALL AFTER PASSIVE DIFFUSION, THERMO-CHEMOTHERAPY AND ELECTROMOTIVE DRUG ADMINISTRATION

Cristian Verri1, Emanuele Liberati1, Marco Casilio1, Renato Massoud2, Giorgio Fucci2, Susanna Dolci3, Pierluigi Navarra4, Fiammetta Torelli1 and Savino M. Di Stasi1

Departments of 1Surgery/Urology, 2Clinical Biochemistry and 3Cell and Biology, Tor Vergata University, via Montpellier 1, 00133 Rome, Italy; 4Institute of Pharmacology, Catholic University, Largo Francesco Vito 00168, Rome, Italy

**Background and Aim:** Device-assisted intravesical mitomycin-C (MMC), including electromotive drug administration (EMDA) and thermo-chemotherapy (TC), shows promise and offers the prospect for greater efficacy than passive diffusion (PD). Integration of drug delivery with tissue pharmacodynamic data provides a means for the rational design of intravesical treatments. The objective of this study was to compare concentration–depth profiles of MMC in the bladder wall after PD, TC and EMDA.

**Materials and Methods:** During each experiment, three full-thickness sections of viable human bladder wall were placed between the two chambers of individual diffusion cells, with urothelium exposed to donor compartments containing 40 mg of MMC in 100 ml water and with serosa-facing receptor compartments containing 100 ml of 0.9% NaCl solutions. Fifteen paired experiments were conducted over a 30-min period. In TC experiments, the two chamber cells were placed in an incubator at 45°C, with the donor compartments filled with heated MMC solutions at 44°C. In EMDA experiments, an anode was placed in the donor compartment and a cathode in the receptor compartment. The electrodes were connected to the current generator and experiments were performed with pulsed direct current of 23 mA. No electric current or hyperthermia were applied in PD control experiments. Bladder wall sections were cut serially into 40-mm slices parallel to the urothelium, the tissues were homogenized and supernatants analyzed by high-performance liquid chromatography for MMC concentration.

**Results:** Concentration–depth profiles of MMC in bladder wall tissues following PD, TC and EMDA are reported below. Data are expressed as the mean ± standard error of the mean (SEM) of 15 replicates per experimental group (μg of MMC/g of wet tissue).

<table>
<thead>
<tr>
<th></th>
<th>PD</th>
<th>TC</th>
<th>EMDA</th>
<th>p-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelium (80-200μm)</td>
<td>53.057±8.240</td>
<td>58.270±8.820</td>
<td>207.991±23.440</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lamina propria (200-1200μm)</td>
<td>18.095±2.139</td>
<td>20.935±3.205</td>
<td>85.339±5.882</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Muscle layer (1200-4000μm)</td>
<td>2.120±0.326</td>
<td>2.424±0.297</td>
<td>24.888±3.645</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*pBoth EMDA vs. PD and EMDA vs. TC.

The mean concentration of MMC transported in urothelium, lamina propria and muscle layers by EMDA significantly exceeded that achieved by PD and TC. Non significant differences were found between PD and TC.

**Conclusion:** EMDA significantly enhances MMC transport into all of the layers of the bladder wall compared to both PD and TC.

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### 150 SUBGROUP ANALYSIS AND UPDATED RESULTS OF A RANDOMIZED STUDY COMPARING SORAFENIB PLUS INTERLEUKIN-2 VERSUS SORAFENIB ALONE AS FIRST-LINE TREATMENT IN METASTATIC RENAL CELL CARCINOMA

Giuseppe Procopio1, Elena Verzoni1, Sergio Bracarda2, Giario Conti2, Valentina Guadalupi1, Cinzia Ortega4, Nicola Nicolai1, Tullio Torelli1, Emilio Bajetta1 and Roberto Salvioni1; on behalf of the ITMO Study Group

1Fondazione IRCCS INT, Milano, 2A.O. Perugia, 3Ospedale S. Anna Como, 4IRCC Candiole, Italy
**Background:** A randomized phase 2 study showed that in the first line treatment of metastatic renal cell carcinoma (mRCC), the combination of sorafenib (So) with interleukin-2 (IL-2) moderately improves the efficacy of therapy when compared to So alone. The subgroup analysis planned in the study design and updated results are reported.

**Patients and Methods:** A total of 128 treatment-naïve patients with mRCC were enrolled in the study. Patients were randomized to receive So (given orally at 400 mg twice daily, continuously) and IL-2, 4.5 MIU subcutaneously, five time a week for four consecutive weeks every six (Arm A), or So alone (Arm B). After the first 40 patients were enrolled, 20 in each arm, a dose reduction of IL-2 was performed in order to improve the safety profile. Therefore, the remaining 44 patients received IL-2 at 3 MIU for 2 consecutive weeks every four.

The study sample size was calculated according to a 'phase 2.5 design'; the progression-free survival (PFS) curves were estimated by the Kaplan-Meier method and compared by means of the log-rank test. Patients were stratified according to different histologies and Motzer’s prognostic criteria.

**Results:** The overall median PFS was 33 weeks for So plus IL-2 compared to 28 weeks for So alone ($p=0.125$). In patients with good prognosis, the median and 1-year PFS were 49 weeks and 47.4% and 41 weeks and 32.1% in favour of the combination treatment. In clear cell histotypes, the median and 1-year PFS were 40 weeks and 37.6%, respectively, compared to 34 weeks and 30.1% in favour of the combined treatment.

When considering the two subgroups of patients receiving full or lower dose of IL-2 separately, the median PFS was 55.5 weeks compared to 31 weeks in favour of the higher dose. Additionally, the 1-year PFS was 50% and 25.1% for full and lower dose of IL-2 respectively.

The most commonly reported adverse events were asthenia, hand-foot syndrome, hypertension and diarrhoea. Grade 3-4 adverse events were reported in 33% of patients in the combination treatment arm and in 22% in the single agent arm.

**Conclusion:** The combination of So plus IL-2 was feasible. Subgroup analysis suggest that patients with clear cell tumours and those with good prognosis benefit more from the addition of IL-2. The improvement in PFS was meaningful in patients receiving higher doses of IL-2.

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**Background:** To assess if an *ex vivo* metabolomic approach can be used to discover metabolic biomarkers that are distinct in prostate cancer and healthy glands and its correlation with metabolites obtained by standard *in vivo* 1H-MRSI.

**Patients and Methods:** We retrospectively reviewed a total of 51 prostate MRI examinations, including morphological imaging, 1H-MRSI and DCE-MRI protocols, carried out from June 2009 to December 2009. All patients underwent 1H-MRSI at 1.5 T. After the radical retropubic prostatectomy RRP, a high resolution 11 T spectroscopy was performed on surgical samples. The compounds of samples were identified and quantified by comparing the spectrum to a collection of reference spectra of pure compounds. Multivariate analysis was applied on 1H-NMR metabolites curve and correlated with those of *in vivo* MRSI. This is used to discern significant patterns in complex data sets and is particularly appropriate in situations where there are more variables than samples in the data set and to classify metabolites in classes.

**Results:** In this study, we show how this approach, applied to 1H-MRSI/DCE-MRI results, allows us to differentiate among the various prostatic diseases in a non-invasive way with 100% accuracy. These findings suggest that multivariate analysis of 1H-MRSI/DCE-MRI can significantly improve the diagnostic accuracy for these pathological entities.

**Conclusion:** This work may be the basis for further development of new *in vivo* MRSI acquisition modalities and may improve diagnostic accuracy level to identify biochemical changes and also metabolic markers for cancer diagnosis.

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**152 ROBOT-ASSISTED LAPAROSCOPIC RADICAL PROSTATECTOMY: ASSESSMENT OF QUALITY OF LIFE AFTER ONE YEAR FOLLOW-UP**

Alessandra Beato, Filippo Annino, Maria Chiara Sighinolfi, Cosimo De Carne, Salvatore Micali, Stefano De Stefani and Giampaolo Bianchi

Department of Urology, University of Modena and Reggio Emilia, Modena, Italy

**Background:** We report the results, in term of quality of life (QoL), of our first 37 consecutive robotic assisted laparoscopic rostectomy (RALP) with more than 12 months follow-up.
**Patients and Methods:** Thirty-seven patients underwent RALP with an energy-free intrafascial (endo- or interfascial) nerve-sparing approach from October 2007 to October 2008. Patients were selected for: Gleason score ≤7(3+4), PSA ≤15 ng/ml, clinical stage ≤T2. The median age was 63 years. Data was collected using the SF-12 Health Survey questionnaire score evaluated at 0 and 12 months. The questionnaire focuses on two domains: mental and physical health (Physical Component Summary, PCS, and Mental Component Summary, MCS). Data were analysed with paired samples t-test.

**Results:** The physical score did not differ significantly before and after RALP \( p=0.5 \) (PCS-pre 50.9 +/- 6.9 vs. PCS-post 50.2 +/- 5.5), while the mental score improved after RALP \( p<0.001 \) (MCS-pre 45.6 +/- 11.0 vs. MCS-post 52.4 +/- 8.8). Urinary continence defined as 0/security pad/day was set at 93% (54/58 pts). These outcomes were consistent with the last question of the ICIQ questionnaire (continence-related QoL) that was not impaired after RALP \( p=0.7 \).

**Conclusion:** RALP is a safe procedure with minimal morbidity for the patients even during the first cases of the learning curve: The improvement in quality of life in term of mental state regarding prostate cancer and the unaffected physical status confirm this statement.

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**NEURO-FUZZY SYSTEM FOR PREDICTING PROSTATE CANCER**

Luigi Benecchi, Anna Maria Pieri, Carmelo Destro Pastizzaro, Nicoletta Uliano, Andrea Prati, Antonio Savino, Roberto Arnaudi, Dario Cerasi, Domenico Potenzoni and Michele Potenzoni

Department of Urology, Fidenza Hospital, Parma, Italy

**Background and Aim:** The fuzzy system and neural network are complementary technologies in the design of adaptive intelligent system. An artificial neural network (ANN) learns from scratch by adjusting the interconnections between layers. A neuro-fuzzy system is simply a fuzzy inference system trained by a neural network-learning algorithm. The aim of our work was to develop a neuro-fuzzy system to predict a positive prostate biopsy. The cases were random divided into a train-test group (800 cases) and validation group (480 cases).

**Patients and Methods:** We retrospectively reviewed 1,280 patients who underwent prostate biopsy. All men had a PSA level of less than 20 ng/ml. Of the 1280 men, 469 (36.6%) had prostate cancer. A neuro-fuzzy system was developed using a coactive neuro-fuzzy inference system model. The model was composed of an input layer with four neurons (PSA, percentage-free PSA, PSA density and age), and an output neuron representing the output value of the predictor. The predictive accuracy of the neuro-fuzzy system was superior to that of total PSA, PSA density, percentage-free PSA and at 90%-.95% of sensitivity even to that of logistic regression.

**Conclusion:** This study presented a neuro-fuzzy system based on both serum data (total PSA, percentage-free PSA, and PSA density) and clinical data (age) to enhance the performance of PSA in predicting a positive prostate biopsy. The predictive accuracy of the neuro-fuzzy system was superior to that of total PSA, PSA density, percentage-free PSA.
**Results:** A total of 256 men entered the study. A total of 79 tumours (30.8%) were found by ultrasound-guided prostate biopsies. The median PSA before the biopsy was 7.05 (range 1.4 to 52.7 μg/l, median age was 62 years (range 36 to 84). Median percent free PSA was 16.67% (range 1.48 to 50.7). Median PSA density was 0.14 (range 0.03 to 0.99). Median PSADT was 4.49 (range –2101 to 554). The median percentage free PSA slope was –0.45 for prostate cancer patients and 0.28 for controls (p<0.001). On univariate and multivariate analysis, the percentage free PSA, lnPSA slope and percentage free PSA slope showed a significant ability to predict the outcome of a 12-core prostate biopsy. At receiver operating characteristic curve analysis, the area under the curve (AUC) of PSA was 0.555 (95% confidence interval 0.492 to 0.617) and the AUC of the slope for percentage free PSA was 0.659 (95% confidence interval 0.597 to 0.717), with a significative statistical difference (p=0.041). A value of percentage free PSA slope equal to zero corresponded to a sensitivity of 65% and a specificity of 60%.

**Conclusion:** We found that the slope for the percentage of free PSA with time curve was an independent predictor of prostate cancer at 12-core prostate biopsy.

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**PSA ACCELERATION**

Luigi Benecchi, Carmelo Destro Pastizzaro, Anna Maria Pieri, Michele Potenzoni, Nicoletta Uliano, Andrea Prati, Antonio Savino, Roberto Arnaudi, Dario Cerasi and Domenico Potenzoni

Department of Urology, Fidenza Hospital, Parma, Italy

**Background and Aim:** PSA kinetic and, in particular, PSA acceleration can offer great opportunities for prostate cancer diagnosis. PSA acceleration is calculated as the slope of lnPSA versus time, where ln is the natural logarithm. The aim of this study was to determine the best interval of time in which PSA acceleration can be calculated with the best result in terms of specificity and sensitivity.

**Patients and Methods:** Between January 2001 to January 2009, all men who underwent transrectal ultrasound-guided prostate biopsy with 12 or more cores and with at least 3 consecutive PSA measurements in at least 365 days entered the study. The ‘acceleration’ of PSA (lnPSA slope) was calculated as the slope of lnPSA versus time, where lnPSA is the natural logarithm of PSA. The PSA acceleration was evaluated in different intervals of time: within 1 year (365 days) before biopsy, 2 years (730 days), 3 years (1095 days), 4 years (1460 days), 5 years (1825 days) and 6 years (2190 days) before biopsy.

**Results:** A total of 741 men entered the study, with 184 PSA measurements, from 3 to 28 for each man. The median interval of time between the first and last PSA assay was 1172 days (range 368–5749). A total of 255 tumours were found at the ultrasound-guided prostate biopsies (34.4%). At the receiver operating characteristic curve analyses, the area under the curve (AUC) of PSA acceleration was better than that of PSA, PSA velocity, PSA slope, and PSA doubling time. Among PSA kinetics, the highest value of the AUC was for PSA acceleration calculated in the period of time between 730 and 1460 days before biopsy.

**Conclusion:** This is the first study that defines the best interval of time in which PSA acceleration can be evaluated. PSA acceleration provides a more accurate discrimination than PSA, PSA velocity, PSA slope, and PSA doubling time for prostate cancer diagnosis. Three or more PSA measurements in a period of time between 730 and 1460 days permits an accurate calculation of PSA acceleration.

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**NOMOGRAPH FOR PREDICTING A POSITIVE PROSTATE BIOPSY**

Luigi Benecchi, Anna Maria Pieri, Carmelo Destro Pastizzaro, Michele Potenzoni, Nicoletta Uliano, Andrea Prati, Antonio Savino, Roberto Arnaudi, Dario Cerasi and Domenico Potenzoni

Department of Urology, Fidenza Hospital, Parma, Italy

**Background and Aim:** A new tool for PSA kinetic is PSA acceleration, the slope of lnPSA versus time, where ln is the natural logarithm. The aim of this study was to develop a nomogram that would be useful for counseling patients in the decision to undergo prostate biopsy.

**Patients and Methods:** We analysed data for all men with 3 or more consecutive PSA measurements in at least 730 days who underwent a transrectal ultrasound-guided prostate biopsy with 12 or more cores in our Department. The factors we evaluated were age, digital rectal examination findings, PSA level, free to total PSA ratio, prostate volume and lnPSAslope.

**Results:** A total of 507 men entered the study and were divided randomly into two groups: one with 300 cases for multivariate logistic regression analyses and nomogram development, and a second group for validation with 207 patients. A total of 153 tumours (30.1%) were found. The stepwise multivariate logistic regression analysis showed that all the factors, except age and PSA, showed a significant ability to predict the outcome of a 12-core prostate biopsy. A nomogram was devised with the results of the model. The area under the curve of the model was 0.801 (95% confidence interval 0.783 to 0.819) and the area under the curve of the nomogram was 0.794 (95% confidence interval 0.777 to 0.810). The area under the curve of the model for validation was 0.795 (95% confidence interval 0.768 to 0.822) and the area under the curve of the nomogram was 0.781 (95% confidence interval 0.757 to 0.804). The nomogram was devised with the results of the model. The area under the curve of the model was 0.801 (95% confidence interval 0.783 to 0.819) and the area under the curve of the nomogram was 0.794 (95% confidence interval 0.777 to 0.810). The area under the curve of the model for validation was 0.795 (95% confidence interval 0.768 to 0.822) and the area under the curve of the nomogram was 0.781 (95% confidence interval 0.757 to 0.804).
interval 0.740-0.853) better than that for PSA, free to total PSA ratio, prostate volume and lnPSAslope alone (p<0.05).

**Conclusion:** We successfully developed an accurate model to predict the outcome of prostate biopsy. Addition of free to total PSA ratio, DRE, prostate volume and lnPSA slope sharply improves the accuracy of our model.

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NEW PERSPECTIVES IN THE SURGICAL MANAGEMENT OF ADVANCED RENAL CELL CARCINOMA IN THE ERA OF TARGETED THERAPIES: PRELIMINARY CASE SERIES FROM A REFERRAL INSTITUTION

Roberto Salvioni1, Nicola Nicolai1, Mario Catanzaro1, Andrea Necchi1, Tullio Torelli1, Angelo Milan1, Luigi Piva1, Davide Biasoni1, Silvia Stagni1, Paolo Girotti1, Antonio Procopio2, Elena Verzoni2 and Emilio Bajetta2

1S.C. Urologia e 2Oncologia Medica B, Istituto Nazionale dei Tumori di Milano, Italy

**Background:** Surgery has been the mainstay of renal cell carcinoma (RCC) therapy for several decades due to the lack of effective alternatives. Currently available for a few years in clinics, targeted therapies (TT) are revolutionizing the clinical course of advanced RCC. Radical nephrectomy is performed before these novel treatments in 67-100% of patients (pts) from published series. New questions addressing the optimal integration of surgery and TT are now arising. We collected a prospective case series aimed to investigate patient outcome with a multimodal approach, where surgery followed or anticipated targeted treatment in patients with locally advanced and/or metastatic RCC.

**Patients and Methods:** From Jan 2007 to Feb 2010, 19 consecutive patients (9 males and 10 females) were admitted to our Institution to be evaluated for an eventual multimodal treatment of advanced, metastatic or bilateral disease. Three cases of sequential TT followed by surgical approach for locally advanced, metastatic or bilateral disease. Three cases of complete remission and of 2 stable disease were achieved; 8 patients with partial response were submitted to surgery. Follow-up ranged from 6 to 32 months. Viable tumour was present in all resected cases. No issues with wound healing, bleeding or thromboembolic events have been encountered. No Grade 3-4 toxicity has been observed while all cases developed TT-induced cutaneous G1-2 late effects.

**Conclusion:** Targeted therapy followed by surgery could be an effective and feasible approach in patients with locally advanced and metastatic RCC. Knowledge of the optimal timing and duration of the pre-surgical medical approach will be derived from more robust data.

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COLO-VESICAL FISTULA: FIRST DESCRIPTION OF SURGICAL LAPAROSCOPICAL TREATMENT WITHOUT INTESTINAL RESECTION

Ettore Mearini, Emanuele Cottini, Giovanni Cochettti, Maria Rita Serva, Francesco Barillaro, Antonella Giannantoni and Carlo Vivacqua

Division of Urology, Andrology and Mini-invasive Techniques, University of Perugia-Terni, Perugia, Italy

**Background:** Enterovesical fistulae comprise a pathological entity of minor influence, possibly arising from evolution of phlogistic intestinal pathologies, neoplastic or more rarely of iatrogenic origin. Mostly, they are colo-vesical fistulae. The standardized treatment includes the removal of the fistulous track, the suture of the bladder wall, the removal of the intestinal segment and the packaging of an intestinal continuity. Conservative surgery, which considers the only removal of the fistulous track, does not represent the therapeutic standard and it is not currently recommended. The laparoscopical approach has not yet been accepted as a treatment of choice and even if it is reserved for selected cases, it is still associated with a high conversion rate and a high postoperative morbidity.

**Case Report:** In August 2008, a 69-year-old man underwent an endoscopic removal of a 2 cm polypoid formation to the level of a diverticulum of sigmoid flexure (ref: Adenoma with reports of phlogosis). Due to the frequent episodes of recurring cystitis for two months, associated with pneumaturia, the patient came to our observation in September 2008. However, these episodes had already appeared 15 days from the execution of the previously mentioned endoscopic examination. An abdominal ultrasound scan, some days before our examination, reported the presence of gas in the bladder, confirmed by CT as well. Via cystoscopy, we noticed hanging faecal material and a projecting and erythematic area at the
level of the vesical cupola, whose biopsy showed only urothelial hyperplasia and chronic phlogosis. Two 10 mm trocars were placed at the level of the right and left iliac pit and another 5 mm trocar in the sovra-umbilical position. During the inspection, a fistulous track vesico-colic was highlighted. The colon was separated from the bladder by dissection of the adhesions and the inflammatory tissue around the fistulous track. However, the diverticular disease appeared macroscopically limited. Therefore, we decided only to resect the fistulous track. The involved bladder wall was resected to the normal mucosa and then the wall defect was closed. In order to protect the sutured tissue, we placed epiploic fat.

Results: The operating time was 210 min with a blood loss of 300 cc. Bowel function resumed during the second postoperative day. After a follow-up of 6 months, cystoscopy and ultrasonography findings were negative.

Conclusion: A surgical treatment which considers only the resection of the fistulous track is described only in two scientific reports. Our case represents the first report of a conservative treatment through a laparoscopic approach. We believe that this strategy can be used on patients with comorbidities for whom colon resection can represent a considerable surgical risk.

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NODAL METASTASES OF PENILE SQUAMOUS CELL CARCINOMA (SCC): PROGNOSTIC PARAMETERS OF A RECENT SERIES OF PATIENTS UNDERGOING LYMPH NODE DISSECTION (LND) WITH/WITHOUT SYSTEMIC CHEMOTHERAPY

Luigi Piva, Mario Catanzaro, Nicola Nicolai, Andrea Necchio, Angelo Milani, Davide Biasoni, Silvia Stagni, Tullio Torelli, Paolo Girotti and Roberto Salvioni

S.C. Urologia, Istituto Nazionale dei Tumori di Milano, Italy

Background: Nodal metastasis from penile SCC is the most crucial event in the history of this disease. Prognosis of patients (pts) with nodal metastasis is commonly considered unsatisfactory, but the majority of the few available reports refer to old series. We analysed our most recent series of pts with lymph node involvement from penile SCC to re-assess factors affecting prognosis.

Patients and Methods: Between 2000 and 2009, 78 consecutive pts with nodal metastasis from penile SCC were referred to our Institution. A total of 68 pts (median age: 58 years) were fully evaluable for disease characteristics and follow-up. Bilateral and pN3 disease were present in 11 (16%) and in 26 (38%) cases. 10 pts underwent inguinal, while 58 (85%) inguinal-pelvic LND. LND was unilateral in 21 and bilateral in 47 cases, respectively and was radical in 64/68 pts (94%). Chemotherapy was delivered as primary treatment in 13 (19%), as adjuvant in 25 (37%) and as a combination of neo-adjuvant and adjuvant in 4 (6%) pts, respectively. Medical treatment was heterogeneous and included cisplatin and 5 fluorouracil with/without a taxane (T/PF) or a combination of vincristine, bleomycin and methotrexate (VBM).

Results: A total of 33 (49%) pts relapsed after a median time of 5 (IQR 3-9) months, while 35 (51%) remained progression-free following a median follow-up of 14(IQR 2.5-52) months. Significant factors associated with relapse were bilateral extension of disease (p=0.0013 log-rank test; HR 4.96, 95% CI 1.86-13.15) and pN3 disease (p=0.002 log-rank test; HR 3.82, 95% CI 1.63-8.95). Systemic chemotherapy prior to or following surgery was not a significant parameter for recurrence (p=0.1989 log-rank test; HR 0.61, 95% CI 0.29-1.29). Nine (27%) out of 33 relapsing pts were rescued with further treatments and are still alive (median overall survival of 10 months; IQR 5-16 months). Currently, 44 (65%) of 68 pts are still alive and without evidence of disease after a median follow-up of 10.5 (IQR 3.75-33.25) months.

Conclusion: Our data indicate that radical surgery currently plays a major role in controlling metastatic penile SCC, and confirm that bilateral and pelvic extension of nodal disease are the most significant unfavorable factors for recurrence. Systemic therapy exerts some effect in advanced disease, but its role still needs to be defined. Few pts can be rescued following further recurrent disease. Early detection and proper surgery remain the most important factors in preventing disease progression.

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STABILIZATION OF UROTHELIAL PRIMARY CULTURE AND CHEMOSENSITIVITY ASSAY IN TRANSITIONAL CELL CARCINOMA (TCC)

Cinzia Fabbiani1, Giovanni Palleschi2, Antonio Luigi Pastore2, Luigi Silvestri2, Andrea Ripoli2, Domenico Autieri2, Vincenzo Petrozza3, Antonella Calogero1 and Antonio Carbone2

1Department of Experimental Medicine Polo Pontino, Sapienza University of Rome, Corso della Repubblica Latina, Italy; 2Department of Urology Polo Pontino, Sapienza University of Rome, via Firenze SNC Terracina (LT), Italy; 3Department of Histopathology Polo Pontino, Sapienza University of Rome, via Faggiana Latina, Italy
**Background and Aim:** Response to arecaidine, a M2 muscarinic agonist, in human urothelial cells grown as primary cultures *in vitro* from either normal or neoplastic tissue was investigated.

**Materials and Methods:** The human urothelial cells were obtained from biopsies of patients with TCC. Biopsies and cores of urothelial tissues were achieved during a transurethral resection of bladder. In addition, effects of arecaidine on survival of the stem-like cell sub-population present in our primary cultures were observed.

**Results:** Six primary cultures, normal or neoplastic, have been established. Normally, about 20 days were needed on average for their establishment *in vitro*. The urothelial tissue was minced and mechanically dissociated. Cells obtained were then cultured in Dulbecco’s modified Eagle’s medium. Arecaidine demonstrated an anti-proliferative effect on all primary cultures. In *vitro* cell proliferation was inhibited after 24 hours following treatment and reached maximum levels of inhibition (80%) after 6 days of treatment with arecaidine 100 Um. Proliferative activity was monitored by a standard 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay. In all our primary cultures, about 1-2% of stem-like urothelial cancer cells, CD133- and OCT4-positive, were detected by immunofluorescence.

**Conclusion:** The present study shows that selective activation of M2 muscarinic receptors may be responsible for a reduced survival and premature cell death at high rates in time- and dose-dependent manners. The antineoplastic properties of antimuscarinic receptor seems to depend on the high presence of M2 receptor (70-80%) on the membrane of normal bladder cells. In conclusion, our data support the possible involvement of muscarinic receptor in the urothelial cancer.

**References**

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**A NOVEL LOCALIZATION OF LOW-AFFINITY NERVE GROWTH FACTOR RECEPTOR (P75) IN NORMAL AND NEOPLASTIC HUMAN PROSTATE. AN IMMUNOHISTOCHEMICAL AND IMMUNOCYTOCHEMICAL STUDY**

**Emanuele Cottini**¹, Giovanni Cochetti¹, Antonella Giannantoni¹, Anna Maria Stabile², Alessandra Pistilli², Mario Rende² and Ettore Meirini¹

¹Division of Urology, Andrology and Mini-invasive Techniques, University of Perugia-Terni, Perugia, Italy; ²Anatomy and Surgery Section, University of Perugia School of Medicine, “Polo Scientifico-Didattico” of Terni, Italy

**Background and Aim:** The biological role of never growth factor and its p75 receptor in prostate cancer is still controversial. The aim of this work was to evaluate the localization of p75 in normal and neoplastic human prostate as prognostic marker.

**Patients and Methods:** Human samples of normal and prostate cancer were analyzed at light and ultrastructural levels (transmission electron microscopy, TEM). At the light microscopical level, p75 immunoreactivity (IR) in normal human prostate was restricted to the basal cells of the acini, at epithelial-stromal junction. This result was confirmed by TEM. Normal prostatic stromal cells were p75 negative, except for nerves and blood vessels. Prostatic intraepithelial neoplasia showed a relevant proliferation of the epithelial compartment, inclusive of the basal cells that remained p75 IR. However, samples of adenocarcinoma, medium to high grade neoplasia showed different patterns of p75 localization. In fact, while basal cells of the epithelial compartment became progressively p75 negative, a novel strong p75 IR was detected in the stromal compartment, adjacent to the neoplastic acini. Ultrastructural analysis showed that the stromal p75 IR was localized on plasma membrane of smooth muscle cells. Other stromal cells were p75 negative. The amount of p75 IR in the stroma seems to be positively correlated to Gleason score.

**Results:** Our study shows a novel morphological localization of p75 in the stroma of prostate tumour. The positive correlation of this stromal localization with the tumour malignancy suggests a progressive dedifferentiation of the smooth muscle cells that are normally p75 negative. This dedifferentiation of neoplastic smooth muscle cells around the neoplastic acini could be relevant for metastatic invasion of the stroma.

**Conclusion:** Our findings of p75 in the stromal compartment of prostate cancer shows that it could be a novel marker for a better definition of the prostatic cancer malignancy and prognosis.

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**DETECTION OF HTR, HTERT AND CKS2 MRNA IN BLADDER WASHINGS: POTENTIAL MOLECULAR MARKERS OF BLADDER CANCER**
Giovanni Cochetti¹, Emanuele Cottini¹, Letizia Mezzasoma², Chiara Del Buono², Cinzia Antognelli², Michele Del Zingaro³, Vincenzo Nicola Talesa² and Ettore Mearini¹

¹Department of Medical-Surgical Specialties and Public Health, Division of Urology, Andrology and Mini-invasive Techniques, University of Perugia-Terni, Perugia, Italy; ²Department of Experimental Medicine, Division of Cell and Molecular Biology, and ³Department of Medical-Surgical Specialties and Public Health, Division of Urology and Andrology, University of Perugia, Perugia, Italy

Background: Although the field of tumour markers in bladder cancer (BC) is rapidly evolving, no ideal marker currently exists. Combined analysis of molecular biomarkers could enhance the diagnostic power of assay. In this exploratory study, we quantified the transcript levels of three different genes associated with carcinogenesis: human telomerase RNA (hTR), human telomerase reverse transcriptase (hTERT) and CDC28 protein kinase regulatory subunit 2 (CKS2).

Patients and Methods: The study included 99 consecutive patients undergoing flexible cystoscopy for needs related and unrelated to bladder cancer (BC). The patients were classified into two age- and sex-matched groups (P=0.693 and P=0.720, respectively). The first one included 36 patients (32 male, 4 female) with a histopathological diagnosis of BC. The mean age ± SD of the BC group was 68.8 ± 10.8 (range 48 to 87) years. The second group (controls) included 63 patients (59 male, 11 female) with a mean age ± SD of 69.9 ± 10.6 (range 41 to 86) years. Tumour stage was determined using TNM (tumour lymph nodes and metastasis) and grading according to the World Health Organization (WHO 1973) guidelines. Tumours were classified as: 72.2% (26/36) superficial [pTaG1 (n=24), pT1G1 (n=2)], 27.8% (10/36) invasive [pT2G3]. At the time of sampling, all controls were BC-free. Messenger RNA amounts were measured by quantitative real-time reverse transcriptase chain reaction in bladder washings of patients with and without BC. Non parametric receiver operating characteristics analysis was performed to assess the accuracy of study variables to discriminate between BC and controls. The diagnostic value of concomitant examination of these markers was evaluated by logistic regression analysis.

Results: Washing fluids transcripts detection of hTR, hTERT and CKS2 genes revealed highly significant differences between BC patients and controls. In particular, hTR, hTERT and CKS2 showed a significant 2.1-fold decrement, 9.3-fold and 8.45-fold increment, respectively, in the expression levels of relative genes compared to controls. The area under the curve (AUC) was 0.67 (95% CI: 0.53-0.80) for hTR, 0.68 (95% CI: 0.54-0.83) for hTERT and 0.72 (95% CI: 0.58-0.86) for CKS2, indicating an average discrimination power between BC and controls, for all these tests when singularly considered. A model including hTR and CKS2 showed a higher clinical performance in comparison to each marker singularly considered. The analysis was also useful when stratifying BC in superficial or invasive forms. Detection of transcripts hTR, hTERT and CKS2 in washing fluid and, most importantly, their combination in different models, represent molecular markers of urothelial malignancy (AUC/hTR/CKS2=0.90, 95% CI: 0.82 - 0.98).

Conclusion: Taken together these findings suggest that hTR, hTERT and CKS2 gene expression and, most importantly, their combination in different models, represent molecular markers of urothelial malignancy. Confirmation of our results in urine might provide a useful non-invasive tool in early detection and clinical evaluation of BC.

164 COST ANALYSIS OF TRANSRECTAL PROSTATE BIOPSY

Andrea Fandella

Casa Di Cura Giovanni XXIII, via Giovanni XXIII 7, 31050 Monastier di Treviso, Italy

Background: The literature reports a mortality and morbidity from prostatic carcinoma that permits a better use of some routine diagnostic tools such as transrectal ultrasound-guided biopsy (TRUSB). The aim of this work is to quantify the overall cost of TRUSB of the prostate and to assess the economic impact of current procedures for diagnosing prostatic carcinoma.

Materials and Methods: The total cost of TRUSB was calculated with reference to 247 procedures performed in 2008. The following cost factors were evaluated: personnel, materials, maintenance - depreciation of the equipment, energy consumption and hospital overheads. A literature review was also carried out to check if our extrapolated costs corresponded to those of other authors worldwide and to consider them in the wider framework of the economic effectiveness of strategies for early diagnosis of cancer of the prostate.

Results: The overall cost of TRUSB (8 samples) was 249.00 Euros, obtained by adding together the costs of: personnel (160.00 Euros); materials (59.00 Euros); maintenance and depreciation of the equipment (12.40 Euros); energy consumption (1 Euro); hospital overheads (17.50 Euros). With extended or saturation biopsies the cost increases due to the additional time needed by pathologists and can be calculated as 300.00 Euros. The literature review points out TRUSB as an invasive tool for diagnosing prostatic carcinoma which is clinically and economically controversial.
Postmortems report the presence of cancer cells in the prostate of 50% of 70-year-old men, while extrapolations calculate a morbidity from prostatic carcinoma in 9.5% of 50-year-old men. It is therefore obvious that randomized prostatic biopsies, methods apart, have a good probability of being positive. This probability varies with the patient’s age, the level of prostate-specific antigen (PSA), the density of PSA/cm3 of prostate volume (PSAD), detection by digital exploration and/or positive transrectal ultrasound.

**Conclusion:** Despite application of all these criteria and critical assessment of the patient’s general conditions, TRUSB is indicated for 16% of the male population over 50 years old, with obvious economic consequences. It has recently been suggested that the ratio between free PSA (antigenic fraction of the total serum PSA) and total PSA could be clinically useful as an effective predictive method regarding TRUSB positivity or negativity. It would appear that free PSA could therefore reduce the number of TRUSB carrie dout.

**165 DIABETES MELLITUS IS A RISK FACTOR FOR PROGRESSION IN RENAL CELL CARCINOMA**

Antonio Vavallo, Giuseppe Lucarelli, Michele Tedeschi, Stefano Vittorio Impedovo, Monica Rutigliano, Silvano Palazzo, Carlo Bettocchi, Michele Battaglia, Francesco Paolo Selvaggi and Pasquale Ditonno

Urology, Andrology and Kidney Transplantation Unit, Department of Emergency and Organ Transplantation, University of Bari, Piazza G. Cesare 11, Bari, Italy

**Background:** An increased risk of renal cell cancer (RCC) among diabetes mellitus (DM) patients has been reported in clinical and experimental studies (1-3). The effect of pre-existing diabetes on prognosis in newly diagnosed RCC patients has not been reported in the literature. In the present study, we investigated the influence of diabetes on clinicopathological features of RCC: histological type, stage, grade and tumour size and on the overall and progression-free survival in RCC patients. It is of great significance to investigate the relationship between diabetes and kidney cancer in order to implement more appropriate strategies for screening procedures, surgical approaches, targeted therapies and follow-up.

**Patients and Methods:** We identified 462 patients treated with radical nephrectomy or nephron-sparing surgery for unilateral sporadic RCC between 1979 and 2000. The clinical features studied were patient age, sex, ECOG performance status, symptoms at presentation and presence of diabetes mellitus. The pathological features studied included histological subtype, tumour size, 2002 TNM primary tumour classification, nuclear grade, coagulative tumour necrosis and presence of sarcomatoid differentiation. To test the association of diabetes with survival end-points, Kaplan-Meier and Cox multivariable logistic regression models were applied.

**Results:** Out of 462 patients (276 males, 186 females, mean age 59.8 years), 76 (16.5%) had diabetes mellitus (11 with type 1 DM and 65 with type 2). An increased incidence of diabetes in RCC patients was found. Mean follow-up was 43 months. Overall survival was 34.3 vs. 67.5 months in diabetic and non-diabetic patients (p<0.05) respectively. Progression-free survival was 26.4 vs. 64.6 months in diabetic and non-diabetic patients, respectively. Disease recurrence occurred in 46 (60.5%) diabetic patients vs. 54 (14.0%) non-diabetic patients (p<0.05). In multivariate analysis diabetes (HR: 4.90; p<0.001) along with stage (HR: 2.01; p=0.01), tumour size (HR: 1.09; p=0.02) and UISS stage system (HR: 1.82; p=0.01) were independent predictors of cancer related-mortality.

**Conclusion:** Patients diagnosed with RCC who have preexisting diabetes were found to have a significantly shorter overall survival, increased risk of recurrence and higher risk for kidney cancer-related mortality compared with those without diabetes.

**References**

**166 LAPAROSCOPIC EXTRAPERITONEAL RADICAL PROSTATECTOMY (LERP) WITH EN-SEAL**

Massimo Madonia, Paolo Soggia, Massimiliano Chessa, Mariano Deriu and Carlo Corbu

Clinica Urologica di Sassari, Viale S. Pietro 43/B, Italy

**Background:** Radical prostatectomy (open, laparoscopic or robot-assisted) is still the treatment of choice for localized prostate cancer. Laparoscopic techniques, proved to have a better control of haemostasis compared to open prostatectomy, but the length of this procedure is usually longer than the standard technique.

**Aim:** To reduce the duration of the procedure maintaining an excellent control of the haemostasis.
**Patients and Methods:** Between 1-31 of January 2010, we performed 6 LERPs. Half of them were carried out using conventional instruments and the other half were performed using a new device to cut and coagulate tissue and blood vessels as to compare the 2 techniques and to test the reliability of the new instrument, both for an accurate evaluation of haemostasis and of the duration of the surgical procedures. L’En-Seal PTC TRIO uses an innovative technology that works on vessels up to 7mm diameters and which achieves seals up to 7 times systolic pressure with minimal thermal spread, sticking, and charring. All these functions are obtained thanks to a multipolar configuration of electrodes and to a device that makes it possible to maintain heating (100°C), but above all, it produces a minimum amount of smoke. The configuration of the instrument makes it possible to take larger samples of tissue in an atraumatic way. The grip is associated with a structure of branches designed with I-Blade geometry which provides a uniform and high compression over the haemostasis area. In both cases, we evaluated the average operative time and the amount of blood loss with the following results: group 1, traditional technique: 170 minutes, with blood loss of 320 ml; group 2, En-Seal: 130 minutes, with blood loss of 290 ml.

**Conclusion:** LERP with the use of En-Seal PTC TRIO allows reduction of the operative time and also maintains excellent intraoperative visibility due to the low production of smoke. It also provides good haemostasis without requiring the use of any metal clips or any other haemostatic devices.

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**RIGHT PELVIC MASS COMPRESSING BLADDER, RECTUM AND OMOLATERAL URETER: CASE REPORT**

Matteo Maggioni¹, Giovanni Longo¹, Riccardo Anceschi¹, Maria Cristina Locatelli¹, Pietro Tombolini¹, Giancarlo Beltramo² and Augusto Maggioni³

¹Urologia, Ospedale San Carlo Borromeo, Milano, Italy; ²Radioterapista, Centro Diagnostico Italiano, Milano, Italy; ³Clinica Urologica I, Università Studi di Milano, Italy

**Background:** Large pelvic masses may represent an important clinical issue, especially regarding surgery. Adequate clinical and radiological evaluation of the mass and of the neighboring anatomical structures, such as the genito-urinary tract, the rectum and neurovascular structures, is of utmost importance for adequate surgical planning.

**Case Report:** A 79-year-old male patient was referred to us for constipation and sudden contraction of diuresis; he had a previous history consisting of COPD, ischemic heart disease, hypertension, NIDDM. The clinical and instrumental evaluation revealed: PSA 84.2, F/T 52.3%, with prostate biopsies not suggestive of neoplastic specimen. The CT scan of abdomen and pelvis detected a right pelvic mass (diameter 10 cm) displacing the bladder and the rectum. Colonoscopy demonstrated compression of rectal ampulla by an extrinsic mass. The retrograde cystouretrography showed a displacement of the prostatic urethra to the left, and footprint along the right side wall of the bladder from extrinsic pelvic mass. At MRI, the right pelvic mass (10.7 × 11 × 6.8 cm) had a cystic pluriconcamerate appearance and was indissociable from the prostate and from the perineal levator ani. The ampulla rectal, bladder, ureter pelvic right were compressed and displaced. The patient underwent exploratory laparotomy, cystic pelvic mass excision and radical prostatectomy, with a final histopathologic diagnosis consisting of: adenocarcinoma of the prostatic ducts of the right lobe, cystic areas with cribriform and papillary aspects. G2, pT3a, pNx; immunophenotype: PSA+, p63-, CA 125-, CK7- and CK20-. The postoperative course was complicated by IMA, which resolved in 5 days after adequate treatment. In 12 days, the bladder catheter was removed with a prompt resumption of micturition; the continence was satisfactory in a few days.

**Results:** The patient underwent radiotherapy and adjuvant hormonal therapy (bicalutamide 50 mg plus leupreolin acetate). At 10 months after surgery, the patient is healthy, with good continence, PSA <0.07, and without evidence of relapse at the clinical and radiologic evaluation (pelvic CT)

**Conclusion:** The use of MRI is the gold standard for evaluation of pelvic masses and the adequate therapeutic approach. Treatment of such masses should be multidisciplinary, even if surgery should consist of radical excision, sometimes also including demolitive surgery in relation to age and comorbidity and life expectancy of the patient; adjuvant and hormonal RT are generally highly recommended.

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**PARA-AORTIC IRRADIATION FOR NODAL RELAPSE OF STAGE I SEMINOMA OF TESTIS: CASE REPORT**

Girolamo Spagnoletti, Anna Maria Leo, Rita Marchese, Raffaella Rignanese, Grazia Anna Nardella, Maria Piserchia and Giuseppe Bove

Department of Radiotherapy, Foggia University Hospital, Italy
Background: Testicular tumours are uncommon but they represent an important group of malignancies in young men. Most patients with seminoma are affected by stage I disease. Adjuvant treatment options for stage I seminoma include postoperative para-aortic nodal irradiation, adjuvant chemotherapy or surveillance. Radiotherapy has been the standard of treatment for the last 50-60 years. Nowadays, surveillance is considered a valid policy since it provides optimal outcomes. Nevertheless, it has not often been adopted because the cost of follow-up is higher and there is concern regarding patient compliance (1). Moreover some authors showed that some conditions, such as tumour size >4 cm and rete testis invasion, are predictors of relapse (1-3). This report describes a case of stage I seminoma with rete testis invasion treated with surgery, which relapsed after two years and was treated with salvage chemotherapy and radiotherapy.

Case Report: A 40-year-old man with stage I pure seminoma infiltrating rete testis was treated with radical left orchiectomy in October 2006. No adjuvant therapy was performed because the patient strongly refused adjuvant treatment and missed the follow-up program. Because of severe abdominal pain, in July 2008, he underwent a chest and abdomen computed tomography (CT) which showed voluminous para-aortic adenopathetic conglomerates starting from the proximal retroperitoneum and reaching the pelvis with compression and dislocation of vessels. Chemotherapy was performed using cisplatin, etoposide and bleomycin. A second CT followed chemotherapy, pointing to a partial response. Radiotherapy was delivered including para-aortic and ipsilateral iliac nodes with a total dose of 36 Gy (1.8 per fraction) and a boost dose of 3.6 Gy (1.8 per fraction) to the macroscopic residual nodes.

Results: Compliance to treatments was good. No acute and late toxicity was observed in relation to radiotherapy or chemotherapy, except for a mild nausea. A thorax and abdomen CT and a positron-emission tomography (PET) were performed two and five months after the end of radiotherapy, respectively: both of them showed a stable nodal disease. The latest CT, in September 2009, pointed to a complete response to treatment. The following PET, in January 2010, confirmed the absence of evident disease, being completely negative.

Conclusion: Patients with stage I seminoma of testis may be safely treated with para-aortic radiotherapy. Surveillance can be a convincing approach in many cases but adjuvant radiation therapy should always be recommended to patients with negative prognostic factors. When a strategy of surveillance is adopted, radiotherapy on para-aortic lymph nodes, which are the predominant site of failure, and chemotherapy are effective treatments at relapse. Seminoma proved to be highly sensitive to radiation therapy and chemotherapy.

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EXPRESSION OF SPANX PROTEINS IN LOW AND HIGH GLEASON SCORE PROSTATE CANCER

Roberto Castiglione1,4, Michele Salemi1,5, Sandro La Vignera1, Rosita Condorelli1, Lucia Olga Vicari1, Cristina Campagna1, Giancarlo Rappazzo2, Angelo Tracia3, Gaetano De Grande6, Rosario D’Agata1, Aldo E. Calogero1 and Enzo Vicari1

1Section of Endocrinology, Andrology and Internal Medicine, Department of Biomedical Sciences, 2Department of Animal Biology, 3Department of Surgical Sciences, Organ Transplant and Advanced Therapies, 4Section of Clinical Pathology and Molecular Oncology, Department of Biomedical Sciences, University of Catania, Catania, Italy; 5Oasi Institute for Research on Mental Retardation and Brain Aging, Troina (ENNA), Italy; 6Unit of Urology, Umberto I Hospital, Siracusa, Italy

Background: Previous genetic studies have investigated the expression of some susceptibility or family genes in prostate cancer (1). The SPANX multi-gene family (human sperm protein associated with the nucleus on the X chromosome) consists of a number of small (15-20 kDa) of very conserved cytoplasmic proteins. SPANX genes comprise five known members (SPANX-A1, -A2, -B, -C, and -D), encoding cancer/testis-specific antigens that are potential targets for cancer immunotherapy. These genes cluster on the X chromosome at Xq27. SPANX-A/D genes are expressed in normal testis and some melanoma cell lines; testis-specific expression of SPANX. Sequence alignments justify a subdivision of this gene family based on the absence (SPANX-A-like) or presence (SPANX-B) of a 18 base-pair sequence stretch in the open reading frame. The SPANX-B-like subfamily is represented by a single gene with the same name. The interest in the SPANX genes is mostly because they are specifically expressed in a variety of tumours as well as in male germ cells. Expression profile analysis showed that at least four of the family members (SPANX-A1, -A2, -B, and -D) are expressed in cancer cells, including highly metastatic
cell lines from melanomas, bladder carcinomas, myelomas, seminomas, embryonal carcinomas and melanoma.

Aim: To investigate the expression of the SPANX protein family in prostate cancer patients with low and high Gleason score.

Patients and Methods: Biopsies of 9 patients (aged 63-79 years, median 74 years) suffering from prostate adenocarcinoma with low, no aggressive phenotype (Gleason grade <7) (n=6) (and/or disease stage I-II) or high, aggressive phenotype (Gleason grade >8) (n=3) (and/or disease stage III-IV) were immunostained for SPANX, using the polyclonal serum against the common SPANX epitope TPTGDSDPQP developed in mouse cells (3). Four-micrometre sections obtained from ten normal skin samples and eight normal prostate tissues were used as normal controls.

Results: Four out of the nine biopsies (44.5%) had epithelial cells with morphological features of carcinoma which stained positive for SPANX protein. The vast majority of the cells (75-80%) were positive to SPANX with a diffuse cytoplasmic and perinuclear localization of the signal. All 4 patients had a low Gleason grade: 5 (3+2), 6 (3+3) and 7 (4+3) in 1, 1 and 2 patients, respectively. The remaining five cases showed no SPANX-positivity (percentage of positivity =0%). Prevalently, these patients had a high Gleason grade which was 8 (4+4) in 3 cases, 7 (3+4) in 1, and 6 (3+3) in the last one. It is noteworthy that SPANX protein expression in prostate cancer was dichotomic: i.e. only absent or present in an elevated number of cells.

Conclusion: These results showed that SPANX protein is expressed in about half of the prostate adenocarcinoma biopsies evaluated and that all had a low malignant phenotype. If these results are confirmed in a larger number of prostate cancer patients, SPANX protein expression may be used as a marker of low cancer malignancy.

References

Girolamo Spagnoletti, Raffaella Rignanese, Valentina Verile, Giovanni Plotino, Vincenzo Oriolo and Giuseppe Bove
Radiotherapy Department, Foggia University Hospital, Italy

Background: Recent analyses of clinical results have suggested that the fractionation sensitivity of prostate tumours is high and many hypofractionated protocols have been tested. In fact the alpha/beta ratio estimates for prostate cancer are much lower than the typical values for many other tumours and many data support a trend towards lower values for prostate tumour than for rectum and bladder. We performed a small randomized trial to compare the acute gastrointestinal (GI) and genitourinary (GU) toxicities of radiotherapy for localized prostate carcinoma using a hypofractionated versus a conventional schedule.

Patients and Methods: From September 2008 to July 2009, 40 patients with cT1-T2N0M0 prostate cancer were randomized to receive either a conventional or a hypofractionated radiation therapy with curative intent.

Patients were stratified according to stage, Gleason score and presenting prostate-specific antigen level; 9 patients were at low risk and 31 patients were at intermediate risk according to Partin classification. The latter received neoadjuvant hormonal therapy that started 2 months before the radiotherapy onset and continued during radiotherapy. Treatments were delivered using four to six coplanar 10-18 MV photon beams at a dose of 72-78 Gy in 36-39 fractions within 7-8 weeks or 64.8-70.2 Gy in 24-26 fractions within 5 weeks. Basing on standard linear-quadratic modeling, the hypofractionated protocol was designed to keep late complications constant in rectal tissues. Gastrointestinal (GI) and genitourinary (GU) toxicity were evaluated before radiation therapy, weekly during treatment and 1-2 months after its completion according to the RTOG/EORTC score system. Efficacy of radiotherapy, based on clinical, radiologic and prostate-specific antigen data, was also evaluated at baseline and afterwards (every 3 months for 2 years and every 6 months subsequently).

Results: All patients completed the whole course of radiotherapy without interruptions. Median follow-up was 6 (2-12) months. None of the patients experienced grade 3-4 toxicity. Grade 1 and grade 2 GI and GU toxicities occurred in 35% and 25%, and 60% and 30%, respectively, for the hypofractionation regimen. The corresponding figures were 25% and 10%, and 65% and 25% for the control group (p>0.5 for all comparisons). Two months after treatment, the majority of GI and GU symptoms were resolved. The results on late effects and tumour control estimates need a longer follow-up: At the moment they are theoretical, although based on the linear-quadratic modeling. According to the linear-quadratic formula in our study design, late toxicity is expected to be equivalent between the two treatment groups. Regarding tumour

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control, assuming a low alpha/beta ratio for prostate carcinoma, we expect an interesting therapeutic gain.

Conclusion: Hypofractionation reveals itself to be a promising regimen for prostate cancer radiotherapy, in the light of modern radiobiological models. Our preliminary results suggest that the hypofractionated schedule is well tolerated. The incidence of clinically significant GI and GU toxicity after conventional and hypofractionated RT appears to be similar.

Encouraged by our findings, we started a moderate dose escalation in the hypofractionated arm in order to maintain a high tumour control when the alpha/beta ratio for prostate cancer is not as low as supposed and to improve clinical benefits even more if these theoretical assumptions are correct.

References

173 EVEROLIMUS IN METASTATIC RENAL CANCER CARCINOMA PROGRESSED ON VEGF-TARGETED THERAPY: A SINGLE-CENTRE EXPERIENCE

Valentina Baldazzi1, Renato Tassi1, Alberto Lapini2, Salvatore Caruso3, Greta Cipriani1, Sara Diaiacci1, Carmine Cerullo1, Carmine Santomaggio1, Marco Carini2 and Roberto Mazzanti1

1Oncologia Medica 2, and 2Urologia 1, AOU Careggi, Italy

Background: mTOR is a serine-threonine kinase involved in regulation of cell growth, proliferation and survival. Abnormal functioning of this pathway is believed to contribute to the pathogenesis and development of many malignancies, in particular renal cancer. Everolimus is a once-daily oral inhibitor of mTOR, forming a complex with the intracellular protein FKBP12. Recently, data obtained by RECORD-1 study showed a prolongation of progression free survival relative to placebo in patients affected by metastatic renal cell carcinoma (mRCC) that had progressed on prior target therapies. Here we present our experience in everolimus administration for patients affected by mRCC.

Patients and Methods: From April 2009 to January 2010, at our institution eight patients received a salvage therapy with daily administration of 10 mg everolimus. They all were affected by mRCC progressed on one or two prior treatment with tyrosine-kinase inhibitors. Six patients previously received a treatment for at least two lines of therapy. The remaining two patients received only a first-line sunitinib administration. The median patient age was 54 (range 35-67) years. All patients presented a Karnowsky Performance Status above 80%. According to Memorial Sloan Kettering Cancer Centre (MSKCC) prognostic score, two patients presented a favourable risk, three patients an intermediate risk and three a poor risk. Treatment was continued until disease progression or unacceptable toxicity or death. Median treatment time was 4 months (and ranged from 1 to 10 months). During the treatment patients underwent clinical examinations and blood tests every three weeks. Every 12 weeks, a total body CT scan was performed.

Results: According to RECIST criteria, there was one complete response (CR), two partial responses (PR) and two cases of stable disease (SD). The remaining three patients progressed on everolimus and did not receive any other treatment. The overall response rate was 62.5%. In our experience, a better response rates was observed in patients presenting a minimal tumour burden. Treatment was usually well tolerated and toxicities were mostly grade 1 or 2 according to Common Terminology Criteria for Adverse Events v3.0. Major adverse events were: fatigue and asthenia, anaemia (5 events grade 1 and 3 events grade 2), hypercholesterolaemia (2 patients with grade 2 toxicities required statine therapy), hypertriglyceridemia (1 patient required a omega 3 fatty acid treatment), hyperglycaemia, dyspnoea, diarrhoea and nail changes. For these toxicities a dose reduction or treatment discontinuation was not required. Moreover, we observed 4 oral mucositis with ulcerations (3 events grade 2 and 1 grade 3) treated with topical drugs. In one patient, oral mucositis required a treatment discontinuation followed by a resumption with a reduced 5 mg daily dose. Two patients presented pruriginous pustular eruption that was treated with topic tetracycline and systemic antihistamines.

Discussion: mTor inhibitors have a distinct mechanism of action from the established standard of care VEGF pathway inhibitors. Therefore, everolimus is an effective therapy after disease progression on a prior targeted therapy based on VEGF inhibitors, especially for those patients still presenting a good performance status and minimal tumour burden. A significant benefit to patients affected by mRCC is provided by VEGF-targeted drugs. However, this treatment is not curative, and disease progression on these drugs is almost certain. For this reason everolimus can be considered a valid and well-tolerated therapeutical option for mRCC patients.
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FLUORESCENT CYSTOSCOPY WITH HEXAMINOLEVULINATE: ASSESSMENT OF THE DIAGNOSTIC ACCURACY FOR NON-MUSCLE-INVASIVE BLADDER CANCER

Alessandro Volpe, Ilenia Zanellato, Michele Billia, Filippo Sogni, Francesco Varvello and Carlo Terrone

SCDU Urologia, AOU Maggiore della Carità, Università del Piemonte Orientale, Novara, Italy

Background and Aim: White light cystoscopy (WLC) is the gold standard for the diagnosis of bladder cancer, but its sensitivity can be improved, especially for the detection of flat lesions such as carcinoma in situ (CIS) or dysplasia. Fluorescent or blue light cystoscopy (BLC) has the potential to overcome the limitations of WLC. The aim of this study was to compare the diagnostic accuracy of WLC and BLC in the diagnosis of non muscle invasive bladder cancer in a single institutional series.

Patients and Methods: A total of 40 patients with a suspicious primary or recurrent bladder tumour at ultrasound or a positive urinary cytology were enrolled in the study. Patients who had intravesical instillations in the 3 months before the procedure were not eligible. After instillation in the bladder of a solution containing 85 mg hexaminolevulinate one hour before the procedure, the patients underwent WLC followed by BLC. All observed lesions were reported in a diagram, then biopsied or resected. Detection and false detection rates of the two techniques were compared. A subset analysis was performed to assess the diagnostic accuracy of WLC and BLC in the diagnosis of non muscle invasive bladder cancer in patients who had undergone previous intravesical treatments to prevent recurrence and progression.

Results: Overall, 158 bladder lesions were detected (58 with BLC only). At pathology, 141 lesions were malignant, while 17 were benign. The detection rate was 67.3% for WLC (95/141) and 97.8% for BLC (138/141). The highest diagnostic advantage for BLC was observed for the diagnosis of carcinoma in situ and for lesions located at the bladder dome (Table I). The false detection rate was 7% for WLC (7/100) and 10.8% for BLC (17/156). Overall, 17/40 patients (42.5%) had a diagnostic advantage with BLC (diagnosis of at least one CIS, dysplastic or papillary lesion that was missed at WLC). The subset analysis showed that the detection rate of BLC is not decreased in patients who underwent previous intravesical treatments when the last instillation is not performed in the 3 months before the procedure.

Conclusion: BLC is a promising technique that has a significantly higher detection rate than WLC. The highest diagnostic advantage with BLC can be obtained for the diagnosis of CIS and of lesions located at the bladder dome. The detection rate of BLC is not decreased in patients who underwent previous endovesical treatments when the last instillation is not performed in the 3 months before the procedure.

Table I.

<table>
<thead>
<tr>
<th>DETECTION RATE</th>
<th>WLC</th>
<th>BLC</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVERALL</td>
<td>67.3% (95/141)</td>
<td>97.8% (138/141)</td>
</tr>
<tr>
<td>DYSPLASIA</td>
<td>58.3% (14/24)</td>
<td>95.8% (23/24)</td>
</tr>
<tr>
<td>PUN-LMP</td>
<td>63.8% (30/47)</td>
<td>97.8% (46/47)</td>
</tr>
<tr>
<td>LG-PUC</td>
<td>78.3% (47/60)</td>
<td>98.3% (59/60)</td>
</tr>
<tr>
<td>CIS</td>
<td>25% (2/8)</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>T1</td>
<td>100% (2/2)</td>
<td>100% (2/2)</td>
</tr>
</tbody>
</table>

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TISSUE RESONANCE INTERACTION METHOD PROBE (TRIMPROB™) A NEW DIAGNOSIS FOR PROSTATE CANCER

Domenico Di Viccaro, Gian Maria Busetto, Maria Rosaria Di Placido, Gabriele Antonini and Costantino Cerulli

Dipartimento di Nefro-Urologia "U. Bracci", Viale del Policlinico 155, 00161 Roma, Italy

Background and Aim: The primary use of tissue resonance interaction method probe (TRIMPROB) is based on emission of electromagnetic energy radiated by a probe across biological tissues affected, with the phenomenon of interference being detected by a receiver. This phenomenon is due to the electromagnetic field interaction with such structures. The diagnostic parameters are based on variations of amplitude of the spectral lines on the monitor and processed by a computer. The aim of our study was to assess the actual clinical utility of TRIMPROB before prostate biopsy, and the ratio between the number of suspects examined TRIMPROB responses with the number of positive prostate biopsies performed later.

Patients and Methods: From March 2007 to July 2009, 458 patients (mean age 67.5 years) with prostatic symptoms were submitted to the TRIMPROB test. In 272 patients there was a normal interference, while 186 patients showed a significant alteration of the red signal on the monitor; hence these patients were recommended to undergo prostate biopsy. Among the 272 patients, only 114 (mean age 60.22 years, mean total PSA of 5.26 ng/ml and negative digital rectal examination), agreed to undergo biopsy.
**Results:** The prostate biopsies were performed by a urologist with a random technique. The result was positive in 51 patients (44.7%). The results obtained (Table I) shows that the sensitivity and specificity of diagnostic TRIMPROB increases for PSA values TOT >4 ng/ml.

<table>
<thead>
<tr>
<th>Total PSA (ng/ml)</th>
<th>Patients (n)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4</td>
<td>32</td>
<td>75%</td>
<td>21.4%</td>
<td>12%</td>
<td>85.7%</td>
</tr>
<tr>
<td>&gt;4</td>
<td>82</td>
<td>85.7%</td>
<td>81.5%</td>
<td>70.6%</td>
<td>91.7%</td>
</tr>
<tr>
<td>Total</td>
<td>114</td>
<td>79%</td>
<td>51.3%</td>
<td>44.8%</td>
<td>83%</td>
</tr>
</tbody>
</table>

**Conclusion:** The TRIMPROB has a good sensitivity and specificity for the diagnosis of prostate cancer but at the moment cannot replace prostate biopsy for the final diagnosis. The results obtained from our study encourage us to integrate the information obtained by this method with that more commonly used and to use the device alongside the recognized tests in the screening protocols for prostate cancer.

**176 POTENTIAL ROLE OF PROTEOMIC ANALYSIS IN PROSTATE CANCER DIAGNOSIS**

Giampaolo Bianchi¹, Maria Chiara Sighinolfi¹, Stefania Bergamini², Elisa Bellei², Elisa Monari², Alessia Cuoghi², Salvatore Micali¹, Stefano De Stefani¹ and Aldo Tomasi²

Departments of ¹Urology and ²Pathology, University of Modena and Reggio Emilia, Italy

**Aim:** Although the introduction of prostate-specific antigen has led to an increase in prostate cancer diagnosis, the role of...
such marker as a screening tool still remains controversial. As a result, the need for novel biomarkers with better diagnostic accuracy has progressively arisen, and proteomics may represent the basis for future research.

**Patients and Methods:** This preliminary study was performed on serum of 19 healthy controls and 12 patients with prostate cancer. The proteomic analysis were carried out on serum samples previous depleted of abundant proteins using a chromatographic technique based on immuno-depletion (Multiple Affinity Remove Column Hu-TL7; Agilent Technology, USA). This technique removes 6 high-abundant proteins, albumin, IgG, transferrin, haptoglobin, IgA and alpha1-anti-trypsin, with high specificity and efficiency allowing the detection of low abundant proteins. Proteomic profile of serum samples was performed by surface enhanced laser desorption/ionization time of flight mass spectrometry (SELDI-TOF MS). This technology is based on the use of ProteinChip Arrays which provide particular surfaces with different chromatographic properties able to bind different protein sets that are directly analyzed by mass spectrometry. Two different types of ProteinChip arrays were used: IMAC30 (immobilized metal affinity capture) and H50 (hydrophobic interactions). Depleted serum samples were loaded on the ProteinChip surfaces and analyzed by SELDI-TOF MS (ProteinChip reader 4000; Biorad). The obtained proteomic profiles were analyzed with specific software in order to discover significant differences between healthy control subjects and patients with prostate cancer.

**Results:** The proteomic analysis identified different cluster peaks for the two different ProteinChip arrays: IMAC30: 64 cluster peaks (42 ranging from 2 to 30 kDa, and 12 from 30 to 100 kDa); H50: 57 cluster peaks (50 ranging from 2 to 30 kDa, and 7 from 30 to 100 kDa). The statistical analysis identified 9 peaks differentially expressed ($p<0.05$) between healthy controls and patients with prostate cancer.

**Conclusion:** These results are preliminary due to the small number of patients recruited. However, the SELDI-TOF MS proteomic analysis may provide a useful tool for further studies with a larger number of patients, in order to identify early potential biomarkers of prostate cancer.

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**POSITIVE SURGICAL MARGIN RATE IN ORGAN-CONFINED PROSTATE CANCER. COMPARATIVE ANALYSIS BETWEEN OPEN AND ROBOTIC SURGERY DURING AND AFTER ROBOTIC LEARNING CURVE IN A SINGLE SURGEON EXPERIENCE**

Giampaolo Bianchi, Filippo Annino, Maria Chiara Sighinolfi, Alessandra Beato, Cosimo De Carne, Salvatore Micali and Stefano De Stefani

Department of Urology, University of Modena and Reggio Emilia, Italy

**Background and Aim:** The learning curve of every procedure could compromise the result of the surgery and this is debatable especially in the case of oncological procedures such as radical prostatectomy. The length of the robotic-assisted radical prostatectomy (RALP) learning curve is not well-established but has been suggested to be around 50 cases. The aim of this study was to evaluate the impact of robotic surgery and of its learning curve on the surgical margin rate in organ-confined disease.

**Patients and Methods:** We evaluated the first 100 consecutive cases of RALP and 50 consecutive cases of open radical prostatectomy performed at our centre by a single experienced surgeon (GB). All pathological findings were prospectively recorded in our hospital database for both groups. Only the pT2 cases were selected for the statistical analysis. The patients have been divided into three groups. Group A: Open surgery; Group B first 50 cases of RALP; Group C following 50 cases of RALP. The three groups were compared with parametric and non parametric tests by means of SPSS software for Windows XP; a statistical significance was considered as $p<0.05$.

**Results:** In Group A, 47 patients had pT2 disease and the positive surgical margin (PSM) rate was 17% (8/47); in group B, 40 patients had pT2 disease and 7 had PSM (17.5%); in group C of the 43 patients with organ-confined disease, 2 had PSM (4.6%). The statistical analysis showed no difference in PSM between the open group and the first 50 RALP cases ($p=0.587$). On the other hand, the comparison between both group A or B with group C showed a statistically significant difference $p=0.05$.

**Conclusion:** RALP is a safe procedure and provides, during its learning curve, comparable results to those of open surgery in term of PSM in organ-confined disease. The comparison between the first and subsequent 50 cases of RALP shows a reduction on PSM rate that seems to confirm the target of 50 cases to achieve the learning curve. Robotic surgery seems to provide better surgical margin outcome, with a statistically significant difference, in organ-confined disease once the surgeon’s experience increases. If these results are confirmed by other series, we could conclude that robotic surgery provides, in expert hands, better results on PSM rate if compared to open surgery for organ-confined disease.
Background: Radical cystectomy represents the treatment of choice for muscle-invasive transitional cell carcinoma of the bladder. The Studer technique is currently considered an adequate procedure for an orthotopic ileal replacement. We report personal modifications to the original technique with postoperative and long-term outcomes for 36 patients.

Patients and Methods: Surgical procedure: After radical cystectomy and pelvic lymphadenectomy, orthotopic diversion is made throughout a 50-60 cm ileal loop that is detubularized except for the proximal 15 cm. After the realization of the posterior face, the neobladder is folded from the right to the left side and sutured in its distal site. The superior hemi-suture is performed transversally, to make the reservoir gain a 'heart-like' shape (Figure 1). The new configured bladder neck, due to its conic feature, can easily be anastomosed to the urethral stump. After the reconstructive step, the neobladder and its chimney are fixed to the levator ani muscle and parietal peritoneum, respectively, to gain a correct placement of the reservoir. We report the outcomes for 36 patients, with particular regard to neobladder morphology.

Results: The postoperative course was uneventful in 86.1% (31/36) of the patients, with regular neovesical-urethral anastomosis in 77.7% (28/36). Mean follow-up was 3.21 +/- 1.4 years, and was assessed with multidetector CT or MRI. As late occurrences, 2 uretero-vesical strictures and 1 case of vesico-ureteral reflux were recorded. Overall renal function was not statistically affected by the procedure (p=0.141). Neobladder-urethral stricture, with an estimated incidence of 16.9% (literature data), was detected in a single patient (2.7%). No pathological alterations in the morphology of the reservoir (i.e. diverticula) have been recorded.

Conclusion: Even if the Studer procedure has been widely described and currently represents a popular orthotopic form of diversion, the technical modifications mentioned here may assist the realization of bladder-urethral anastomosis, reducing post-surgical complications (i.e. leakage, stenosis), and improving morphological outcomes of the reservoir.

CARDIAC METASTASIS OF APPARENT TRANSITIONAL CELL CARCINOMA ORIGIN

Maria Chiara Sighinolfi, Salvatore Micali, Alessandro Mofferdin, Filippo Annino, Giovanni Saredi, Stefano De Stefani and Giampaolo Bianchi

Department of Urology, University of Modena and Reggio Emilia, via del Pozzo 71, 41100 Modena, Italy

Case Report: A 79-year-old man presented to our institution with ultrasonographic diagnosis of a bladder mass. The patient’s history revealed a previous superficial transitional cell carcinoma with frequent relapse (last transurethral resection of Ta tumour performed 5 years before, no further endoscopical controls). Chronic renal failure with dialysis and chronic atrial fibrillation were also reported. The patient underwent transurethral resection of the bladder and the pathologic findings were a high-grade, stage T2 urothelial carcinoma. An abdominal contrast CT scan was performed, and confirmed the presence of a bladder tumour with peri-vescical fat and right seminal vesicle infiltration. However, in addition to these findings, a right ventricular mass 4.3 cm in size was discovered and confirmed with a magnetic resonance image of the thorax. Such imaging procedures described an enhancing right ventricular mass with infiltration into the myocardium, consistent with metastatic disease (Figure 1). Cardiac metastasis from transitional cancer represents a rare event and there are few clinical reports of such cases (1, 2). A case of cardiac mass from squamous cell carcinoma of the bladder has been described more recently (3). Even if clinical presentation is usually typical, with signs and symptoms deriving from cardiac injure (dyspnoea, oedema), the patient described in our case was asymptomatic and the finding was occasional. Another point of the present report to be highlighted is the absence of a proper oncological follow-up of the previous superficial bladder cancer: in fact, cystoscopy with cytology are mandatory, also in the case of patients undergoing dialysis. In fact, when diagnosed, a cardiac mass is often life threatening, as it leads to significant diagnostic and therapeutic challenges.
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THE IMPACT OF THE EXTENT OF LYMPH-NODE DISSECTION ON BIOCHEMICAL RELAPSE AFTER RADICAL PROSTATECTOMY IN NODE-NEGATIVE PATIENTS


S. Orsola-Malpighi Hospital, Department of Urology, Bologna, Italy

The therapeutic role of pelvic lymph-node dissection (PLND) and the impact of its extension on cancer outcome are still unclear. To assess the impact of the number of lymph-nodes (LN) retrieved at PLND during radical prostatectomy (RP) on biochemical relapse (BCR) in node-negative patients.

Patients and Methods: In all, 1,510 consecutive patients had a retropubic (n=1,199) or laparoscopic (n=311) radical prostatectomy between 25 October 1995 and 30 June 2009; 1,343 of these patients with a minimum follow-up of 12 months were evaluated. Seven (0.5%) had incomplete pathological data and were excluded. Four hundred and thirty-nine (32.7%) had Nx status and 103 (7.7%) had LN positive disease and were excluded, therefore 794 (59.1%) had pN0. Eleven patients (0.8%) had pT0 disease and were excluded. A total of 81 patients (6.0%) were submitted to neoadjuvant therapy (NHT) and were excluded; among 727 (54.1%) remaining patients, 97 (13.3%) had incomplete follow-up data and were excluded. Among the remaining 630 valuable patients, immediate adjuvant hormonal deprivation was administrated in 16 patients (2.5%) and were excluded. The study included 614 patients with pT2-4N0. Overall the mean number of nodes obtained at RP was 10.8±6.4 (median 10, range: 1-36). The population was divided into two groups: group 1 (n=295, 48.0%) had 1 to 9 LNs with a mean of 5.7±2.3 LNs (median: 6); group 2 (n=319, 52.0%) had 10 or more LNs with a mean of 15.6±5.1 LNs (median: 14). The parameters analyzed were age, PSA, clinical and pathological Gleason score and stage, margin status, LN group and adjuvant radiotherapy (ART). When LN groups were compared, there was no significant difference regarding PSA, clinical and pathological stage, margin status, LN group and adjuvant radiotherapy (ART). When LN groups were compared, there was no significant difference regarding PSA, clinical and pathological stage, margin status or ART while group 1 tended to have a significantly slightly higher mean age and lower clinical and pathological Gleason score. BCR was defined as PSA greater than 0.2 ng/mL. BCR-free survival was estimated using the Kaplan-Meier method. Cox regression was applied to analyze survival rates.

Results: Mean follow-up was 62.5±39.7 months (range 12-159 months). Among 614 patients, 130 (21.2%) presented BCR. Figure 1 shows the Kaplan-Meier curve for BCR-free survival with patients stratified by LN group. Group 2 showed a significantly lower risk than group 1 (HR=0.658, 95% CI: 0.464-0.934, p=0.019). At multivariate analysis, LN group, PSA, clinical and pathological Gleason score, pathological stage and ART all showed an independent significant relationship with BCR.
Conclusion: In node-negative patients, a more extensive PLND do positively affect BCR-free survival. Even if the extent of PLND may indirectly influence the BCR because of the stage shift (the Will Rogers phenomenon), a more extensive PLND may have a therapeutic role by removing the micrometastasis.

181 ACCURACY OF PET/CT WITH 11-C-CHOLINE IN THE RESTAGING OF RECURRENT PROSTATE CANCER PATIENTS WITH A SINGLE LESION AT BONE SCINTIGRAPHY


Department of Urology, S. Orsola-Malpighi Hospital, Bologna, Italy

Background and Aim: Bone scintigraphy (BS) still remains the gold standard in the assessment of osseous metastatic disease in prostate cancer (PCa). Although the combinations of therapeutic treatments of bone disease can achieve a degree of local control, across the vast majority of metastatic PCa they provide only palliation. However, before each therapeutic planning, it is very important to know the exact number of lesions and the site of the disease. The aim of this study was to assess the accuracy of 11C-choline PET/CT in the restaging of PCa after radical prostatectomy (RP) in patients with a single osseous lesion diagnosed at BS.

Patients and Methods: Between December 2003 and August 2009, 1,324 consecutive patients underwent 11C-choline PET/CT for PCa staging and restaging. We retrospectively evaluated 20 consecutive patients (mean age 70 years, range 64-80 years) with PSA relapse after RP (median PSA (ng/ml): 5, range 0.3-23) who presented a single positive lesion at BS and who underwent 11C-choline PET/CT within 3 months. All but one avoided hormonal therapy before PET/CT. Results of BS and PET/CT were compared and physicians reporting consensus was obtained with the confirmation achieved by a follow-up period of at least 6 months.

Results: On a patient basis, 11C-choline PET/CT visualized the bone lesion in 14/20 patients (70%) and confirmed the single localization of disease in 7, while multiple sites of bone disease were detected at PET/CT in the remaining 7; on a lesions basis, PET/CT demonstrated 27 bone lesions in 14 patients. Furthermore, 3 out of the 7 patients with multiple bone lesions at PET/CT presented different localizations of non-osseous disease, such as a single pelvic lymph node metastasis, a lung metastasis and a local recurrence. On the other hand, 6/20 (30%) patients were false-negative at PET/CT; of these, in 3 cases a clear osteoblastic lesion was seen on CT attenuation correction images, 1 patient was under hormonal treatment before PET/CT and in 2 cases the bone metastasis was confirmed during follow-up with progressive bone disease at BS.

Conclusion: PET/CT with 11C-choline can shows additionally bone lesions in about 50% of the patients, and can add information regarding different sites of non-osseous metastasis in about 20%. Our results suggest that 11C-choline PET/CT can provide complementary information to BS in patients with a single bone lesion, thus helping to choose the correct patient management.

182 THE IMPACT OF POSITIVE SURGICAL MARGINS AFTER RADICAL PROSTATECTOMY ON BIOCHEMICAL RELAPSE IN PATIENTS WITH PT2 AND PT3 DISEASE

R. Schiavina, A. Franceschelli, E. Brunocilla, S. Concetti, F. Manferrari, A. Bertaccini, M. Garofalo, M. Borghesi, V. Vagnoni, A. Baccos, C. Rocca, C. Pultrone and G. Martorana

Department of Urology, S. Orsola-Malpighi Hospital, Bologna, Italy

Aim: To assess the impact of positive surgical margins (R1) after radical prostatectomy on biochemical relapse (BCR) in patients with pT2 and pT3 disease.

Patients and Methods: From October 1995 to June 2009, 1,510 consecutive PCa patients underwent RP at our Department; 1,343 with a minimum follow-up of 12 months were evaluated. Patients with pN1, pT0, pT4, neoadjuvant therapy, adjuvant radio- or hormonal therapy, incomplete data regarding pathological stage (p-stage) or follow-up data were excluded. The resulting 884 patients (66%) were divided into pT2 (n=536, 60.6%), pT3a (n=272, 30.8%) and pT3b (n=75, 8.5%) groups. The parameters analysed in the multivariate analysis were age, PSA, clinical and pathological Gleason score (c-Gs and p-Gs), clinical and pathological stage (c-stage and p-stage) and margin status (presence of uni- or multifocal positive margin, R1 vs. negative margins, R0). BCR was defined as PSA greater than 0.2. BCR-free survival was estimated using the Kaplan-Meier (KM) method. Cox regression was applied to analyse survivals rates.

Results: On a patient basis, 11C-choline PET/CT visualized the bone lesion in 14/20 patients (70%) and confirmed the single localization of disease in 7, while multiple sites of bone disease were detected at PET/CT in the remaining 7; on a lesions basis, PET/CT demonstrated 27 bone lesions in 14 patients. Furthermore, 3 out of the 7 patients with multiple bone lesions at PET/CT presented different localizations of non-osseous disease, such as a single pelvic lymph node metastasis, a lung metastasis and a local recurrence. On the other hand, 6/20 (30%) patients were false-negative at PET/CT; of these, in 3 cases a clear osteoblastic lesion was seen on CT attenuation correction images, 1 patient was under hormonal treatment before PET/CT and in 2 cases the bone metastasis was confirmed during follow-up with progressive bone disease at BS.

Conclusion: PET/CT with 11C-choline can shows additionally bone lesions in about 50% of the patients, and can add information regarding different sites of non-osseous metastasis in about 20%. Our results suggest that 11C-choline PET/CT can provide complementary information to BS in patients with a single bone lesion, thus helping to choose the correct patient management.
showed a significantly higher risk of BCR than did R0 (HR=2.541, \(p=0.001\)). At multivariate analysis, margin status, PSA and p-Gs showed a significant relationship with BCR. On the contrary, in pT3a and pT3b patients, R1 cases did not show a significantly higher risk of BCR than R0 (\(p=0.365\) and \(p=0.938\), respectively). Finally, the pT2 and pT3a patients (n=808, 91.4%) were divided into 4 groups: group 1= pT2R0 (n=418, 51.7%), group 2= pT2R1 (n=118, 14.6%), group 3= pT3aR0 (n=183, 22.6%) and pT3aR1 (n=89, 11.0%): Only group 1 had a significantly lower risk of BCR than the other 3 groups (\(p<0.001\), Figure 1). At multivariate analysis, patient group, PSA, c-stage, c-Gs and p-Gs showed a significant relationship with BCR.

**Conclusion:** In our populations, patients with positive margins are at higher risk of BCR only in pT2. Patients with pT2R1 seem to have a risk of BCR similar to those with pT3aR0/1. These results may have an impact on the indication for adjuvant radiotherapy after radical prostatectomy.

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**INGUINAL LYMPHADENECTOMY FOR PENILE CANCER AND MELANOMA: OUR EXPERIENCE WITH 22 CASES**

Stefano De Stefani, Giovanni Saredi, Maria Chiara Sighinolfi, Francesco Fidanza, Salvatore Micali and Giampaolo Bianchi

Department of Urology, University of Modena and Reggio Emilia, via del Pozzo 71, 41100 Modena, Italy

**Background:** Inguinal lymphadenectomy has a key role in the management of patients affected by penile, vulval, anal and cutaneous malignancies (1). Malignant tumours of the skin, most commonly malignant melanoma arising on the leg or thigh, may metastasize to the inguinal nodes (2). Therapeutic inguinal lymphadenectomy is the recommended surgery for these patients in order to prevent further dissemination of the disease (1, 2). Prophylactic lymphadenectomy, which has been demonstrated to be very helpful in early stages of penile cancer, has not been shown to improve survival in melanoma (3). Therefore the benefit of prophylactic lymphadenectomy or ‘modified’ groin lymphadenectomy proposed by Catalona in terms of a lower percentage of early and late postoperative complications cannot be supported in such cases (3). However, when required, lymphadenectomy should be more extensive and invasive as these patients have been already submitted to previous operation for biopsy of the sentinel lymph node. Radical removal of superficial and deep inguinal nodes implies a deep knowledge of local anatomy, the execution of correct surgical procedures and the adoption of technical tricks which allow the best results to be obtained, minimizing side-effects. We prospectively evaluated clinical outcomes of extended inguinal lymphadenectomy performed for both penile cancer and melanoma, with particular regard to peri- and postoperative morbidity and complications.

**Patients and Methods:** From June 2006 to July 2008, a total of 22 inguinal lymphadenectomies were performed at our institution. Except for 3 cases of penile cancer, the remaining procedures were carried out for melanomas located in lower limbs. A pelvic lymphadenectomy was contextually performed in 5 patients (laparoscopic approach in 2, open surgery in 3 cases). In a single case, the procedure was associated with inguinal hernioplasty and in another case with laparoscopic ovariectomy. The mean age of the patients was 59 +/- 17 (range: 18-81) years, for a total of 11 males and 11 females.

**Results:** When performing an inguinal unilateral lymphadenectomy (15 cases), the mean operative time was 140 (range: 90-225) minutes. The mean number of nodes retrieved per site was 13 +/- 4.6 (range: 5-20). Inguinal nodal metastases were found in 11 patients (microscopical or singular node location in 5 cases). Mean hospitalization was 14.7 +/- 9.5 (range: 2-39) days. The postoperative course was uneventful in 16 patients (72%). In the remaining patients, the following complications were found: 5 mild cutaneous necroses which spontaneously recovered, 1 lymphocele that required periodical drainage (bilateral inguinal lymphadenectomy).

**Conclusion:** Inguinal lymphadenectomy with saphenous-sparing technique according to Catalona’s procedure represents an important step in the management of penile cancer. Such practice can be effectively offered even to patients with melanoma of the leg, where an extended retrieval of both superficial and deep nodes is advised; moreover, these patients have often undergone previous inguinal procedures, such as sentinel node retrieval, and may...
experience a higher cutaneous complication rate following lymphadenectomy. Despite these considerations, our series confirms the feasibility of the procedure, with acceptable outcomes in terms of operative time, hospitalization and complication rate.

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YORK MASON TRANS-SPHYNYERIC TRANS-RECTAL REPAIR OF IATROGENIC RECTO-URINARY FISTULA: CASE REPORT

Roberto Sanseverino, Giorgio Napodano, Olivier Intilla, Umberto Di Mauro and Tommaso Realfonso
U.O.C. di Urologia, Ospedale Umberto I, Nocera Inferiore, Italy

Background: Recto-urinary fistula formation is a very important complication of surgery for prostatic disease. Spontaneous closure is rarely successful and reconstructive procedures are usually performed. Although several surgical approaches have been proposed in the literature, successful repair is often difficult. We report a case of a 73-year-old male with recto-urethro-vesical fistula developing after high intensity focused ultrasound (HIFU) treatment for prostate cancer. We performed a fistula repair with a posterior trans-sphincteric trans-rectal (York Mason) approach.

Case Report: One month after the HIFU treatment, the patient presented at our institution for faecaluria. Diagnostic cystoscopy and colonoscopy revealed a wide recto-urethro-vesical fistula. The patient initially underwent diverting colostomy. Cystoscopy was performed and a catheter was left draining the urinary bladder; after being placed in the jackknife prone position, an analococygeal incision was made. After external and internal sphincteric dissection, each sphincter muscle was tagged with color-coded sutures; coccygeal resection was performed. Vertical incision of the posterior rectal wall allowed exposure of the fistula, showing the catheter in the prostatic urethra. The next step of this procedure was the incision around the fistula, followed by the excision of the fistulous tract. After surgical placement, the procedure was completed by suture of rectal wall and approximation of sphincter muscle. The surgical procedure lasted 4 hours. Blood loss was 300 cc; no transfusion was required. The bladder remained continuously drained for 8 weeks until a cystogram and colonoscopy were obtained to confirm complete healing of the fistula.

Conclusion: The York Mason technique provides easy identification of recto-urethro-vesical fistula and excellent surgical exposure with minimal postoperative morbidity. It is a highly effective option for treating an iatrogenic recto-urinary fistula.

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COMBINED EXTRAPERITONEAL LAPAROSCOPIC RADICAL NEPHRECTOMY AND PROSTATECTOMY

Roberto Sanseverino, Olivier Intilla, Umberto Di Mauro, Giorgio Napodano, Mario Iacone and Tommaso Realfonso
U.O.C. di Urologia, Ospedale Umberto I, Nocera Inferiore, Italy

Background: We report the case of a 58-year-old male affected by kidney and prostate cancer; the patient underwent a laparoscopic retroperitoneal left radical nephrectomy and preperitoneal nerve-sparing radical prostatectomy during the same operative session.

Case Report: The patient was placed in a lateral position. A retroperitoneal access was realised by ballon trocar. Renal hylum was exposed. The artery and the vein were isolated and then clipped by HemOlock clips. The ureter was identified and clipped with HemOlock clips. The kidney was then completely isolated and placed in an endobag. A regional lymphadenectomy was carried out using laparo clips. The endobag was pulled out through the skin incision. Afterwards, the patient was placed in the supine position. After creating the preperitoneal space by balloon trocar dissection, five trocars (2 × 5 mm and 3 × 10 mm port) were placed in the hypogastrium, allowing immediate access to the space of Retzius; bilateral pelvic lymphadenectomy was then performed. Bilateral incision of endopelvic fascia anticipates the introduction of a sovrapubic trocar. We proceeded with haemostatic transacted suture of Santorini plexus with Vicryl™; another stitch was passed for back bleeding. A needle holder, inserted through the sovrapubic trocar, lifted up the prostate base, while the endoretractor pushed the bladder laterally. This solution allows an easy bladder neck dissection. The urethra was then transected. The vas deferens were isolated and then cut; mobilization of seminal vesicles preceded incision of Denonvilliers’ fascia. Section of the
prostatic pedicles was achieved with Hem-O-lock and endoshears. After cutting the Santorini plexus and urethra, the prostate was placed in endobag. A Tachosil™ sponge was applied on the bundles using laparoscopic dedicated applier. A water-tight urethrovesical anastomosis with double running suture as described by van Velthoven was performed.

The operative time and estimated blood loss were 340 minutes and 800 ml, respectively. Kidney and prostate weight were 600 g and 40 g, respectively. Histological evaluation revealed a clear cell renal carcinoma (pT3bG2) and prostate adenocarcinoma [pT2b, Gleason score 7 (4+3)].

Conclusion: This experience supports the feasibility of performing simultaneous laparoscopic interventions during the same surgical session. This approach obviates the need for repeated anaesthesia, and reduces psychological stress and total hospital stay.

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FIBROEPITHELIAL POLYP OF GLANS PENIS: A CASE REPORT

Giorgio Napodano, Alfonso Baio, Umberto Di Mauro, Tommaso Realfonso and Roberto Sanseverino

U.O.C. di Urologia, Ospedale Umberto I, Nocera Inferiore, Italy

Background: Fibroepithelial polyps are benign mesodermic tumours that can be observed in renal pelvis, ureter, bladder, urethra and penis; regardless of site, they are histologically similar. Fibroepithelial polyps of penis are a very rare occurrence and they have been previously reported as complication of phimosis or long-term condom catheter use. We report a case of fibroepithelial polyp of glans penis associated neither with phimosis nor long-term condom catheter use.

Case Report: A 35-year-old man presented at our institution for a penile lesion which had appeared fifteen months before. The patient had never used a condom catheter; his past medical history did not reveal any relevant pathology, nor were any specific symptoms recorded.

On physical examination, a cauliflower-like lesion was observed at the ventral side of the glans penis, near the urethral meatus. The lesion measured 7 × 5 × 2 cm.

After placement of the urethral catheter, a wide local excision of the mass was performed under locoregional anaesthesia. The glans skin was repaired with 4/0 absorbable suture.

No postoperative complications were registered. The lesion had a polypoid macroscopic appearance, tough elastic consistency and white colour. Microscopic examination revealed a fibroepithelial polyp. After 60 months, no recurrence was observed.  

Conclusion: Fibroepithelial polyps of glans penis are rare benign mesodermic tumours. In contrast with the literature reported, in our case, the lesion was not associated with long-term condom catheter use or phimosis.

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USING BENIQUEE IN VIDEO-LAPAROSCOPIC RADICAL PROSTATECTOMY BY EXTRAPERITONEAL COMBINED ANTEROGRADE AND RETROGRADE. OUR EXPERIENCE

Vincenzo Ferrara, Behrouz Azizi, Carlo Vecchioli, Willy Giannubilo and Antonio Garritano

Operative Unit of Urology, Ospedale Civile di Jesi, Ancona, Italy

Background and Aim: The spread of video-laparoscopic radical prostatectomy, due to the development of technological tools, the experience gained in many centres in recent years and the success of minimally invasive treatments for the treatment of localized prostate cancer (e.g. brachytherapy) have provided input for many different experiences, accelerating the diffusion of laparoscopic pelvic surgery. However, with regard to laparoscopic radical prostatectomy, there is no completely standardized technique. Therefore, all variants of the technique derived from the different experiences in different centres are invaluable. The aim of our work was to demonstrate the laparoscopic approach and the benefits of using a Beniquee-positioned urethra in a retrograde incision after the bladder neck. The retrospective evaluation of video-laparoscopic radical prostatectomy performed at the UOC di Jesi with this technical device has demonstrated unquestionable technical advantages in the course of surgery. Therefore, we present the procedure we used routinely in the last 150 cases of video-laparoscopic radical prostatectomy.

Patients and Methods: For the study in question, the last 150 extraperitoneally video-laparoscopic radical prostatectomies were taken into account, namely those from January 2006 to September 2008 at the UOC of Urology of Jesi. Our technique provides an extraperitoneal approach and is characterized by some stages:

- using only two surgeons, assisted by a nurse;
- use of four trocars, including 3 of 10 mm and two of 15 mm;
- isolation of bundles proceeding by combined anterograde and retrograde approaches.

This approach allowed, in our experience, a better visualization of vascular bundles - nervous, both at the prostatic apex and along their course, so as to be best isolated from the prostatic capsule, proceeding by blunt (by retrograde) and cold-cutting (in the sense anterograde). This procedure was used in the last
150 consecutive patients. The average age was 66 years. A total of 140 patients had a preoperative Gleason score (GS) less than or equal to 7, 8 patients had GS=4+3, and 4 +4= 2 GS. Overall, 87% of patients had initial PSA 10 ng/ml. 52% had intraprostatic disease at final histology.

Results: With regard to surgical results, our technique did not result in longer surgery times (the average time was 140 minutes), nor of blood loss (mean 220 cc). The hospital stay was of 7 days. Catheterization average was 5-6 days. The complication rate was 4.1%, distributed as follows: 2 lesions of the rectum, 3 urinary fistulas, 1 stenosis of the neck. From the standpoint of oncological and functional results, there was a higher rate of positive margins of 17.3% and the continence rate was 96%. The recovery of erectile function amounted to 48%.

Conclusion: Use of Beniquee is, in our experience, very useful since: 1) it allows the prostate to be moved depending on the convenience of the surgeon, making sure to save a gateway to the abdomen; 2) avoids the necessity for a third surgeon, being handled by an appropriately trained nurse; 3) compresses the vessels of the plexus of Santorini when it is recorded, avoiding bleeding, without it having to be tied before them. Although the results obtained are not yet definitive because of the short follow-up and the lack of a control group, laparoscopic nerve-sparing prostatectomy performed with this approach allows satisfactory results in terms of clinical and pathological functional, with minimal morbidity.

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ROLE OF CRYOTHERAPY IN THE TREATMENT OF PERI-HILAR RENAL TUMOURS

Vincenzo Ferrara, Behrouz Azizi, Carlo Vecchioli, Willy Giannubilo and Antonio Garritano
Operative Unit of Urology Ospedale Civile di Jesi, Ancona, Italy

Background: Recent years have witnessed the development of many conservative approaches in the treatment of renal neoplasms. Many of these techniques, such as video-laparoscopic partial nephrectomy, have become the gold standard of treatment of these tumours. But clinical practice makes use of these approaches difficult, as in cases where the patient has a solitary kidney, surgical or functional congenital complication, or in situations in which the contralateral kidney presents pre-existing conditions and a radical nephrectomy could affect the overall renal function. Partial nephrectomy, however, has limitations in its technical feasibility not solely related to the size of the tumour, but also due to its position within the kidney and its proximity to the hilum. Therefore, parallel to the partial nephrectomy, it may be necessary to resort to other less invasive ablative techniques, which achieve equally radical results. Among the techniques of ablation, cryotherapy is the oldest. In 1845, James Arnott hypothesized that low temperatures could be used to destroy diseased tissue. In practice, cryotherapy probes that can be cooled with liquid nitrogen or argon are used. They may have different thickness and length and are chosen depending on the technique used (open, laparoscopic, percutaneous) and the size of the tumour. Temperatures of -187°C or -195°C, can be achieved leading to tissue necrosis via: 1) the formation of ice crystals in the extracellular space, with increase in osmolarity, invocation of liquids and subsequent cell lysis and 2) the phenomena of oedema, vascular occlusion and thrombosis in microcirculation. Usually 2 cycles of freezing are carried out separated by about 15 minutes of thawing. This serves to increase the release of cytotoxic factors by cells affected, by increasing further the effect that results from the necrotic tumour cells.

Materials and Methods: In our Urology Department, this technique is used for laparoscopy or retroperitoneoscopy (usually 3 trocars). Through this approach, the tumour is isolated and then pierced by the biopsy cryoprobe. Two cycles of freezing of about 15 minutes each, separated by 15 minutes of thawing, are then performed. It is not usually necessary to proceed with haemostasis since the renal vessels are thrombosed directly due to the freezing. A unique haemostatic device we use is the inclusion of a ‘cigarette’ of Tabotamp and/or Floseal in the hole remaining after removal of the cryoprobe. A drain is left in place and removed on day 2. The follow-up consists of an MRI the next day, after 3 months, after 6 months and then annually.

Results: A total of 13 treatments were performed from July 1999 to the present, including 4 for parahilar tumours. The technique was very safe in these cases, since freezing was not harmful to the great vessels, whose wall is preserved by the heat of constant blood flow within them. Of the 13 patients, 1 underwent nephrectomy due to bleeding postoperatively in the second day, the other 11 had no complications, and were discharged in 4 days and have no current signs of recurrent tumour. The follow-up period was 5 years and 8 months.

Conclusion: These results concur with those of other reports showing cryotherapy to be the treatment of choice for parahilar tumours < 4 cm, where it is necessary to retain the kidney.

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SIMULTANEOUS LAPAROSCOPIC NEPHROURETERECTOMY AND CYSTECTOMY: OUR EXPERIENCE

Vincenzo Ferrara, Behrouz Azizi, Carlo Vecchioli, Willy Giannubilo and Antonio Garritano
Operative Unit of Urology, Ospedale Civile di Jesi, Ancona, Italy
**Aim:** We present a preliminary report for the treatment of patients with muscle-invasive bladder cancer and concomitant upper urinary tract tumours who may be candidates for simultaneous cystectomy and nephroureterectomy. Other clinical conditions such as dialysis-dependent end-stage renal disease and non-functioning kidney are also indications for simultaneous removal of the bladder and kidney.

**Patients and Methods:** Two patients underwent simultaneous laparoscopic radical nephroureterectomy (unilateral) and radical cystectomy at our institution. In both patients, urinary diversion was performed by monolateral uretero-skin anastomosis. Demographic data, pathologic features, surgical technique and outcomes were retrospectively analysed.

**Results:** The laparoscopic approach was technically successful in both cases without the need for open conversion. Median total operative time was 390 min. Median estimated blood loss and hospital stay were 755 ml and 7.5 days, respectively. There were no intraoperative complications.

**Conclusion:** Laparoscopic nephroureterectomy with concomitant cystectomy is technically feasible. Except for a lengthening of the operative time, there are substantial technical differences compared to the open technique, with undoubted advantages in terms of postoperative pain and morbidity associated with surgery.

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**SILS EXTRAPERITONEAL RADICAL PROSTATECTOMY**

Vincenzo Ferrara, Willy Giannubilo, Behrouz Azizi, Carlo Vecchioli and Antonio Garritano

Operative Unit of Urology, Ospedale Civile di Jesi, Ancona, Italy

**Aim:** The surgical technique for video-laparoscopic extraperitoneal radical prostatectomy carried out through a single incision of 2.5 cm below the navel, is presented.

**Materials and Methods:** The technique involves the placement of a port of a new concept, the SILS-port, which has 3 channels through which instruments and a camera are inserted.

Oncological and functional results of 10 patients undergoing SILS prostatectomy were compared with the last 10 patients treated at our facilities with video-laparoscopic extraperitoneal increasingly radical prostatectomy (“conventional” technique).

**Results:** There were no substantial differences between the two techniques, except for a modest lengthening of the operative time.

**Conclusion:** This technique has been shown to be feasible, secure and less invasive.

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**MULTIDISCIPLINARY SALVAGE SURGERY FOR METASTATIC NSGCT: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE**

Lorenzo Ruggera, Oliviero Lenardon, Martina Zanin, Lorenzo Buttazzi, Daniele Maruzzi, Antonio Marin, Claudio Rustici and Antonio Garbeglio

U.O. di Urologia, Ospedale S. Maria degli Angeli, Pordenone, Italy

**Background:** Salvage surgery in nonseminomatous germ cell tumour (NSGCT) is an integral part of the multidisciplinary treatment, aiming to remove residual masses after salvage chemotherapy. Surgery in metastatic disease may even be beneficial for patients with persisting marker elevations after chemotherapy (‘desperation surgery’), or patients with late tumour relapse. In view of late relapse, the extent and completeness of the primary resection is an important issue and, therefore, surgery should be performed in specialised centres. Herein, we report 2 cases of multidisciplinary salvage surgery for metastatic non-seminomas.

**Case Report:** Case 1: A 30-year-old man underwent left inguinal orchiectomy in January 2000. Histological examination revealed an NSGCT (mature teratoma 70%, choriocarcinoma 20%, embryonal carcinoma 5%, necrosis 5%), with blood vascular invasion. At the diagnosis LD, AFP and hCG-beta were 1786 IU/l, 586 ng/ml and 140000 mIU/ml, respectively. The thoracoabdominal CT scan detected the presence of multiple retroperitoneal (9×7×8 cm in diameter), pulmonary and liver metastases. Following the orchiectomy, 4 cycles of PEB chemotherapy (cisplatin, etoposide, and bleomycin) were given which resulted in partial response of the tumour markers (AFP and hCG-beta were 26 ng/ml and 55 mIU/ml, respectively). Therefore, the patient underwent the second-line VIP chemotherapy (etoposide, ifosfamide, cisplatin). After this, hCG-beta value was normal; AFP was 17.9 ng/ml. The thoracoabdominal CT scan revealed the persistence of multiple metastases localized in the retroperitoneum, in the liver, and bilaterally in the lungs. Multidisciplinary salvage surgical approaches were adopted, consisting of first-line retroperitoneal lymphadenectomy and partial hepatic metastasectomy, histologically revealing teratoma and necrosis, respectively. Subsequently, the patient underwent percutaneous embolization of the right portal vein in order to induce the hypotrophy of the right liver, and bilateral lung metastasectomy (necrosis). Conclusive surgical treatment was the right hepatectomy (histological finding: fibrosis). At the follow-up of 10 years, the patient has no evidence of disease (NED).

**Case 2:** A 23-year-old man underwent left inguinal orchiectomy in May 2007. Histological examination revealed an NSGCT (mature teratoma 40%, immature teratoma 32%,...
embryonal carcinoma 25%, choriocarcinoma 2%, yolk sack tumour 1%), with blood vascular invasion. At diagnosis, AFP and hCG-beta were 2208 ng/ml and 6785 mIU/ml, respectively. The thoracoabdominal CT scan revealed the presence of multiple retroperitoneal, pulmonary and mediastinal metastases. Overall, the retroperitoneal masses had a maximum diameter of about 40 cm. As a result, 4 cycles of PEB and 2 cycles of VIP chemotherapy were given. Serum levels of AFP and hCG-beta at the end of the chemotherapy were 15.6 ng/ml and 3 mIU/ml, respectively. The thoracoabdominal CT scan detected the persistence of the multiple retroperitoneal, mediastinal, and pulmonary metastases. Patient underwent multidisciplinary salvage surgery: extended retroperitoneal lymphadenectomy (mature teratoma), pulmonary metastasectomy (yolk sack tumour and necrosis), and mediastinal metastasectomy (necrosis). At the end of the therapy, the tumour markers were normal (AFP 2.8 ng/ml; hCG-beta <2 mIU/ml). At the follow-up of 34 months the patient had NED.

**Conclusion:** Success in the treatment of NSGCT, as one of the few examples of a curable adult solid neoplasm, is achieved through combined efforts of a multidisciplinary team. The role of surgery has changed with time. Resections of residual masses after chemotherapy have become an important adjuvant treatment modality. In some cases, radical resections using unusual and risky surgical approaches represent the last attempt to cure patients who have previously failed all other therapeutic options. Extensive surgical procedures are associated with higher complications rates and, therefore, require excellent knowledge and understanding of potential hazards, careful diagnostic work-up and planning of the procedure in cooperation with an experienced team, as well as experience with extensive resections by various surgical approaches and additional resection procedures involving other specialties.

**194 PRELIMINARY PATHOLOGICAL FINDINGS OF AN ONGOING PROSPECTIVE ANALYSIS COMPARING NEEDLE CALIBRE IN TRANSPERINEAL PROSTATE BIOPSY**

Giovanni Saredi, Maria Chiara Sighinolfi, Francesco Fidanza, Christian Guarasci, Salvatore Micali, Stefano De Stefani and Giampaolo Bianchi

Department of Urology, University of Modena and Reggio Emilia, Italy

**Introduction:** Transperineal prostate biopsy has been developed in recent years as an adequate alternative to the transrectal approach. An 18-G needle is the most common needle calibre used to obtain prostatic tissue: This standard derives from the transrectal approach, which requires this needle size. The use of larger calibre has been previously invoked for breast cancer, in order to increase the amount of tissue harvested during biopsy and improve histological sampling. The feasibility of the transperineal biopsy with a 16-G needle has been previously evaluated in a prospective trial comparing 16-and 18-G size (1): no differences were found in terms of pain and adverse events. We aim to present our preliminary data about cancer detection rate among patients randomly assigned to receive a 16-G or 18-G prostate biopsy.

**Patients and Methods:** Five hundred and thirty-one patients undergoing transperineal prostate biopsy were prospectively and randomly divided into two groups. The first one (258 patients, Group A) received a transperineal prostate biopsy using a 16-G needle and the second group (273 patients, Group B) underwent transperineal prostate biopsy with an 18-G needle. Anaesthesia was obtained with a single perineal injection at the prostatic apex in all patients. Statistical analysis was carried out using parametric and non-parametric tests.

**Results:** The mean age of patients and PSA values were similar between groups (p=0.34 and p=0.46, respectively). Seventy-two prostate tumours (27.9%) were detected with the 16-G needle and and 71 (26%) with 18- G needle procedure (p=0.346). Fifty-three cases of high-grade prostatic intraepithelial neoplasia (HGPIN) were found among patients of group B and 49 among patients of group a (p=0.495). Atypical small acinar proliferation (ASAP) was detected in 9 patients of group A, and in 7 patients in group B (p=0.356).

**Conclusion:** To our knowledge, this is the first report evaluating the use of different needle calibres in transperineal prostate biopsies. This topic has been previously debated for breast cancer: In this field, the quality of tissue samples was found to be significantly superior with a 16-G needle (2). This finding was confirmed by further researches, as a larger specimen may lead to an improved diagnostic accuracy. When dealing with prostate cancer, the only report concerning biopsy specimen size is that from Iczkowski et al. (3) who found that needle core length on sextant biopsy may influence the cancer detection rate, especially at the apex. Although our previous ongoing analysis is not able to draw definitive conclusions, the study is currently ongoing to assess whether the use of a 16-G needle can improve the quality of the specimen and reduces its fragmentation (as it appears to do, unpresented data), in order to improve diagnostic accuracy and reduce the finding of uncertain forms.

**References**

INTEGRATED MULTIDISCIPLINARY APPROACH TO METASTATIC RENAL CARCINOMA IN AN EXPERIMENTAL PROJECT OF URO-ONCOLOGY COOPERATION

Daniele Masala¹, Pompeo Brigante¹, Maurizio Carrino¹, Domenico Di Lorenzo¹, Domenico Taglialetela¹, Alberto Masala¹ and Giacomo Carteni²

¹Dipartimento Nefro-Urologico e UOC Urologia, and ²UOC Oncologia Ospedale A. Cardarelli, Napoli, Italy

Background: In relation to a sharp increase in the number of requests for advice aimed at the surgical treatment of uro-oncological diseases and particularity for kidney cancer, from January 2009 at our Institution, an experimental Uro-Oncology service for continuous pre-and post-surgery interdisciplinary consulting and assistance has been established, involving initially patients with locally advanced or metastatic renal adenocarcinoma in anticipation of a subsequent extension on the remaining kinds of urological cancer. In the period between January 1st, 2009, and February 5th, 2010, 97 patients with renal cancer were seen (including 12 cases of small size renal tumours which were operated by partial nephrectomy). According to an internal uro-oncologic protocol, the entire group of patients operated in our Urology Department by radical nephrectomy are divided into 2 groups: multidisciplinary follow-up or adjuvant chemotherapy.

Patients and Methods: In keeping with modern international guidelines which require an extension of renal cell carcinoma surgical indications even at very advanced and metastatic cases and the close cooperation between urologists and oncologists, from January 1st, 2009 to February 5th, 2010 at our Urology Department, we performed a total of 78 radical nephrectomy for renal tumour distributed as follows: 27 radical nephrectomy with ‘open’ technique and 51 radical nephrectomy with ‘laparoscopic’ technique. As part of a multidisciplinary Uro-Oncology Hospital protocol, all 97 patients were studied and preliminary assessed with blood chemistry tests, renal ultrasound, multiphasic CT abdomen (with and without contrast) and chest X-ray, of which 78 were then selected for radical surgery and 7 judged unsuitable for surgical treatment. These were addressed by us directly to oncology consultation for starting primary chemotherapy. The patients which were operated by radical nephrectomy, based on definitive histological response, were systematically divided into two groups to follow two well-coded paths: Group A, patients with localized disease and Group B, patients with locally advanced and metastatic disease. The follow-up of the first group is fully managed by urologists, while patients in Group B, after a preliminary urological inspection performed 20-25 days after surgery, are invited to a uro-oncology multidisciplinary consult, which is necessary for planning subsequent diagnostic and therapeutic monitoring. The Uro-Oncology Interdisciplinary Service, active in our Hospital for only 1 year and currently still experimental for only cases of kidney cancer, was designed with the intent to provide a real continuous care pathways, secure and complete, to sick uro-oncology patients: from diagnosis to surgery or oncological therapy, to the follow-up, both short- and long-term. Such care pathways, when finally codified and extended to all uro-oncological diseases, will provide a dedicated call-centre, a specific section on the corporate website and a modern Uro-Oncology Service with a dedicated healthcare team composed of urology and oncology medical specialists, as well as staff nurses and technicians.

Results: In previous recent years, the follow-up of patients with renal cell carcinoma in our experience has been characterized by a high number of drop-outs, probably related in part to the excellent surgical result in the immediate postoperative and in part to the uncertainty of patients, and often to failure by their doctor to identify the person responsible for follow-up management itself (urologist or oncologist). In contrast, since it was activated, the Uro-Oncology Interdisciplinary Advisory and Assistance Service offers patients with renal cell carcinoma specific behavioral procedures, deadlines to be supplemented by specialist advice, in a shared multi-protocol. This is leading to a very significant reduction of patients ‘lost to follow-up’ and a significant rating factor and adherence in patients, which is also perceived by us as increased confidence and uptime.

IMPROVED DETECTION OF LOW-GRADE PROSTATE CANCER BY PSA-IGM ASSESSMENT

Michela Verna¹, Paolo Pengo¹, Andrea Gallotta¹, Danilo Zani², Silvia Costa², Antonette E. Leon³, Massimo Gion³, Giorgio Fassina¹ and Luca Beneduce¹

¹XEP TAGEN SpA, Marghera Venice, Italy;
²Department of Urology, University of Brescia, Italy;
³ABO Association, Regional Centre for the Study of Biological Markers of Malignancy, AULSS 12, Venice, Italy
Background and Aim: The assessment of circulating immune complexes of prostate-specific antigen (PSA) with IgMs (PSA-IgM) has been shown to achieve a higher diagnostic accuracy compared to the PSA test, thus demonstrating the value of PSA-IgM assay for prostate cancer detection. Moreover, the detection of prostate cancer (PC) can be further enhanced when PSA-IgM determination is used in combination with PSA. The aim of the study was to further investigate the correlation of serum levels of PSA-IgM and Gleason score of PC, by assessing the occurrence of PSA-IgM in patients with different grading of prostate cancer and in a control group consisting of patients with benign prostatic hyperplasia (BPH) by comparison with PSA.

Patients and Methods: Serum samples from 37 patients with PC (25 patients with Gleason score 6 mean age ± SD=68±2.9, and 12 patients with Gleason score 8, mean age ± SD=65±7.6 years) and 44 BPH patients (mean age ±SD=68.4 ± 6.4 years) were collected. Serum levels of PSA were measured in by automatic analyzer (Immulite 2000, Medical System, Italy). Serum levels of PSA-IgM were measured with Prostate-IC kit (Xeptagen, Italy).

Results: Serum levels of PSA-IgM were significantly elevated above the cut-off (151 AU/ml) in 13 out of 37 PC patients (sensitivity=35%) compared to 3 out of 37 patients (sensitivity=8%) with PSA levels above the cut off of 10 ng/ml. When patients were stratified according to Gleason score, 9 out of 25 PC patients (36% sensitivity) with a Gleason score of 6 and 4 out of 12 PC patients with a Gleason score of 8 (33%) were positive for PSA-IgM assay compared to 12% of sensitivity (3/25) in the group with Gleason score 6 and to 0% of sensitivity (0/12) in the group with Gleason score 8 achieved with PSA test. Moreover, 12 out of 44 BPH patients (73% specificity) and 42 out of 44 BPH patients (95% specificity) were positive for PSA-IgM. When the combination of PSA-IgM and PSA was assessed by decision tree analysis without compromising the specificity, an improvement of sensitivity up to 48% (12/25) was obtained only in the group of patients with Gleason score 8 since PSA did not identify any patients with Gleason score 8.

Conclusion: These results demonstrate for the first time evidence of similar diagnostic value of the PSA-IgM test in moderately and well-differentiated prostate cancer in contrast to the PSA test. Co-determination of PSA-IgM and PSA at a higher cut-off value might provide a notable enhancement of detection of low-grade prostate cancer.

Background: To date few reports has been published on the surgical outcomes of patients submitted to radical prostatectomy (RP) for prostate cancer who had undergone previous TURP. The objective of the present study is to assess incidence and location of the positive surgical margins in there patients.

Patients and Methods: A total of 2,408 men treated with RP for prostate cancer were consecutively enrolled in 135 centres. Patient features (age, body weight and height, BMI), preoperative tumour characteristics (digital rectal examination, clinical stage, PSA, bioplastic gleason score) bioplastic records (number and site of cores, of positive cores and percentage of positive scores, number of re-biopsies) general (SF-12) and specific (UCLA-PCI, IIEF) QoL scores, preoperative urologic parameters (continence status, previous catheterization and TURP), intra and perioperative records (nerve sparing, including mono- or bilateral, bladder neck preservation, complications, day and size of catheterization) pathological outcomes (Gleason score, pT, N+, positive surgical margins, including the number and the site) were recorded. We analysed overall positive surgical margins (PSM), the number (single or multiple) and the site (apex, bladder neck, left, right and posterior) of PSMs with Spearman correlation coefficient, logistic regression and unpaired samples t-test.

Results: As expected, clinical stage (p<0.001), bioplastic Gleason score (p=0.001) and number of positive cores at biopsy (p<0.001) were the most significant favouring factors for PSM, while the high number of positive bioplastic cores (p<0.001) and the choice of a nerve-sparing approach (p=0.025) seems to determine avoidance of positive margins. The apex was the most common site of PSM, and in 54% of case it was the single localization of PSM, while left and right margins were more frequently involved in multiple PSM (60% and 63.5%, respectively). Bladder neck preservation was strongly correlated with positive surgical margins at bladder neck site (correlation coefficient: -0.218; p<0.001), while nerve-sparing surgery was not related to the site of PSM.
More relevant data were the correlation with previous TURP: In the overall PSM outcomes, there was no correlation between TURP and PSM (coeff.: 0.33; p=0.101). However, TURP seems to reduce the risk of PSM at the apex (coeff.: -0.43; p=0.036) and improve the risk at the bladder neck (coeff: 0.40, p=0.049). Unpaired samples t-test confirmed these data: overall: 32% PSM without TURP vs. 23% PSM with TURP: p=0.101; apex: 14% PSM without TURP vs. 5% PSM with TURP: p=0.036; bladder neck: 2% PSM without TURP vs. 5% PSM with TURP: p=0.049.

Conclusion: In this study, previous TURP was associated with lower incidence of PSM at the apex and higher incidence of PSM at the bladder neck.

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EARLY CONTINENCE RECOVERY AFTER RADICAL PROSTATECTOMY: RESULTS FROM THE M.I.R.R.O.R. (MULTICENTRE ITALIAN REPORT ON RADICAL PROSTATECTOMY OUTCOMES AND RESEARCH) GROUP

Mauro Gacci1, Alchiede Simonato2, Virginia Varca2, Marco Carini1, Giulio Nicita1, Andrea Decensi3, Aldo Franco De Rose2, Massimo Maffeizzini3, Ottavio De Cobelli4, Roberto Salvioni5, Andrea Briganti6, Ciro Imbimbo7, Vincenzo Mirone7 and Giorgio Carmignani2

1Department of Urology, University of Florence, Italy; 2Urology Clinic, “L. Giuliani” Genova, Italy; 3Department of Oncology, Ospedali Galliera Genova, Italy; 4Department of Urology, IEO Milano, Italy; 5Department of Urology, Istituto Tumori Milano, Italy; 6Department of Urology, HSR Milano, Italy; 7Department of Urology, University Federico II, Napoli, Italy

Aim: To evaluate the predictive factors for the early (1-month) continence recovery after radical prostatectomy (RP) in a multicentre prospective observational study.

Patients and Methods: A total of 2,408 men treated with RP for prostate cancer (PCa) were consecutively enrolled in 135 centres. Patient feature (age, body weight and height, BMI), preoperative tumour characteristics (digital rectal examination, clinical stage, PSA, biotical Gleason score) biotical records (number and site of cores, positive cores and % of positive scores, number of re-biopsies) general (SF-12) and specific (UCLA-PCI, IIEF) QoL scores, preoperative urological parameters (continence status, catheterization and TURP), operative records (nerve sparing [NS], including mono- or bilateral, bladder neck preservation [BNP], complications, days and size of catheter) pathologic outcomes (Gleason score, pT, N+, positive surgical margins) were recorded. We analysed continence outcomes 1 month postoperatively, defining urinary continence as: group A) Fully continent; group B) Minimal stress incontinence, requiring 0-1 pad a day; group C) Urinary incontinence requiring more than 1 pad a day. Statistical assessment included Spearman correlation coefficient and logistic regression, and an unpaired samples t-test comparing group A vs. group B-C.

Results: Preoperatively, 2,190/2,448 (89.5%) men were classified as A, 51 as B (2%) and 10 as C (0.4%), while for 197 (8%) men the data were missed. At 1 month, the continence status of 2,027/2,190 (92.5%) men with both pre- and postoperative data was available: 646/2,027 (31.9%) men were A, 832 (41.0%) B and 549 (27.1%) C. At univariate analysis, age, body weight, positive DRE and clinical stage, prostatic biopsy (Gleason, N° and % of positive cores), catheter features (diameter and days of catheter use), prostate weight, PCS-12 (Physical Component Summary of SF-12) scores had worsened continence, while preoperative catheterization, patient’s desire to preserve sexual function, NS and BNP, MCS-12 (Mental Component Summary of SF-12), UF and SF (Urinary Function and Sexual Function of UCLA-PCI) and IIEF scores had significantly improved postoperative continence. These data were confirmed by t-test. At multivariate analysis, only BNP (p<0.001), UF (p=0.021), SF (p=0.010) and IIEF scores (p=0.028) were determinants for postoperative continence.

Conclusion: Bladder neck preservation may aid in an earlier return of continence following RP. Baseline urinary function is a relevant predictive factor for full continence 1 month postoperatively. Baseline sexual function, measured by IIEF-5 or SF scores (UCLA-PCI domains), was identified as a significant factor predicting early continence recovery after RP.

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DESIRE TO PRESERVE SEXUAL ACTIVITY AND DECISION FOR A NERVE-SPARING PROSTATECTOMY: RESULTS FROM THE M.I.R.R.O.R. (MULTICENTRE ITALIAN REPORT ON RADICAL PROSTATECTOMY OUTCOMES AND RESEARCH) GROUP

Mauro Gacci1, Alchiede Simonato2, Virginia Varca2, Marco Carini1, Giulio Nicita1, Andrea Decensi3, Aldo Franco De Rose2, Massimo Maffeizzini3, Ottavio De Cobelli4, Roberto Salvioni5, Andrea Briganti6, Ciro Imbimbo7, Vincenzo Mirone7 and Giorgio Carmignani2

1Department of Urology, University of Florence, Italy; 2Urology Clinic, “L. Giuliani” Genova, Italy; 3Department of Oncology, Ospedali Galliera Genova, Italy; 4Department of Urology, IEO Milano, Italy; 5Department of Urology, Istituto Tumori Milano, Italy; 6Department of Urology, HSR Milano, Italy; 7Department of Urology, University Federico II, Napoli, Italy
Background and Aim: With survival from prostate cancer increasing, quality of life and of sexuality have become very important targets in treating those patients. Preoperative counseling should include sexual counseling in order to identify the patient’s desire to preserve erectile function and to inform patients about the feasibility of a nerve-sparing approach. The aim of the present study was to investigate factors affecting the patient’s desire and surgeon’s final decision to preserve erectile function after radical prostatectomy in Italian experience.

Patients and Methods: A total of 2,408 men treated with radical prostatectomy for prostate cancer were consecutively enrolled in 135 Urology Departments in Italy. Patients characteristics, general (SF-12) and specific (UCLA-PCI, IIEF) quality of life (QoL) data, urological and prostate cancer preoperative parameters, intraoperative and perioperative results and pathological outcomes were recorded. Univariate (Spearman) and multivariate (log regression) analyses were performed in order to identify parameters that can influence both patient’s desire to preserve sexual activity and the final decision to perform a nerve-sparing approach.

Results: Age (p=0.001), physical component of SF12 (PCS12: p=0.003), Sexual Function of UCLA-PCI (p=0.008) and IIEF score (p<0.001) were the main determinant of “patient’s desire to preserve sexual activity”. The outcomes of multivariate analysis for “final decision of nerve-sparing approach” are reported.

Conclusion: Age, prostate biopsy (bioptical Gleason score and percentage positive cores) and patient’s desire to preserve sexual activity are the main determinants of the choice of a nerve-sparing approach. The amount of sexual activity, assessed either by the specific score of IIEF and UCLA-PCI SF and SB domains, seems less important than the patient’s actual desire to preserve sexual activity.

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BLADDER METASTASIS FROM BREAST ADENOCARCINOMA: TWO CASE REPORTS

Francesco Fidanza, Corradino Di Pietro, Giovanni Saredi, M. Chiara Sighinolfi, Filippo Annino, Giammarco Isgrò, Stefano De Stefani and Giampaolo Bianchi

U.O Urologia, Policlinico Universitario di Modena, Italy

Background: Breast cancer is the most commonly diagnosed cancer among women ranging from 50 to 70 years old years. Metastatic dissemination is the major cause of mortality. Currently, only 19 cases of bladder metastasis are reported in the literature. We report two cases of bladder metastasis from breast adenocarcinoma.

Case Report: Case 1: A 70-year-old female was submitted to radical right mastectomy (for lobular breast cancer T2 N1 Mx) in 1988. In 2004, for bilateral ovarian metastases, the patient underwent total abdominal hysterectomy and bilateral salpingectomy followed by adjuvant chemotherapy. In 2008 after an episode of macrohaematuria, the patient was submitted to cystoscopy, showing multiple bladder neoplasms, constituting solid, non papillary, oedematous areas.

Case 2: A 78-year-old female with prior left quadrantectomy (1998) for breast lobular adenocarcinoma (T2 N1 Mx) subsequently underwent left radical mastectomy in 2005 for local recurrence, followed by adjuvant chemotherapy and radiation therapy. In 2008, the patient came to our observation for bilateral hydronephrosis and acute renal failure. Ureteral stents were placed bilaterally, during the procedure multiple solid, oedematous bladder neoplasms were found. In both cases transurethral bladder resection (TURV) was performed. Pathological examination found breast cancer metastasis.

Discussion: Bladder localization for metastatic breast cancer is very rare. Few cases were diagnosed in alive patients. Metastatic spread of the disease occurs, on average, 90 months after diagnosis of the primary tumour. In our series, the diagnosis was always made for the living patient and bladder localization represented, in one case, the only place of recurrence. CT scan showed in one case the presence of bilateral hydronephrosis without apparent injury to the bladder and in the other case, no alteration of the excretory axis bilaterally. For this reason, unlike the literature, we believe that no radiological investigation is able to provide the most accurate information; our experience demonstrates the crucial role of cystoscopy, highlighting the features of the bladder wall. Although metastatic bladder cancer should be considered a rather rare occurrence, in the presence of persistent macrohaematuria, it is always necessary to perform a cystoscopy in order not to neglect primary or secondary neoplastic bladder disease. This attitude can also be useful in the diagnosis of rare events such as bladder metastasis from breast cancer.

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A RARE CASE OF ANGIOSARCOMA OF THE KIDNEY: LITERATURE REVIEW

Matteo Maria Gerardini, Laura Scopesi, Paolo Mirando, Maurizio Ruggieri, Marco Lorenzo Berardinelli, Gianluca Ricci and Mario Mensi

Azienda Ospedaliera della Provincia di Pavia, Ospedale Civile di Voghera, Italy
Case Report: A rare case of renal angiosarcoma is described in a 71-year-old male. In January 2009 a 71-year-old male was admitted for macroscopic hematuria. A renal ultrasound revealed a mass in the right kidney. The CT scan and the lung radiography confirmed the renal tumour and revealed multiple lung and liver metastases. A liver biopsy and subsequent histopathological tests revealed a sarcoma of the liver of metastatic origin. We sent the patient to the Oncology Division and he started chemotherapy. After one month, the patient was admitted to the Emergency Department with acute abdominal pain and anaemia due to the rupture of the renal mass, and a radical right nephrectomy was performed. The final histopathological test revealed a primary renal angiosarcoma. Our patient survived for only 1 month after surgery. This is a very rare and aggressive malignant tumour with poor prognosis and with fewer than 25 cases described in the literature.

References

MICROABSCESSES AT PROSTATE BIOPSY: A NEW CLINICAL-PATHOLOGICAL ENTITY

Giuseppe Pastore1, Francesco Pinto1, Angelo Totaro1, Alessandro Calarco1, Emilio Sacco1, Andrea Volpe1, Marco Racioppi1, Alessandro D’Addessi1, Gaetano Gulino1, Francesco Pierconti2 and Pier Francesco Bassi1

1Department of Urology, and 2Department of Pathology, “A. Gemelli” Hospital, Catholic University, Rome, Italy

Background: Microabscesses are pathological entities consisting of a neutrophil inflammatory infiltration of the epithelial gland cells without evidence of microbial presence. Microabscesses are rarely described in genito-urinary inflammatory diseases. For the first time, our Department of Pathology described the evidence for microabscesses on tissue from prostatic biopsies with gross evidence. We present a prospective study, not randomized, consisting of the evaluation of total and free PSA variations and modifications of lower urinary tract symptoms (LUTS) after a cycle of antimicrobial therapy with a quinolone orally administered to patients with prostate biopsy positive for microabscesses.

Patients and Methods: Between December 2007 and May 2009, we administered a cycle of antimicrobial therapy with quinolonic agent (Levofloxacin) for 15 consecutive days to 74 patients with prostatic biopsy results positive for microabscesses but negative for cancer submitted to prostate biopsy for abnormal PSA values. LUTS were assessed by IPSS questionnaire administered before and 3 months after the biopsy. Total serum PSA levels were measured 3 months after the biopsy. We divided the population with microabscesses into two groups on the basis of prevalence of microabscesses: group I (fewer than 25% of microabscesses); group II (more than 25% of microabscesses)

Results: The mean total PSA serum level and IPSS score before biopsy were 8.7 ng/ml (±4.1) and 19.9 (±6.7) respectively. The mean total PSA serum levels and IPSS measured three months after biopsy were 5.1 ng/ml (±1.8) and 13.8 (±5.2) respectively. These data show a significant reduction of PSA serum level and an improvement of LUTS after quinolonic therapy (p<0.005). No difference was identified between groups I and II.

Conclusion: We observed a strong reduction both of total PSA serum value and LUTS after 15 days of antimicrobial therapy with quinolone in a population of patients with microabscesses after prostate biopsy. The identification of this new clinicopathological entity and its treatment might reduce the number of patients who need rebiopsy and relief of LUTS.

203 MALIGNANT TESTICULAR GERM CELL TUMOUR IN FATHER AND SON

Paolo Chierigo1, Alfonsino Visonà2, Oliviero Puccetti3, Mojtaba Rahmati1, Maurizio Lazzarotto1, Davide Brotza1, Massimiliano Bernabei1 and Nicola Franzolin1

1Unità Operativa Complessa di Urologia, Ospedale De Lellis, via De Lellis 1, 36015 Schio, Italy; 2Unità Operativa di Anatomia Patologica, and 3Unità Operativa di Oncologia, Ospedale Boldrini, via Boldrini 1, 36016 Thiene, Italy

Aim: To report a case of testicular germ cell tumour (TGCT) in a father and his son, arising in the son at an age 15 years earlier than in the father, according to the evidence found in the literature.

Background: TGCTs are the most common solid malignancy in Caucasian males aged from 15 to 40 years, accounting, between these ages, for 60% of all malignancies. TGCTs show an annual increase of 3-6%. They can occur in a sporadic or familial manner (about 2%). Risk factors are cryptorchidism, Caucasian ethnicity, family occurrence and personal history of TGCT. Cryptorchidism is the best
established risk factor, with a risk of 2: 5–8. 8. Asians and Africans have a low risk of TGCTs. Their descendants maintain a low risk even while living in areas of high risk. The risk for a brother of a TGCT case is 8–10, and between fathers and sons is 6–10. For most other types of cancer the familial risk rarely exceeds 4. Attempts to find genetic markers of testicular cancer have yielded conflicting results. Disease anticipation is an earlier age-at-onset (AAO) of disease in subsequent generations, or an increased severity of disease in children compared with their parents. DA has been observed in a number of genetically triggered diseases, both neoplastic and not, and is called genetic anticipation. It has been demonstrated (3) in cancer of the breast, ovary, testicle, colorectum, pancreas, in Hodgkin’s lymphoma, Crohn’s disease, Parkinson’s disease, multiple sclerosis, schizophrenia, rheumatoid arthritis, type II diabetes, Grave’s disease and primary pulmonary hypertension.

Case Report: Case 1: A 46-year-old Caucasian male presented in 1993 with a 2-month history of right testicular pain, and swelling of 10 days. Ultrasound was suspicious for malignancy. αFP and βHCG were normal. Examination revealed a heavily enlarged testis. A right inguinal orchiectomy was performed. The pathological diagnosis was classic seminoma, 5×4×3.5 cm, with vascular invasion, focal infiltration of tunica albuginea, rete testis and epididymis, without spermatic cord involvement. Chest and abdomen computerized tomography (CT) scan was normal. A right modified retroperitoneal lymph node dissection was performed: 11 out of 32 nodes were ipoistive for embryonal carcinoma. Tumour was pT2pN2M0, stage 2B. The patient received 4 cycles of PEB (cisplatin, etoposide, bleomycin). A right modified retroperitoneal lymph node dissection was performed: 11 out of 32 nodes were ipoistive for embryonal carcinoma. Tumour was pT2pN2M0, stage 2B. The patient received 4 cycles of PEB (cisplatin, etoposide, bleomycin).

Case 2: A 31-year-old male, the son of the patient in Case 1, found a painful swelling in the right testis in June 2009. There was no history of trauma, infection, cryptorchidism, torsion or previous malignancy. Ultrasound revealed a 4-cm mass. Physical examination confirmed the suspicion of tumour. αFP and βHCG were normal; LDH was 2.7 times the upper level. A right inguinal orchietectomy was performed. The pathological diagnosis was classic seminoma, 5×4×3.5 cm, with vascular invasion, focal extension to rete testis, and focal infiltration of tunica albuginea. Chest and abdomen CT scan were normal. The tumour was pT2N0M0S2, stage 1S. The patient received carboplatin, only 1 cycle, AUC 7. LDH dropped quickly and returned to normal levels. A survey of the literature was performed from 1972 (1) until today. The AAO of TGCT in the parent generation (G1) and next generation (G2), histology and stage were registered. The mean AAO for all G1 and G2 patients were calculated. The first report of father-son TGCTs was issued in 1972. From 1972 to 1992, only 31 pairs have been described worldwide, and from 1992 to 1999, sixteen further cases. Based on staging and histology, 45% of pairs have more severe disease in G2 compared with G1, 35% have the same severity, and 20% have less severe disease in G2. The mean AAO for G1 is 43.3 years and the mean AAO for G2 is 27.0 years. The mean difference in AAO for G1 versus G2 is 16.3 years. In our report, the father had right TGCT at 46 years; his son developed right TGCT at 31 years. Neither of them had a history of cryptorchidism. At present they both remain free from illness. The son had not been performing self-examinations despite his father’s history of TGCT. The appearance of TGCT in both father and son might indicate a genetic transmission. In our case, the 15-year difference in the AAO may express a GA. Raghavan in 1980 was the first to suggested GA in father-son testicular tumours (2).

Conclusion: some cases of TGCT may have a genetic transmission; it is mandatory for a son to begin testicular self-examination about 20 years before the time of occurrence of TGCT in his father.

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ROBOT-ASSISTED LAPAROSCOPIC PROSTATECTOMY VERSUS BRACHYTHERAPY IN THE TREATMENT OF LOW-RISK PROSTATIC CANCER: RETROSPECTIVE EVALUATION OF FUNCTIONAL AND QUALITY OF LIFE RESULTS

Claudio Giberti, Fabrizio Gallo, Emilio Gastaldi, Luciano Chiono and Maurizio Schenone
Dipartimento di Chirurgia, Divisione di Urologia, Ospedale San Paolo, Savona, Italy

Aim: To compare retrospectively the functional and quality of life (QoL) outcomes reported during the first year of follow-up after robot-assisted laparoscopic prostatectomy (RALP) versus brachytherapy (BT) in the treatment of low-risk prostate cancer (CaP).

Patients and Methods: In December 2009, we retrospectively compared the outcomes reported by two groups of 150 patients each who underwent bilateral nerve sparing RALP (Group 1) or BT (Group 2), respectively, in the period between May 2005 and September 2009 (mean follow-up 19.3 months). All the patients had similar
preoperative characteristics. Before treatment all patients were invited to fill in three different questionnaires concerning urinary function (IPSS), erectile function (IIEF-5) and quality of life (QoL) (EORTC-QLQ-PR25). Both groups of patients were monitored during the follow-up by physical examination, PSA assays and compilation of IPSS, IIEF and EORTC-QLQ-PR25 questionnaires. Functional and QoL outcomes were evaluated by comparing the two groups of patients in terms of postoperative mean questionnaire score values at one, three, six, nine and twelve months after surgery.

Results: There were no statistically significant differences in preoperative characteristics between the two groups of patients. Concerning the postoperative compilation of the IPSS questionnaire, a significant increase of mean total IPSS score was reported by Group 2 with respect to Group 1 patients at one (12.2 vs. 5.0), three (12.1 vs. 4.7), six (13.0 vs. 4.3) and nine (10.1 vs. 4.5) months, while it decreased to baseline in both groups of patients after twelve months (4.7 vs. 4.3) from surgery. As regards IIEF questionnaire score assessment, 60 and 65 patients of Group 1 and 2, respectively, were excluded from the evaluation of the results due to a preoperative total IIEF score ≤21, allowing the evaluation of 90 and 85 patients of Group 1 and 2, respectively. As expected, a decrease of mean total IIEF score was reported during the follow-up among both groups of patients with respect to the preoperative values. In particular, a significant decrease of mean total IIEF score was reported by Group 1 with respect to Group 2 patients at one (7.2 vs. 15.9), three (9.1 vs. 16.7) and six (9.3 vs. 16.5) months, while similar scores were reported by the two groups of patients at nine (15.8 vs. 17.4) and twelve (20.1 vs. 20.5) months. Concerning the EORTC-QLQ-PR-25 questionnaire, significantly higher scores were reported by Group 1 with respect to Group 2 patients (65 vs. 35) at one month of follow-up. On the contrary, significantly higher scores were reported by Group 2 with respect to Group 1 patients at six (73 vs. 50) and nine (62 vs. 43) months of follow-up.

Conclusion: Between the two groups, patients who underwent BT reported a significant increase of IPSS score due to postoperative urinary irritative disorders during the first nine months after surgery. On the contrary, patients who underwent RALP reported a significant decrease of IIEF score during the first six months due to the transitional erectile dysfunction. The data assessed by the compilation of EORTC-QLQ-PR-25 questionnaire substantially confirmed these aspects, showing the different limitations of quality of life in the two groups of patients mainly represented by erectile dysfunction and urinary incontinence among Group 1 patients in the first 6 months and irritative disorders among Group 2 patients in the first 9 months.

References

THE ROLE OF SURGERY IN RENAL CELL CARCINOMA: A SINGLE-CENTRE EXPERIENCE FROM 1979 TO 2009

Silvano Palazzo, Stefano Impedovo, Giuseppe Lucarelli, Pasquale Ditonno, Pasquale Martino, Carlo Bettocchi, Michele Battaglia and Francesco Paolo Selvaggi
Dipartimento dell’Emergenza e dei Trapianti di Organi, Università Aldo Moro di Bari, Italy

Background and Aim: Until recently, renal cell carcinoma (RCC) was considered mainly a surgically treated disease due to its chemo- and radioresistance. Refinements in surgical technique and the introduction of minimally invasive approaches have improved patient care and bear the promise of even more improvements to come. The aim of this study was to analyse the effects of surgery type on the postoperative period and the long-term survival in a population of 622 patients surgically treated for RCC.

Patients and Methods: We identified 622 patients treated with radical nephrectomy (n=518) or nephron-sparing surgery (n=104) for unilateral sporadic RCC between 1979 and 2009. The clinical features studied were patient age, sex, ECOG performance status, symptoms at presentation and surgery type. Patients with a palpable abdominal mass, flank pain, gross hematuria, acute onset varicocele, weight loss or paraneoplastic syndromes were considered symptomatic at presentation. The pathological features studied included histological subtype, tumour size, 2002 TNM primary tumour classification, perinephric fat invasion, nuclear grade, coagulative tumour necrosis and presence of sarcomatoid differentiation. The Heidelberg classification and Fuhrman grading system were used to assign histotype and nuclear grade of differentiation, respectively. Survival curves were estimated by using the Kaplan-Meier method. The log-rank test and the Cox regression analyses were used for univariate and multivariate analysis.

Results: A total of 622 patients, 387 men (62.3%) and 235 women (37.7%), with a median age at diagnosis of 59 (range: 19-85) years, were included in the study. The number of patients that presented with pathological stage T1, T2, T3 and T4 was 270 (43.4%), 75 (12.1%), 251 (40.4%) and 26 (4.1%), respectively. Most were asymptomatic (n=287, 46.2%). Nodal
metastases were recorded in 39 patients (6.2%) and 52 (8%) had distant metastasis. The mean tumour size was 6.3 (range: 0.5-25) cm. Fuhrman grade was I in 139 (22.3%) patients, II in 251(40%), III in 194 (31.2%), and IV in 38 (6.5%). Clear cell RCC was the predominant subtype (n=455, 73.1%); the remaining cases were papillary (n=95, 15.3%), chromophobe (n=57, 9.1%) and sarcomatoid subtypes (n=15, 2.5%). An extraperitoneal flank incision over the 11th or 12th rib was the preferred approach (66%). An incision below the 12th rib and a thoraco-abdominal approach was used in 29.2% and 0.6% of cases, respectively. Laparoscopic nephrectomy was performed in 26 cases (4.1%) Table I shows the effects of the different surgical approaches on bleeding, ileus and hospital stay.

Table I.

<table>
<thead>
<tr>
<th>Surgical approach</th>
<th>Flank</th>
<th>Anterior</th>
<th>Laparoscopic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding (ml)</td>
<td>520</td>
<td>675</td>
<td>50</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Ileus (days)</td>
<td>3.3</td>
<td>4</td>
<td>2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>7.3</td>
<td>9.2</td>
<td>5.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The median follow-up was 94 (range: 3-234) months. A total of 132 patients (21.2%) experienced recurrence following surgery and 112 (18%) died of RCC at a median of 60 months. The 5- and 10-year overall survival rates were 70% and 61%. Cancer-specific survival (CSS) rates were 78% and 75% at 5 and 10 years respectively. On univariate analysis the following variables were statistically significant: sex, incidental finding, size, stage, Fuhrman grade and tumour necrosis. The Cox regression model showed that sex, stage and Fuhrman grade were significantly associated with CSS. Cox multivariate distribution analysis confirmed the same statistical significance (Table II).

Table II.

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>P (univariate)</th>
<th>P (multivariate)</th>
<th>EXP (coef)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.003</td>
<td>0.025</td>
<td>0.46</td>
</tr>
<tr>
<td>Incidental finding</td>
<td>0.028</td>
<td>n.s</td>
<td>-</td>
</tr>
<tr>
<td>Size</td>
<td>0.000</td>
<td>n.s</td>
<td>-</td>
</tr>
<tr>
<td>Stage</td>
<td>0.000</td>
<td>0.000</td>
<td>0.13</td>
</tr>
<tr>
<td>Fuhrman grade</td>
<td>0.000</td>
<td>0.018</td>
<td>0.31</td>
</tr>
<tr>
<td>Necrosis</td>
<td>0.010</td>
<td>n.s</td>
<td>-</td>
</tr>
<tr>
<td>Histotype</td>
<td>n.s</td>
<td>n.s</td>
<td>-</td>
</tr>
</tbody>
</table>

We experienced a progressive increase in nephron-sparing surgery (NSS) (38.4% in the period 2004-2009 vs. 21.7% before 2004) due to the better prognosis of incidentally diagnosed tumour, the excellent outcome of NSS and the increase in the number of lower stage lesions diagnosed in the past five years (72.3% stage T1-T2 in the period 2004-2009 vs. 48.6% before 2004).

Conclusion: Radical nephrectomy has been the gold standard for treatment of RCC since it was first described by Robson et al. In 1963. In recent years, decreasing tumour stage (migration), coupled with improved surgical adjuncts and techniques has resulted in the establishment of NSS as a viable surgical option for patients with renal tumours. The introduction of laparoscopic nephrectomy has accelerated the evolution toward minimally invasive surgical management of RCC. Preservation of as much renal function as possible and reduced rates of complications are two goals of new minimally invasive approaches to RCC; other goals are to identify early markers of disease, prognosis, or responsiveness to therapy.

206 EFFECTS OF MINIMAL ANDROGEN EXPOSURE ON PROSTATE CANCER, PIN, AND NORMAL PROSTATIC TISSUE. RESULTS OF A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, PRE-SURGICAL TRIAL OF FINASTERIDE VS. FLUTAMIDE: IMPLICATIONS FOR CHEMOPREVENTION

Massimo Maffezzini1, Fabio Campodonico1, Matteo Puntoni2, Rodolfo Hurle3, Ottavio De Cobelli4, Giorgio Carmignani5, Rodolfo Montironi6, Hunert Bartels7 and Andrea Decensi2

1Department of Urology, and 2Medical and Biostatistical Oncology, E.O. Ospedali Galliera, Genova, Italy; 3Clinical Institute Humanitas, Gavazzeni, Bergamo, Italy; 4European Institute of Oncology, Milano, Italy; 5Department of Urology, University Clinic of Genova, Italy; 6Department of Pathological Anatomy, University of Ancona, Italy; 7University of Arizona, Tucson, U.S.A.

Background: Antiandrogens are known to play a central role in the metabolism of prostatic cells. The effect of minimal doses is not currently documented.

Patients and Methods: A total of 125 patients with a diagnosis of low- and intermediate-risk prostate cancer and concomitant PIN who were candidates for surgery were randomised to finasteride 5 mg/d, or flutamide 250 mg/d, or placebo for 4 to 6 weeks immediately before surgery. Biochemical parameters, as well as immunohistochemistry, and morphometric studies were performed. In particular, karyometric analysis, a novel technique, was used to study chromatin arrays.

Results: The statistically significant variations observed consisted in the increase of LH levels in the flutamide arm, as well as, a reduction of PSA, total and fractions, in both treatment arms. The most significant finding of the study was
represented by a clear cut inhibitory effect on progression in the finasteride arm, as documented by karyometry, both on cancerous and on PIN lesions.

Conclusion: Minimal antiandrogen exposure, specifically, with finasteride, exerts an inhibitory effect on the progression of cancer and PIN, establishing a proof of principle in favour of the use of the drug in chemoprevention trials.

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AMPLE VARIABILITY OF PROSTATIC BIOPSY SAMPLING IN PATIENTS WITH CLINICALLY INTRACAPSULAR DISEASE. A COMPARISON OF BIOPSIES AT DIAGNOSIS AND REPEAT BIOPSIES ON THE SURGICAL SPECIMEN

Massimo Maffezzini1, Fabio Campodonico1, Rodolfo Hurle2, Ottavio De Cobelli3, Giorgio Carmignani4 and Rodolfo Montironi5

1Department of Urology, E.O. Ospedali, Galliera, Genova, Italy; 2Clinical Institute Humanitas, Gavazzeni, Bergamo, Italy; 3European Institute of Oncology, Milano, Italy; 4Department of Urology, University Clinic of Genova, Italy; 5Department of Pathological Anatomy, University of Ancona, Italy

Background: Treatment choice for prostate cancer hinges on biopsy results and on the characteristics of the host. We sought to compare the results of biopsies at diagnosis with biopsies after surgical removal of the gland.

Patients and Methods: The data regarding patients participating in a pre surgical chemoprevention trial were collected and analysed, comparing the biopsies obtained at diagnosis with repeat biopsies from the surgical specimen after surgical removal of the gland. The biopsies, i.e. both the diagnostic and the repeated biopsy, were considered as adequate for the present study if: i) a minimum of 10 good quality cores (i.e. 20 mm length) were included, and, ii) the entire material was available for central pathology review.

Results: Among the total of 125 patients entered into the pre-surgical study, 73 patients met both the criteria for inclusion in the present analysis. The repeated biopsy on the removed gland was positive for cancer tissue in 28 out of 73 cases (38.4%), and negative in the remaining 45 cases (61.6%). Among the concordant positive cases, a discrepancy in the Gleason score was apparent, specifically, the Gleason score of 4+3 was confirmed only in one third of the repeat biopsies.

Conclusion: Repeat biopsies are influenced mainly by variability in the in vivo, and the ex vivo, technique nevertheless, the risk of missing or under-grading tumour tissue, or both, is relevant and bears implications for candidates for active surveillance, as well as, those for focal therapy.

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THE SYSTEMIC ABSORPTION OF GEMCITABINE AFTER EARLY INSTILLATION IS SIGNIFICANTLY DIFFERENT IN LARGE VS. SMALL TURBT

Fabio Campodonico, Matteo Puntoni, Francesca Mattioli and Massimo Maffezzini

SC Urologia, EO Galliera, Genova, Italy; Cattedra di Farmacologia Università di Genova, Genova, Italy

Aim: To evaluate the systemic quantitative absorption, pharmacokinetics, and toxicities of gemcitabine administered intravesically at the recommended, high-concentration dose of 40 mg/ml, immediately after transurethral resection.

Patients and Methods: The study included fifteen consecutive patients with recurrent, low- or intermediate-risk non muscle-invasive bladder cancer, candidates for a single intravesical instillation of gemcitabine after resection. The extent of resection was defined as “small” if ≤6 excursions of the resecting loop were needed to eliminate lesion and “large” if >6 excursions were needed. Gemcitabine, 2000 mg in 50 ml saline, was instilled immediately postoperatively and held in the bladder for 1 h. Pharmacokinetics of gemcitabine and its metabolite 2’-2’ difluorodeoxyuridine (dFdU) were determined in plasma by high-performance liquid chromatography. Local and systemic toxicity were assessed.

Results: The highest mean gemcitabine concentrations were 1.38 μg/ml in small and 2.47 μg/ml in large resections. The difference was largest at 15 min after instillation (1.10 vs. 2.47 μg/ml, p=0.001). A significant difference was found between the time and type of resection for gemcitabine plasma levels (p=0.02) but not for dFdU. Toxicity never exceeded grade 2. At a mean follow-up of 2 years, 9 patients (60%) were recurrence free.

Conclusion: The systemic absorption of a single postoperative intravesical instillation of high concentration gemcitabine is proportional to the extent of resection; peak plasma concentrations reached at 15 min are below the levels of intravenous administration.

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RETROSPECTIVE ANALYSIS OF CANCER-SPECIFIC SURVIVAL IN 126 PATIENTS WITH RENAL CELL CARCINOMA WITH TUMOUR THROMBUS EXTENSION

Siracusano Salvatore1, Simonato Alchiede2, Schiavina Riccardo3, Carmignani Giorgio2, Martorana Giuseppe3, Ciciliato Stefano1, Varca Virginia2, Maisonneuve Patrick4 and Belgrano Emanuele1

1Department of Urology, E O. Ospedali, Galliera, Genova, Italy; 2Clinical Institute Humanitas, Gavazzeni, Bergamo, Italy; 3European Institute of Oncology, Milano, Italy; 4Department of Urology, University Clinic of Genova, Italy; 5Department of Pathological Anatomy, University of Ancona, Italy

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Conclusion: The systemic absorption of a single postoperative intravesical instillation of high concentration gemcitabine is proportional to the extent of resection; peak plasma concentrations reached at 15 min are below the levels of intravenous administration.
Background: It is well known that surgical treatment is the first-choice therapeutic strategy in patients suffering from renal cell carcinoma with tumour thrombus extension. In this context, 5 year survival does not exceed 60% and 20%, without and with metastasis, respectively. The aim of this study was to analyse retrospectively cancer-specific survival (CSS) in a group of patients with renal carcinoma stage pT3b and at the same time to assess lymph node involvement as a possible prognostic expression of survival.

Patients and Methods: A total of 126/1,251 patients (10.0%) treated at the Urology Clinics of Trieste, Genoa and Bologna in the period between 1985 and 2005 were included. Patients had a mean age of 66 (range 24-68) years and mean follow-up of 48 (range 0-240) months. Disease was clear cell adenocarcinoma stage pT3b with tumour thrombus involvement of the renal vein in 101/126 (80%), of the infrahepatic cava in 20/126 (16%), and the intrahepatic cava in 5/126 (4%). In all patients, the surgical treatment consisted of radical nephrectomy with removal of the tumour thrombus, which in some cases entailed thoraco-phreno-laparatomic access or mini-invasive access by an abdominal diaphragmatic approach. Application of Kaplan-Meier test and multivariate analysis enabled us to assess CSS and observe whether age, sex, tumour stage and grade, side and bi-laterality, lymph node involvement and presence of metastases could represent independent predictive variables of mortality in this category of patients.

Results: CSS in 126 patients with tumour thrombus extension compared to 1,125 without it is shown in the Table below.

<table>
<thead>
<tr>
<th>CSS at follow-up</th>
<th>24 Months</th>
<th>48 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal vein thrombus (101/126)</td>
<td>79%</td>
<td>62%</td>
</tr>
<tr>
<td>Infrahepatic cava thrombus (20/126)</td>
<td>89%</td>
<td>77%</td>
</tr>
<tr>
<td>Intrahepatic cava thrombus (5/126)</td>
<td>40%</td>
<td>-</td>
</tr>
<tr>
<td>Absence of thrombus (1125/1251)</td>
<td>95%</td>
<td>90%</td>
</tr>
</tbody>
</table>

In particular, multivariate analysis showed that positive lymph node result and/or the presence of metastases are the only independent predictive variables of mortality.

Conclusion: Patients with tumour thrombus extension have a worse CSS rate compared to patients with renal carcinoma but without tumour thrombus extension. Among patients with tumour thrombus extension, lymph node involvement and/or the presence of metastases are the only variables which determine the outcome of these patients.

PARA VESICAL PARAGANGLIOMA: CASE REPORT AND LITERATURE REVIEW

Salvatore Siracusano\textsuperscript{1}, Stefano Ciciliato\textsuperscript{1}, Rossana Bussani\textsuperscript{2}, Nicoletta Lampropoulou\textsuperscript{1}, Francesco Visalli\textsuperscript{1} and Emanuele Belgrano\textsuperscript{1}

\textsuperscript{1}Clinica Urologica ed \textsuperscript{2}Istituto di Anatomia Patologica, Università degli Studi di Trieste, Italy

Background: Neoplasias of paragangliar tissue have been found in almost all viscera and tissues, including vagina and urinary bladder. Paragangliomas of the urinary bladder are rare and represent 0.06% of all bladder cancer cases and about 10% of all tumours of the extra-suprarenal paragangliar system (1, 2). We describe a case report of a paraganglioma localized in a para-vescical space for which a conservative surgical approach was adopted.

Case Report: A 58-year-old woman suffering from suprarenal adenoma underwent an abdominal ultrasound scan, which evidenced the presence of a latero-vescical lesion with a maximum diameter of 35 mm. A CT scan confirmed the ultrasound diagnosis and cytoscopy did not show endoluminal productive processes. The patient underwent surgical excision of the mass through extra-peritoneal access. The histopathological and immunohistochemical analysis (positivity for CD56, vimentin and chromogranin A) are compatible with the diagnosis of paraganglioma for which, owing to the lack of recurrent lesions, adjuvant therapy is not necessary. Eight months after the surgical treatment, the patient is in good health and CT scan has not shown any evidence of disease relapse.

Conclusion: Vescical paragangliomas are rare tumours. In the case report described here, the clinical evidence was accidental and rather unusual for its localization. The treatment of these tumours is exclusively surgical. In the literature, vesical paragangliomas are usually treated with partial cystectomy. In the case described here, the favourable localization of the tumour in a para-vescical site and its complete cleavage from the bladder justified a conservative approach.

References

ITEM GENERATION OF A QUALITY OF LIFE QUESTIONNAIRE SPECIFIC FOR ILEAL ORTHOTOPIC NEOBLADDER

Salvatore Siracusano\textsuperscript{1}, Cristina Lonardi\textsuperscript{2}, Mauro Niero\textsuperscript{2} and Urodynamics Club of Triveneto (Giuseppe Benedetto\textsuperscript{3},

1Clinica Urologica Università di Trieste, Italy; 2Clinica Urologica Università di Genova, Italy; 3Clinica Urologica Università di Bologna, Italy; 4Unità di Epidemiologia IEO di Milano, Italy
Background: Among urinary diversions after radical cystectomy, ileal orthotopic neobladder (IOB) seems particularly promising from the patient’s point of view since it allows the use of their urethra. Besides its main intuitive advantages over other solutions (maintenance of anatomic voiding and preservation of preoperative body image), shortcomings of IOB have been underlined in literature, such as nighttime incontinence, sexual dysfunction, etc. Comparative studies on quality of life (QOL) in IOB have been conducted by using generic measures such as SF-36 and/or cancer specific tools (FACT, QLQ-30, HAD). To date therefore, no tools are available, neither for monitoring IOB dysfunction, etc. Comparative studies on quality of life (QOL) in IOB have been conducted by using generic measures such as SF-36 and/or cancer specific tools (FACT, QLQ-30, HAD). To date therefore, no tools are available, neither for monitoring IOB patients’ QOL over time, nor for conducting appropriate comparative studies. The aim of the present contribution is that of describing structural components, as well as specimens, of the questionnaire development.

Patients and Methods: Up to 35 IOB (mean age 63.3 years; males=28) from 7 Italian centres were selected for interview, in order to represent the main types of clinical condition: continent=21; nighttime incontinent=10; totally incontinent=2; hypercontinent=2. The technique of narrative interviewing was adopted because of the specific object of the study, aimed at exploring how patients see their QOL over time, nor for conducting appropriate comparative studies. The domains given above did not result from any particular theoretical pre-determined framework (functional approach, needs-based approach or others). The guide for the interview narrative only asked patients to narrate the trajectory of their disease. Interviewees usually started from early cancer symptoms and proceeded by talking about decision-making on adopting IOB. We are confident that our study collected a reasonable sample of the issues that tap into the typical problems of living with IOB.

Conclusion: After this provisional development, the IOB questionnaire will enter a phase of international development. A side qualitative study will try to shed light on the mechanism of the response shift in IOB patients that could better address the questionnaire development.

212 COMBINED ROLE OF SERUM ASSAYS OF PSA-IGM AND PSA FOR THE DIAGNOSIS OF PROSTATE CANCER

Danilo Zani1, Silvia Costa1, Alberto Pettenò1, Claudio Simeone1, Sergio Cosciani Cunico1, Antonette Leon2, Massimo Gion2, Giorgio Fassina3 and Luca Beneduce3

1Department of Urology, University of Brescia, Italy; 2ABO Association, Regional Centre for the Study of Biological Markers of Malignancy, AULSS 12, Venice, Italy; 3Xeptagen SpA, Marghera, Venice, Italy

Background and Aim: The assessment of serum levels of prostate-specific antigen (PSA) is the a widely used important tool for the detection of prostate cancer (Pca). PSA is still considered the best marker in the field of Pca, although its main limitation is that it is not cancer specific
but rather organ specific. Therefore, the PSA test may lead to many unnecessary biopsies for a correct diagnosis. PSA may be detected in the bloodstream of patients with PCa associated with immunoglobulin M (IgM) to form complexes (PSA-IgM), whose levels are measured for the diagnosis of PCa. Recently, it has been demonstrated that testing for serum levels of the immune complexes PSA-IgM may improve the diagnostic performance of the test of total PSA. The aim of the study was to evaluate a possible association of the PSA-IgM assay with the PSA test for the selection of patients to be subjected to trans-rectal ultrasound (TRUS) guided prostate biopsy.

**Patients and Methods:** Serum samples from 67 male patients, 33 affected by organ-confined PCa that underwent radical prostatectomy with Gleason score from 5 to 7 and 34 affected by benign prostate hypertrophy (BPH) that underwent endoscopic treatment, were collected by the Department of Urology, Spedali Civili of Brescia, and immediately snap frozen at 80°C. Serum levels of PSA-IgM were assessed using Prostate-IC (Xeptagen, Italy) while PSA levels were determined by automatic analyzer (Immuliite 2000, Medical System, Italy).

**Results:** Patients were stratified into two groups according to age: the first group consisted of 24 patients with PCa and 20 with BPH aged between 60 and 70 years and the second group consisted of 9 patients with PCa and 14 with BPH aged between 70 and 80 years. Serum levels of PSA and PSA-IgM were analysed in the two groups using cut-off values of 4 ng/ml for PSA and 145 AU/ml for PSA-IgM respectively. In the first group, 18/24 PCa patients were positive for PSA (75% sensitivity) with a specificity of 50% (10/20 BPH patients) compared to 10/20 PCa patients which were identified with PSA-IgM assay but with a higher specificity of up to 70% (6/20 BPH patients). The association of both biomarkers gave a sensitivity of 38%, identifying 9/24 patients with prostate cancer but with a significant improvement of specificity up to 90%, since 18/24 patients with BPH were negative for at least one test. In the second group of patients, aged 70-80 years, PSA test had a sensitivity of 67% (6/9 PCa patients) and specificity of 78% (3/14 BPH patients) compared to a sensitivity of 44% calculated for PSA-IgM test (4/9 PCa patients) with a specificity of 71% (4/14 BPH patients). The association of PSA and PSA-IgM had a sensitivity of 30% (3/9), with the highest specificity (93%, 13/14 BPH patients).

**Conclusion:** The results of the study demonstrate the valuable diagnostic value of PSA-IgM assay compared to total PSA test in patients with organ-confined PCa. The association of PSA-IgM and total PSA improves the diagnosis of PCa and better discriminates between BPH and PCa. Therefore, the diagnosis of PCa can be improved by utilising both tests and thus reducing the number of negative prostate biopsies.

**References**


**213 PHOTODYNAMIC DIAGNOSIS IN NON-MUSCLE-INAVERSE BLADDER CANCER: EXPERIENCE WITH HEXAMINOLEVULINATE**

Lorenzo Gatti1, Nicola Pesenti1, Nicola Arrighi2, Alessandro Antonelli1, Claudio Simeone1, Regina Tardanico2 and Sergio Cosciani Cunico1

1. Department of Urology University of Brescia, Italy; 2. Section of Pathology Spedali Civili Brescia, Italy

**Background:** Bladder cancer is the seventh most common cancer in men and the seventeenth most common in women. Approximately 75%-85% of patients with bladder cancer present non muscle-invasive cancer. Bladder cancer has a high prevalence and poor prognosis if diagnosed late or treated inadequately, and treatment is also associated with high economic cost. Photodynamic diagnosis (PDD) used in addition to conventional cystoscopy is a sensitive aid in the identification of bladder cancer, particularly for flat lesions. For this reason, PDD is recommended for the detection of the carcinoma in situ by EAU guidelines. The aim of the study was to evaluate the diagnostic accuracy of PDD with hexaminolevulinate (HAL) in 76 consecutive patients with non muscle-invasive bladder cancer.

**Patients and Methods:** From October 2008 to December 2009, 76 patients, 63 males and 13 females, underwent bladder resection with use of PDD; 21 were at first observation, 9 second look and 46 were suspected of recurrence of known disease. A total of 209 histological specimens was analysed by an expert uropathologist. Fifty-five of these specimens came from the first observation group, 26 from the second look group and 125 from the group with suspected recurrence. According to EAU guidelines, the histological classification used was 2004 WHO/ISUP. An instillation of 50 mg of HAL was given 1 hour before cystoscopy and transurethral resection of bladder performed by using Storz D Light System®, which allows both white and blue light bladder inspection. Resection was conducted in all suspicious area in white or blue light.
Results: All patients maintained HAL in the bladder for an hour and nobody showed sign of systemic side-effects. Histological results of 209 biopsies obtained from 76 analyzed patients had shown 84 benign areas and 125 malignant lesions; 40 (31.7%) of these were missed during standard white light cystoscopy but detected under blue light. Twenty-seven biopsies were carcinoma in situ (67.5%), 2 were high-grade papillary urothelial carcinoma (5%) and 11 were low-grade papillary urothelial carcinoma (27.5%). Sensitivity, specificity, PPV and NPV for the diagnosis of non muscle-invasive of bladder cancer were 98.4%, 28.8%, 71.9% and 94.7%, respectively. In the “first observation cases”, 34 biopsies were positive for malignant disease and 7 were evident only in PDD. In “second-look cases”, 18 biopsies were positive for malignant lesion and 4 were missed in white light. In cases of suspected recurrence-prostate cancer, 74 specimens were positive for tumoural lesion and 19 were evident only in PDD.

Conclusion: The results show that addition of PDD to HAL improves quality of tumour resection by comparison with conventional white light cystoscopy alone. In particular, detection of carcinoma in situ is increased. The low specificity can improve by surgeon experience.

References

215 COMPLEX RENAL CYSTIC LESIONS: ASSESSMENT WITH CONTRAST-ENHANCED US (CEUS) AND COMPUTER TOMOGRAPHY

Massimo Valentino1, Alessandro Bertaccini2, Michele Bertolotto3, Pietro Pavlica4, Libero Barozzi4 and Giuseppe Martorani2

1Dipartimento Emergenza/Accettazione, Chirurgia Generale e dei Trapianti, UO di Radiologia, Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, via Massarenti 9, 40138 Bologna, Italy;
2UO Urologia, Dipartimento Chirurgie Specialistiche ed Anestesiologia, Università di Bologna, Policlinico S. Orsola-Malpighi, via Palagi 9, Bologna, Italy;
3UCOdi Radiologia dell’Università di Trieste, Ospedale di Cattinara, Strada di Fiume 447, 34149, Trieste, Italy;
4UO di Radiologia Barozzi, Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, via Massarenti 9, 40138 Bologna, Italy

Patients and Methods: A total of 102 consecutive patients with 108 atypical cystic renal masses at CT underwent CEUS. Overall, 36 masses were resected, the remaining 72 lesions were followed up for periods ranging from 9 months to 4.5 years. CT Images and US digital cine clips of all lesions were retrospectively evaluated by blind readers. Basing on CT appearance the lesions were assigned a Bosniak classification. Similar criteria modified for US imaging were used to score atypical cysts at CEUS. For each lesion, the number of septa, thickness of wall and septa, presence of calcifications, and contrast enhancement were evaluated with both techniques. The scores of resected masses were correlated with pathology reports.

Results: At CT, lesions were scored as category II (n=44), IIF (n=26), III (n =20), and IV (n =18). All type IV and 18/20 type III lesions were surgically removed. All category IV and 12/18 category III lesions of the surgical group were malignant. All class II and IIF cysts were stable after follow-up periods ranging from 9 months to 4.5 years. In 94/108 (87%) lesions, CT and CEUS scores were equivalent, while in 14 lesions (13%), there were differences. CEUS depicted more septa than CT, or upgraded wall thickness, resulting in Bosniak score upgrade in 8 lesions from category II to IIF. Two category III lesion at CT were scored as category IV at CEUS. Two category IIF and 2 category III lesion at CT were scored as category III and IIF at CEUS, respectively.

Conclusion: CEUS shows similar findings to CT in most complex cystic renal lesions. Complex cystic renal masses are characterized effectively with CEUS; this technique could be considered an alternative to CT in the follow-up of complex cysts and particularly in patients with renal insufficiency. It can be performed during the routine US examination, has no risk due to the use of radiation and iodinated contrast media, and has a lower cost.

216 CREATION OF A PROSTATE CANCER TISSUE BANK: NEW TECHNIQUE

Luca Carmignani, Stefano Picozzi, Robert Stubinski, Stefano Casellato, Giorgio Bozzini, Luca Lunelli and Domenico Arena

Urology Department, IRCCS Policlinico San Donato, via Morandi 30, 20097, San Donato Milanese, Milan, Italy

Background: Tumour tissue banking has an important role in basic research. The only approved and currently used
protocol is the modified Bova’s technique (1), which removes prostatic capsule and obtains 0.5 cm thick samples from the apex to the prostate base. Samples are stored at \(-150^\circ C\) and detached in 4 parts (2×2 cm), thus leading to a 70% of tumour identification and isolation. The aim of the study is to validate a new technique for creating a prostate cancer tissue bank.

**Patients and Methods:** This study was first approved by our Ethical Committee and each patient signed a consent form. Prostatic tissue is immediately collected from the prostate surgically removed specimen, with six cores (3 in the tumour site + 3 on the other side). Prostatic cores are collected from the site previously indicated as tumoural by the biopsy; a hand-assisted biopsy is used to better identify nodules. An ink injection mark is made to ensure the sample is taken from the tumour site. A further check is carried out by repeating a biopsy in the same site. The pathology report ensures correct sample collection, identifying ink injection into the tumour site and tumour evidence in the repeated biopsy. Patients with tumour microfocus evidence were excluded from the study.

**Results:** Between September 2008 and June 2009, 42 patients were enrolled. Four revealed a tumour microfocus and were excluded from the study, leaving 38 pts. The mean age was 60.6 (range 52-72) years. Preoperative mean PSA was 8.13 (range 3.4-40) ng/ml. Mean weight of the prostate surgical removed was 48.6 (range 25-140) g. Pathological TNM evaluation (according to 2002 TNM) was 2 pts pT2a, 2 pT2b, 28 pT2c, 6 pT3a, 1 pT3b, and 1 pT4. Definitive histological report revealed the tumour in one lobe in 20 pts, and in two lobes in 18 pts. Tumour width (maximum diameter) ranged between 2 mm and 28 mm. In 30 cases, biopsies collected from the tumour site were correct, with a mean of 45% of tumoural involvement of the core (range 10-90%). A negative biopsy was observed in 4 cases of mismatch between the previous biopsy report and the definitive report and in 4 cases in which the cores collected did not reveal tumour. Overall tumour detection rate was 88% (30/34).

**Conclusion:** This technique has a good tumour detection rate (88%), is simple, fast and does not require other persons and materials to store the samples. The technique does not change the pathological definitive TNM, does not require other pathological examinations, and does not require big space for storage. Core storage is made simpler by the use of RNALater, thus avoiding immediate cooling and leading to indefinite RNA protection. Biomarkers and immuno-histochemical research is made possible by including samples in tissue microarrays (2). This technique a prostate cancer tissue bank of good quality to be obtained, even in an institution which is not academic, nor able to obtain funds or samples from other centres.

**References**


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**SHORT- AND LONG-TERM COMPLICATION EVALUATION IN PATIENTS WHO UNDERGO TRANSRECTAL PROSTATIC BIOPSY**

Luca Carmignani, Stefano Picozzi, Matteo Spinelli, Salvatore Di Pierro, Gabriella Mombelli and Ercole Negri

School of Urology, University of Milan, Italy

**Background:** Prostatic biopsy, despite technical and material development, still presents complications. The aim of the study was to prospectively evaluate both short- and long-term complications occurring as a consequence of this procedure.

**Patients and Methods:** Between January and October 2009, any patient who underwent prostatic biopsy and accepted to enter the study was enrolled by our Urology Departments. This study was first approved by our Ethical Committee and each patient signed a consent form. Prostatic biopsy was proposed following EAU guidelines. Before the procedure, all patients had a full blood test examination with coagulation PT and PTT check. Patients taking anticoagulant drugs their therapy to a low molecular weight heparin. In patient taking platelet antiaggregant drugs the therapy was maintained. Patients with immunodeficiency disorders, taking a double antiaggregation therapy, performing a second biopsy or a biopsy of the anastomosis after a RRP were not enrolled. Fourteen prostatic cores were collected following the Gore scheme. After the procedure, the patients were clinically observed for two hours. A phone call was made after 3, 7, and 30 days to check possible complications, submitting to all the same approved questionnaire. A total of 204 patients entered this study and 198 (97%) answered the phone call. The mean age was 64.5 (41-84) years. Mean PSA was 7.94 (1.5-19) ng/ml. Overall, 82 patients had a positive DRE and 94 had a positive TRUS. 26 pts had a platelet antiaggregant therapy and 2 an anticoagulant one.

**Results:** The following Table shows the complications experienced by the study group.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhage</td>
<td>17</td>
</tr>
<tr>
<td>Fever</td>
<td>11</td>
</tr>
<tr>
<td>Pain</td>
<td>28</td>
</tr>
<tr>
<td>Infection</td>
<td>5</td>
</tr>
</tbody>
</table>

Infective major complications happened within 3 days of the procedure being done. Major bleeding complications occurred within 2 hours. There is no statistical evidence of any difference in complications ($p<0.05$) between patients with antiaggregant or anticoagulant therapy and other patients. Perineal pain (17.2%) tended to gradually resolve, but 3.5% reported a perineal pain after 30 days. Haemospermia was frequent after the procedure (in 68.3% of the patients who had sexual intercourse 3 days after the biopsy). In this typical aspect, there is a statistical difference between patients in anticoagulant or antiaggregant therapy and other patients.

**Conclusion:** There is no need to keep the patient under observation for more than two hours after a prostatic biopsy, hence the procedure can also be done as an outpatient clinic procedure and not only as a day surgery one. As reported in the literature, platelet antiaggregant and anticoagulant drugs increase the risk of haemospermia.

**219 DYNAMIC CONTRAST-ENHANCED AND DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING AND PROSTATE CANCER DETECTION: PRELIMINARY RESULTS**

Anna Lia Valentini1, Francesco Pinto2, Angelo Totaro2, Emilio Sacco2, Andrea Volpe2, Marco Racioppi2, Beatrice Gui1, Francesco Pierconti3, Lorenzo Bonomo1 and Pier Francesco Bassi2

1Istituto di Radiologia, 2Urologia, and 3Istituto di Anatomia Patologica, Università Cattolica del Sacro Cuore, Policlinico ‘A. Gemelli’, Roma, Italy

**Background:** A prospective multi-disciplinary study was performed to determine the accuracy of dynamic contrast-enhanced (DCE) and diffusion-weighted (DW) magnetic resonance imaging (MRI) for prostate cancer (PCa) detection in patients with persistent elevation of serum PSA levels and previous negative transrectal ultrasound (TRUS)-guided prostate biopsies.

**Patients and Methods:** A total of 11 consecutive patients with persistent elevation of serum PSA levels (greater than 4 ng/ml) and previous negative TRUS-guided prostate biopsies formed the study group. Patients were studied with three-dimensional (3D) T1-weighted images with spoiled gradient echo multi-phases for DCE-MRI and 2D echo planar imaging for DWI. Four weeks after the MRI, patients underwent a TRUS-guided transperineal prostate biopsy with 24 random cores plus additional biopsies of suspicious areas, if present, detected on functional MRI. Each MRI examination was discussed with the radiologist in order to define the exact location of the suspicious areas before the TRUS-guided biopsy.

**Results:** DCE-MRI and DW-MRI showed 29 suspicious areas. Histopathology showed PCa in 5 (17.2%); atypical small acinar proliferation (ASAP) in 3 (10.3%); chronic inflammation in 5 (17.2%); glandular atrophy/fibrosis in 12 (41.3%), atrophy alone in 2 (7%) and micro-abscess in 2 (7%). The detection rate for DCE-MRI (OA=82.7%; 4/5 PCa and 1 ASAP) was better than that for DWI (OA= 58.6%).

**Conclusion:** Pre-biopsy DCE-MRI can provide best quality of cancer detection and allow target biopsies. DW-MRI demonstrated high false-positive rate caused by overlapping of apparent diffusion coefficient (ADC) for both benign and malignant lesions.

**220 PROGNOSTIC ROLE OF SUPPRESSOR OF THE CYTOKINE SIGNALLING (SOCS3) METHYLATION IN PATIENTS WITH PROSTATE CANCER: PRELIMINARY ANALYSIS ON RADICAL PROSTATECTOMIES AND PROSTATIC BIOPSIES**

Francesco Pinto1, Alessandro Calarco1, Angelo Totaro1, Emilio Sacco1, Alessandro D’Addessi1, Andrea Volpe1, Marco Racioppi1, Francesco Pierconti2, Maurizio Martini2, Luigi La Rocca2 and Pier Francesco Bassi1

1Urologia, and 2Istituto di Anatomia Patologica, Università Cattolica del Sacro Cuore, Policlinico ‘A. Gemelli’, Roma, Italy

**Background and Aim:** Suppressor of the cytokine signalling (SOC) proteins are a family of inhibiting proteins playing a focus role in the negative regulation of cytokine signalling. The alterations of gene and the consequent defective expression of SOC proteins may contribute to the tumour progression and metastatic processes. Methylation of SOCS3 gene has been demonstrated to be involved in disease genesis and progression in many types of solid tumours. The primary
The objective of the study was to determine the methylation status of SOCS3 in vivo in patients with prostate cancer. This might allow identification of a prognostic marker and a category of patients that might benefit from alternative and targeted therapies with demethylating agents, already actuated in other tumours.

Patients and Methods: The analysis of the methylation status of SOCS3 promoter was performed for 3 groups of patients: 1) 9 patients submitted to prostate biopsy with a diagnosis of benign prostatic hyperplasia (BPH); 2) 30 patients who underwent radical prostatectomy (RP) for localized or locally-advanced prostate cancer (PC) in which analysis was performed on RP specimens; 3) 10 patients in which the analysis was performed on the biopsy and RP specimens. All the explored cases had never been treated with any hormonal therapy before the study.

Results: All the BPH cases showed an unmethylated status of SOCS3 promoter. Of the 30 RP, all 10 cases with PC Gleason score 6 showed SOCS3 promoter to be unmethylated; conversely, it was methylated in 7 out of 9 cases of PC Gleason score 7 (3+4), 2 out of 2 PC Gleason score 7 (4+3), 4 out of 6 Gleason score 8 and in all 3 cases of PC Gleason score 9. In the group of patients in which the methylation status was assessed in the prostatic biopsy and in the RP specimens, a 70% concordance was found with a discrepancy in 1 case, while in 2 patients, it was not possible to assess the methylation status because of the short positive sample length of the prostatic biopsy (<4 mm).

Conclusion: The SOCS3 gene does not appear to be methylated in patients with BPH after biopsy and in the non aggressive prostatic tumours, while the promoter was methylated in most cases with a more aggressive disease. The methylation status seems to be identifiable also in the biopsy sample at the moment of the diagnosis. These results, even if in a small series, seem to be promising for a prognostic role of this biomarker and, possibly, therapeutic target with the use of demethylating agents.
term continence rate is satisfactory as well as the sexual activity, and it ensures good functional and oncological results, particularly in young patients.

Table I. Y-shaped ileal neobladder: comparison between urodynamic results at 1 and 11 years of follow-up.

<table>
<thead>
<tr>
<th>Urodynamic parameters</th>
<th>1-Year (mean ± SD)</th>
<th>11-Years (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum cystometric capacity (ml)</td>
<td>300 ± 60.5</td>
<td>395.3 ± 65.7</td>
</tr>
<tr>
<td>Neobladder contractions: minimum pressures (cmH20)</td>
<td>32.5 ± 13.8</td>
<td>49.5</td>
</tr>
<tr>
<td>Neobladder contractions: maximum pressures (cmH20)</td>
<td>64.17 ± 35</td>
<td>115 ± 26.3</td>
</tr>
<tr>
<td>Post-void residual volume (ml)</td>
<td>124.5 ± 196</td>
<td>86.7 ± 203</td>
</tr>
</tbody>
</table>

References


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IS REPETITION OF SATURATION BIOPSY USEFUL? SINGLE-CENTRE EXPERIENCE

Giandavide Cova, Francesco Beniamin, Giovanni Luca Drago Ferrante and Luigi Maccatrozzo
Struttura Complessa di Urologia, Ospedale Civile di Treviso, Italy

Background: The management of patients at high-risk of harbouring prostate cancer after an initial negative biopsy is always a challenge. Super-extended prostate biopsy schemas were introduced with the aim of improving cancer detection but, on the other hand, the risk of discovering an insignificant cancer is high. We report our centre experience to evaluate the diagnostic value of repeated saturation prostate biopsies.

Patients and Methods: Between December 2005-December 2009, 346 consecutive patients underwent saturation biopsy (mean age 62 years, mean PSA 13.5 ng/ml). Every patient had a previous prostate biopsy (mean cores number 8). The indications were presence of PIN high-grade (114 pts) or ASAP (82 pts), abnormal PSA velocity (122 pts) or abnormal DRE (38 pts). After a median follow-up of 6 months, because of persistence of risk factors, 76 patients underwent second saturation biopsy, and after a mean follow-up of 12 months, 17 patients underwent a third saturation biopsy. Every procedure was performed under local anesthesia (periprostatic nerve block) using a pre-defined 24 cores scheme with a median core length of 1.8 cm.

Results: A total of 135 prostate tumours were detected at first saturation biopsy (39%), 16 at second saturation (21%) and 3 at third saturation (17%). The tumours detected at second or third set were considered significant in 11 patients (mean Gleason score 7) and 7 patients underwent radical prostatectomy (4 pT2 Gleason score 6 and 3 pT3 Gleason score 7). No increased side effects or serious complications were reported in repeated procedures.

Conclusion: Even if one single saturation biopsy does not exclude the presence of prostate cancer, repeated super-extended biopsy does not improve cancer detection rate which dramatically decreases (from 39% to 21 and to 17%), so patients with persistent risk factors have only a remote possibility of harbouring prostate cancer. The probability that carcinomas missed at first mapping were insignificant was high and even when carcinomas were considered significant, the prevalence of intracapsular disease with a low Gleason score in patients who underwent radical prostatectomy suggests a possible overdiagnosis and overtreatment. According to our experience, repetition of saturation biopsy has a low diagnostic yield and the prevalence of low aggressive cancers perhaps suggests other therapeutic options such active surveillance but other clinical studies are required.

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PROSTATIC URETHRA PRESERVATION DURING RADICAL PROSTATECTOMY: DESCRIPTION OF THE TECHNIQUE AND OUTCOMES

Remigio Pernetti, Eugenio Brunocilla, Mascia Guidi, Barbara Barbieri and Giuseppe Martorana
Clinica Urologica, Università degli studi di Bologna Alma Mater Studiorum, via P. Palagi 9, 40138 Bologna, Italy

Background and Aim: The radical prostatectomy remains the gold standard for the treatment of prostate cancer. In the last years were developed so many surgery procedures to preserve the urinary function without reducing oncological results. We aimed to describe an anatomic, reproducible technique of prostatic urethra preservation (PUP) and the associated perioperative and long term outcomes.

Patients and Methods: Data of 27 radical prostatectomies, made by the same surgeon, with the technique of the PUP, from 2007 to 2009, were prospectively collected and analysed. The surgical procedure consists into preserving 1.0-1.5 cm of prostatic urethra during the bladder neck dissection. Tumour characteristics, perioperative complications and postoperative urinary control were evaluated both at 1 and 3
weeks and 1, 4 and 12 months, by means of patients’ visits and submission of a questionnaire; continence was defined as 0–1 pads per day.

**Results:** The mean age was 67±5 years. Mean PSA was 6.6±2 ng/ml. A total of 21 patients had Gleason’s score of 3+3 and 6 patients had Gleason’s score of 3+4. Only 2 patients had positive margins (apex and lateral), nobody had positive distal prostatic urethral margin. The continence rate at 1 week was 57%, at 3 weeks was 65%, at 4 months was 92%. The PSA value at 1 month was <0.01 ng/ml.

**Conclusion:** With this technique, it is possible to avoid bladder neck mucosa eversion and reconstruction. The technique is associated with a quick and satisfactory relief of urinary function and a good cancer control.

### 224 PATHOLOGICAL FEATURES AND ADVERSE PROGNOSIS OF NEUROENDOCRINE BLADDER TUMOURS

**Marco Oderda**¹, Michele Ruoppolo², Francesco Marson¹, Francesca Pisano¹, Luca Molinaro³, Donatella Pacchioni³, Alessandro Tizzani¹ and Paolo Gontero¹

¹Department of Urology, Molinette Hospital, University of Turin, Turin, Italy; ²Treviglio, Italy; ³Department of Biomedical Sciences and Human Oncology, University of Turin, Italy

**Background:** Neuroendocrine bladder tumours are rare entities with a very aggressive behaviour and an abysmal prognosis. Their spectrum comprises small cell carcinomas (SCC), carcinoids and large cell neuroendocrine bladder carcinomas (LCNBC). Aim of this study is to retrospectively evaluate the outcome of a series of 14 consecutive bladder neuroendocrine neoplasms observed in 2 institutional hospitals.

**Patients and Methods:** We analysed the charts of 14 patients affected by neuroendocrine bladder tumours for clinical information and follow-up status; immunohistochemical study was performed for chromogranin-A and synaptophysin. The main endpoint was to evaluate the overall survival (OS) and the cancer-specific survival (CSS) of the cohort. Subanalysis of survival based on the type of treatment received was attempted.

**Results:** The mean age was 70.2 years; 11 tumours were SCC, 2 LCNBC and 1 was an adenocarcinoma with both muciparous and neuroendocrine features. Median follow-up was 6.5 months. The 6-months CSS rate was 57.1%, while the 2-years CSS rate was 21.4%. CSS and OS rates coincided. The median survival for the cohort was 7 months. There was no statistically significant difference in survival between patients who underwent surgery and those who did not.

**Conclusion:** Independently from the therapy performed, the prognosis of neuroendocrine bladder tumours is very poor. Nowadays, it seems that an early diagnosis does not affect so much the survival, as an effective and specific treatment of this neoplasms is currently lacking.

### 225 MINILAPAROTOMY (MINILAP) AND RADICAL RETROPUBIC NERVE SPARING PROSTATECTOMY: OUR EXPERIENCE

**Giuseppe Coraci**, Maria Karydi, Leonardo Mosè Salamè, Salvatore Biancorosso, Pietro Liberti, Bruno Mazzoccoli, Francesco Pietropaolo, Giuseppe Salamone and Gianfranco Savoca

U. O. di Urologia, Fondazione San Raffaele-G. Giglio, Cefalù, Palermo, Italy

**Background:** Radical retropubic prostatectomy is the standard treatment of clinically localized prostate cancer. Several techniques have been developed in order to reduce the aggressiveness of the chirurgical procedure and to reduce the impact on the quality of life. The minilap (minilaparotomy) technique, permits to reduce the length of the incision (6-8 cm) and facilitates the recovering of patients without interfering with the functional or oncological results. The purpose of our study is to evaluate the feasibility of the minilap technique reporting our experience during the nerve sparing radical retropubic prostatectomy.

**Patients and Methods:** We reviewed 310 consecutive patients who underwent radical prostatectomy from January 2007 to September 2009 in our institution. Ninety-three (30%) of these patients were treated with conventional RRP while 217 patients (70%) with minilaparotomy RRP. Two hundred and eight (67%) had a localized disease (T1-T2), and 60 patients of these (28.8%) received nerve-sparing surgery. The minilap technique was carried out with a 6-8 cm infraumbilical vertical incision from the pubic symphysis towards the umbelicus. The oncological outcomes were mainly limited to the positive surgical margins rates evaluation. The potency rate was calculated with the IIEF-5 score questionnaire pre and postoperatively, while continence was evaluated through ICI-q-SF questionnaire and number of pads used daily. The functional outcomes were calculated at 3-6-12 months after surgery.

**Results:** Positive surgical margin rate was 16.1% in the RRNS group, while 16.3% in the mini lap RRNS group. The potency rate (IIEF-5>22) in the mini lap group at 3 months was 56.6%, at 6 months 68.1%, at 12 months 70.8%. Further more, 76.3%, 87.5% and 92% maintained a complete continence at 3, 6, 12 months respectively in the mini lap
group. Either potency or continence rates were similar to both
groups during the follow-up period. The advantage of the
mini lap group to the standard group was related to less
postoperative pain, and shorter hospitalization.

**Conclusion:** The results we obtained suggest that there are
no statistically significant differences comparing standard
RRPNS and mini lap RRPNS evaluating positive surgical
margins, potency rate and complete continence rate at 3, 6,
12 months. A statistically significant difference in favour of
minilap RRPNS was related to less postoperative pain, and
shorter hospitalization. The mini lap technique represents an
easily reproducible technique with similar oncological and
functional results to standard RRP.

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**BLUE NEVUS OF THE PROSTATE GLAND**

Nicola Tosi1, Federico Lanzi1, Lorenzo Masieri1, Maria
Grazia Raspolini2, Florence Graziano Vignolini1, Saverio
Giancane1, Sergio Serni1, Leonardo Pescitelli3 and Alberto
Lapini1

1Department of Urology, University of Florence, Careggi
Hospital, viale Pieraccini 18, 50139, Florence, Italy;
2Department of Human Pathology and Oncology, University
of Florence, Careggi Hospital, viale Morgagni 85, 50134,
Florence, Italy;
3Department of Dermatology, University of Florence, via
della Pergola 58, 50121, Florence, Italy

**Background and Aim:** To present a case of adenocarcinoma
associated with blue nevus of prostate found at histological
examination after radical prostatectomy

**Case Report:** A patient of 68 years under therapy with
tamsulosin for obstructive symptoms. During the first
urological evaluation, a digital rectal examination was
performed showing a prostate significantly increased in
volume with normal consistency. PSA was 5.4 ng/ml with a
high free/total ratio. It was associated treatment with
dutasteride and a trimestral PSA monitoring. Six months after
dutasteride with a α-blocker, PSA was 4.6 ng/ml and 8.1
ng/ml after 1 month of 5-ARI suspension. The patient was
submitted to a 12-sample transperineal prostatic biopsy. At
transrectal ultrasound prostate size was 65x50x65 mm with
periurethral calcifications without evident alterations.
Histopatological evaluation revealed prostatic adenocarcinoma, Gleason 3+3 in 2 samples in the median
side of right lobe. Considering preoperative features and the
high score of IIEF-5 questionnnaire it was performed a
bilateral nerve sparing antegrade prostatectomy with pelvic
lymphadenectomy.

**Results:** In September 2009, surgery was performed.
Intraoperatively, surgeons’ inspection of the prostate showed
no significant alterations in consistency, aspect and cleavage
planes. Definitive histological examination confirmed
the presence of adenocarcinoma, Gleason 3+3, involving
less than half of the right lobe with no lymph node metastasis
(pT2a, pN0). The uropathologist found the presence of blue
nevus in almost all evaluated prostatic slides without lymph
node involvement. Immunohistochemistry was positive for
HMB45, MART-1, S100, Ki67 <1% of cells and negative for
CD68 resulting suggestive for prostatic melanosis.
Dermatological examination of the patient was negative in
finding epidermal blue nevi.

**Conclusion:** Blue nevus is a benign lesion of the skin
characterized by the presence of dermal dendritic and/or
fusiform melanocytes. Extracutaneous localization of blue
nevus is very rare, found mainly in uterine cervix. There
are only four reports in the literature of melanosis of
prostate seen in association with prostatic adenocarcinoma.
Although in literature the definition of pigmented lesions
of prostate is still debated, the most accepted considers
the blue nevus as a lesion with melanin pigment into the
stromal layer, and melanosis inclusion into the epithelial
layer. In dermatology, a malignant blue nevus is described
as a melanoma that occurs in a context of blue nevus.
There is currently no evidence in the literature of
extradermatological malignant blue nevi, so we considered
regular skin examinations appropriate, as proposed by
dermatological protocol, and a standard follow-up of
prostatic adenocarcinoma.

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**PATHOLOGICAL STAGE OF PROSTATE CANCER
USING PARTIN’S TABLES: EXTENDED VERSUS
LIMITED PELVIC LYMPHADENECTOMY**

Vincenzo Maria Altieri, Pietro Palumbo, Rossella Manco,
Roberto Castellucci, Simona Di Francesco, Pietro Castellan
and Raffaele Lanfranco Tenaglia

Clinica Urologica-Ospedale SS Annunziata, Università G.
D’Annunzio-Chieti, Italy
Background and Aim: In the European Association of Urology Guidelines on Prostate Cancer (PCa) an extended pelvic lymphadenectomy (EPLND) is now recommended, instead of a dissection limited to the obturator fossae (iPLND) (1). EPLND is considered an important procedure for the detection of lymph node metastases in PCa; however, the therapeutic benefit of EPLND in PCa management is currently under debate (2). The aim of this study was to evaluate the applicability of Partin’s table in consecutively enrolled patients with PCa and compare the predicted versus actual pathologic stage (3). Thus, we wanted to assess the incidence of lymph node metastasis and the role of PLND in PCa, in which patients and to what extent it should be performed.

Patients and Methods: In total, 94 patients with PCa, no prior hormonal treatment, who underwent radical prostatectomy between 2007 and 2009, were evaluated as to the number of lymph node metastasis and organ extension. Preoperative, twenty (21.0%) patients had a Partin’s table predicted probability of lymph node invasion of ≥ 1%. In addition, seventy-four (78.7%) patients had a probability of PCa organ confined of >80%, fourteen (14.9%) of range 40% to 70% and six (6.4%) of <40%. Eighty-four (89.3%) patients had a probability of extraprostatic extension of <30% and ten (10.6%) of >30%. Predicted probability of seminal vesicles invasion was of 1% in seventy-four (78.7%) patients and only two (2.1%) greater than 10%. For all patients, was performed a meticulous PLND along the external iliac vein, obturator nerve and internal iliac (hypogastric) vessels.

Results: Lymph nodes positive for metastasis were found in twelve (13.0%) of patients. Invasion of the seminal vesicles was identified in four (4.2%) of eight (8.5%) patients with extracapsular extension tumour. Tumour was fixed or invades adjacent structures other than seminal vesicles in four (4.2%) patients.

Conclusion: The current work showed that the lymph nodes metastasis rates and organ extension rates were found to be similar than that predicted by the scoring system. We propose validation of Partin’s tables in a larger cohort for its global applicability. Therefore, EPLND should be performed in all patients with PCa who are indicated on the nomograms predicting pathologic stage of PCa at high risk to develop lymph node metastasis, as indicated by PSA ≥10 ng/ml and/or biopsy Gleason of 7 or greater. Other patients should be treated with EPLND to reduce the risk of complications.

References

228 TUMORAL INVOLVEMENT OF PROSTATIC APEX IS AN INDEPENDENT PROGNOSTIC FACTOR OF PROGRESSION AFTER RADICAL PROSTATECTOMY

Lorenzo Masieri, Federico Lanzi, Nicola Tosi, Michele Lanciotti, Graziano Vignolini, Saverio Giancane, Sergio Semin, Marco Carini and Alberto Lapini

Department of Urology, University of Florence, Careggi Hospital, Viale Pieraccini 18, 50139, Florence, Italy

Aim: The aim of our study was to investigate histopathologically and oncologically the role of tumoural involvement of prostatic apex in patients undergone radical prostatectomy.

Patients and Methods: We retrospectively evaluated 566 consecutive patients who underwent radical retropubic antegrade prostatectomy (RRAP) for clinically localized prostate cancer. Prostate was analysed in parallel sections of 24 mm perpendicular to the urethral axis. We defined neoplastic involvement of apex as neoplastic extension into the distal 8 mm of prostate. In cases of positive lymph nodes, patients were addressed to early adjuvant hormonal treatment. Biochemical recurrence (BCR) was defined as two consecutive values of PSA >0.2 ng/ml. Kaplan-Meier method was used to evaluate biochemical recurrence, the log-rank test to estimate the difference between the analysed variables (apex involvement, preoperative PSA, Gleason Score, pathological staging and surgical margins status) and Cox multivariate analysis to evaluate statistical independency of each variable.

Results: The mean follow-up was (range) 26.5 (3-84) months. Neoplastic involvement of prostatic apex (Apex+) was present in 395 (60.9%) patients. BCR-free survival at 36 months for N0/Apex+ patients was 52.6% months, while in patients N0 without apical involvement (Apex-) was 71.0% (p=0.0162). Survival curves were compared in terms of pathological staging (pT2, pT3a, pT3b, pT4), Gleason score (<7 vs. 7 vs. >7), preoperative PSA (<10 vs. 10-20 vs. >20) and surgical margins (positive vs. negative), resulting statistically significatives: p<0.001, p<0.001, p<0.001 and
Aim: To present our technique of urethral preservation and vesico-urethral anastomosis during open antegrade radical prostatectomy (ARP) in a series of 916 consecutive patients (pts) evaluating functional and oncological outcome.

Patients and Methods: From January 2000 to December 2008, 916 pts underwent radical prostatectomy for clinically localised prostate cancer. We performed an antegrade radical prostatectomy characterized by blunt dissection of vesico-prostatic junction that allows complete preservation of bladder neck. By the antegrade approach, it is possible to anatomically prepare urethral sphincter with an excellent visualization of the apex, due to cranial traction of the completely mobilized prostate. At this point, the urethra can be resected with maximum respect for anatomical boundaries of urethral sphincter, minimizing the risk of leaving prostatic tissue in situ. Mucosal eversion of bladder neck with Vycril® Rapid 3/0 is a crucial point for vesico-urethral anastomosis created using four sutures of 3/0 Polysorb® around a Foley 18 Fr catheter. The catether is usually removed on postoperative day 15. Patients with preoperative obstructive symptoms were evaluated with uroflowmetry. Patients were evaluated every 3 months postoperatively for the first 2 years, every 6 months for the next 2 years, and then annually. In cases of postoperative reduced urinary flow and/or urinary incontinence (≥1 pad/day), patients were evaluated with uroflowmetry and urodynamic study.

Results: The mean follow-up (SD, median, range) was 31.7 (21.8; 26; 6-105) months. Tumoral involvement of the apex was found in 519 pts (56.7%), while apical-positive surgical margins were discovered in 73 pts (73/519; 14.1%). Of these, 22 (30.1%) developed biochemical recurrence. Overall, 878 (95.8%) pts completely fulfilled our continence criteria (no pads) at a minimum follow-up of 12 months; 12 pts used 1 pad/day (1.3%), while 27 pts used 2-3 pad/day (2.9%). At the first month, continence was obtained in 476 pts (51.9%), in 372 (40.7%) at 3 months, in 52 (5.7%) at 6 months, and in 16 (1.7%) at 1 year. Overall, 4 pts (0.4%) developed anastomotic contracture at a mean of 6.5 (5-9) months: Of these, 2 pts were non nerve-sparing radical prostatectomized, 1 monolateral and 1 bilateral nerve-sparing ARP (p=NS). All these pts were treated by endoscopic cold incision of anastomotic stricture. Overall 1 pt developed mid urinary incontinence after endoscopic treatment; at a mean follow-up of 27.7 (15-47) months, 3 patients were continent and without signs of obstruction at uroflowmetry.

Conclusion: Our technique of urethral preservation allows a complete definition of the anatomical boundaries of bladder neck, apex and striated sphincter, with the maximum saving of the urethra. This approach provides optimal functional results, in terms of low rates of anastomotic contracture and high rates of recovery of continence, with excellent oncological results in terms of low incidence of positive surgical margins.

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HEMANGIOENDOTHELIOMA OF URINARY BLADDER – REPORT OF A CASE

Daniele Masala¹, Daniele Mattace Raso¹, Pompeo Brigante¹, Alberto Masala¹, Gianfranco De Dominicis² and Oscar Nappi²

¹Dipartimento Nefro-Urologico e UOC Urologia, ²UOC Anatomia, Istologia e Citologia Patologica, Ospedale A. Cardarelli, Napoli, Italy

Background: Vascular tumours can occur almost anywhere in the human body. Epithelioid hemangioendothelioma (EHE) represents a rare endothelial vascular tumour, typical of yong adults, which was first described by Weiss and Enzinger in 1982 in soft tissues. It can occur in different locations such as lung, heart, liver, and bones, rarely in the pleura or thyroid...
gland; however, they are extremely rare in the urinary bladder. In the 2002 WHO classification of soft tissue tumours, EHE is classified as an angiocentric vascular tumour of intermediate malignant potential, also with metastatic evolution, composed of epithelioid endothelial cells. Here we describe the fourth case in the literature. The patient underwent radical surgery and the definitive histological response was made difficult by the rarity of the disease and the complex differential diagnosis with other diseases such as bladder sarcoma. The use of immunohistochemical analysis was essential for the certainty of diagnosis.

Case Report: We report a case of extremely uncommon location of primary EHE of the urinary bladder in a 32-year-old young man with anamnesis of left nephrectomy for an invertebrate distal ureteral stenosis. The patient came to our attention in April 2007 with gross haematuria and soprapubic pain. The bladder ultrasound was positive for a huge and large based neoplasm involving the entire wall of the bladder and enveloping the right urethral meatus. Multiphasic CT scans of the abdomen and pelvis were performed and were positive for voluminous bladder tumour involving the entire bladder wall, with involvement of the prostate and the slope of the rectum-sigma and the pelvic cavity. Obvious swelling of the lymph node chains was apparent at the pre-sacral, iliac-obturator, lumbar-aortic. We decided to refer the patient to a staging TURB and the histological report was “solid undifferentiated highly malignant bladder neoplasia with full-thickness infiltration of suburothelial connective and muscle wall”. After a multidisciplinary uro-oncological consultation, no neo-adjuvant chemotherapy was performed because of the poor results described in the literature and 2 months after (in May), the patient directly underwent a radical cystectomy with uretero-cutaneostomy and bilateral iliac-obturator, pre-sacral and lumbar-aortic lymphadenectomy and a simultaneous segmental resection of the rectum-sigma. The morphological aspect showed a tumour composed of cells with a nucleus of medium size, round/oval or spindle-rhyme, with optically empty or eosinophilic cytoplasm, sometimes forming a small vacuole. The cells were organized into solid nests in a fibrous stroma and sometimes myxoid. In some areas they formed alveolar and pseudovascular spaces. The cells were positive for the immunohistochemical study for CD34, CD31 and pancytokeratin. These aspects were consistent with a malignant vascular neoplasm with aspects of malignant (high grade) EHE. The tumour involved the whole bladder and prostate, and infiltrated the seminal vesicles and “ab-extrinsically” infiltrated the rectal wall to the limit with the submucosa. All the lymph nodes analysed were only inflammatory and disease-free. In agreement with our oncologist, no adjuvant chemotherapy was necessary and we decided to refer the patient for careful follow-up with abdomen ultrasound, CT scan of abdomen and pelvis and total body PET CT.

Conclusion: Prognostic predictors for this lesion are not available for tumours arising from the bladder. However, at the other more common sites, such as soft tissue, indicators of a poor prognosis include nuclear atypia, increased mitotic figures, tumour cell spindling, and necrosis. Gross haematuria is reported in all of the other 3 cases described in the literature. All of these factors were present in our patient. Regarding the treatment plan, radiotherapy has no place in the management of these tumours. Similarly, chemotherapy rarely affects these lesions; therefore, the only option is surgical debulking or, if possible, complete or near total excision. Our patient is still alive, presently in a good general condition, has a strict follow-up with abdominal and pelvic multiphasic CT scan at 6 and 12 months and PET CT total body at 1 year and 6 months.

References

231 UROTHELIAL RELAPSE OF THE URETHRA DURING FOLLOW UP OF THE SUPERFICIAL TRANSITIONAL CELL CARCINOMA (TCC) OF THE BLADDER

Gerardo Pizzirusso, Gian Luigi Boschi, Carlo Calcopietro and Claudio Dal Pozzo

U.O. Urologia, Ospedale Civile di Faenza, Azienda USL Ravenna, viale Stradone 9, 48018 Faenza, Italy

Background: Transitional cell carcinoma (TCC) can grow in any part of the urinary tract, in the urethra also. The urinary tract is evaluated almost exclusively before cystectomy and reconstruction of neobladder. We evaluated all patients during
the follow up for TCC. Excluding TCC of the bladder or upper urinary tract, we enrolled 21 patients with uncertain or positive urinary cytology and submitted them bladder and urethral biopsy. Finally, we obtained 16 patient with TCC of the urethra. These patients were submitted to surgical or intravesical treatment

**Patients and Methods:** From June 2008 to June 2009, we evaluated 211 patients during follow up for TCC. Exclusion criteria: negative urinary cytology, cystoscopy and with computerized tomography urography. In 21 patients, there was uncertain or positive urinary cytology. These patients were submitted to bladder and urethral biopsy: there were 16 patients (7.6%, 11 men and 5 women, mean age 76 ± 4.4 years) with TCC of the urethra (carcinoma in situ, CIS, or high grade T1). These patients had already been submitted to intravesical treatment for TCC of the bladder. The male patients were treated by transurethral resection for the staging and following cystectomy. To Cystectomy, or intravesical treatment with bacillus Calmette-Guerin (BCG) was proposed to the female patients and they were informed of the risk factors of progression; all were treated by BCG, performed according to Lamm schedule and following cystoscopy and cytology. Ten male patients were submitted directly to cystectomy (urethrectomy only in positive surgical margin). The mean follow up was 10.3 ± 2.4 months.

**Results:** The histological examination showed 9 pT1 high-grade TCC of the urethra and 1 CIS, with bladder specimen negative for TCC. All 10 patients were alive at the last follow-up, and without endoscopic or cystological evidence of cancer relapse; the only patient that refused cystectomy died after 4 months from metastatic disease. The female patients are alive and without cancer relapse too; one showed recent urethral relapse and was been submitted to cystectomy. **Conclusion:** Our results undoubtedly are limited by the short-term follow-up, and more data are clearly needed. The aim of the study was to re-evaluate the urothelial cancer of the urethra. In fact, TCC of the urethra is not uncommon (in our experience, occurring in 7.6% of the patients in follow-up), and quickly aggressive. This localization can be the expression of the progression of the original bladder cancer (according to the grading, and localization on the bladder neck). The mean onset time was 23.2 ± 6.4 months. The time of contact of chemotherapeutic drugs with the urethra is too short to be of great benefit. We believe that the gold standard treatment is cystectomy.

**References**


to distant metastasis and to lower cancer-specific survival \((p=0.008\) and \(p=0.001\), respectively; relative risk of developing distant metastasis, 2.7; relative risk of death from disease 2.87). Furthermore, the presence of CCC was an independent predictor of distant metastasis and death in a multivariable analysis.

**Conclusion:** Although helpful for staging purposes in other types of cancer (1), detection of occult LN metastasis was not useful for bladder cancer in our experience. With regards to the role of CCC, the preliminary data of the present study, although limited by a small sample size, show very good correlation with pathological stage and clinical outcome, both in terms of time to distant metastasis and cancer-specific survival. Our data need confirmation in larger samples and after longer follow-up; nevertheless, searching for CCC may be promising for the prognosis of patients with invasive bladder cancer.

**References**


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**233 ULTRASONIC VERSUS ATERMAL DISSECTION FOR NERVE SPARING LAPAROSCOPIC RADICAL PROSTATECTOMY**

Ivan Martines, Marcello Scarica, Gaetano De Rienzo, Stefano Alba and Arcangelo Pagliarulo

Università degli Studi di Bari, Sezione di Urologia e Andrologia, Piazza G. Cesare 11, Bari, Italy

**Background and Aim:** Over the last 6 years in this Urology Department, open radical retropubic prostatectomy was performed by a laparoscopic preperitoneal approach. Later along the learning curve, a nerve-sparing technique was also applied, using Harmonic Scalpel® ultrasonic dissection at an earlier stage, and cold (athermal) clip dissection later on. The goal of the present work was to compare our data regarding the two techniques used for dissection, in terms of erectile function (EF) recovery, blood loss and margin status.

**Patients and Methods:** From February 2005 until September 2008, 164 nerve-sparing laparoscopic radical prostatectomies were performed using the same surgical equipment. The neurovascular bundle was spared using Ace Harmonic Scalpel® (Ace)and tissue irrigation with isotermic saline solution in 77 cases (37 bilateral, 40 monolateral), while cold-clip dissection was performed in 82 cases (35 bilateral, 47 monolateral). At the time of surgery, all patients had a median age of 59 (range 50-74) years and an International Index of Erectile Function (IIEF) score >20. Postoperatively, all patients underwent penile rehabilitation as follows: Intracavernous injections of prostaglandin E1 (5 μg twice a week x 10 weeks) and Sildenafil 100 mg thereafter, according to patient’s compliance. Time to recovery of erectile function and differences in the EF domain score of the IIEF at 3, 6, and 12 months were studied between the two groups. Also differences in blood loss (median) and margin status were calculated among the two techniques. For statistical analysis, a non parametric \(\chi\)-square test was used at 5% level of significance.

**Results:** Recovery of erectile function (IIEF >20): Overall recovery rate after a minimum follow-up time of 12 months was 63% (101/159). Comparison of ACE vs. cold-clip dissection respectively resulted in an overall recovery rate of 57% (44/77) and 69% (57/82), in a median time to recovery of 9 and 6.5 months. Sildenafil support was required in 64.5% (31/48) and in 58% (35/60) of potent patients respectively. The other patients did not require any pharmacological support after 12 months of minimum follow-up. Blood Loss: median blood loss was 430 ml and 680 ml for patients undergoing ultrasonic vs. cold-clip dissection/preservation of the neurovascular bundle, respectively. Surgical margin status: surgical margins were positive in 14% and 11.6% of patients respectively, regardless of pathological stage.

**Conclusion:** Taking into account the limit of the retrospective nature of the study and differential surgical skills of the surgeons at the time of ultrasonic compared to cold-clip dissection, this study shows that ultrasonic nerve-sparing technique translates to 57% rate of erectile function recovery, although significantly lower compared to that with athermal dissection. Higher positive surgical margins may be the result of an early phase of the learning curve. On the contrary, ultrasonic dissection may confer an advantage in terms of blood loss.

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**234 PREVALENCE OF METABOLIC SYNDROME AND ITS COMPONENTS IN MEN WITH HORMONE-NAİVE PROSTATE CANCER**

Simona Di Francesco, Michele Nicolai, Antonio Como, Vincenzo Altieri, Pietro Castellan, Manuel Campanelli and Raffaele Lanfranco Tenaglia

Clinica Urologica e Andrologica-Università degli Studi G. D’Annunzio Chieti, via dei Vestini 5, 66100 Chieti, Italy

**Background:** The metabolic syndrome (MS) is characterized by central obesity, insulin resistance, high serum glucose levels, dyslipidaemia and systemic arterial hypertension. MS is a known risk factor for breast cancer and a causal factor
for cardiovascular mortality. Men with prostate cancer (PCa) have higher rates of non-cancer mortality than men in the general population, with some of this excess attributed to hormonal treatment. At present, there are conflicting reports as to the causal relationship between MS and PCa and there is limited literature regarding the association between MS and PCa at the initial diagnosis, without the influence of hormonal therapy. The present study aimed to evaluate the prevalence of MS and its components in men with PCa at initial diagnosis and compared it with the prevalence in age-matched controls.

**Patients and Methods:** This was a controlled cross-sectional study. We evaluated 80 men, including 40 patients who were hormone-naive, with a histological diagnosis of prostate adenocarcinoma (group 1), and 40 age-matched controls without any history of benign or malignant prostate disease, with a normal PSA ($\leq 3$ ng/ml) and absence of suspicious lesions (group 2). MS was defined according to the Adult Treatment Panel III criteria. Men were excluded from the study if they had a Karnofsky performance status (KPS) lower than 70%, disseminated disease, history of thyroid disease, liver disease or renal insufficiency, glucocorticoid use in the previous 6 months, history of any form of hypogonadism and any history of hormonal therapy or chemotherapy for PCa.

**Results:** There was no significant difference in mean age between the two groups (65.9 $\pm$ 7.57 group 1 vs. 65.05 $\pm$ 6.45 group 2). Men in the group with prostate cancer had significantly higher body mass index (BMI) compared with the control group (28.06 $\pm$ 3.42 vs. 25.45 $\pm$ 3.24). Among 80 participants, 30% of the men in the group 1 met the criteria for MS. This prevalence was significantly higher in the PCa versus the control group (32.3% vs. 15.2%). Analysis of various components of MS revealed that men of group 1 had significantly higher overall prevalence of hyperglycaemia (35% vs. 20.2%) and hypertriglyceridaemia (40% vs. 25%) compared with the group 2. There was no significant difference in the prevalence of arterial hypertension between the two groups (50.2% vs. 40.8%).

**Conclusion:** This is the first cross-sectional study showing the higher prevalence of MS in men with PCa at initial diagnosis versus controls, without influence of hormonal therapy. On the basis of the findings of our study, one might speculate the possibility that MS may play a role in the development of PCa and that the higher prevalence of MS in men with prostate cancer may be, at least partly, responsible for higher cardiovascular mortality in this population and worse prognosis of PCa. We recommend the investigational field be expanded with larger sample sizes and cohort studies to further delineate this association and to elucidate the full effects of obesity, hyperglycaemia and hypertriglyceridaemia patterns on prostate cancer development and progression.

### 235 CAN HIGH-GRADE TRANSITIONAL CELL CARCINOMA IN THE PROSTATIC URETHRA REPRESENT A RISK FACTOR FOR DISEASE PROGRESSION?

**Stefania Cicuto**, Daniele Tiscione, Valentina Pecorari, Sandro Bosetti and Gianni Malossini

Ospedale S. Chiara, Trento, Italy

**Background:** Transitional cell carcinoma (TCC) is a multifocal disease of the urinary tract that can also involve the prostatic urethra (PU). In patients with bladder TCC, the incidence of superficial involvement of the PU is 12-40%. We investigated whether high-grade TCC in the PU represents a risk factor for disease progression.

**Patients and Methods:** The data of 185 consecutive male patients with high-grade bladder TCC who were treated at our institution were reviewed. All patients were initially treated with intravesical instillations (BCG, mitomycin-C and gemcitabine). Patients were followed up by cystoscopy, urine cytology and repeat biopsy to detect persistent and/or progressive disease.

**Results:** Fifteen patients (8%) had high-grade TCC in PU. The median age of the patients was 72 (60-87) years and median follow-up was 46 (1-287) months. Nine patients (60%) had a simultaneous high-grade bladder TCC and four patients (27%) had both high-grade and multifocal bladder TCC. Six patients (40%) were treated with cystoprostatectomy because of failure of treatment to eradicate superficial disease or disease progression. The cystoprostatectomy specimen showed prostatic stromal invasion in four patients and multifocal carcinoma *in situ* in PU in the other two patients. Six patients (40%) with high-grade TCC in PU and nineteen patients (11%) with high-grade bladder TCC died due to progression of the disease, while the median survival was 50 (1-117) and 62 months (4-236) respectively.

**Conclusion:** Our long-term data support high-grade and multifocal bladder TCC as representing an important risk factor for superficial urothelial cancer in the PU; furthermore, high-grade TCC in the PU is an important risk factor for disease progression. We recommend cystoprostatectomy in patients with high-grade TCC with PU involvement.

### 236 CORRELATION BETWEEN THE GLEASON SCORE OF PROSTATE BIOPSIES AND RADICAL PROSTATECTOMY

**Roberto Castellucci**¹, Rossella Manco¹, Vincenzo Maria Altieri¹, Pietro Palumbo¹, Enrico Penitente²,

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Our study found that the concordance between the GS of prostate biopsies and RRP was 40.4% and that the prostate biopsy underestimated the GS in 44.7% of patients. Concordance was not affected by age nor by PSA. In conclusion, only the accuracy of GS determined by needle biopsy in patients with prostate cancer seems to be unreliable. However, the biopsy GS is included among other prognostic factors in therapeutic decision-making, such as patient’s age and health, clinical stage and serum PSA level, but it could produce an underestimated value.

References

237 LONG-TERM BIOCHEMICAL CONTROL OF PROSTATE TUMOURS FOLLOWING STANDARD OR HYPER-FRACTIONATED CONFORMAL RADIATION

Riccardo Valdagni1, Alan E. Nahum2, Tiziana Rancati1, Tiziana Magnani, Barbara Avuzzi and Claudio Fiorino3

1Prostate Program, Scientific Director’s Office, Fondazione IRCCS Istituto Nazionale dei Tumori, via Venezian 1, Milan, Italy;
2Department of Physics, Clatterbridge Centre for Oncology, Bebington, Merseyside, UK;
3Medical Physics Department, San Raffaele Scientific Institute, via Olgettina 60, Milan, Italy

Background and Aim: In 1993, a prospective, non-randomized study of prostate cancer patients using 3D conformal radiotherapy (3D-CRT) with two different fractionation regimens (standard 2.0 Gy/day, STD; hyperfractionated 1.2 Gy BID, HFX) was activated. The choice of utilizing HFX radiobiologically, as suggested by Fowler et al. (IJROBP, 1995), was based on the need to reduce late toxicity and, at the same time, safely increase radiation doses. In our previous report (Valdagni et al., Rad Oncol, 2005), HFX was found to decrease late rectal and urinary toxicity with similar 3-year biochemical control rates as STD. Here, we report the long-term results with respect to biochemical control and analyse the implications for the alpha/beta ratio of prostate cancer.

Maria Raffaella Olivieri1, Stefano Ricciardulli1, Antonio Como and Raffaele Lanfranco Tenaglia1

1Clinica Urologica, Ospedale "SS. Annunziata", and
2Dipartimento di Anatomia Patologica, Ospedale "SS. Annunziata", Università G. D’Annunzio*, via dei Vestini 5, Chieti, Italy

Background: The Gleason score (GS) is an important prognostic factor for patients with prostate cancer (1). Prostate biopsy findings provide important information when considering treatment options. Incorrect histological grading can result in inappropriate treatment and possible liability. In our study, we examined the concordance between the results from prostate biopsy and retropubic radical prostatectomy (RRP) specimens.

Patients and Methods: Between January 2008 and January 2010, we retrospectively reviewed 95 patients with clinically localized prostate cancer confirmed by transperineal biopsy guided by transrectal ultrasound. A 12-core biopsy technique was performed in all cases. All patients underwent RRP and patient’s medical records were reviewed. We excluded patients who had incomplete data and who underwent neoadjuvant hormone therapy because of the inherent difficulties in pathological interpretation of the specimen GS subsequent to androgen deprivation therapy. The biopsies and RRP specimens were reviewed by one staff pathologist of our institution and pathological interpretation of the specimen GS subsequent to hormone therapy because of the inherent difficulties in pathological interpretation of the specimen GS subsequent to androgen deprivation therapy. The biopsies and RRP specimens were reviewed by one staff pathologist of our institution and tumour grade was determined according to the Gleason scoring system (2). We compared the GS of the needle biopsy and the RRP. The overall correlation between GS for needle-biopsy and RRP specimens were evaluated by analyzing the following parameters: Age, the preoperative serum prostate-specific antigen (PSA) level and laterality concordance. A “downgrade” was defined as the converse.

Results: Of the 85 men who underwent RRP, 47 patients satisfied the inclusion criteria. Patient age ranged from 57 to 76 (mean, 66.3) years and preoperative serum PSA level ranged from 1.6 to 44.0 (mean, 8.52) ng/ml. GS ranged from 3 to 8 for biopsy-core specimens, and from 4 to 9 for RRP specimens. Biopsy involvement was unilateral in 27 (57.4%) and bilateral in 20 (42.6%). Compared to biopsy, RRP GS was concordant in 19 (40.4%), upgraded in 7 (14.9%) and downgraded in 21 (44.7%). When biopsy involvement was unilateral, 19 out of 27 (70.3%) patients had bilateral involvement on RRP. In patients with bilateral biopsy involvement 18 out of 20 (90.2%) had bilateral involvement on RRP. Both GS and laterality were concordant in only 21.2%.

Conclusion: Prior studies have suggested that prostate biopsy underestimates prostatectomy GS and a high percentage of patients with an unilateral involvement disease in biopsy show a bilateral involvement in RRP specimens (3).
Patients and Methods: Between 1993 and 2003, 370 pts entered the study. Three-hundred and thirty pts, 179 in the STD and 151 in the HFX, were evaluable for this long-term analysis. Pre-treatment and treatment variables were similar in the two groups. Conformal treatment consisted of a four-field technique for prostate and/or pelvic nodes, and a five-field boost with rectal shielding in the final part of the treatment. Median doses were 79.2 Gy and 74 Gy for HFX and STD patients, respectively; median follow-up was 7.5 years. The two fractionation regimens were compared in terms of 7.5-year biochemical relapse-free survival (according to ASTRO definition, bRFS) by univariate (log-rank test) and multivariate analyses (Cox regression hazard model).

Results: The 7.5-year bRFS was 53.4% (4.4%, 95% CI) and 65.4% (4.0%) for HFX and STD, respectively (p=0.13); HFX was associated with a poorer outcome in NCCN low+intermediate pts (7.5-year bRFS: 66.3% vs. 76.3%, p=0.048) while no differences were seen for high-risk patients (7.5-year bRFS: 44.1% vs. 45.3%). Multivariate analysis revealed that NCCN risk grouping (high vs. low+intermediate: OR: 0.59, p=0.009) and age (< vs. ≥70 years: OR: 0.67, p=0.03) were the main predictors of poorer bRFS. Interestingly, when considering the subgroups of low+intermediate risk patients <70 years, the poorer outcome of HFX was more evident (7.5-year bRFS: 47.1% vs. 70.9%, p=0.078), while no difference was seen for older patients (7.5-year bRFS: 69.4% vs. 72.0%, p=0.76).

Conclusion: The long-term bRFS results of this non-randomized trial comparing HFX and STD fractionation are consistent with high (~10) alpha/beta value for high-risk patients and a much lower value for low/intermediate-risk patients (below 3). However, the statistical power of the study is not strong enough to fully clarify this issue. Interestingly, a higher alpha/beta is exactly what one would expect if the proportion of hypoxic tumours were higher in the high-risk group. The impact of age on the outcome of HFX on younger low+intermediate patients is consistent with an incomplete repair effect (between fractions) in older patients (something similar has been described for normal tissue injury, Paulino, Semin Radiat Oncol 2010).

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238 TRANSRECTAL ULTRASOUND-GUIDED PROSTATIC BIOPSY: OUR EXPERIENCE

Pietro Palumbo, Rossella Manco, Vincenzo Maria Altiere, Roberto Castellucci, Vittore Verratti, Lucia Anna Mastroserio and Raffaele Lanfranco Tenaglia

Clinica Urologica, Ospedale "SS. Annunziata", Universita "G. d'Annunzio", via dei Vestini 5, Chieti, Italy

Background: Many studies have affirmed that only patients with prostate-specific antigen (PSA) >10 ng/ml and a palpable nodule seems to have an adequate detection rate with few, directed biopsies (1). Transrectal ultrasonography has two potential roles in the diagnosis of prostate cancer: To identify lesions suspected of malignancy and to improve the accuracy of prostate biopsy. Ultrasound-guided transrectal 18-G core biopsy has become the standard way to obtain material for histopathological examination (2). After our experience of three years, we review the technique and its indications.

Patients and Methods: Between January 2007 and December 2009, 234 patients underwent transperineal guided biopsy. Patients were aged from 46-85 (mean 65.5) years. Every patient underwent digital rectal examination. Antibiotic prophylaxis was used to reduce risk of complications after prostate biopsy. The standard technique that we used included 10-cores of peripheral zone, divided into 5-cores for lobe; 6-cores in far-lateral lobar region and 4-cores in mid lobar region.

Results: The incidence of prostate cancer in the biopsies of our groupe was 101 (43.0%). The number of patients that had prostate cancer in the mid and lateral core biopsies was 38 (37.6%); 56 (55.4%) patients had a single mass in the lateral core biopsy and 7 (6.9%) patients a single tumour in the mid lobar biopsies.

Conclusion: Prior studies showed that the vast majority of tumours were detected in the far-lateral lobar region of prostate, an area well-sampled by the technique of laterally directed sextant biopsy. Our study confirmed these data. It seems that the direction of the biopsies may well be as important as the number of cores.

References

239 CELECOXIB AND BLADDER CANCER: NEW MOLECULAR TARGETS

Patrizia Ancona, Ivan Martines, Annamaria Salerno, Arcangelo Pagliarulo and Vincenzo Pagliarulo

Sezione di Urologia e Andrologia, Università degli Studi di Bari, Piazza G. Cesare 11, Bari, Italy

Background: Celecoxib (CLX), a selective cyclooxygenase-2 (COX-2) inhibitor, initially approved for the treatment of

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rheumatoid arthritis and osteoarthritis, as several studies have shown, has a chemopreventive effect on different tumours, as a consequence of angiogenesis inhibition, and induction of apoptosis. We conducted the first phase II on the role of CLX in reducing progression and relapse of disease in non muscle-invasive bladder cancer. To further define the molecular mechanism of CLX and to optimize the clinical application in the treatment of TCC, we performed a gene expression study on a stabilized superficial bladder carcinoma cell line (J82) treated with CLX in vitro. The goal of the present study was to identify the genes related to the molecular action of CLX using cDNA microarray.

Materials and Methods: J82 bladder cancer cells were grown in monolayer and treated in presence and absence of 75 μM CLX. After incubation for 24 h, total RNA was extracted, and the cDNA synthesized as follows. In vitro transcription was performed in the presence of biotinylated UTP and CTP and carried out using the Gene Chip IVT Labeling Kit (Affymetrix, Santa Clara, California, USA). A total of 15 μg of biotinylated cDNA were fragmented randomly. The cDNA fragment was hybridized for 16 hours at 45°C with the human genome U133A GeneChips containing a total of 22283 genetic markers and then stained with streptavidin/phycoerythrin. The arrays were analyzed on a Genearray scanner using standard Affymetrix protocols. The final data analysis was performed using Affymetrix Microarray Suite 5.0 software.

Results: We examined the changes in expression of 5570 genes of the cell line J82 in presence and absence of treatment with CLX for 24 hours. The isolated genes were functionally classified as surface receptors related to signal transduction (11 genes), intracellular transport (10 genes), the immune response (6 genes) and response to external stimuli (6 genes). Among them, for further discussion based on some of their characteristics, we selected the following genes: TRIB3, interleukin 6, PTX3. After treatment with CLX, these genes were found to be down-regulated and generally involved in the immune response.

Conclusion: These preliminary results have identified some of the genes that may be involved in the molecular mechanisms responsible for the chemopreventive activity of CLX in bladder cancer.

240 POST-CHEMOTHERAPY RETROPERITONEAL LYMPH NODE DISSECTION: CORRELATION BETWEEN MASS DIMENSION AND RESIDUAL VITAL CELLS

Paolo Destefanis1, Carlo Luigi Augusto Negro1, Beatrice Lillaz1, Andrea Bosio1, Alessandro Bisconti1, Claudia De Maria1, Mariateresa Carchedi1, Andrea Buffardi1, Patrizia Lista2, Libero Ciuffreda2 and Dario Fontana1

1Divisione Universitaria di Urologia 2, and 2Divisione di Oncologia Medica 1, Ospedale San Giovanni Battista Molinette, Torino, Italy

Background and Aim: Patients with advanced NSGCT have long-term freedom from disease progression when chemotherapy is combined with resection of residual masses. The appropriate integration of chemotherapy (CHT) and surgery (PC-RPLND) is crucial to achieving long-term survival. The objective of this report was to analyse the outcome of surgery in patients with metastatic germ cell tumours treated with CHT at a single institution, with a particular regard to the relationship between mass dimension and residual vital tumour cells.

Patients and Methods: Between February 2003 and October 2009, 19 patients underwent RPLND 1 month after CHT for metastatic germ cell tumour (mean age 33.5 years). All patients were treated with 3 or 4 cycles of BEP chemotherapy according to the prognostic class. Orchiectomy revealed: seminoma in 2 cases, mixed GCT in 11, no tumour in 4, IGCNU in 1 and embryonal carcinoma in 1. All patients but 2 had a complete serological response (these 2 did not respond to second-line CHT either). At the CT scan post-CHT, none of the patients had a complete regression of the mass, but there was a mean reduction of 37%.

Results: Seven patients presented with a primitive retroperitoneal mass. Five patients underwent adjunctive surgery, 2 mediastinal surgery, 4 thoracic and ENT surgery and 1 brain metastasectomy. PC-RPLND was radical in 16 patients. Three patients underwent a second RPLND, in one case with IORT. RPLND revealed: necrosis in 3 cases (16%), teratoma in 8 (42%), vital GCT in 8 (42% - 1 yolk-sac tumour, 4 seminoma and 3 embryonal carcinoma). Patients with vital GCT underwent second-line CHT (4 cases), HDCHT + staminal cell transplantation (1 cases); one patient refused treatments. Mean pre-CHT and post-CHT mass dimension in vital GCT group were 12.2 cm and 9.5 cm (p=0.61); comparing vital GCT group and teratoma/necrosis group: mean pre-surgery mass dimensions were 9.5 cm in the vital group and 5.4 cm in the teratoma/necrosis group (p=0.227); no statistical differences were found in mean pre-CHT α-FP (p=0.21) and β-HCG (p=0.17) between the two groups. Two patients were lost at follow-up; at a mean follow-up of 26.4 months (1-75 months), only 1 patient died, one patient had a liver relapse, whilst the others were free from disease.

Conclusion: There are no criteria that can reliably predict tumour viability in residual masses. We observed a high rate of vital GCT in resected masses (42%), without finding statistically significant differences in mass dimensions or pre-CHT serum markers between patients with vital GCT and teratoma/necrosis; this is probably due either to the small number of patients, even if our data do suggest a trend in the correlation with mass dimension. Our results in terms of survival, at 26 months follow-up, are good, with only one death.
MICROSURGICAL “TESTIS-SPARING” SURGERY FOR NON-PALPABLE TESTICULAR LESIONS

Carlo Luigi Augusto Negro, Paolo Destefanis, Andrea Bosio, Alessandro Bisconti, Beatrice Lillaz, Claudia De Maria, Mariateresa Carchedi, Andrea Buffardi, Massimiliano Timpano, Carlo Ceruti Dario Fontana and Luigi Rolle

University Department of Urology, Ospedale “San Giovanni Battista - Molinete”, Turin, Italy

Background: With the increased use of trans-scrotal ultrasound (US), the unexpected detection of nonpalpable hypoechoic testicular lesions has become more frequent, in particular in patients with infertility. Definitive guidelines do not yet exist for the management of these lesions, although there is general consensus on immediate exploration of lesions, due to emerging literature that reports the the presence of malignant tumours. We report our series of patients with hypoechoic testicular lesions undergoing surgical exploration with the aid of the operating microscope.

Patients and Methods: A total of 13 patients were considered for microsurgical exploration of non-palpable hypoechoic testicular lesions, from April 2003 to October 2009. Hospital records, US and operative reports were retrospectively reviewed.

Results: The side of the lesion was left in 6 and right in 7 cases; the mean size of the hypoechoic areas was 4.3 (range 1.7-6) mm. In 5 patients, the lesions were incidentally discovered during evaluation for azoospermia. All patients had normal α-FP, β-HCG and LDH. The microsurgical technique allowed the lesion to be identified and successfully excised in all patients. Intraoperative frozen section examination showed a benign lesion in 11 cases, intratubular germ cell neoplasia (ITGCN) in 1 and seminoma in 1. Patients with ITGCN and seminoma underwent radical orchietomy. The definitive histological analysis confirmed the frozen section examination in all cases but 2, in which a diagnosis of seminoma and teratoma were made, and radical orchietomy was performed. Patients were clinically and ultrasonographically evaluated with a median follow-up of 41 months. No complications occurred and no new hypoechoic lesions were discovered.

Conclusion: Microsurgical exploration of the testis combined with frozen section examination represents a safe, effective and reliable technique in cases of nonpalpable hypoechoic testicular lesions. This approach leads to significant advantages and should be considered especially in patients with a solitary testis or presenting bilateral lesions and wishing to father a child.

BOSNIACK 4TH TYPE CYST: SINGLE PRESENTATION OF A TRANSITIONAL UROTHELIAL CANCER

Lorenzo Gatti1, Alessandro Antonelli1, Regina Tardanico2, Danilo Zani1, Sergio Cosciani Cunico1 and Claudio Simeone1

1Cattedra di Urologia e Divisione Clinicizzata di Urologia, Università degli Studi di Brescia; 2° Servizio di Anatomia Patologica, Spedali Civili di Brescia, Italy

Background: Cysts of kidneys are frequently found in adults, usually during ultrasound examination or computed tomography (CT). Clinical attitude in asymptomatic injuries may vary from total abstention to surgical treatment, depending on the neoplastic risk of the cyst, which nowadays is determined by the application of the Bosniak classification. This classification is based on the cyst’s characteristics, which emerge from the preoperative CT findings, but also from ultrasound and RMN, evaluating wall thickness, presence of intraluminal septa, density of content, presence of calcifications and presence of contrast enhancement. Intracystic neoplasms, included among parenchymal kidney neoplasms, originating from the tubule of the kidney, generally have a conventional histotype and are characterized by a low aggressiveness. Therefore, these can be treated with a conservative intervention which leads to healing in almost all cases.

Case Report: We describe a clinical case diagnosed with imaging investigations, because of the presence of septa and solid lesion characterized by enhancement contrast, as a Bosniak’s 4th class cyst. Intraoperatively, once the cyst was opened, the solid lesion was identified, which from the visual analysis was characterized by typical peculiarities of a transitional carcinoma. Therefore it was decided to send a sample for an extemporaneous biopsy, which confirmed the macroscopic diagnostic hypothesis. For this reason, the most indicated procedure was a surgical intervention of nephroureterectomy. The appropriateness of the therapeutic decision was confirmed by the result of the definitive histological exam which found a transitional urothelial cancer. In the light of the facts, the hypothesis is that the cancer had developed inside of an excluded dilated calice, simulating a complex cyst.

Conclusion: We report this case because of the possibility that a neoformation with imaging characteristics of Bosniak’s cyst may mask a urothelial cancer, deeply modifying the therapeutic approach. The risk of performing a tumour excision, in the case of a transitional urothelial cancer, is to leave neoplastic cells which are potentially risky for recurrence, with serious clinical issues in the future for the patient. This case report underlines how the diagnostic accuracy, supported also by clinical experience, is primarily important and allows
the best approach to be chosen, depending on the type of the lesion that has to be treated: conservative in the 4th class type, with a demolitive intervention for the transitional urothelial forms, in order to ensure the therapeutical gold standard of care is provided to the patient.

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PALLIATIVE RADIOTHERAPY FOR BLADDER CANCER: A SMALL RETROSPECTIVE STUDY

Girolamo Spagnoletti, Giuseppe De Nobili, Rita Marchese, Anna Maria Leo, Raffaella Rignanese and Giuseppe Bove

Radiotherapy Department, Foggia University Hospital, Italy

Background: Curative treatment of bladder cancer is based on radical cystectomy or transurethral resection followed by radiotherapy and concomitant chemotherapy. Unfortunately, tumours are usually found at advanced stages, or the general condition of the patient is reduced and aggressive therapy is therefore contraindicated. In these situations, palliative treatment is of extraordinary importance. In this retrospective study, we analysed the utility of palliative radiotherapy in advanced bladder cancer and evaluated the results of the different fractionation regimens.

Patients and Methods: From October 2006 to December 2009, 25 patients (pts) with grade III urothelial carcinoma of the bladder (T2-4N0-2) received palliative external radiotherapy. All patients (21 males and 4 females) presented with haematuria and local pain and their medical conditions or disease status prevented an operation or a radical multimodal therapy. The mean age was 77 (range: 63-87) years. Many different fractionation schedules were used: conventional irradiation with 20-30 fractions up to 40-54 Gy in 16 cases and hypofractionated radiotherapy with 1-3 fractions of 6-10 Gy once a week in 9 cases. Treatments were carried out with three or four 10-18 MV photon beams.

Results: Half of all patients (12 pts) achieved complete remission of the initial symptoms and one fourth (6 pts) showed a partial remission. On the whole, three out of four patients experienced symptomatic relief. Haematuria improved in 76.5% of affected patients (13/17 pts). Pain and/or dysuria decreased in 41.7% of complaining patients (5/12 pts). The mean duration of response was 17 weeks (range 3-118). A comparison between hypofractionated and conventional regimens suggested a more important and rapid improvement in symptoms control with the shorter courses. The rates of complete clearing of haematuria were 22.2% (2/9 pts) in the conventional fractionated group and 50% (4/8 pts) in the hypofractionated group. Among the short schedules we used, 6 Gy fractions were found to be the least useful treatment: up to 3 fractions, we observed only a slight benefit. We did not notice any significant difference in the toxicity of the two schedules. Acute genitourinary toxicity was observed in 48% of patients (12 pts) but no significant late toxicity was noted. The overall survival rates were 24% at one year (6 pts) and 12% at two years (3 pts). Nine patients are still living with persistent tumours and one of them has reached 34 months after completion of radiotherapy. Survival was longer in the conventional fractionated group but this is probably due to the better condition of patients selected for the longer therapy. Among dead patients, we recorded a mean survival of 32 (range 4-120) weeks.

Conclusion: Radiation is a very effective palliative agent for patients with locally advanced carcinoma of the bladder. It has an important role, especially in cases of bleeding but it can alleviate pain as well. In our experience, symptoms were more effectively palliated with short fractionation regimens than with conventional treatment. We found that efficacious regimens are: 3 fractions of 7 Gy, 2 fractions of 8.5 Gy and, if necessary, a 10 Gy single dose. When 6 Gy fractions are used, they should be total more than 3 in number. We conclude that hypofractionated radiotherapy may be the palliative treatment of choice because it delivers palliation that is effective, minimally toxic and less distressing for patients. However, multidimensional parameters such as biological prognostic factors, performance status and comorbidities of patients should be always considered in order to select patients who would benefit from a palliative approach, or from a radical treatment with conventional fractionation and much higher doses.

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EVOLUTION OF CHEMOTHERAPY IN METASTATIC SQUAMOUS CELL CARCINOMA OF THE PENIS

Giorgio Pizzocaro1,2, Luigi Piva1 and Nicola Nicolai1

1Istituto Nazionale Tumori IRCCS, via Venezian 1, Milano, 20133, Italy;
2Urologic Clinic II Milan University, S. Giuseppe Hospital, via S. Vittore 12, 20100 Milano, Italy
**Background and Aim:** Squamous cell carcinoma (SCC) of the penis is a severe disease that metastatizes first to inguinal nodes and then to pelvic ones. Distant metastases are rare and death occurs due to ulceration, infection and hemorrhage. The aim of this study was to evaluate progress and efficacy of chemotherapy to prevent metastasis in high-risk patients and to cure advanced disease. Single-agent chemotherapy was first studied at Memorial SKCC in New York with sequential bleomycin, methotrexate and cisplatin and these three drugs were secondarily tested as multiple agents (BMP) on 14 patients with advanced disease achieving 2 complete and 8 partial remissions (1) at the cost of severe toxicity. At INT, Milano, the first Author thought that SCC of the penis could have the same responsivity to chemotherapy as SCC of the head and neck. So far, we have used the combination vincristine, bleomycin, methotrexate (VBM) for both N-positive and unresectable metastatic nodes and followed the progress of chemotherapy for head and neck cancer.

**Patients and Methods:** VBM was given weekly for 8-12 courses for both adjuvant and neoadjuvant chemotherapy: 1 mg vincristine i.v. on day 1, bleomycin 15 mg i.m. 6 and 24 hours after vincristine and methotrexate 30 mg orally on day 3. Thirteen patients were treated in the neoadjuvant setting and 25 as adjuvant (1) between 1979 and 1990. In 1991, we started to give 3 courses of adjuvant PF (cisplatin and 5FU) and 4 courses were given in the neoadjuvant setting (1). Starting in 2004, we gave taxol, cisplatin and 5-FU in unresectable patients (2).

**Results:** The results of combined surgery and chemotherapy compare favourably with results of surgery alone, with or without complementary previous radiotherapy.

<table>
<thead>
<tr>
<th>Adjuvant therapy</th>
<th>No. of patients</th>
<th>Alive, NED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical surgery alone</td>
<td>38</td>
<td>15 (39%)</td>
</tr>
<tr>
<td>VBM chemotherapy, 12 courses</td>
<td>25</td>
<td>21 (84%)</td>
</tr>
<tr>
<td>PF chemotherapy, 3 courses</td>
<td>30</td>
<td>28 (93%)</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VBM, 12 courses</td>
<td>13</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>PF, 4 courses</td>
<td>25</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>TPF, 4 courses</td>
<td>6</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>M.D. Anderson Centre (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC(I), 4 courses</td>
<td>7</td>
<td>4 (57%)</td>
</tr>
</tbody>
</table>

These results were confirmed also at M.D. Anderson [T: taxol; C: carboplatin; I: ifosfamide (3)].

**Conclusion:** Adjuvant and neoadjuvant chemotherapy in combination with radical surgery, improved significantly the survival of patients with fixed or ulcerated and even of patients with fixed or ulcerated and unresectable nodes and results improved with improving chemotherapy.

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**CATEGORIZATION OF PERIOPERATIVE COMPLICATIONS DURING THE EARLY EXPERIENCE OF ROBOTIC RADICAL PROSTATECTOMY**

Gianluca D’Elia, Paolo Emiliozzi, Gianfranco Ortolani, Antonio Iannello and Umberto Anceschi

Ospedale San Giovanni, Piazza San Giovanni in Laterano, Roma, Italy

**Aim:** To evaluate the prevalence of intraoperative and postoperative complications according to a modified Clavien System associated with preliminary experience of robotic radical prostatectomy.

**Patients and Methods:** Fifty patients, with a mean age of 64.2 years, submitted to robotic radical prostatectomy in a 14-month period were assessed for perioperative complications. The modified Clavien system suggested by Stolzenburg for laparoscopic radical prostatectomy was used to grade intraoperative and postoperative complications: grade I and II represented minor complications, whereas grade III, IV and V represented major complications.

**Results:** Two patients had intraoperative complications (4%): These were rectal injuries, which were intraoperatively recognized and successfully repaired with double-layer suture and peritoneal flap interposition. Seven patients had postoperative complications (14%): These were anaemia requiring blood transfusions in 3 patients who underwent an intrafascial procedure (6%), fever (6%) and prolonged urinary leakage (2%). No perioperative mortality was observed. According to the the modified Clavien system, perioperative complications were graded as follows: Intraoperative grade III complications in 4% of the patients; postoperative grade I complications in 6%, grade II complications in 6% and grade III complications in 2%.

**Conclusion:** During our initial series of 50 cases, robotic radical prostatectomy was associated with a major intraoperative complication rate of 4%. Postoperative major and minor complications were 2% and 12%, respectively. A standardized reporting system for perioperative complications is helpful to critically analyse outcomes and to provide comparable data among urologists. Larger prospective trials are needed to clearly identify predicting factors of perioperative complications associated with robotic radical prostatectomy.
ROBOTIC RADICAL PROSTATECTOMY: DOES PROCTORING AFFECT PERIOPERATIVE AND PATHOLOGIC OUTCOMES

Gianluca D’Elia, Paolo Emiliozzi, Gianfranco Ortolani, Antonio Iannello and Umberto Anceschi

Ospedale San Giovanni, Piazza San Giovanni in Laterano, Roma, Italy

Background: Robotic radical prostatectomy has evolved into the preferred surgical treatment of localized prostate cancer because of its short learning curve when compared to laparoscopic radical prostatectomy. We report the perioperative and pathologic outcomes of our initial series of 50 robotic radical prostatectomies performed by two surgeons utilizing a proctored step-by-step approach.

Patients and Methods: Fifty patients with low-risk prostate cancer underwent robotic radical prostatectomy over a 14-month period. Two surgeons performed all the procedures. The senior surgeon proctored the junior surgeon after the first 25 cases. Perioperative data and pathological results were retrospectively reviewed. Perioperative outcome measures included: Operative time, estimated blood loss, transfusion rate, perioperative complication rate according to modified Clavien system, median hospital stay, mean catheterization time. Pathological outcome measures encompassed positive surgical margin rate and prostate weight. Perioperative outcomes were also analysed using prostate weight as a continuous variable by multivariate regression.

Results: The mean age was 64.2 years. Mean body mass index (BMI) was 26.6. The first 20 procedures were performed via an extraperitoneal approach, whereas the last 30 cases were performed via a transperitoneal approach. An intrafascial nerve-sparing procedure was performed in 14 patients. Mean operative time was 221 minutes. Mean estimated blood loss was 216 cc. Blood transfusion was needed in 3 patients. Median hospital stay was 4 days, mean catheterization time was 11 days. The intraoperative complication rate was 4% (two rectal injuries, which were intraoperatively recognized and successfully repaired with double-layer suture and peritoneal flap interposition). Overall positive surgical margin rate was 22% (11/50). It was 19% for pT2 disease (8/42) and 37.5% for pT3 disease (3/8). The most frequent location of positive margins was the prostate apex (pT2 50%; pT3 100%). Mean prostate weight was 53 g. No correlation between prostate weight, perioperative outcomes and positive margins was found at the multivariate regression analysis (p>0.5).

Conclusion: Robotic radical prostatectomy has a low perioperative complication rate and acceptable pathological outcomes even during proctoring. Two surgeons accomplished their learning curve within 50 cases without putting outcomes at risk. Perioperative and pathological outcomes seem to be unrelated to prostate weight. After this initial experience, robotic radical prostatectomy has replaced our previous standards of open and laparoscopic radical prostatectomy.

URO-CT AS TAILORED-IMAGING FOR DETECTION AND EVALUATION OF RENAL AND TRANSITIONAL CANCER

Federico Lanzi1, Simone Agostini2, Tommaso Lombardi2, Lorenzo Masieri1, Nicola Tosi1, Graziano Vignolini1, Francesco Mondaini2, Sergio Serni1 and Alberto Lapini1

1Department of Urology, University of Florence, Careggi Hospital, Viale Pieraccini 18, 50139, Florence, Italy; 2Department of Radiology, University of Florence, via delle Oblate 1, 50141, Florence, Italy

Background and Aim: Uro-CT performed as a single bolus of organioiodate contrast and four acquisition phases (SBT-CT) is the gold standard in evaluating renal and transitional tumours. In literature, the usefulness of multibolus techniques (SPLIT-CT) in obtaining a diagnostic value similar to standard CT, reducing radiation exposure by performing only 2 or 3 phases of acquisition, is widely demonstrated. The aim of this study was to propose the personalization of Uro-CT performed as an SBT-CT or a multibolus bi-triphasic CT and to define the indications for this technique.

Patients and Methods: From January to June 2008, 203 Uro-CT were performed to detect, in staging or follow-up of renal or urothelial tumours with or without urological comorbidities. Of these, 101 were a standard single-bolus with tetraphasic acquisition, while in 102 patients the examination was tailored depending on urological pathology and the patient’s performance status: 35 patients (34%) underwent standard SBT-CT and 67 (66%) underwent SPLIT-CT. CT always starts with a direct acquisition phase which is necessary to gain a panoramic view that allows the radiologist to produce a tailored imaging technique. SPLIT-CT consists of a first 70 ml contrast bolus; if necessary it is possible to perform an arterial acquisition phase 25-30 seconds after the first injection; 7 minutes later a second contrast bolus of 50 ml is injected, followed by a third bolus (50 ml) 45 seconds later. Combined phase acquisition is usually performed 25-30 seconds after the third bolus. We adopted the SPLIT-CT: To evaluate and follow-up urothelial tumours and small renal lesions (≤4 cm); in case of gross haematuria or in microscopic haematuria with positive urinary cytology and/or positive FISH test without previous
diriment ultrasonography; in preoperative staging of patients with urothelial muscle-invasive tumours; to study patients with urothelial tumours involving urethral meatus; hydronephrosis without high creatinine serum level and previous non concluding US. Standard CT technique as single-bolus with tetraphasic acquisition was performed in patients with large renouretheral tumours and hepatic, splenic or surrenalic lesions of uncertain interpretation at previous ultrasonography or discovered during preliminar direct CT.

Results: SPLIT-CT allowed a contextual representation of vessels, renal parenchyma and excretory system with an high detection rate. SPLIT infusion technique applied 170 ml of organioiodate contrast versus 100-120 ml of SBT-CT. Measured dosimetric levels (range) of bi-triphasic SPLIT technique and SBT-CT were 12.7 (6-18), 20.8 (10-30) and 25.4 (12-38) mSv respectively.

Conclusion: Uro-CT is the gold standard in evaluating renal and transitional tumours but with high radiation levels. We propose the personalization of Uro-CT on the base of the pathological and clinical status of each single patient. The SPLIT infusion technique allows a detailed study with a dosimetric reduction up to 50%, becoming fundamental in patients with long-life expectancy or young female patients found to have no tumours. The limitation of the procedure is represented by a higher dose of contrast infusion that must be considered in patients with renal failure, contrast intolerance and monoclonal gammopathy.

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INCIDENTAL DETECTION OF SCROTAL TUMOURS AT ULTRASONOGRAPHY IN PATIENTS WITH CHRONIC SCROTAL PAIN

Federico Lanzi1, Simone Agostini2, Francesco Mondaini2, Lorenzo Masieri1, Nicola Tosi1, Graziano Vignolini1, Tommaso Lombardi2, Sergio Serni1 and Alberto Lapini1

1Department of Urology, University of Florence, Careggi Hospital, Viale Pieraccini 18, 50139, Florence, Italy; 2Department of Radiology, University of Florence, via delle Oblate 1, 50141, Florence, Italy

Background and Aim: Chronic scrotal pain (CSP) is defined as a condition of constant or intermittent pain, persisting at least 3 months, and interfering with normal activity; it is estimated that patients with CSP represent 3.1% of all uroandrological examinations. Usually scrotal masses are detected during physical examination, while more rarely they are detected incidentally during scrotal ultrasound (US). The aim of our study was to report our experience in detection of scrotal masses during US performed for CSP.

Patients and Methods: From January to June 2009, 58 consecutive patients were evaluated with US as an extension of a physical uroandrological examination (PE) for CSP. None of the patients had positive suspected scrotal masses at PE. We identified two groups on the basis of the presence (Group A, 31 pts, 53%) or absence (Group B, 27 pts, 47%) of a PE diriment on an identifiable aetiopathogenetic element of pain. Scrotal US with funicolar extension was performed with high-frequency probes (7.5 and 10 MHz), multifrequency probes (7-13 MHz), and integrated with color Doppler and functional manoeuvres.

Results: US in Group A better defined clinical elements, with a concordance of 71% with PE. In 3 cases (9.7%), a didymal lesion was found that was identified as seminoma at definitive histopathological evaluation and in 1 case (3.2%) a millimetric epididymal lesion, purportedly an adenomatoid tumour, was better defined with MRI, avoiding a surgical procedure. In Group B, US was unable to identify an aetiopathogenetic element of pain according to PE in 41% of cases. In this group, 2 (7.4%) didymal tumours ≤3 mm were found. One tumour was treated with a US-guided conservative surgery. Histopathological analysis revealed a low-stage seminoma. The second case showed stable dimensions in a close follow-up, and was supposed to be a sertolinoma or a leydigoma.

Conclusion: In the literature, the possibility of scrotal pain determined by dydimal-epidydimal tumours is reported. In our study, patients underwent US to complete uroandrological physical examinations without palpatory evidence of suspected masses. US was not conclusive in discriminating aetiopathogenetic elements of chronic scrotal pain; in spite of that, it was possible to identify very low-stage tumours. US remains a simple, non-expansive and non-invasive examination that must be performed to complete specialist examination.

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ASSESSING FEASIBILITY AND SAFETY OF LESS ADRENALECTOMY: INITIAL EXPERIENCE

Fabio Neri1, Francesco Berardinelli1, Luca Cindolo1, Stefano Gidaro1,2, Fabiola R. Tamburro1 and Luigi Schips1

1Urology Unit, “S. Pio da Pietrelcina” Hospital, Vasto (CH), Italy; 2Department of Surgical and Experimental Sciences, Chieti-Pescara University, Chieti, Italy

Background and Aim: LESS is one of the most interesting surgical advances. We performed a LESS adrenalectomy in five patients to assess feasibility, safety, and perioperative outcomes.
Patients and Methods: Five patients with non-functional adrenal masses underwent TriPort™ adrenalectomy. Demographics, perioperative and pathological records were collected, together with postoperative data. TriPort™ was used through a 3-cm subcostal incision with 10 mm 30°optic and two 5 mm instruments. The specimens were entrapped in a 10 mm bag and extracted together with the Triport™.

Results: TriPort™ adrenalectomy was successfully completed in all cases. The mean operative time was 200 min (mean blood loss 40 ml). No perioperative complications were recorded. Pathological examination confirmed 2 cases of adenoma, 2 of lung cancer metastasis and 1 myelolipoma.

Conclusion: LESS adrenalectomy is feasible and safe, with favourable perioperative and short-term outcomes. It is technically more challenging than standard laparoscopy and requires advanced surgical skills. Prospective studies are needed for further conclusions to be drawn.

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JACKSON STAGING SYSTEM IS MORE PREFERABLE THAN TNM SYSTEM IN PENILE CANCER FOR SELECTION OF CANDIDATES FOR Cavernous-Sparing Surgery

Edoardo Austoni1,2 and Giovannalberto Pini3

1Chair of Urology, University of Milan, Italy; 2GVM Mangioni Hospital Lecco, GVM Salus Hospital Reggio Emilia, GVM Villalba Hospital Bologna, Italy; 3School of Urology, University of Modena and Reggio Emilia, Italy

Background: The TNM staging for penile cancer classifies tumours as T2 malignancies with varying degrees of invasiveness and does not differentiate infiltration of the corpus spongiosum (CS) from infiltration of the corpora cavernosa (CC). These uncertainties in staging can negatively impact the radicality of the surgical procedure. Such a difference is, in surgical practice, a fundamental prerequisite for erectile-sparing surgery. On the contrary, Jackson’s classification distinguishes in stage I tumours, the infiltration of the glans and foreskin, without invasion of the CC; in stage II tumours the invasion of CC without inguinal metastases; in stage III tumours those lesions (independently of infiltration) presenting with inguinal/iliac lymph nodes metastasis. Hence, Jackson’s classification can distinguish tumours that do not infiltrate (S1) the CS from those that do (S2). The objective of penile cancer surgery should combine oncological radicality with the preservation of sexual function.

Thanks to the most recently acquired understanding of penile functional anatomy and to a correct clinical staging (Jackson system), these objectives may be attained by the ‘cavernous-sparing’ procedure in many patients suffering from penile cancer. We report our surgical results for clinical Jackson S1 with a mean follow-up of 9.5 years.

Patients and Methods: We usually perform conservative laser therapy for superficial S1 tumours (Ta-T1). The recommendation for S1 tumours (T2 of the corpus spongiosum), namely amputation, would be much too radical. If the tumour has not invaded the CC (S1), conservative surgery of the CC can be proposed and performed by anatomical dissecting the two morphological/functional units the procedure is termed cavernous-sparing surgery (spongious cavernous disassembly, Austoni 1987). The apex of cavernous bodies was covered by a medium thickness dermal-epidermal graft harvested from the thigh. From 1990 and 2009, we submitted 68 patients, mean age 65.5 (55-83) years to glansectomy by cavernous-sparing surgery, for S1 Jackson stage.

Results and Discussion: Cancer infiltration of the CS are more frequent and generally do not infiltrate the CC; instead, the less common infiltration of the CC has a greater malignant potential. Moreover, the invasion of the CS by an epithelial glans tumour is common, because the epithelium and the lamina propria are less than 1 mm thick. On the other hand, a tumour of the coronary sulcus requires greater malignant potential to reach the CC (epidermis, subcutaneous, darts, Buck’s fascia, albuginea are thicker than 8 mm). We reported tumour recurrences/ progression, erectile and orgasm function (PTS-QOL evaluation), and surgical complications. With a mean follow-up of 9.5 years, there were no local recurrences in any of the 68 patients, and 6 (9.6%) cases of metastasis to inguinal lymph nodes; 54 (87.1%) patients did not report any difference on spontaneous erection, rigidity and penetrative capacity in comparison with the past. Orgasm recovery was reported in 51 patients (82.2%). No major surgical complication were reported, and only 6 (9.6%) patients required multiple medications for partial loss of the dermoeipidermal grafts; one patient required meatoctomy.

Conclusion: From our experience, cavernous-sparing selective glansectomy for S1 tumours (T2 of the CS) offers the same oncological radicality as amputation of the penis, with a significant impact on the quality of life of patients (PTS-QOL evaluation). Use of the TNM staging system risks overstaging the disease, and only Jackson’s classification could overcome this bias by offering patients the opportunity of an erectile-sparing surgery.

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251 PHALLOPLASTY AFTER PENILE CANCER TREATMENT: OUR EXPERIENCE

Austoni Edoardo¹,² and Pini Giovannalberto³
¹Chair of Urology, University of Milan, Italy; ²GVM Mangioni Hospital Lecco, GVM Salus Hospital Reggio Emilia, GVM Villalba Hospital Bologna, Italy; ³School of Urology, University of Modena and Reggio Emilia, Italy

Background: The objective of penile cancer surgery is to combine oncological radicality with the preservation of sexual function. These objectives may be attained thanks to the recent improvements in the penile functional anatomic knowledge and in the clinical staging of the tumour. Today, the ‘cavernous-sparing’ procedure can be performed in many cases. However, advanced tumours require extensive wide local excision or internal radiation therapy. Therefore, for these cases, complex reconstructive procedures are carried out. Reconstructive penile surgery makes ample use of free grafts and pedunculated flaps are often combined with a prosthetic implant. We describe our experience in phalloplasty techniques.

Patients and Methods: Penile partial amputation followed by internal radiation therapy for advanced PC, normally can result in a concealed penis inside the scrotum with severe sclerolipomatosis. In these cases, we performed a corporeal-glânduloplasty with cavernosum-lysis and wide lipectomy to achieve a good enhancement of the concealed penis. Then multiple advancement of scrotal and infrapubic flaps was carried out while the shaft was covered by medium thickness dermal-epidermal grafts. In cases of severe amputation, when the penis is fully concealed inside the scrotum together with the urethral meatus, a scrotal approach was followed by cavernosum-lysis, legamentolysis and minimally invasive soft prosthetic implant, to maintain the achieved penile enhancement. Then dermal-epidermal medium thickness graft and buccal mucosa graft was performed for penile shaft, and for neoglanduloplasty. In cases of total penectomy, our phalloplasty follows the original Mulchay technique, which foresees isolation of the right or left abdominal rectum muscle and dissection proximally at the umbilical level. Maintaining its pedicle to the inferior epigastric vessels infrapublically, the rectum muscle flap is then rotated and used to fashion the neophallus, finally covered by dermal-epidermal medium thickness multiple grafts.

Results and Discussion: All patients treated for concealed penis, consequent to partial penectomy and radiotherapy, regained a penile length sufficient to urinate in a standing position, and recovered the previous erection. Patients treated with cavernosumlysis and ligamentolysis and soft prosthesis minimally invasive implant with multiple dermal-epidermal and buccal mucosa grafts regained previous coital and orgasm ability and reported satisfactory aesthetic results. Patients treated with total phalloplasty by Mulchay procedure reported satisfactory aesthetic results, while poor functional coital results were reported due to the full loss of sensitivity. Our follow up is discussed.

Conclusion: Phalloplasty after penile cancer surgery requires ample use of free grafts, pedunculated flaps, and is sometimes combined with prosthetic implants. Pedunculated flaps offer best elasticity, but are not available after radiotherapy. Free grafts are more rigid and their adhesion capacity and elasticity are strictly related to their own thickness: the thinner the graft, the greater its capacity for attachment, and the higher the risks of retraction. Multiple medium thickness free grafts will fully take in 10 days. Prosthetic implants are useful to maintain the penile enhancement after corporoplasty and facilitate coital activity in case of erectile dysfunction.

252 USE OF FIBRIN GEL (TISSUCOL) AS HEMOSTATIC AGENT DURING LAPAROSCOPIC PARTIAL NEPHRECTOMY: OUR EXPERIENCE

Daniele Tiscione, Stefania Cicuto, Lorenzo Luciani, Valentino Vattovani, Franco Coccarelli and Gianni Malossini
Ospedale S. Chiara, Trento, Italy

Background: Laparoscopic partial nephrectomy (LPN) is increasingly performed all over the world and represents a valid procedure for the management of small renal tumours. Control of bleeding and urine leakage is one of the most technically challenging step in LPN, although there is no consensus about the best approach of these injuries. We describe our experience to control bleeding during LPN using fibrin gel (Tissucol) as a type of sealant.

Patients and Methods: Between October 2008 and July 2009, 14 patients underwent LPN. In all cases, tissue gel was used alone, without suture renorrhaphy. The following parameters were recorded: patient demographics, tumour characteristics at computerized tomography, warm ischemia time, length of surgery, estimated blood loss, postoperative complications, renal function loss, pathologic and follow-up data.

Results: The median patient age was 58 (range 44-77) years. The median tumour size was 3.1 (range 1.5-5) cm; 10 masses were exophytic and 4 deep. After application of the tissue sealant, haemostasis was immediate in all cases. Median operative time was 174 (range 140-200) minutes, while the median warm ischaemia time was 14 (range 11-19) minutes. Estimated blood loss ranged from 150 to 500 (median 330) cc. Twelve cases were discharged after 5 days.
without complications. Average individual renal function loss was 9%. Postoperative complications included haematoma treated conservatively (n=1) and urine leakage requiring double J ureteral stenting (n=1). There were no open conversions.

Conclusion: Sutureless LPN for exophytic lesions may be an effective ‘add on’, reducing bleeding and urine leakage, as well as reducing warm ischaemia time, length of surgery and renal function loss. In our experience, sutureless LPN for deep lesions may not be a safe procedure. Further prospective studies are necessary to validate the role of fibrin gel during LPN.

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NEPHRON-SAVING LAPAROSCOPIC SURGERY FOR RENAL CELL CARCINOMA OF 4-7 cm
Andrea Polara, Luca Aresu, Alessandro Cielo, Francesco Maritati, Massimo Occhipinti and Gaetano Grosso

Casa di Cura Polispecialistica Pederzoli, via Monte Baldo 24, 37019 Peschiera del Garda, Verona, Italy

Background: Nephron-sparing surgery is standard of care for small-sized kidney neoplasms. In the literature, a laparoscopic approach has shown advantages in terms of morbidity but longer operative time, ischaemia time and more bleeding than open techniques in the early learning curve; furthermore, long-term oncological results are needed. We analysed mid-long term oncological results of 59 patients affected by 4-7 cm-sized neoplasms (pT1b RCC), treated with laparoscopic nephron-sparing surgery.

Patients and Methods: Since 2004, in our Institution, 248 patients have undergone laparoscopic nephron-sparing surgery, 59 of them were affected by RCC of 4-7 cm (41 males, 18 females, mean age 62 years, mean neoplasm diameter 4.8 cm). Lumboscopic access was preferred in most cases, while transperitoneal procedure was adopted in 10% of patients in relation to placement of neoplasm.

Results: In all cases, isolation of renal artery was performed and warm ischaemia was applied (9 min mean warm ischaemia time, 7-18 min) tractioning vessel loop. Biopsies on the resection bed were performed in 2 cases; gelatin matrix was used in 30% of cases. Mean operative time was 80 min, conversion rate 0%, transfusion rate 0%, mean hospital stay 4 days. Complications: 4 respiratory failures, 2 openings of collecting system. Surgical margins presented focal infiltration in 4 cases, 2 of them developed cancer recurrence at different site from resection area and radical nephrectomy was performed. Mean follow-up was 2.4 years, (1-5 years). At five-year follow-up 0.2 mg/dl mean increase of creatinine was registered.

Conclusion: Laparoscopic approach is safe and feasible for treatment of RCC in expert centres. Radical nephrectomy is still the gold standard for pT1b RCC although a strong increasing demand of nephron-sparing surgery. Our experience with larger neoplasms is promising further implementation of this procedure even for pT1b RCC in relation to our mid-long term results.

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SINGLE LAPAROSCOPIC ROBOT-ASSISTED RADICAL PROSTATECTOMY (RARP) LEARNING CURVE OF A NAIVE SURGEON
Giancarlo Albo¹, Sara Melegari¹, Carlo Ambroso¹, Bernardo Rocco¹, Luigi Santoro², Serena Detti³, Fabrizio Verweij¹ and Ottavio De Cobelli¹,³

Divisions of ¹Urology and ²Epidemiology and Biostatistics, European Institute of Oncology, via Ripamonti, 435 -20141-Milan, Italy; ³Faculty of Medicine, University of Milan, Italy

Background: Radical prostatectomy is considered the gold standard therapy for localized prostate cancer (1) Minimvasive approaches have been developed in the last years to decrease perioperative morbidity and to improve functional outcomes. The first laparoscopic prostatectomy was performed in 1992, but this technique has not spread because of its long learning curve. Robotic procedures, thanks to 3D vision, x10 magnification and instruments with 7 degrees of freedom, have allowed a shorter learning curve and consequently a greater use if this technique. In this study, we evaluated single laparoscopic robot-assisted radical prostatectomy (RARP) learning curve of a naive surgeon.

 Patients and Methods: From November 2006 to September 2009, 423 RARP were performed at European Institute of Oncology, following the Patel technique (2) and posterior reconstruction of rhabdosphincter (3) using a 4-arm Da Vinci System (Intuitive).

A total of 222 procedures were carried out by the samelaparoscopic-naive operator, trained in open surgery. We analysed three groups, each one of 74 consecutive patients: Group 1 (G1): patients treated in the first 12.5 months from the beginning of experience; Group 2 (G2): patients treated in the subsequent 12.5 months; Group 3 (G3): patients treated from 25th to 35th month from the beginning of experience.

We analysed surgical time (min), bleeding (ml), hospital stay
Patients’ characteristics were comparable in the three groups (age, PSA, staging, Gleason score). Surgical time decreased in the first two groups, and was longer in the third (264±77 vs. 215±34 vs. 241±51; p=0.0001). This trend may be related to the increased number of lymphadenectomies carried out in the last group of patients (G3 33%, G1 24%). Concerning the blood loss, there was a small rise in the three groups (208±123 vs. 266±165 vs. 275±179; p=0.011). A shorter hospital stay was found in the third group (4.3±2.0 vs. 3.1±2.3 vs. 3.9±2.2; p<0.0001). There was no significant difference as far as catheterization (6.7±3.2 vs. 7.5±7.2 vs. 6.8±2.9; p=0.20) and positive surgical margins rate (18.9% vs. 14.9% vs. 18.9%) are concerned. Nor was any difference detected in urinary continence, and sexual potency considering patients with at least 3 months of follow-up, in which urinary continence was achieved in 68-76% (p=0.67) and spontaneous erections in 15-26% (p=0.52). The 89 patients younger than 65 years reached spontaneous erections in 20-41% with no difference in the three groups (p=0.26).

Conclusion: The RARP learning curve had no impact on oncological, perioperative and functional outcomes.

References
1 EAU Guidelines 2009.

A METACHRONOUS BLADDER METASTASIS OF RENAL CELL CARCINOMA: A CASE REPORT

Sara Melegari, Giancarlo Albo, Bernardo Rocco, Fabrizio Verweij and Ottavio de Corbelli

Department of Urology, European Institute of Oncology, via Ripamonti 435 20141 Milano, Italy

Background: The incidence of kidney cancer has been growing in recent decades. According to SEER data (http://seer.cancer.gov/), it is estimated 54390 and 13010 patients died because of this tumour in 2008. Five-year relative survival rates were 89.9% for localized disease, 61.3% for regional lymph node spread and 9.9% for distant metastasis. Staging and grading have influence on the prognosis (1). Although organ-confined, RCC (renal cell carcinoma) can recur at any time after nephrectomy; the percentage of survival rate and metastases risk can be estimated, according to the Mayo Scoring System on the basis of pathological stage, tumour size, regional lymph node status, nuclear grade and the presence of necrosis. RCC usually metastasizes via the haematogenous and lymphatic system, involving the lung (50-60%), lymph node (40-60%), liver (30-40%), bone (30-40%), brain (5%), bowel (4%), pancreas (1%), and rarely adrenal gland, parotid gland, pharynx (2). We describe the case of a 65-year-old patient affected by bladder transitional cell carcinoma (TCC), kidney RCC and adenocarcinoma of the prostate.

Case Report: The bladder TCC was firstly diagnosed elsewhere in 1993; the patient underwent TURBT for a TCC T2G2. No adjuvant therapy was performed and a regular endoscopic follow up was maintained. The bladder tumour recurred twice: in 1997 (TCC T1G1), and in 2006 (TCC T1G2 associated with carcinoma in situ). He was administered a 36-month BCG immunotherapy following SWOG schedule. In 2005, a cT2N0M0 prostate tumour was diagnosed (Gleason score 4+4; PSA 37.7 ng/ml). An abdominal CT scan revealed incidental presence of kidney cancer. Thus, the patient underwent a left radical nephrectomy and lymphadenectomy for a RCC pT3a pN0, Fuhrman III grade. The tumour was <10 cm, with necrosis inside. The patient underwent subsequently radiation therapy for prostate cancer (66 Gy). No evidence of diseases recurrence was found in the immediate three years of regular follow-up. In February 2009, a 5 mm lesion was found during cystoscopy performed as a follow-up for the TCC. This lesion was endoscopically resected and found to be a clear cell RCC. RCC metastasis was confirmed after comparison with the histology of the primary kidney cancer. Immunohistochemistry was positive for CK AE1/AE3, CK 7, CK 20, CD10 and beta-catenin, and negative for C-KIT, PSA and FAP. We performed a metastasectomy as it was a typical secondary neoplasm. In this case, the diagnosis of bladder metastasis was metachronous, 36 months after the nephrectomy. According to the Mayo Clinic score system, the patient was at high risk, with a 62.9% probability of metastasis at 3 years.

Conclusion: During RCC follow-up, every lesion should be considered as a metastasis of possible RCC, even if it is not present in a typical site, such as the bladder. The 3-year survival rate is 80% in cases of single metastasis, and the mean time to diagnosis is 28 months after nephrectomy (3). Management of these lesions is very inhomogeneous, as complete resection, excision, or radiotherapy is justified and can contribute to long-term survival. Complete resection of RCC single metastases seems to be associated.
with 5-year survival rates between 35% and 60%. The longer the disease-free interval is, the longer the survival. Synchronous metastasis seems to correlate to a worse prognosis than metachronous (2). Thus patients with metastatic RCC should be offered metastasectomy if the likelihood that complete resection of all sites of disease is high. Even though more data are required to reach a conclusion, and although the curative impact of metastasectomy can still be considered uncertain, operative intervention can also provide effective palliation for symptomatic metastatic disease.

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Bacillus Calmette-Guérin: Treatment for Superficial Transitional Cell Carcinoma (TCC) of the Bladder

Samanta Fornia, Stefania Ferretti, Davide Campobasso, Antonio Barbieri, Umberto Maestroni, Francesco Ziglioli and Pietro Cortellini

U.O. Urologia Azienda Ospedaliero-Universitaria di Parma. V. Gramsci 14, 43126 Parma, Italy

Background and Aim: Intravesical immunotherapy with bacillus Calmette-Guérin (BCG) has been the gold standard among the treatment options for superficial transitional cell carcinoma (TCC) of the bladder at high and intermediate risk of recurrence and progression since 1976. The aim of this work was an evaluation of the risk of recurrence, tumour progression, survival and tolerability of this therapy for patients affected by high-risk superficial transitional cell carcinoma of the bladder (according to EORTC '96).

Patients and Methods: A total of 196 high-risk TCC patients were enrolled for intravesical immunotherapy with BCG after transurethral resection and histological confirmation of non muscle-invasive bladder cancer from 01/02/1999 to 31/07/2008. Each patient received an instillation of BCG weekly for 6 weeks followed by a 3-week cycle after 3 and 6 months, and then each 6 months up to 3 years. The follow-up was carried out with biopsy after 3 months and cystoscopy and urinary cytology every 3 months. Recurrence was defined by the presence of positive cystoscopy or urinary cytology, followed by histological confirmation. Therapy was interrupted in case of intolerance, side-effects (medium or severe), recurrence or tumour progression.

Results: The following patients were treated: 70 Ta (36%: 48 G3, 18 G2, 4 G1), 101 T1 (52%: 87 G3, 12 G2, 2 G1), 2 T2 (1%: G3) and 23 CIS (12%); 52% had a recurrence. In 105 (54%) cases, the tumour was single, while 91 (46%) were multifocal. The mean follow-up period was 35 months. The mean treatment period was 14.5 months. Only 25 patients (31%) out of 81, completed the therapy of 36 months: 102 (52%) patients stopped therapy due to intolerance (45%), recurrence (31%) and for personal reasons (20%). In total, 196 patients were treated, 147 (75%) of them are disease-free, with a mean follow-up period of 39 (range 3-112) months. The remaining 25% (49 patients) had recurrence (mean disease-free time: 22 months, range 3-66 months). Overall, 25 cases (14%) had tumour progression; in 4 cases it was rapid (<6 months from diagnosis), while 2 manifested well after the beginning of the therapy (34 and 53 months), both with negative endoscopy imaging and cytology, but high stage (T4B N+). Twenty-one patients were treated with radical cystectomy, 2 with partial cystectomy, 1 with radiotherapy, 2 with systemic chemotherapy, 1 with topical chemotherapy. Eight patients treated with cystectomy died due to tumour after a mean period of 18 months. Total survival rate was 84% (31 patients of this study have died, 18 due to progression of disease).

Conclusion: The results of our study are in line with the literature and underline a high survival rate in the mid-term but with significant toxicity. We think, however, that remarkable diagnostic efforts should be made in order to identify those patients with tumour of stage >T1 (premature recurrence) and those with ‘deep’ recurrence (for example CT or MRI every 6/12 months) in which premature cystectomy could guarantee advantages in terms of survival.

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Perioperative Complications in Robot-Assisted Laparoscopic Radical Prostatectomy

Giancarlo Albo, Sara Melegari, Bernardo Rocco, Serena Detti, Fabrizio Verweij and Ottavio De Cobelli

Department of Urology, European Institute of Oncology, via Ripamonti 435, 20141 Milano, Italy
Background and Aim: Robotic-assisted laparoscopic radical prostatectomy (RALP) is in widespread and rapidly expanding use in the last decade as a surgical approach for prostate cancer. The number of RALPs rose from 766 in 2002 to 48000 in 2007, and RALPs nowadays account for the majority of radical prostatectomies performed in the United States. The feasibility and safety of this procedure have been well established since its introduction in 2000, and reports from high-volume centres suggest excellent short- and medium-term functional and oncological outcomes for patients undergoing this procedure. Although there is no level I evidence to support its use over conventional laparoscopic radical prostatectomy or open radical prostatectomy, RALP is a procedure with limited blood loss, favourable complication rate and short hospital stay. Perioperative complications considered as any deviation from the standardized RALP pathway are often recorded in the literature. Murphy, in his study on 400 patients, described complications in 63 of them (15.75%). Mottrie et al. performed a study on 184 patients and described complications in 22 of them (11.9%). The aim of the present study is the analysis of complications in our experience of RALP.

Patients and Methods: From 1st November 2006 to 29th January 2010, 486 RARPs were performed at the Urology Division of the European Institute of Oncology. We defined as perioperative complications any deviation from the standardized RALP pathway and we stratified these data into five grades according to the classification described by Clavien et al.

Results: Of 486 treated patients, 69 (14.2%) had one complication. From the day of surgery to 30 days after, we recorded 72 complications: 7 infections, 5 fistulas/leak, 33 bleeding/hematomas, 3 cardiopulmonary events, 1 neurological complication, 1 pain complication, 22 other complications. According to the Clavien-Dindo classification, 24 were grade 1 events (deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions), 34 were grade 2 (event requiring pharmacological treatment with drugs other than such allowed for grade 1 complications), 2 were grade 3a (event requiring surgical, endoscopic or radiological intervention not under general anaesthesia), 11 were grade 3b (event requiring intervention under general anaesthesia), 1 was grade 4b (multi-organ dysfunction).

Conclusion: As all innovative therapies, there is not much information regarding the incidence of complications and reintervention after robot-assisted radical prostatectomy. In our experience, we reported 14.2% complications in 486 patients; these data are similar to the incidence of complications reported in the literature. Fourteen (2.8%) of these cases were serious (grade ≥3) and required surgical intervention. These data can help the physician in correct counselling of the patient.

258 DOES ROBOTIC SURGERY AFFECT KATTAN’S POSTOPERATIVE 5-YEAR CANCER-FREE SURVIVAL FORECAST MORE THAN OPEN SURGERY

Deliu Victor Matei1, Bernardo Rocco1, Sara Melegari1, Giancarlo Albo1, Serena Detti1, Antonio Brescia2 and Ottavio De Cobelli1

1Urology Division, European Institute of Oncology, Milan, Italy; 2San Giuseppe Hospital, Robotic Oncologic Urology Division, via San Vittore 12, 20123 Milan, Italy

Background: The value of robotic surgery in prostate cancer has been shown but some concern persists, mainly for the real incidence of positive surgical margins (SM) rates in centres with limited robotic experience (<500 cases). In fact, Kattan’s algorithm of cancer-free survival (CFS) forecast combines clinical stage, biopsy Gleason score (GS) and PSA in its preoperative variant and pathology data (stage, GS, seminal vesicles, lymph nodes and SM status) in its postoperative variant. As a consequence, the pre- to postoperative variance is mostly due to pathological up- or understaging/grading and the presence of positive SM.

Patients and Methods: We retrospectively analysed 91 RALP (robot-assisted laparoscopic prostatectomy) and 183 RRP (retropubic radical prostatectomy) carried out by a single surgeon between 09.1999 and 09.2009; pre and postoperative Kattan 5-year CFS forecast was calculated for 90 and 163 patients with available data. Up/downstaging and grading, and SM status were analysed. The variance in CFS was calculated subtracting the preoperative calculated value from the postoperative CFS forecast; the difference would thus be negative, null or positive.

Results: SM+ rate was 26.7% in RALP vs. 22.1% in RRP cases. Considering the nerve-sparing procedures, SM+ was 25.7 vs. 20.7% respectively, while considering only pT2 patients, it was 17.5 vs. 16.1% respectively. Pathological upstaging from cT1c was found in 34% of RALP vs. 37% of RRP, while postoperative upstaging from cT2 was 56% vs. 57% respectively. No statistical significance was reached. The table presents the preoperative to postoperative variance of the CFS forecast. A negative difference means a worsened CFS forecast, mostly due to upstaging and to the SM+.

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Only if the CFS forecast improved after the surgery did the average of the difference show a slight statistical trend \((p=0.08)\) in favor of RALP patients. The higher average difference score (22\% in the RALP group vs. 13\% in the RRP group) in those cases in which the postoperative forecast clearly improved could be due to: 1) the more severe selection criteria in the RALP group during the learning curve; 2) the pathological stage shift: 45.4\% of pT2 in the RRP group vs. 52.2\% in the RALP group.

**Conclusion:** Kattan’s nomogram of 5-year CFS probability forecast, by combining clinical and pathological data, allows univariate statistical analysis to be performed, mimicking multivariate analysis. Our study shows no statistical difference in SM+ and upstaging rates between RRP and robotic surgery and thus no difference in the hypothetical influence of the type of surgery on the clinical outcome. The present study’s limitations are that it is a retrospective one and that RALP were performed after having obtained a good open surgical experience, although still on the learning curve. Further studies are required to assess the influence of robotic surgery on the real clinical outcome more tha on the CFS probability forecast.

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**ROBOT-ASSISTED REPAIR OF RECTOVESICAL FISTULA RESULTING FROM ROBOTIC RADICAL PROSTATECTOMY**

Deliu Victor Matei, Bernardo Rocco, Gennaro Musi, Stefano Zambito, Gabriella Mombelli and Ottavio De Cobelli

European Institute of Oncology, Urology Division, via Ripamonti 435, Milan, Italy

**Background:** Rectovesical fistula (RFV) is a rare complication of radical prostatectomy (1-11\%) and represents a major complication of this procedure. Surgical reconstruction remains the mainstay in the management. Recently, numerous reports of laparoscopic and robotic surgical repair of these fistulas have shown that these techniques can be effectively and safely used with added advantages of short hospital stay, reduced morbidity and lower blood loss. Robot-assisted surgery has the advantage of facilitating intracorporeal suturing, making laparoscopic reconstruction easier. However, the steep learning curve and the high cost of robotic surgery are limiting factors. We present a case of surgical robotic repair of a RFV, describing the technique.

**Case Report:** A 53-year-old man, dialysed and diabetic, underwent robotic radical prostatectomy for localized prostate cancer (iPSA 4.9; GS 3+3; pT3a pNx R0 M0). The procedure was complicated by a haematoma between the rectum and the bladder, spontaneously drained into the rectum through a fistula matured after 14 days from the procedure, probably on an ischaemic preexisting field. Right excluding colostomy was performed. Conservative management with continuous drainage using a Foley catheter failed, and after 5 months, the patient was referred for robotic surgical repair. Under general anaesthesia, the patient was prepared and positioned in the steep extreme Trendelenburg position (30\°). A 3-arm Da Vinci System and 5-port transperitoneal access were used with a port configuration identical to that commonly used for robotic prostatectomy and the peritoneum was incised at the level of the lowest point of the pouch of Douglas. Blunt and sharp dissection was used to separate the rectum from the bladder until the fistula was visualized. The borders of the fistula on the bladder and rectal side were prepared and separately closed using a running reabsorbable mono-filament stitch with lapratypes. Tissucol was used to cover the sutures and Tabotamp Fibrillar was positioned between rectum and bladder as omentum was not available. The peritoneum was then sutured over the Douglas cul-de-sac and a suction drain was positioned. Fistula repair was successful with an operative time of 170 min without blood loss. The patient was discharged on day 5. The Foley catheter was removed on day 30, after having obtained a good voiding cystogram. At a 1-month follow-up, the patient remains free of fistula recurrence. The colostomy was scheduled to be closed after a 3-month follow-up.

**Conclusion:** Robotic repair of RFV appears feasible and represents an attractive alternative to both open and pure laparoscopic approaches as it makes reconstructive procedures very easy to perform.

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**LAPAROSCOPIC ROBOT-ASSISTED MICROWAVE ABLATION OF SMALL RENAL CARCINOMA**

Deliu Victor Matei1, Bernardo Rocco1, Fabrizio Verweij1, Federica Mazzoleni1, Gennaro Musi1 and Andrea Nordio2

1Urology Division, European Institute of Oncology, via Ripamonti 435, 20141- Milan, Italy; 2San Giuseppe Hospital, Robotic Oncologic Urology Division, via San Vittore 12 – 20123, Milan, Italy

**Background:** The laparoscopic partial nephrectomy requires experience and a longer learning curve, especially for renal reconstruction time, which may consequently prolong the ischaemia time. The advent of robot-assisted laparoscopic surgery has proved successful in prostate cancer surgery, encouraging a growing number of centres to apply this technology also to renal surgery, with a potentially shorter
learning curve for minimally invasive nephron-sparing surgery (NSS). Different minimally invasive approaches have been recently developed. Microwave (MW) ablation requires neither ischaemia, tumour excision, nor renal reconstruction, thus making the technique more simple and the learning curve shorter.

**Patients and Methods:** An 81-year-old male presented at our Hospital asking for therapy for a single upper polar renal tumour found during a CT-scan required for anaemia. Surgery, open or robotic seemed to us too invasive with regard to the patient’s age, the size of the tumour, and the comorbidities (diabetes, former stroke, hypertension, high serum-creatinina and anaemia). We chose a transperitoneal access. A 3-arm Da Vinci System with a bedside assistant was used for the procedure. Three trocars (two 8-mm robotic trocars and one 12-mm trocar for the optic) were placed in a triangulated configuration; and one additional 10 mm assistant port was placed at 6-7 cm medially with respect to the lower robotic trocar. The colon was mobilized, incising the peritoneum from the spleen attachments to the iliacal vessels and parallel to the descending colon, allowing identification of the upper renal pole. Intraoperative US allowed the precise identification of the tumour site and Gerota’s fat layer covering the tumour was then removed. A needle biopsy was performed and frozen section assessed, showing a renal cell carcinoma. A 17-G MW probe was then inserted into the tumour until its tip reached the deepest margin of the lesion under US control. Thermoablation using a 35-W microwaves generator (HS Amica Apparatus for Microwave ablation®, HS SpA, Rome, Italy) was performed. Periodic US allowed control such that thermoablation front entirely covered the lesion. MW time was 5 min. No bleeding occurred at needle extraction. Overall operative time was 90 min.

**Results:** The patient was dismissed on day 2, with stable haemoglobin and serum creatinine levels. The level of pain (colour scale) was 1. Non analgesic therapy was given. CT scan performed after 1 month and US scan performed after 6 months showed complete destruction of the tumour and no relapse.

**Conclusion:** In our initial experience, robotic-assisted microwave ablation seems to be a safe and effective treatment for small renal tumours in patients with high surgical risk or who refuse surgery.

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**INGUINOSCROTAL HERNIA CONTAINING OCCULT BLADDER CANCER: CASE REPORT**

Domenico Viola, Ahmad Hind, Ferdinando Martino, Leonardo Manoni, Roberto Rossi Cesolari and Sergio Leoni

U.O.C. Urologia, Arcispedale S. Maria Nuova, viale Risorgimento 80, 42100 Reggio Emilia, Italy

**Background:** We report an unusual case of invasive urothelial bladder cancer arising within the herniated dome of the bladder in a inguinoscrotal hernia.

**Case Report:** An 80-year-old man was referred to our Department complaining of 3 months persistent macroscopic haematuria and LUTS. An abdominal contrast-enhanced CT scan, performed 1 month earlier, had ruled out renal masses or stones and had showed herniation of the bladder dome into a left inguinoscrotal hernia. The bladder was described as being free of any luminal mass, although dysmorphic, with thickening of the herniated bladder wall. Physical examination was unremarkable, except for pallor and the evidence of a non reducible left-sided inguinoscrotal swelling. The prostate was slightly enlarged and fibrous on palpation. Laboratory investigations revealed severe chronic anaemia (Hb 8 g/dl) and the patient underwent blood transfusion. Flexible and rigid cystoscopies were carried out, but we were not able to inspect the herniated bladder dome due to a very narrow and tight isthmus, which did not allow the progression even of the 16 Fr. flexible scope. Urine cytology for malignant cells was negative. We then decided to perform an inguinal hernioplasty, dissecting the bladder dome free from the hernial sac and a TURP. During the operation, the herniated bladder was extremely hard on palpation and it was consequently resected and sent for frozen sections, which revealed a high-grade transitional cell carcinoma. A partial cystectomy was finally performed and the definitive histology showed a 3.5 cm ulcerated hard mass, consistent of undifferentiated transitional cell carcinoma, infiltrating the bladder wall, with negative margins and foci of carcinoma in situ in the remaining mucosa. Hernioplasty with polypropylene mesh and TURP were completed uneventfully. The patient was discharged on the 5th postoperative day in good condition and is now undergoing adjuvant chemotherapy. Approximately 1-3% of inguinal hernias in adults are associated with herniation of the bladder, which is seldom indentified preoperatively and it is an exceptional site for neoplasm (1), with fewer than 15 cases reported in the literature since 1943 (2). In patients with urinary symptoms and bladder hernias, accurate diagnostic investigations that allow the evaluation of the herniated bladder wall are of paramount importance and mandatory to exclude the presence of neoplasm.

**References**


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**INTROOPERATIVE RADIOTHERAPY FOR LOCALLY ADVANCED PROSTATE CANCER: A MATCHED PAIR ANALYSIS**

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Background: Oral metastases represent 1% of all oral tumours and rarely are the first manifestation of a primary tumour arisen elsewhere. Renal cell carcinoma, breast cancer, lung cancer and prostate cancer can metastasize to the oral cavity, but only few cases are reported in the literature as being the first appearance of the disease. Prognosis is generally poor, since, at the moment of the diagnosis, the primary tumour has already widely metastasized.

Case Reports: We present 8 unpublished cases of oral metastasis of renal cell carcinoma, 7 of which were the first sign of the primary tumour: the mean age was 63.5 (range 78–45) years; 6 were males and 2 females. Both bone and soft tissues were involved: 3 cases were localized in the parotid gland, 2 arising within the gingiva, 2 in the mandible (condyle and body) and 1 on the tongue. Clinical signs and symptoms were various and related to the involved organs: swelling, teeth mobility, epulis-like lesions, alitosis, chin numbness, pain and facial palsy were the most common. Radiological features were often non specific and did not contribute to the diagnosis. Differential diagnoses with many benign oral conditions (i.e. abscesses, osteomyelitis, periodontal pathologies, granulomatous gingivitis, piogenic granuloma, giant cell granuloma, epulis), with primary oral tumours (squamous cell carcinoma, lymphoproliferative disorders and salivary gland tumours) and, at least in one case, with metastases were carried out.

Conclusion: Since clinical and radiological features of the oral lesions are non-contributory for the diagnosis, this can be difficult without the biopsy, which is mandatory. Pathology often reveals poorly differentiated clear cell cancer, therefore our diagnoses were made on the basis of immunohistochemistry (vimentin and CD10), especially when the primary tumour was unknown.

References
SOLUBLE E-CADHERIN SERUM LEVEL VARIATIONS IN PATIENTS WITH PROSTATE CANCER AFTER RADICAL RETROPUBIC PROSTATECTOMY

Fortunata Iacopino1, Francesco Pinto2, Alessandro Bertaccini3, Alessandro Calarco2, Gabriella Proietti1, Angelo Totaro7, Giuseppe Martorana3, Pier Francesco Bassi2 and Gigliola Sica1

1Institute of Histology and Embryology, and 2Department of Urology, Faculty of Medicine, Catholic University of the Sacred Heart, Largo F. Vito 1, 00168 Rome, Italy; 3Department of Urology, Alma Mater Studiorum, University of Bologna, via Palagi 9, 40138 Bologna, Italy

Background: Recently, new biomarkers have been proposed to be integrated with prostate-specific antigen (PSA) in order to increase its diagnostic and prognostic value. In fact, PSA is known to have some limitations, particularly in distinguishing indolent from aggressive cancer and predicting outcome after specific therapy. E-cadherin (E-cad) is a calcium-dependent adhesion glycoprotein found in epithelial tissue where it maintains proper cell-to-cell structure. Much data indicate that prostate cancer (PCa) can develop abnormalities in E-cad expression. In addition, it has been reported that proteolytic cleavage of the mature E-cad (120 kDa) form delivers different fragments that are shed into the extracellular space and are measurable in the serum of patients suffering from several types of cancer, including PCa. In particular, there is a significant difference in the expression level of the 80 kDa fragment in serum of healthy individuals vs. patients with benign prostatic hyperplasia (BPH) and between BPH vs. localized and metastatic hormone-refractory PCa. Elevated expression of the fragment at the time of diagnosis is associated with a significantly increased risk of biochemical failure. In this study, we investigated the variations in the serum concentrations of 80 kDa soluble fragment (sE-cad) due to the surgical treatment in patients affected by PCa.

Patients and Methods: Sixty-one patients with localized or locally advanced PCa, who did not receive any previous treatment, were enrolled into the study. Local or locally advanced PCa was defined according to the current TNM classification. Patients were submitted to radical retropubic prostatectomy. Serum samples were collected before and after surgical treatment with standard procedure and kept at -80°C till the time of E-cad determinations, which were performed using ELISA kit (human E-cadherin EIA kit, Zymed Lab., San Francisco, USA).

Results: The sE-cad levels were 6.01 ± 2.70 (mean ± SD) μg/ml and 4.62 ± 2.30 μg/ml before and after prostatectomy, respectively. The decrease in sE-cad concentrations was highly statistically significant (p<0.0001, paired Student’s t-test). In particular, the reduction in sE-cad levels after the surgical treatment was seen in 50/61 patients (82%) and it was more than 20% in 34/50 cases (68%). Nevertheless, an increase in postoperative sE-cad levels was observed in 11/61 patients (18%); it was higher than 20% in 5/11 cases (45%). The sE-cad levels before and after surgery were correlated (r=0.6993, p<0.0001, Pearson’s correlation coefficient) while no correlation between preoperative sE-cad levels and PSA concentrations was found. There was no statistically significant difference in sE-cad levels observed before and after the surgical treatment in relation to perineural invasion and surgical margin infiltration. sE-cad levels before prostatectomy were significantly higher in patients with G3 tumours with respect to those with G2 tumours (p<0.02, unpaired Student’s t-test). The 80 kDa fragment concentrations both before and after surgery were higher in tumours with Gleason score 7 with respect to those with Gleason score <7 (p<0.002 and p<0.05, respectively, unpaired Student’s t-test).

Conclusion: Our findings clearly indicate that prostatectomy determines a statistically significant reduction in the levels of sE-cad in patients affected by localized or locally advanced PCa. The preoperative concentrations of the marker are higher if the tumour is less differentiated which suggests that sE-cad might be proposed as a marker of tumour aggressiveness at the diagnosis.
cancer (CPEC). Emiconfluent starved cultures were treated with recombinant Prok1 (5nM) alone or associated with antiProk1 monoclonal antibody or solvent. Cells were harvested 48 hours after the treatment and stained with propidium iodide for flow cytometry of the cell cycle by FACSCaliber or recovered for protein extraction for Western-blot analysis, or for mRNA extraction for semiquantitative RT-PCR. Cells grown on slides were also treated and harvested after 46 h for TUNEL assay. A wound assay was performed for the evaluation of cell motility after overnight incubation. For ERK phosphorylation assay cell cultures were harvested after 5, 10, 20 and 60 min following treatment.

Results: An increase of the cell number in the S phase, with a decrease of cell counts in pre-G1 and G0/G1, and a significant reduction of the percentage of fragmented nuclei was found after Prok1 treatment ($p<0.05$ vs. control). Treatment induced an increase of migration in CEPC only. All these effects were abolished when antiProk1 monoclonal antibody was added. Prok1 induced a rapid and transient phosphorylation of ERK in EPN and more sustained effects on CEPC; these effects were abolished by pretreatment with PD98059 (50 nM). Semiquantitative PCR showed an increase of prokineticin receptor 2 (Prok-R2) transcript in treated cells.

Conclusion: Our study demonstrates that Prok1 is a mitogenic factor for prostate epithelia and may be a target for a new therapeutic approach for the control of prostate cancer development and/or progression.

267 CYBERKNIFE ROBOTIC IMAGE-GUIDED STEREOTACTIC RADIOThERAPY FOR ISOLATED RECURRENT PRIMARY, LYMPH NODE OR METASTATIC PROSTATE CANCER

Barbara Alicjia Jereczek-Fossa, Laura Fariselli, Giancarlo Beltramo, Cristiana Iuliana Fodor, Luigi Santoro, Dario Zerini, Federica Gherardi, Carmen Ascione, Isa Bossi Zanetti, Roberta Mauro, Livia Corinna Bianchi, Achille Bergantin, Andrea Vavassori, Giovanni Battista Ivaldi, Ottavio de Cobelli, Bernardo Rocco, Giancarlo Albo, Epifanio Scardino, Gennaro Musi, Fabrizio Verweij, Deliu Victor Matei, Orecchia Roberto

Departments of 1Radiotherapy, 2Medical Physics, 3Urology and 4Epidemiology and Statistics, European Institute of Oncology, Milan, Italy; 5Cyberknife Centre CDI, Milan, Italy; 6Radiotherapy Unit Carlo Besta Neurological Institute Foundation, Milan, Italy

Aim: To evaluate the outcome of robotic Cyberknife-based stereotactic radiotherapy (CBK-SRT) for isolated recurrent primary, lymph node or metastatic prostate cancer.

Patients and Methods: Between 05/2007 and 12/2009, 34 patients were treated (38 lesions: group $P =$15 pts re-irradiated for local recurrence; group $A =$4 pts re-irradiated for local anastomotic recurrence; group $LN =$16 pts treated for single lymph node recurrence; group $M =$3 pts treated for metastasis). Median age, initial PSA (iPSA), pre-SRT PSA and Gleason score (GS) were 62.5 years, 9.7 ng/ml, 3.2 ng/ml and 7, respectively. In all but 4 pts, $[^{11}C]$choline-positron-emission tomography/computed tomography ($[^{11}C]$choline PET/CT) was performed. CBK-SRT consisted of re-irradiation in the case of 27 lesions and in 11, CBK-SRT was the first radiotherapy. Median dose was 30 Gy/4.5 fractions (group $P$ 30 Gy/5 fractions, group $A$ 30 Gy/5 fractions, group $LN$ 34 Gy/3 fractions, group $M$ 36 Gy/3 fractions). In 21 pts, androgen deprivation was added to CBK-SRT, and was of a median duration of 16.5 months.

Results: All patients completed planned CBK-SRT. No acute bowel toxicity was observed. Acute urinary toxicity included 2 G1 events, 2 G2 events and 2 G3 events. Late toxicity included urinary (4, 3 and 1 G1, G2, G3 events, respectively) and rectal events (2 and 1 G1 and G2 events, respectively). The median follow-up was 12 months (0-30 months). Of 33 evaluable lesions, biochemical response was observed in 27 cases. PSA stabilization was seen for 4 lesions and in 2 cases PSA progression was reported. At the time of last follow-up, disease progression was observed in 10 pts (5, 1, 3, 1 in P, A, LN and M groups, respectively). In-field progression was seen In only 2 cases progression. Median time to biochemical progression was 10.3 (range, 5.0-18.2) months. At the time of the analysis (January 2010), 14 patients were alive with no evidence of disease, 14 were alive with disease and 6 alive with unknown status of disease (non evaluable).

Conclusion: Cyberknife-based SRT is feasible approach for isolated recurrent primary, lymph node or metastatic prostate cancer, offering good in-field tumour control and low toxicity profile. Further investigation is warranted in order to identify those patients who benefit most from this treatment modality. The optimal combination with androgen deprivation should also be defined.

268 POSITIVE SURGICAL MARGIN IN THE RETROPUBIC RADICAL PROSTATECTOMY: OUR EXPERIENCE

Stefano Zambito, Giancarlo Albo, Carlo Ambruosi, Epifanio Scardino and Ottavio De Cobelli

Istituto Europeo Oncologico, via Ripamonti 435, 20141 Milano, Italy
**Background and Aim:** Positive margin rates in published series have ranged from 11% to 48%. The rate of postoperative recurrence for patients with a positive surgical margin has been variably reported between 19% and 50%. Overall, approximately 35% of patients experience failure within 10 years following RRP. The impact of margin status on patient outcome after radical prostatectomy remains in question.

**Patients and Methods:** We analysed data from 953 patients who underwent radical prostatectomy for clinically localized prostate cancer at our centre between 1999 and 2008. We excluded patients with follow-up less than 20 months. Surgical procedures were performed by different surgeons using standardised techniques. All patients included here underwent an open retroperitoneal approach. A positive margin was defined as tumour extension to the inked surface of the resected specimen. Biochemical recurrence was defined as two consecutive values of PSA >0.2 ng/ml. We examined the relationship of positive surgical margins to biochemical progression.

**Results:** The overall positive surgical margin rate was 20.5%. In 74% of patients, a single positive margin was identified, while 26% had 2 or more positive margin sites. Positive margin in the apex was present in 28% of the positive margins; 41% in patients with organ-confined tumours and 59% in those with extracapsular disease. A total of 54% and 30% of men who had a positive margin received respectively adjuvant radiotherapy (31% radiotherapy alone and 23% associated with hormonal therapy) and hormonal therapy (7% hormonal therapy alone) at a median postoperative follow-up of 49 months. Overall 14.5% had biochemical recurrence in the positive surgical margin group with median time to recurrence of 35 months; 39% had not received any treatment post surgery. In these patients, 17% had recurrence in comparison with 14% in those patients that had received at least one treatment. PSA at diagnosis in patients with recurrence was 17 ng/ml vs. 11 ng/ml in patients without recurrence. Overall, 12% of the patients had positive nodes and of these, relapses occurred in 17%. The 4-year biochemical progression-free survival rates was 91.3% for the positive surgical margin group in low-risk disease vs. 85% in the positive surgical margin group in intermediate and high-risk disease.

**Conclusion:** Our results for relapse are similar to those in the literature. Patients with low-risk disease have a favorable long-term outcome regardless of margin status and may be candidates for expectant management even with positive surgical margins, sparing them the side-effects and costs of treatment.

**MANAGEMENT OF SUSPECTED UPPER URINARY TRACT-URETHERAL CARCINOMA IN PATIENTS WITH ONLY POSITIVE URINARY CYTOLOGY: ROLE OF FISH**

**Background:** Upper urinary tract-urothelial carcinoma (UC-UUT) is a relatively uncommon malignancy characterized by an abnormal karyotype similar to that seen in bladder UC, whose frequency is increasing. Diagnostic evaluation of suspected UC-UUT was made using cytosourethroscopy, selective upper-tract urinary cytology, retrograde ureteropyelography and biopsy of suspected lesions if detectable (1). In all cases, with or without a positive imaging result, multi-target fluorescence in situ hybridization (FISH) (2) of selective upper-tract cytology was more sensitive than urine cytology alone (85.7% vs. 23.8%) confirming its utility in UUT-UC management.

**Patients and Methods:** On the basis of FISH in urine specimens in 3 patients with selective upper urinary tract washings/brushing suspected for UT-TCC and despite imaging and cystoureteroscopy negativity, the patients underwent nephroureterectomy with open approach. The first case had monosintomatic haematuria and negative anamnensis for UC-TCC. The second had received a diagnosis of bladder TCC (TaG3) ten years before, treated with endoscopic resection and BCG instillation. He underwent regular follow-up, which was negative. The third patient discovered a bladder TCC (T1G3) three years before.

**Results:** Surgery confirmed suspected diagnosis in all cases. The first case was of TCC carcinoma in situ, staging pT3N0 G3 vasc1. In the second and third cases, pathohistological analysis detected no macroscopic evidence of disease but pTis of pelvis and upper tract of ureter.

**Conclusion:** Only few studies have been targeted to establish the role of FISH in UT-TCC diagnosis. Although the use of Urovysion test, approved for bladder TCC management, shows screening of a huge number of cells for their FISH signals, it is time consuming using traditional microscopy analysis and relies on operator subjectivity. In selected cases, FISH seems to be a more harmful approach, allowing a semiquantitative evaluation, recently associated with tumour invasion and recurrence risk. The sensitivity of urinary cytology is known to correlate closely with pathological tumour grade: even if selective upper-tract cytology of high-grade lesions, including carcinoma in situ, has a reported accuracy of detection of almost 80% for well-differentiated tumours, the accuracy is only 10% to 40% (3).
In conclusion, the dilemma of positive cytology and FISH analysis without evident disease remains, but, in our little experience, surgery has shown to be an indicated treatment that always needs to be considered. Thus FISH could be considered as a complementar study to urinary cytology in all cases without macroscopic evidence of disease.

References

270 ZOLEDRONIC ACID INCREASES THE EXPRESSION OF NDRG1 GENE IN HUMAN ANDROGEN-INDEPENDENT PROSTATE CANCER PC3 CELLS

Monica Marra 1, Matteo Ferro 2, Vincenzo Altieri 2, Silvia Zappavigna 1, Gaia Giuberti 2, Daniele Santini 3, Giuseppe Tonini 3, Alberto Abbruzzese 4 and Michele Caraglia 1,

1Department of Biochemistry and Biophysics, Second University of Naples, via Costantinopoli 16, 80138 Naples, Italy; 2Institute of Urology, “Federico II” University of Naples, Dipartimento di Scienze Ostetrico-Ginecologiche, Urologiche e Medicina della Riproduzione, via Pansini 5, 80100 Naples, Italy; 3Medical Oncology, University Campus Bio-Medico, via Alvaro del Portillo 200, 00128 Rome, Italy

Background and Aim: Zoledronic acid (ZOL) is an aminobisphosphonate able to affect the isoprenylation of intracellular small G-proteins such as Ras (1). Aminobisphosphonates have a definite direct anti-tumour activity but a limited in vivo activity. N-myc downstream-regulated gene 1 (NDRG1) is a member of the NDRG gene family that is necessary but not sufficient for p53-mediated caspase activation and apoptosis and it seems to be a novel marker of androgen-induced differentiation in the human prostate cancer (2). Despite the large clinical use of zoledronic acid, its molecular targets are still not completely defined. The aim of this study was to identify new molecular targets of zoledronic acid (3) and determine if ZOL up-regulates genes involved in androgen-differentiation.

Patients and Methods: Proliferation assays on human prostate androgen-independent PC3 and DU145 and androgen-dependent LNCaP cell lines and Western blot, and real-time-PCR were carried out.

Results: As first step toward the understanding how ZOL influences the gene expression profile of human androgen-independent PC3 prostate adenocarcinoma cell line, we performed DNA microarrays to analyse the posttranscriptional modifications induced by ZOL treatment. We have identified down-modulated and up-regulated genes and checked for modulation of mRNA and of the relative encoded proteins. NDRG1 mRNA was up-regulated by ZOL in a dose-dependent manner after 48 h of treatment. Similar effects were observed at protein product levels, with an approximately 2-fold change recorded in cells treated with 50 mM ZOL, a concentration able to induce 50% growth inhibition. Interestingly, gefitinib, sorafenib and tipifarnib used at their IC50s were also able to induce changes in NDRG1 expression, but 50 mM ZOL was about 2-fold more potent. On the other hand, cytotoxic agents such as docetaxel did not have any effect. We then investigated if these effects are dependent on the inhibition of isoprenylation induced by ZOL. The addition of farnesol (FOH) or geranylgeraniol (GGOH) to ZOL-treated cells had poor effect on the regulation of NDRG1 expression induced by ZOL.

Conclusion: In conclusion, ZOL induces a strong regulation of the expression of NDRG1 at both mRNA and protein levels that appears to be dose-dependent and specific. NDRG1 changes could at least in part be independent of the inhibition of isoprenylation induced by ZOL. The study of the biological relevance of these effects on the anticancer effects of ZOL is ongoing with small interference RNA approaches.

References

271 UROTENSIN II RECEPTOR IS INVOLVED IN THE REGULATION OF MOTILITY OF PROSTATE ADENOCARCINOMA CELLS AND PREDICTS THE CLINICAL OUTCOME OF PROSTATE CANCER PATIENTS

M. Caraglia 1, M. Marra 1, R. Franco 2, A. Sgambato 3, S. Zappavigna 1, S. Striano 4, L. Marra 4, L. Gallo 6, G. Botti 2, M. Ferro 5, V. Altieri 3, E. Novellino 6, A. Molinari 7, A. Budillon 8 and P. Grieco 6
Background and Aim: Urotensin II (U-II) is a potent vasoconstrictor peptide and its receptor (UTR) was correlated with human corticoadrenal carcinoma proliferation (1). Prostate cancer is the most frequently diagnosed malignancy. Although initially effective, hormone therapy fails for the majority of initial responders, as subpopulations of tumour cells gain capacity to proliferate in an androgen-deprived environment. The Gleason score is a widely acknowledged system able to predict the aggressiveness of prostate cancer (2) but searching for homogenous criteria of evaluation is of paramount importance. In this study, the potential involvement of UT-II in human prostate tumourigenesis was evaluated both in vivo and in vitro. As a novel approach, molecular features, such as markers of cell cycle regulation and blood vessel formation, are potentially relevant prognostic factors.

Patients and Methods: We evaluated the expression and functional role of UTR on human prostate adenocarcinoma both in vivo and in vitro. Proliferation assays were performed on human prostate androgen-independent PC3 and DU145 and androgen-dependent LNCaP cell lines. Western blot analysis, RT-PCR, invasion and motility assay, scanning electron microscopy, FACS analysis, in vivo expression of UTR in 195 prostate specimens, histology and immunohistochemistry were all utilised.

Results: UTR mRNAs and protein were expressed at high levels only on androgen-dependent LNCaP cells. UTR assessment in vivo in 195 human prostate tissue samples showed that it was always expressed at intermediate intensity in hyperplastic tissues and at high intensity in well-differentiated carcinoma (Gleason 2-3). The expression was low in Gleason score 4 and absent from tumours of Gleason score 5. We evaluated the effects of an antagonist of UTR urantide on migration and invasion of LNCaP cells. Urantide induced a dose-dependent decrease of the area occupied by migrating and invading LNCaP cells whose characteristic amoeboid movement seems to be an advantageous behavior that sustains their malignancy. These effects occurred by down-regulating the autophosphorylation of FAK and the integrin surface expression on LNCaP cells. The effects on cell motility and invasiveness were likely due to the inhibition of RhoA activity induced by both urantide and shRNA UTR transfection.

Conclusion: These data suggest that UTR can be considered an additional therapeutic target and a diagnostic marker in differentiated prostate adenocarcinoma (European Patent Application EP2118130, licensed to Pharmabullet srl, Salerno, Italy).

References

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EFFICACY OF LOW-DOSE KETOCONAZOLE IN CASTRATION-RESISTANT PROSTATE CANCER: A SINGLE INSTITUTION EXPERIENCE

Cinzia Ortega1, Veronica Prati1, Valentina Coha1, Leonardo D’Urso2, Giovanni Muto2 and Massimo Aglietta1

1Medical Oncology Unit, Institute for Cancer Research and Treatment, Candiolo, Turin, Italy; 2Urology Unit, S. Giovanni Bosco Hospital, Turin, Italy

Background: The management of rising PSA in castration-resistant prostate cancer (CRPC) remains controversial. Among the options, second-line hormonal therapy is commonly used. Ketoconazole, an antimycotic that affects the synthesis of androgens and other steroids, has shown direct cytotoxic effects in prostate cancer. This retrospective study describes our experience with low doses of ketoconazole and prednisone treatment for CRPC.

Patients and Methods: From 4/2007 to 12/2009, 26 patients, with progressive CRPC who were previously treated with maximal androgen blockade received 200 mg ketoconazole orally 2 times daily, orally replacement prednisone (5 mg bid) and maintained LHRH-agonists. Performance status of all patients was ECOG0. Overall, 11/26 patients had bone and no visceral metastases, 5/26 patients had nodal metastases and 8/26 both. All patients had low tumour burden. Sixteen out of 26 patients received concomitant zoledronic acid. PSA response was defined as a >50% fall in PSA from baseline and PSA nadir was calculated. Progression was defined by objective disease progression or PSA increase of >50% above

1Department of Biochemistry and Biopysics, Second University of Naples, Naples, Italy;
2Pathology Unit, and 8Experimental Pharmacology Unit, National Institute of Tumours, Fondazione “G. Pascale”, Naples, Italy;
3Institute of General Pathology, “Giovanni XXIII” Cancer Research Center, Catholic University of Sacred Heart, Rome, Italy;
4Uro-gynecological Department, National Institute of Tumours, Fondazione “G. Pascale”, Naples, Italy;
5Department of Urology, and 6Department of Pharmaceutical and Toxicological Chemistry, University of Naples Federico II, Naples, Italy;
7Department of Technology and Health, Italian National Institute of Health, Rome, Italy
nadir or >25% above baseline. Patients were monitored clinically and with serial PSA measurements every 1-month.

Results: Median age was 74.9 (range: 59.6-82.3) years; median PSA was 64.9 (range: 4-888.2) ng/ml; median duration of the treatment was 6.18 (range: 1.6-35.3) months. Ten out 26 patients (38.5%) showed a decrease in PSA >50%, with a median duration of PSA response of 4.5 (range: 1.17-23.07). Toxicity was mild and no patients discontinued therapy because of side-effects. Three out of 26 patients had WHO G2 nausea and moderate elevated transaminases. No acute hepatitis or adrenal insufficiency was observed.

Conclusion: Our data confirm the length and duration of second-line hormonal therapy reported by the literature. Low-dose ketoconazole is an effective and well-tolerated treatment in patients with CRPC and should be considerate in the subset of patients with low-volume disease and a rising PSA level despite maximal androgen blockade.

References

273 DOCETAXEL RETREATMENT IN DOCETAXEL-PRETREATED CASTRATION-RESISTANT PROSTATE CANCER

Giuseppe Di Lorenzo1, Giovannella Palmieri1, Carlo Buonerba1, Alfredo Marinelli1, Sabino De Placido1, Vincenzo Altieri2, Matteo Ferro2, Mariano Marsicano2, Vittorino Montanaro2, Giovanni Castelluzzo2 and Antonio Tesone2

1Dipartimento di Endocrinologia ed Oncologia Clinica e Molecolare, and 2Institute of Urology, Dipartimento di Scienze Ostetrico-Ginecologiche, Urologiche e Medicina della Riproduzione, “Federico II” University, via Pansini 5, 80100 Naples, Italy

Background: Although the taxanes represent the most active chemotherapeutic agents for first-line treatment of metastatic castration-resistant prostate cancer (CRPC), all patients experience disease progression after taxane-based treatments. No prospective trials have been reported so far on docetaxel retreatment after first-line therapy with docetaxel in CRPC.

Aim: To determine the activity and tolerability of docetaxel re-treatment in CRPC failing first-line docetaxel-based therapy.

Patients and Methods: Between June 2005 and January 2009, 45 patients who respond to docetaxel and progressed after a period of biochemical remission of at least 5 months were retreated enrolled in a prospective multicentre trial. Primary end point was the biochemical response (partial response >50% prostate-specific antigen (PSA) decline, according to Bubley’s criteria) evaluated every cycle; secondary end points were toxicity, progression-free survival (PFS) and overall survival (OS).

Results: Partial PSA responses were observed in 11 patients (24.5%), 4 (25%) of whom had objective responses. The treatment was well tolerated, with grade 1-2 neutropenia, thrombocytopenia, vomiting, and peripheral neuropathy noted in 18 (40%), 11 (24.5%), 8 (17.8%), and 6 (13.3%) patients, respectively. The most common grade 3 toxicity was neutropenia, noted in 8 patients (17.8%). Median PFS was 5 months and median OS was 13 months.

Conclusion: Docetaxel retreatment preserves antitumour activity and is well tolerated in patients with pretreated CRPC. Further randomized trials are needed to confirm our preliminary results.

References

274 DOCETAXEL AND CARBOPLATIN IN DOCETAXEL-PRETREATED CASTRATION-RESISTANT PROSTATE CANCER: PRELIMINARY RESULTS

Giuseppe Di Lorenzo1, Giovannella Palmieri1, Carlo Buonerba1, Adriana Faialla1, Pasquale Rescigno1, Matteo Ferro2, Vincenzo Altieri2, Mariano Marsicano2, Vittorino Montanaro2, Giovanni Castelluzzo2 and Antonio Tesone2

1Dipartimento di Endocrinologia ed Oncologia Clinica e Molecolare, and 2Institute of Urology, Dipartimento di Scienze Ostetrico-Ginecologiche, Urologiche e Medicina della Riproduzione, “Federico II” University, via Pansini 5, 80100 Naples, Italy

Background and Aim: Prostate cancer is the second leading cause of cancer mortality among men in the U.S. To the Authors’ knowledge, there is no proven, effective, second-line therapy for...
docetaxel-refractory disease. Recent data suggest that platinum salts may be effective when combined with taxanes in metastatic castration resistant prostate cancer (cRPC). In this multicentre, single arm, phase II study, we show preliminary results of docetaxel-and carboplatin combination.

**Patients and Methods:** Patients were treated with intravenous docetaxel at a dose of 60 mg/m2 plus carboplatin at an area under the curve of 4 once every 21 days until they had either disease progression or unacceptable toxicity.

**Results:** To date, twenty-five patients have been enrolled. Therapy was tolerated reasonably well; Grade 3 leukopenia (graded according to the Common Toxicity Criteria grading system) was the most common adverse event (experienced by 48% of patients), but there was only one episode of febrile neutropenia reported. Prostate-specific antigen (PSA) declines ≥50% were noted in 6 patients (24%), and measurable responses were observed in 12%. Pain reduction and QoL improvement were observed in 6 patients (24%). The median progression-free survival was 4 months, and the median overall survival was 11 months. Patients were more likely to respond to the combination if they had previously responded to docetaxel.

**Conclusion:** In men with CRPC who developed progressive disease during or shortly after treatment with docetaxel, the addition of carboplatin resulted in modest additional activity. Taxane-refractory CRPC is an area of unmet need, and the current trial has provided evidence that platinum chemotherapy may be an important therapeutic option.

**References**


**275 ENDOVESICAL GEMCITABINE IN RECURRENT PREVIOUSLY TREATED NON-MUSCLE-INVASIVE BLADDER CANCER**

Vincenzo Altieri1, Luigi Castaldo1, Alessandra Di Lallo2, Aniello Zito3, Giovanni Ruggiero4, Riccardo Autorino1 and Massimino D’Armiento1

1Institute of Urology, “Federico II” University, Naples, Italy;
2Department of Urology, “A. Cardarelli” Hospital, Campobasso, Italy;
3Department of Urology, “A. Maresca” Hospital, Torre del Greco, Napoli, Italy;
4Department of Urology, “GEPOS” Nursing Home, Telese Terme, Italy

**Background and Aim:** The incidence of local recurrence of superficial transitional cell carcinoma of the bladder (TCCB) is reduced by intravesical adjuvant therapy after transurethral resection (TUR), but not abolished. Our aim was to evaluate the efficacy and tolerance of intravesical instillations of Gemcitabine in relapsing Ta-T1 ‘low-risk’ bladder tumours.

**Patients and Methods:** Between December 2006 and September 2008, 42 patients with non-muscle-invasive recurrent bladder cancer were enrolled in a multicentre single arm phase II study. All patients already had recurrent disease; the average relapse rate was 1.8. All patients had undergone previous endovesical chemophrophylaxis (with doxorubicin and/or mitomycin C). The last previous instillation was at least 3 months before enrollment in the study. After a complete transurethral resection, all patients underwent intravesical therapy of gemcitabine at 2000 mg/50 ml with 4 weekly instillations followed by 6 monthly instillations. Primary end-points: 12 months recurrence and progression rates. Secondary end-points: Time to recurrence, average recurrence time, time to progression, side-effects, quality of life.

**Results:** A total of 17 patients (40.5%) were recurrence-free at 12 months; 4 patients (9.5%) progressed to T1G3; the average recurrence time was 7.5 months; because of a relapse, only 27 patients completed all the scheduled treatment (induction + maintenance), but only one patient dropped out because of toxicity (chemical cystitis).

**Discussion/Conclusion:** Despite statistical significance not being reached, endovesical gemcitabine enabled 40% of patients to be free from recurrence at 12 months, in a population of previously relapsing and treated patients. A few (4) patients progressed (3 out of 4 referred from the same centre) to T1G3. Tolerance was very good, as commonly accepted. After further validation, our data support a possible therapeutic role of gemcitabine in frequently recurrent non muscle-invasive bladder cancer.

**Reference**

1 Serretta V et al: Gemcitabine in intravesical treatment of Ta-T1 transitional cell carcinoma of bladder: Phase I-II study on marker lesions. Urology 65(1) 65-69, 2005

**276 DEFINING AN mRNA EXPRESSION SIGNATURE OF GLEASON GRADE**

Kathryn L. Penney1,3, Jennifer A. Sinnott2,3, Katja Falla1,4, Yudi Pawitan4, Yujin Hoshida5, Peter Kraft1,2, Michelangelo Fiorentino6, Sven Perner7, Stephen Finn6, Stefano Calza4,
Richard Flavin6, Matthew L. Freedman5,9, Sunita Setlur10, Swen-Olof Andersson11, Neil Martin12, Philip W. Kantoff9, Jan-Erik Johansson11, Hans-Olov Adami1,4, Mark Rubin13, Massimo Loda5,6,10, Todd R. Golub5,14, Ove André10, Meir J. Stampfer1,3 and Lorelei A. Mucci1,3

1Department of Epidemiology and 2Biostatistics, Harvard School of Public Health, Boston, MA, U.S.A.; 3Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital, and Harvard Medical School, Boston, MA, U.S.A.; 4Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; 5The Broad Institute, Cambridge, MA, U.S.A.; 6Department of Pathology, Dana-Farber Cancer Institute, Boston, MA, U.S.A.; 7Department of Pathology, University of Ulm, Ulm, Germany; 8Department of Biomedical Sciences and Biotechnologies, University of Brescia, Brescia, Italy; 9Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, U.S.A.; 10Department of Pathology, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, U.S.A.; 11Department of Urology, Örebro University Hospital, Örebro, Sweden; 12Department of Radiation Oncology, Harvard Radiation Oncology Program, Boston, MA, U.S.A.; 13Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY, U.S.A.; 14Department of Pediatric Oncology, Dana-Farber Cancer Institute, Boston, MA, U.S.A.

Background: Gleason grade, a measure of prostate tumour differentiation, is a strong predictor of prostate cancer survival. We reasoned that distinct sets of genes or pathways affect or are affected by the de-differentiation process and sought to identify an mRNA signature that distinguishes high from low Gleason grade.

Patients and Methods: Using the Illumina complementary DNA (cDNA)-mediated annealing, selection, extension, and ligation (DASL) assay, we measured the mRNA expression of 6100 genes in prostate tumour tissue from patients in the Swedish Watchful Waiting cohort (N=358) and Physicians’ Health Study (PHS, N=109). We compared individuals with Gleason score ≤6 (both Gleason patterns ≤3) to those with Gleason score ≥8 (both patterns ≥4).

Results: After performing individual t-tests, 107 genes in the Swedish cohort and 2 genes in the PHS remained significant at the 0.05 level after Bonferroni correction. We built a signature using Prediction Analysis of Microarrays in the Swedish data. The most parsimonious model that minimized misclassification (18%) had 157 genes. The area under the ROC curve was 0.91. When this signature was applied to the PHS the misclassification remained low (15%) and the area under the ROC curve was 0.94. Using Gene Set Enrichment Analysis, pathways involved in cell-cycle, pyrimidine, and one-carbon metabolism were significantly (FDR<0.10) enriched in high-grade tumours, whereas propanoate metabolism was enriched in low-grade cancer cases. We identified sets of genes that differentiate low from high Gleason grade in a Swedish Cohort and replicated our findings in the PHS. When examining the first two principal components of the 157-gene model in the pooled cohorts, we noted less variation in gene expression among the low-grade than high-grade tumours - initial loss of differentiation may occur in the same genes and pathways in most individuals, but a more complete loss of normal structure can occur in different ways.

277 PROSTATE-SPECIFIC MEMBRANE ANTIGEN (PSMA) EXPRESSION AND PROSTATE CANCER SURVIVAL

Julie Kasperzyk1,2, Stephen Finn3, Whitney Hendrickson1, Richard Flavin3, Michelangelo Fiorentino3,4, Edward Giovannucci1,2, Meir Stampfer1,2, Massimo Loda3,5 and Lorelei Mucci1,2

1Department of Epidemiology, Harvard School of Public Health, Boston, MA, U.S.A.; 2Channing Laboratory, and 3Department of Pathology, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, U.S.A.; 3Department of Pathology, Dana-Farber Cancer Institute, Boston, MA, U.S.A.; 4Pathology Unit, Addari Institute of Oncology, Sant' Orsola-Malpighi Hospital, Bologna, Italy

Background: Prostate-specific membrane antigen (PSMA) is a transmembrane protein that is highly expressed in normal prostate tissue and is up-regulated in prostate tumours and metastatic disease sites. In vitro and animal studies of prostate cancer have shown a positive correlation between PSMA expression and angiogenesis, as well as a down-regulation of PSMA in the presence of testosterone and vitamin D. Overexpression of PSMA in prostatectomy specimens has been linked to biochemical recurrence of prostate cancer, though no studies have examined prostate cancer survival. The objective of the study was to assess whether high PSMA expression in tumour tissue is associated with prostate cancer-specific death and markers of tumour proliferation, apoptosis, and angiogenesis in a US-based, prospective cohort.
Patients and Methods: Archival prostatectomy and TURP tissue was collected from participants of the Physicians’ Health Study (n=347) and Health Professionals Follow-Up Study (n=558) diagnosed with prostate cancer from 1983-2004. PSMA protein expression intensity, measured across nine tissue microarrays (TMA), was visualized by immunohistochemistry and imaged using a semi-automated quantitative image analysis system (Ariol). Cell proliferation (visualized by Ki67) and apoptosis (evaluated using the TUNEL assay) were also measured in these tumour specimens; microvessel density, a measure of tumour angiogenesis, was evaluated in a subset of 414 cases. As of August 2009, 81 patients had died of prostate cancer during an average follow-up time of 11.7 years. We used Cox proportional hazards regression to calculate multivariable hazard ratios (HR) and 95% confidence intervals (CI) of lethal prostate cancer.

Results: Higher PSMA expression was noted in tumours with more advanced tumour stage and higher Gleason score. PSMA expression was associated with a non-significant increase in prostate cancer-specific death: HRQ1=1.00 (referent), HRQ2=0.85, HRQ3=1.54, HRQ4=1.55; p-trend=0.11, adjusting for age at diagnosis, year of diagnosis, and TMA. These associations were attenuated after further adjusting for PSA at diagnosis and Gleason grade: HRQ1=1.00 (referent), HRQ2=0.67, HRQ3=0.78, HRQ4=0.90; p-trend=0.81. Using Spearman’s rank correlation, PSMA expression was not significantly correlated with markers of tumour proliferation (p=0.15), apoptosis (p=0.59), or angiogenesis (p=0.20).

Conclusion: High tumour PSMA expression was modestly associated with an increased risk of prostate cancer-specific death among a cohort of 905 survivors. However, PSMA expression did not predict mortality independent of clinical factors.

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A PHASE II PROSPECTIVE STUDY OF KETOCONAZOLE IN CASTRATION-RESISTANT PROSTATE CANCER (CRPC) PATIENTS.

V. Guadalupi, M.O. Giganti, I. Testa, S. Villa, N. Nicolai, D. Biasoni, R. Salvioni, R. Valdagni, E. Bajetta and G. Procopio

Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy

Background and Aim: Treatment of advanced prostate cancer also includes the use of an androgen-suppressive hormone therapy followed at failure by chemotherapy with taxotere. Both the timing of chemotherapy and the role of the new hormonal treatment have not yet been clearly defined. The aim of the present study was to verify the efficacy of ketoconazole in patients with CRPC previously treated or untreated with chemotherapy.

Patients and Methods: From April 2008 to September 2009, 37 CRPC patients have been treated in our Institution with ketoconazole. The primary endpoint of the study was to assess the efficacy of ketoconazole in terms of biological marker response (PSA response); the secondary endpoints included the evaluation of clinical benefit, progression-free survival and the safety profile of the drug in CRPC patients previously treated or untreated with chemotherapy. Ketoconazole was administered by oral route at the dose of 200 mg every 8 hours continuous dosing until the onset of serious adverse events or disease progression. PSA value assessments were carried out every two months of therapy. The study was based on a two-step design with an interim efficacy analysis carried out on the first 14 patients accrued.

Results: The main characteristics of the patient population were: median age 75 (range 60-88) years; baseline mean PSA value 28.8 (4.3-1000) ng/ml; 27 patients previously surgically or radiotherapy treated for their primary disease; 30 patients previously challenged with least two lines of hormone therapy; 15 patients previously treated with taxotere. Biochemical responses accounted for: 2 CR (5%), 5 PR (13%), 11 SD (29%), and 13 PD (35%). Six patients are not yet evaluable for efficacy. Overall disease control has been achieved in 18 out of 37 patients (47%). Clinical benefit (RC+RP+SD>6 months) has been observed in 29% of cases (11 out of 37 patients). Among 15 patients resistant to chemotherapy, 5 (33%) cases with clinical benefit have been recorded. Treatment was feasible and well tolerated without inducing grade 3-4 adverse events. The most common grade 1-2 adverse events observed consisted of asthenia (27%), vomiting (8%), abdominal pain (8%) and diarrhoea (3%).

Conclusion: Treatment with low-dose ketoconazole is feasible and well tolerated. The efficacy was also satisfactory in patients previously treated with chemotherapy.

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A NEURAL NETWORK-BASED PREDICTIVE MODEL FOR LATE RECTAL BLEEDING AFTER 3D-CRT IN PROSTATE CANCER PATIENTS

Stefano Tomatis1, Tiziana Rancati2, Claudio Fiorino3, Vittorio Vavassori4, Gianni Fellin5, Elena Cagna6, Flora Anna Mauro7, Giuseppe Girelli8, Giovanni Frezza9 and Valdagni Riccardo8

1Department of Medical Physics, Fondazione IRCCS – Istituto Nazionale dei Tumori, Milan, Italy; 2Scientific Director’s Office, Prostate Program, Fondazione IRCCS, Milan, Italy;
Background and Aim: A model exploiting artificial neural networks (ANN) has been developed to correlate dosimetric and clinical variables to late rectal bleeding (LRB) in prostate cancer patients undergoing radical radiotherapy (RT). Our aim was to assess the utility of this model.

Patients and Methods: Data for a total of 718 men included in the AIROPROS 0102 trial were analysed. This multicentre protocol was characterized by the prospective evaluation of LRB through self-assessed questionnaires (minimum follow-up: 36 months). RT doses were between 70 and 80 Gy. Information was recorded on co-morbidity (with particular attention to hypertension, cardiovascular history, diabetes mellitus, auto-immune diseases), previous abdominal surgery (rectum-sigma resection, kidney resection, cholecystectomy, appendectomy), use of drugs (anticoagulants or antiaggregants, antihypertensives, hypoglycaemic or insulin). Rectal dose–volume histograms of the whole treatment were recorded for all patients and the percentage volume of rectum receiving more than 20, 30, 40, 50, 60, 70 and 75 Gy (named V20Gy\textsubscript{r} V75Gy) were considered. Only LRB of grade ≥2 was considered for this study (52/718 events).

The overall population was split into a train and a verify set. The train set was used to optimise the inner fitting weights of the ANN by means of a back propagation training algorithm. The verify set was used as an independent set to verify the generalisation capabilities of the model and avoid data over fitting.

Results: The previously described data formed a set of 22 variables, which was subjected to a genetic algorithm for selecting a suitable subset of input data able to better predict LRB by discarding parameters with a less predictive power. At the end of the process, six variables were identified, namely the V75Gy\textsubscript{r} continuous variable), surgery (yes/no), seminal vesicles irradiation (yes/no), use of anticoagulants (yes/no), mean rectal dose (continuous variable) and presence of haemorrhoids (yes/no). The resulting ANN classifier was able to correctly predict LRB with sensitivity and specificity values of 63% and 62%, respectively, for the overall population. Following ROC analysis, the area under the ROC curve was 0.66.

Conclusion: The results obtained with the ANN model are slightly superior to those achieved with nomograms. These models might help radiation oncologists predict RT-related late rectal morbidity and possibly avoid unnecessary worsening of quality of life, introducing treatment corrections to better tailor the treatment to the individual patient’s characteristics.

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280 [111In-DTPA-D-Phe]-OCTREOTIDE SCINTIGRAPHY IN METASTATIC HORMONE-REFRACTORY PROSTATIC ADENOCARCINOMA WITH HIGH CHROMOGRA NIN A

G. Villa\textsuperscript{1}, C. Borzone\textsuperscript{2}, G. Sambuceti\textsuperscript{1} and G. Carmignani\textsuperscript{2}

\textsuperscript{1}U.O. Medicina Nucleare e \textsuperscript{2}Clinica Urologica, A.O. San Martino di Genova, Italy

Background: Chromogranin a (CgA) is well established as a serum marker for neuroendocrine tumours and has also been associated with some non-neuroendocrine tumours, suggesting a possible role for somatostatin analogues such as octreotide in the treatment of these tumours. Neuroendocrine (NE) cells are found in hormone-refractory prostatic adenocarcinoma (HRPC), and their incidence is considered a promising prognostic indicator for the development of androgen-independent disease. NE cells are derived from non-NE prostate cancer cells and secrete factors that can act in a paracrine manner to stimulate the survival, growth, motility, and metastatic potential of prostatic carcinoma cells. Expression of CgA, neuron-specific enolase and the androgen receptor are modulated during NE differentiation and serve as molecular markers for NE cells. Neuroendocrine tumours (NETs) are visualized by different radiolabelled somatostatin analogues that bind 5 distinct somatostatin receptor types (named SSTR1-5) that show different tissue distribution. The subtypes SSTR2 and SSTR5 are the most commonly expressed in NETs. to date, the most widely used radiolabelled somatostatin analogue for planar and single photon-emission computed tomography (SPECT) is [111In-DTPA-D-Phe]-octreotide. The aim of this study was to explore the possibility, using imaging, of identifying metastatic lesions from metastatic, comparing the results with the measured plasma CgA levels in order to identify those patients who might benefit from octreotide therapy.

Patients and Methods: 111In-octreotide scintigraphy (Octreoscan, 185 MBq) was performed on 12 patients affected by HRPC, all with metastatic bone disease and with
CgA levels elevated above the normal range (>98 ng/ml (IRMA-CIS Bio Inter, Gir sur Yvette, France). A bone scan was performed two weeks prior to the investigation with OctreoScan. Chemotherapy was not administered to any patient before the octreotide scan as it reportedly reduces the number of cellular receptors for somatostatin analogues (Mencoboni et al, Anticancer Res. 2006).

Results: In 4 of 12 patients (33%), at least one metastasis was positive at OctreoScan scintigraphy. Of the 90 lesions detected with 99mTc-labelled HDP bone scintigraphy, 12 were visualized with the octreotide scan technique, thus accounting for a 13% detection rate. Two patients showed uptakes in nodes and in the liver. A significant correlation was demonstrated between uptake activity of the lesions at OctreoScan scintigraphy and level of CgA.

Conclusion: Our data suggest that in prostate cancer and its bone metastases, somatostatin receptors (subtype 2 and 5) are present and can be visualized with OctreoScan, but their expression is weak. We suppose that other conjugates should be tested for receptor-mediated therapies which are better at addressing cancer-specific somatostatin receptors present in HRPC. More promising results were obtained by different groups using Ga-68-DOTATOC PET/CT (Luboldt et al, Mol Imaging Biol 2010; Buchmann et al, Nucl Med Commun 2008). DOTATOC is a new somatostatin receptor, labelled with the positron-emitting Ga-68, characterized by a favourable spatial resolution and high sensitivity.

References

Background and Aim: Thermo-chemotherapy is a promising method for the treatment of carcinomas, particularly those on the body surface or inside cavities such as bladder. Synergo: 101® SB-TS-1 is a system of application of endocavitary microwave hyperthermia associated with intravesical administration of medications for the treatment of non muscle invasive bladder cancer. Several in vivo studies tested the combination of hyperthermia, mitomicin-C (MMC) and chemotherapy, and demonstrated the safety and efficacy of this device in the treatment of superficial bladder cancer. The aim of this work was to identify the ideal Synergo treatment defined as optimum-reached temperature and time of treatment.

Patients and Methods: A total of 108 patients affected by superficial transitional cell cancer (TCC) of the bladder were enrolled in a multicentric fashion. They underwent at least 6 weekly thermochemotherapy treatments with 40 mg MMC. We analysed all the treatment data and stratified therapies in relation to the temperature reached and the exposure time at each temperature.

Results: Heat therapy was primarily effective in preventing the recurrence of TCC in patients at first episode of illness than in patients with at least one relapse or a highly recurrent disease (p=0.002). In contrast, there were no differences in disease-free survival between patients at intermediate risk and those at high risk of relapse according to EORTC (p=0.0182). We split the treatments into three temperature groups, each with similar number of treatments (group 1, average T≤41.5°C; group 2, 41.6°C<average T≤41.9°C; group 3, average T> 41.9°C) and no differences were apparent in relapse prevention (p=0.0396). Multivariate analysis of disease-free survival between patients who underwent treatment with T≥40°C shows it as being significant in cases where the median time beyond this temperature value was ≥305 minutes; the DFS was significantly better than for patients who did not exceed this duration (p=0.039, HR 2.9). No statistically significant differences for treatments with T>41°C (p=0.631), T> 42°C (p=0.0414), and T>43°C (p=0.0837). Stratifying patients according to clinical history (the first episode, recurrent disease, a disease highly relapse) and class of risk (high-risk and intermediate risk) showed those highly diseased patients at higher risk to benefit most from treatment with T>40°C for a duration >305 minutes (p=0.007, p=0.006). Analysing the entire treatment data confirmed the ideal cut-off temperature to be 40°C: the higher the treatment time beyond this value, the greater the DFS. In particular, univariate and multivariate analyses showed that patients have a median duration ≥82% at T≥40°C have a lower likelihood of developing recurrence than patients who do not reach this value (p=0098, HR 2: 19). The analysis of the entire treatment (induction and maintenance) showed no statistically significant difference between incidence of disease recurrence and temperatures >41°C (p=0.35), >42°C (p=0.43) and >43°C (p=0.0701). There was no correlation between average temperature of treatment and DFS.

Conclusion: Our experience has helped to define that ideal intravesical thermotherapy should exceed 40°C, for a duration greater than 305 minutes in the induction phase and a median >85% above this value for the entire treatment.

283 BIOLOGICAL THERAPY FOR CONTINENCE RECOVERY IN PATIENTS PREVIOUSLY SUBMITTED TO RADICAL PROSTATECTOMY: EFFECT OF A NEW SOFTWARE-CONTROLLED DEVICE (PHYBACK PBK-2C) FOR PELVIC FLOOR REHABILITATION

Debora Marchiori, Alessandro Bertaccini, Claudio Ferri and Giuseppe Martorana

Urology Department, Alma Mater Studiorum University, Bologna, Italy

Background: Retropubic radical prostatectomy (RRP) is affected by urinary incontinence (UI) that even if temporary or mild can severely impact patients’ quality of life. Many devices have been used to stimulate muscle tone, such as electrical stimulation or biofeedback by endorectal devices. Here we present the results of our experience testing a new non-invasive device, characterized by sovrarubic skin electrodes named PBK-2C that has been demonstrated to restore muscle strength by enhancing either a local releasing of humoral factors, such as endothelial vascular growth factor (VEGF), nitric oxide and prostacycline, with anti-inflammatory effect, and increasing vessel density and pain relief [1-4].

The aim of this prospective study was to assess PBK-2C in patients affected by post radical prostatectomy incontinence.

Patients and Methods: Between May 2005 and January 2010, a total of 322 patients aged >65 years, suffering from mild to moderate incontinence (1 pad or a minipad/daily) were submitted to 10 consecutive sessions of PBK-2C therapy lasting 25 minutes each. Follow-up was at 1-6 and 12 months only for the patients who gained a benefit from this therapy. Patients who had a poor or no response were subsequently submitted to electrical stimulation.

Outcomes were defined by a subjective self-assessment as any response, improvement or complete recovery of continence.
Results: A total of 50% of the patients achieved cure and 20% a significant improvement, while 30% had no response at 1 month, respectively. At 6 months, the group of continent patients was in a stable condition; 78% of those who referred an improvement at one month gained continence status, while 22% still improved without becoming totally leak-free. At 12 months, only 5% complained of a mild leakage.

Discussion: The aim of pelvic floor muscle exercises in patients with UI is to improve the strength and coordination of peri-urethral muscles. The innovation of PBK over traditional transanal/vaginal electrical stimulation is its effect on local tissues resulting in an accelerated repair and activated microcirculations in damaged areas by generating voltage impulses instead of stimulating the muscle contraction. The non-invasive approach and the local neoangiogenic effect seem the more interesting characteristics of this device because the electrical effect is not directly on rectal mucosa and it could be worth increasing vascular density in post-ischaemic tissues such as those surrounding the external sphincter damaged by surgery.

Conclusion: The results that we obtained in post prostatectomized patients affected by moderate or mild incontinence by working with PBK-2C are very encouraging and we intend to apply this device in cases of severe incontinence.

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BENEFITS OF CONTRAST-ENHANCED SONOGRAPHY FOR THE ASSESSMENT OF INCIDENTAL TESTICULAR LESIONS: COMPARISON WITH HISTOLOGICAL FINDINGS

Massimo Valentino1, Alessandro Bertaccini2, Michele Bertolotto3, Pietro Pavlica4, Giuseppe Martorana2 and Libero Barozzi4

1 Dipartimento Emergenza/Accettazione, Chirurgia Generale e dei Trapianti, UO di Radiologia, Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, via Massarenti 9, 40138 Bologna;
2 UO Urologia, Dipartimento Chirurgie Specialistiche ed Anestesiolegia, Università di Bologna, Policlinico S. Orsola-Malpighi, via Palagi 9, Bologna;
3 UC di Radiologia dell’Università di Trieste, Ospedale di Cattinara, Strada di Fiume 447, 34149, Trieste;
4 UO di Radiologia Barozzi, Azienda Ospedaliero-Universitaria di Bologna, Policlinico S. Orsola-Malpighi, via Massarenti 9, 40138 Bologna, Italy

Aim: To quantitatively and qualitatively assess perfusion with contrast-enhanced ultrasonography (CEUS) in testicular focal lesions incidentally discovered.

Patients and Methods: From April 2006 to December 2009, all patients referred to the Radiology Unit with acute or chronic testicular discomfort underwent ultrasonography (US) with color-Doppler evaluation. Twelve patients with US findings of small testicular focal lesion were studied with CEUS and the results were compared with histological findings. In 8/12 patients, the lesion was less than 5 mm in size and nonpalpable. Enhancement data yielded perfusion measurements, including mean value over entire recorded replenishment curve, and curve slope. Time to peak value were compared with final diagnosis to define a possible correlation.

Results: Final pathological diagnosis was seminoma for 8 patients and benign tumours in 4 patients. The typical enhancement pattern of testicular tumours was hypoechogenic relative to normal parenchyma, with poor color Doppler signal in 7/12 patient. CEUS showed strong enhancement of all the lesions, with much more rapid wash-in and wash-out of ultrasonographic contrast agents of malignant lesions. The curves obtained in seminomas revealed an early arrival time and time to peak intensity in all the malignant lesions, with a significant difference in the time to enhancement, time to peak intensity, peak signal intensity, and enhancement duration between the malignant and benign tumours (p<0.001).

Conclusion: CEUS provides innovative data in the assessment of small and nonpalpable testicular focal lesions. The time–intensity curve analysis correlates well with pathological results. Therefore, this technique may be useful for the characterization of small testicular lesions incidentally discovered, and should be performed routinely to increase diagnostic confidence and help in the management of these lesions.

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ACTIVE SURVEILLANCE IN LOW-RISK PROSTATE CANCER PATIENTS: A 5-YEAR SINGLE INSTITUTION EXPERIENCE
Background: Since 2005, we have been proposing active surveillance (AS) as an alternative to radical therapies in low-risk prostate cancer (PCa) patients (pts). We here report on our 5 year experience.

Methods: Between Mar 05 and Nov 07 the AS institutional protocol (SAINT) was applied to 75 patients. Entry criteria were as follows: informed consent, initial PSA (iPSA) ≤10ng/ml, clinical stage ≤T2a (2002 TNM), GPS ≤3+3, positive biopsy cores ≤20%, max core length containing cancer ≤50%. F-up was scheduled with PSA and DRE every 3 mos, TRUS every 6 mos and re-biopsy every yr for the first 2 yrs and every 2 yrs afterwards. Pts drop out the protocol due to PSA doubling time (DT) ≤3yrs, total PSA >10ng/ml, disease upgrading and/or upsizing (upg/ups) at re-biopsy or due to PSADT, 1 due to PSA > 10 ng/ml, 6 due to protocol drop out, 9 due to anxiety is considered. To date, no unfavorable outcome has been observed. iPSA, age, stage, GPS, number of positive cores at biopsy, max core length containing cancer, PSADT and DRE did not significantly associate with PCa progression.

Conclusion: AS is feasible in selected men with early prostate cancer. Ongoing studies are trying to optimize AS protocols in order to be efficient to detect pts with disease progression: 1 yr re-biopsy is an important check, which can be used as a diagnostic clarification point. Further follow-up is needed to detect the effect of deferred treatment on disease control.

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A QUANTITATIVE ANALYSIS OF QUALITY OF LIFE IN PATIENTS UNDERGOING ACTIVE SURVEILLANCE: EARLY RESULTS

Lara Bellardita1, Andrea Luciano Spatuzzi1, Riccardo Valdagni1, Maria Olga Giganti1, Tiziana Rancati2, Nicola Nicolai2, Nicola Nicolai2, Tiziana Magnani1, Raffaella Visini1 and Simona Donegani1

1Scientific Director's Office, Prostate Program, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy;
2Department of Urology, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy;
3Department of Radiotherapy, Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy; and the Multidisciplinary Clinic Working Group; Fondazione IRCCS - Istituto Nazionale dei Tumori, Milan, Italy

Background: Active surveillance (AS) is a relatively new strategy in the management of prostate cancer (PCA) patients (pts), aimed at avoiding overtreatment. It is still not well defined whether this approach contributes to psychological distress, given that men are living with untreated PCA. The objective of this study is to detect and investigate quality of life (QoL) changes in pts undergoing AS.

Methods: Pts participating in the PRIAS protocol are evaluated. QoL data are collected by 4 psychologists of the Prostate Program multidisciplinary team (MT) through: SCL-90 (Symptom Check List-90); MINI-Mac (Mini Mental Adjustment to Cancer) and FACT-P (Functional Assessment of Chronic Illness Therapy-Prostate). QoL evaluation has been planned for a 5 yr period, through 8 screening phases. We here present a preliminary evaluation concerning 67 pts and their initial attitude towards their prostate disease and the QoL evolution (25 pts considered) at 9 mos after PRIAS acceptance.

Results: Between Nov 2007 and Feb 2010, 67 pts entered the QoL study (70% of all PRIAS pts); median age is 66 yrs, >50% of pts is still employed; >80% is married and >70% in good economic condition. 7/67 pts dropped out from PRIAS protocol (4 for histological upgrading/upsizing, 2 for PSA doubling time < 3 years and 1 due to personal choice). Preliminary analysis reveals that:

- 29% pts chose AS because of trust in the MT and 33% because of fear of toxicity related to active PCA treatments
• SCL-90 shows a normal (T-points <60) psycho-emotional condition for most pts (max deviation from normal condition for Somatization and Obsessive-Compulsive behaviour in 16% pts)
• MINI-Mac points out a good attitude towards PCa 25/67 pts completed the QoL at 9 mos after AS beginning. The preliminary analysis of these data shows that:
• 54.5% pts arose some doubts about AS during the first 3-6 mos, however only 9% still reports doubts at 9 mos
• between 3 and 9 mos (MINI-Mac results) fatalism, fighting spirit, anxious preoccupation and avoidance are reduced

FACT-P reveals positive trends when considering social/family, emotional and functional well-being, while a slight negative course is reported for physical well-being (between 3 and 9 mos)

Conclusion: Despite the limited number of pts, we think that exhaustive information, good communication between pts and clinicians and on-demand psychological support can help to cope with anxiety and uncertainty related to AS acceptance.

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