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A PROSPECTIVE, MULTICENTER EVALUATION OF PREDICTIVE FACTORS FOR POSITIVE SURGICAL MARGINS AFTER NEPHRON SPARING SURGERY FOR RENAL CELL CARCINOMA: THE RECORd1 ITALIAN PROJECT

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CONFLICT OF INTERESTS PAGE

All authors have no conflicts of interest to declare.

Micro Abstract

The early oncological goal of any partial nephrectomy is to achieve negative surgical margins. Several factors have been advocated as predictors of PSMs after NSS. In our study, age, upper pole tumor location, standard PN and Fuhrman 3-4 nuclear grade were found to be independent predictors of PSMs at multivariable analysis. Further evaluation are required to verify the oncological impact of the PSM on local and systemic recurrence.

Abstract

Purpose. To evaluate the predictors of positive margins in one of the largest available prospective multi-institutional study.

Material and Methods. We evaluated all patients who underwent nephron sparing surgery for radiologically diagnosed kidney tumors between January 2009 and December 2012 at 19 urological Italian centers (RECORd project). Preoperative and anthropometric data, co-morbidities, intra-operative and post-operative outcomes and histological findings were analysed. The negative and positive SM were compared according to the clinical and surgical variables. Multivariable logistic regression models were applied to analyse predictors of PSM.

Results. Eight hundred consecutive patients were evaluated. 761 (95.1%) and 39 patients (4.9%) achieved negative and positive surgical margins, respectively. Patients with PSMs were significantly older compared to those with negative margins (median age: 66.6 vs. 61.8 years, respectively, p=0.001). A higher incidence of PSMs was observed when NSS was performed for renal masses located in the upper pole (p=0.001). A lower rate of PSM was found in those patients treated with simple enucleation rather than standard partial nephrectomy (1.6% vs. 7.4% respectively, p<0.0001). Higher incidence of PSMs was found in Fuhrman 3-4 tumors (11.3%, p<0.0001). At multivariable analysis, age (OR: 1.04, p=0.01), upper pole tumor location (OR: 2.85, p=0.005), standard PN (OR: 3.45, p=0.004) and Fuhrman 3-4 nuclear grade (OR: 4.81, p=0.001) were found to be independent predictors of PSMs.

Conclusions. In our multi-institutional report, young age, simple enucleation, middle or lower tumor location and low grade tumor demonstrated to be independent predictors of negative surgical margins.

Introduction

Nephron-sparing surgery (NSS) has become the standard of care for the conservative management of clinically localized renal cell carcinoma (RCC) whenever technically feasible [1,2], offering equivalent oncological results [3,4] and lower renal function impairment [5,6] in comparison to radical nephrectomy. The excision of the tumor with a minimal margin of healthy parenchyma surrounding the neoplasm is currently considered the standard technique for partial nephrectomy (PN), in order to minimize the risk of positive surgical margins (PSM) and achieve optimal local cancer control [1]. In recent years, large series have reported the results of simple enucleation (SE) of renal masses showing equivalent functional and oncological results to standard PN [7]. In all cases, NSS may result in incomplete cancer removal, thus causing PSM, which may need additional follow up and can lead to a potentially increased risk of local recurrence and disease progression [8-10]. In the absence of randomized trials providing strong clinical evidences, several factors have been advocated as predictors of PSM after NSS, such as tumor size [11], pathological stage [9], Fuhrman grade [12], indication to NSS (elective vs. imperative) [11] and surgical volume [13]. Conversely, the surgical approach (open vs. minimally invasive), as well as surgical technique (Standard PN vs. SE), appear to be unrelated to margins status, according to the largest currently available evidences [7, 14-18]. We aimed to evaluate the predictors of PSM after NSS for RCC in one of the largest available prospective multi-institutional study.

Material and Methods

The Italian Registry of Conservative Renal Surgery (RECORd Project) is a 4-Year prospective observational multicenter study promoted by the Leading Urological No profit foundation Advanced research (LUNA) of the Società Italiana di Urologia (SIU). The RECORd project includes all patients who underwent conservative surgical treatment for radiologically diagnosed kidney

tumors between January 2009 and December 2012 at 19 urological Italian centers, upon the approval of the study protocol by the local ethical committee and patients acceptance of the written informed consent. Overall, information about 1055 patients were collected. In the present study only malignant lesions were analysed and 255 (24.2%) cases with benign histology were excluded. An online database was generated and it comprises 5 main folders: 1) anthropometric and preoperative data; 2) imaging, indications and co-morbidities; 3) intra-operative data; 4) post-operative data; 5) histological analysis. All data were centrally recorded on a data server. All preoperative anthropometric characteristics were collected: gender, age, body mass index (BMI). Surgical indications were defined as elective (localized unilateral RCC with healthy contra-lateral kidney), relative (localized unilateral RCC with the coexistence of co-morbidities such as diabetes, hypertension or lithiasis that could potentially affect kidney function in the future) and absolute (bilateral tumors, multiple tumors, moderate to severe chronic kidney disease or in case of neoplasia involving an anatomically or functionally solitary kidney). Performance status was assigned according to the Eastern Cooperative Oncology Group (ECOG) criteria [19]. Mode of presentation was distinguished according to the Patard classification [20]. In all patients clinical workup included at least abdominal computed tomography (CT) scans and chest X-rays. Chest and brain CT scans were obtained only when indicated by signs and symptoms. Tumors were classified according to their location on the longitudinal plane (upper pole, middle part, and lower pole) and on the transverse plane (anterior surface, posterior surface, lateral margin, medial margin, peri-hilar) of the kidney. According to the degree of depth into the kidney, tumors were also subdivided into three growth pattern categories: 1) prevalently (≥50%) exophytic, 2) prevalently endophytic (<50% exophytic), and 3) entirely endophytic. All intra-operative data including centre surgical volume, surgical approach and technique, the decision whether or not to clamp the renal vessels, type of ischemia, ischemia time, esteemed intra-operative blood loss (EBL) and operative time

were recorded. Analysing full dataset of 1055 cases, centres were divided in low- and high-volume, low and very high-volume according to the threshold of 50 and 65 interventions of NSS per year, respectively. The minimally invasive (video laparoscopic or robot assisted) and open approaches as well as the surgical technique, performed in the form of standard PN and SE, were adopted according to the centres' and surgeons' preference. Standard PN has been defined as the excision of the tumor comprising a minimal margin of healthy peritumoral renal parenchyma [7]. SE has been defined as the blunt tumor excision without removing a visible rim of parenchymal tissue around the pseudocapsule [7]. All surgical specimens were processed according to standard pathological procedures at each institution by experienced uro-pathologists. For surgical margins evaluation the specimens were fixed in 10% buffered formalin, and grossly analysed. The size, the colour, the gross aspect (solid to cystic) were recorded and the surgical margin was marked with ink. After tumor dissection, samplings were performed in order to obtain tissue blocks where tumor, healthy parenchyma, and surgical edges were comprised and further blocks with tumor, renal capsule and peritumoral fat were enclosed. The margin was considered positive when tumor tissue was marked with ink. The margin was considered negative when no-neoplastic renal tissue was observed on the inked edges. Tumors were pathologically staged according to the American Joint Committee on Cancer TNM classification [21]. The renal epithelial neoplasms classification, outlined in the 2004 WHO monograph, was used to assign the histological type [22]. The Fuhrman classification was used to assign the nuclear grade [22]. No central pathological slide review was performed. All the postoperative medical and surgical complications, occurring within 30 days, were recorded. The severity of surgical complications was graded according to the modified Clavien system [23].

Statistical Analysis

Categorical variables were reported as number and percentage. Continuous variables were reported as mean (SD) or as median and IQR, as appropriate. The Student t test and the Mann-Whitney U test were used to compare continuous variables and the Pearson's chi square test was used to compare categorical variables. The negative and positive SM were compared according to the clinical and surgical variables. Multivariable logistic regression models considering factors that were significantly related to SM status at univariable analysis were applied to analyse predictors of PSM. Statistical significance in this study was set as $p \leq 0.05$. All reported p values are two-sided. Analyses were performed with SPSS version 20.0 (SPSS Inc, Chicago, IL, USA).

Results

Overall, 800 patients were evaluated. Table 1 reports the clinical characteristics of the entire cohort according to the surgical margin status: 761 (95.1%) achieved negative surgical margins (NSM), while 39 patients (4.9%) had PSMs at the final pathological examination. Patients with PSM were significantly older compared to those with NSM (median age: 66.6 vs. 61.8 years, respectively, p=0.001). Conversely, no statistically significant differences were found among patients with positive and negative margins in terms of gender, BMI, indication to NSS (elective/relative vs. imperative), symptoms at the time of diagnosis, ECOG performance status, number of lesions, clinical stage and tumor side. Median (IQR) clinical diameter was 3.3 (2.3-4) cm and 3.2 (2.0-3.9) cm in those patients with NSM and PSM, respectively (p=0.6). A significantly higher incidence of PSMs was observed when NSS was performed for renal masses located in the upper pole compared with mesorenal or lower pole tumors (p=0.001). On the contrary, the tumor growth pattern (exophytic/endophytic) and localization (anterior, posterior, medial, lateral) did not significantly affect the surgical margins status.

Table 2 summarizes the most relevant intra-operative data. The incidence of PSMs was significantly lower after minimally invasive NSS compared to open procedures (3.0% vs. 6.2% respectively, p=0.04). According to the adopted surgical technique, a lower rate of PSM was found in those patients treated with SE rather than standard PN (1.6% vs. 7.4% respectively, p<0.0001). Conversely, margin status was not significantly affected by the centre's surgical volume, considering both low- vs. high-volume centres and low- vs. very high-volume centres. Margin status was not significantly affected by operative time, EBL, hilar clamping, ischemia time and intra-operative complications. Furthermore, no significant differences in terms of tumor histotype, pathological diameter and pathologic tumor evaluation (intra-capsular vs. extra-capsular) were found among patients with negative and positive surgical margins, respectively (Table 3); interestingly, the incidence of PSM was higher in Fuhrman 3-4 tumors when compared to those with lower nuclear grade (11.3% vs. 3.1% respectively, p<0.0001, Table 3).

Results from multivariable logistic regression analysis considering factors that were significantly related to SM status are summarized in Table 4. Age (OR: 1.04, p=0.01), upper pole tumor location (OR: 2.85, p=0.005), standard PN (OR: 3.45, p=0.004) and Fuhrman 3-4 nuclear grade (OR: 4.81, p=0.001) were found to be independent predictors of PSMs. Conversely, the surgical approach (open vs. minimally invasive) was not an independent variable (OR: 1.36, p=0.48) at multivariable analysis.

Discussion

When performing NSS for RCC, the complete removal of the tumor and the avoidance of PSMs is of paramount importance, to reach optimal long-term oncological control [1]. Currently,

the incidence of PSM after elective NSS ranges from 0% to 7% [10]. Our series report an overall incidence of PSMs of 4.9%, which is comparable to the results of other NSS series, regardless of the surgical approach (open vs. minimally invasive) [9]. To our knowledge, this is one of the largest, multi-institutional prospective study evaluating the predictors of positive surgical margin and it is the first that included both open and minimally invasive NSS in the analyses.

In our multi-institutional study, the PSMs rate was slightly higher in those patients treated with open rather than minimally invasive (either laparoscopic or robot-assisted) NSS at univariable analysis (6.2% vs. 3.0%, respectively, p=0.04). Conversely, the surgical approach failed to confirm its independent role as predictor of PSM at multivariable analysis (Table 4). In a recent matched-pair analysis comparing open and robot-assisted PNs from 23 centres, Ficarra et al. found no significant difference in PSM rate among open (5.5%) and robot-assisted (5.7%) PN (p=0.98) [16]. Similarly, Springer and coworkers, showing results from a retrospective single-institutional study of 340 open and laparoscopic PN for cT1 RCC, found comparable incidence of PSMs between the two groups (1.7% vs. 1.2%, p=0.09) [24].

It appears still controversial whether the age at the time of surgery could be a predictor of PSMs. In our report, the rate of positive margins were found to be slightly higher in those patients older than 65 years, even if this data was not statistically significant at univariable analysis (Table 1, p=0.07). Conversely, at the multivariable logistic regression analysis, age as continuous value demonstrated to be significant and independent predictor of PSMs (OR: 1.04, p=0.01, Table4). Such result could be easily explained. Basically, in older patients renal function could be much more impaired because of medical or cardiovascular co-morbidities than younger counterparts. In this scenario, urologists attempt to spare as much healthy parenchyma as possible during NSS, in order to minimize the loss of postoperative renal function, thus increasing the risk of PSMs. This result is different than other reported in Literature. Ani et al. found that age was not

independently associated with the higher risk of PSMs at multivariable analysis (OR: 0.99, p=0.3) [9]. Similarly, Yossepowich and co-workers did not found any correlation between age and surgical margin status at both univariable (OR: 1, p=0.77) and multivariable (OR: 1, p=0.81) analysis [11].

Despite the previous, historical recommendations to remove at least 1 cm of normal appearing renal parenchyma around the tumor in order to ensure negative margins [25], the current indications for NSS have been progressively changed: indeed, according to the recognized oncological safety of NSS even for T1b RCC [3, 26] and to the need for preservation of as much functioning healthy parenchyma as possible to minimize the loss of renal function [27], NSS has moved from maximal parenchymal resection to a minimal tissue removal [20]. In this scenario, several non-randomized studies demonstrated the oncological safety of simple tumor enucleation in comparison to standard PN for the treatment of cT1 RCC, with a quite lower incidence of PSMs with respect to those observed after standard PN [7,28,29]. Minervini et al, in the retrospective SATURN study, found a PSM rate of 0.2% and 3.4% after SE and traditional PN, respectively ($p<0.001$) [7]. Similarly, in our study the incidence of PSM was significantly lower in those patients treated with SE ($p<0.0001$, Table 1), even at multivariable analysis the surgical technique was confirmed as an independent of PSM (OR: 3.45, p=0.004, Table 4). The reason of such results, however, should be carefully analyzed. In fact, the blunt enucleation of the tumor along the inflammatory pseudocapsule, rather than a traditional resection of the surrounding healthy parenchyma, could allow to a better respect the natural cleavage plane, avoiding entering within the mass in case of irregular shape and leaving positive margins behind. Moreover, an extensive and established experience of surgeons performing SE in this series could be another possible explanation of such result. Therefore, present data should be regarded at least as a proof of non-inferiority in terms of local cancer control of SE versus standard PN but prospective randomized series are awaited to shed light on this oncological issue.

Longitudinal location (polar vs. mesorenal), exophytic, hilar location and clinical dimension of the tumor (parameters that belong to the PADUA classification) [30] could be significant pre-operative factors able to predict the complexity of the NSS and could be related to the risk of complications as well as of PSM. It seems reasonable that, the higher is the surgical complexity, the more challenging is to achieve local control and complete resection. In our study, the rate of PSM after NSS was significantly higher only for upper polar tumors, rather than mesorenal or lower polar lesions (9.3% vs. 2.6% vs. 3.8%, respectively, p=0.001). Moreover, the polar location (superior vs. mesorenal/inferior) demonstrated to be an independent predictor of PSM at multivariable analysis (OR: 2.85, p=0.005, Table 4). A worse exposure of the surgical field in the upper pole tumors in both right and left side tumors may render the resection of the tumor more difficult, especially when performing minimally invasive procedures. To our knowledge, no previous series reported a correlation between tumor polar location and the risk of PSM. Nevertheless, in the present series, the rate of PSM was not influenced by the tumor growth pattern, the hilar location and the rim location. This agrees with the data reported by other recently published papers. Khalifeh and coworkers, in a multi-institutional, retrospective study of 943 consecutive robot-assisted PN, showed that surgical margin status was not significantly compromised by the hilar location, endophytic rate and the tumor complexity according to the nephrometric score [7].

Currently, there are no convincing correlations among tumor size, clinical stage and incidence of PSM after NSS. Yossepowitch et al. retrospectively evaluated a cohort of 1390 patients with a mean tumor diameter of 3.5 cm, demonstrating that increasing tumor size was associated with a lower incidence of positive margins both at univariate and multivariate analyses (P=0.05) [10]. Conversely, comparable incidence of PSM between patients with tumors ≤ 4 cm and > 4 cm has been found in other retrospective open and laparoscopic series [31,32]. In a recent

report from the Ontario Cancer Registry evaluating 788 open and laparoscopic PNs, Ani et al. found significant correlations between increasing tumor size and margin status, with a 4-fold higher risk of PSM in pT1b tumors (p=0.002) [8]. In our study the mean tumor dimension and the clinical and pathological stage failed to correlate with PSM status. This finding corroborate the oncological safety of NSS even in cT1b renal tumors, regardless of the surgical approach and technique adopted.

The correlation between high nuclear grade and the incidence of PSM still remains controversial. Intuitively, the presence of more aggressive and infiltrative cancer with irregular shape and infiltrative growth pattern may render the tumor dissection more challenging thus enhancing the incidence of PSM. Higher nuclear grade and more unfavourable cancers have been shown to be related to the complexity of the renal tumors, according to their anatomical and topographic characteristics [33]. In the present study, positive margins were significantly higher in patients with Fuhrman 3-4 RCC compared to those with nuclear grade 1-2 ($p<0.0001$). Furthermore, higher tumor grade was found to be an independent predictor of PSM at multivariate analysis (OR: 4.81, p=0.001, Table 4). Bensalah et al, retrospectively evaluated a cohort of 775 patients treated with PN and found comparable results: a greater frequency of high-grade tumors was found in patients with PSMs rather than in those with NSM (30% vs. 19.4%, respectively) [11]. Contrasting results have been recently reported in other studies [8], in which nuclear grade was neither associated nor independent predictor of PSMs.

In literature, the surgical indication (elective/relative vs. imperative) demonstrated to play a role in the prediction of PSMs after partial nephrectomy. Yossepowitch et al, after adjusting for clinical tumor size, found that the imperative indication was an independent predictor of PSM [10]. Conversely, in the present study the incidence of PSM was not statistically influenced by the surgical indication. Indeed, even if the rate of positive margins was quite higher in patients treated

with imperative NSS (8.5%) compared to those with elective procedure (4.6%), this finding did not reach the statistical significance (p=0.18). However, the low number of patients treated with imperative indications in our report could have reduced the statistical power of our analysis.

The actual clinical and oncological impact of PSMs after NSS is at least controversial. Indeed, according to the currently available evidences [10], the presence of a positive margin could lead to an higher risk of local recurrence in the ipsilateral kidney, especially in those patients with high grade tumors. Conversely, at intermediate- and long-term follow-up, the metastatic progression and cancer specific mortality rates were found to be comparable among patients with positive or negative surgical margins [10].

We believe that the high number of patients treated and of variables analyzed, as well as the prospectively maintained database, are the main strengths of our study. Moreover, its multicenter nature might increase the external validity of the data compared with the single-center, single-surgeon setting and provide a valid snapshot of the incidence and predictors of PSM in a European country in the last 4 years. As study limitations, the absence of a central pathological review, which would have influenced the interpretation of the specimens and the final diagnosis of surgical margin status, and the lack of assessment of the surgical complexity according to nephrometric scores represent the most important limitations of the present paper.

Conclusion

The early oncological goal of PN is to achieve negative margins. In our multi-institutional report of open and minimally invasive NSS, the overall rate of PSM is 4.9%. Older age, standard PN technique, upper polar tumor location and high grade tumor are all independent predictors of

PSMs. Further evaluation and follow-up is required to verify the oncological impact of the PSM on local and systemic recurrence.

Clinical Practice Points

- The excision of the tumor with a minimal margin of healthy parenchyma surrounding the neoplasm is currently considered the standard technique for partial nephrectomy (PN), in order to minimize the risk of positive surgical margins (PSM) and achieve optimal local cancer control
- This study (RECORd project) includes all patients who underwent conservative surgical treatment for radiologically diagnosed kidney cancers between January 2009 and December 2012 at 19 urological Italian centers.

- Results from multivariable logistic regression analysis showed that age (OR: 1.04, p=0.01), upper pole tumor location (OR: 2.85, p=0.005), standard PN (OR: 3.45, p=0.004) and Fuhrman 3-4 nuclear grade (OR: 4.81, p=0.001) were found to be independent predictors of PSMs.
- Conversely, the surgical approach (open vs. minimally invasive) was not an independent variable (OR: 1.36, p=0.48) at multivariable analysis.
- Further evaluation and follow-up is required to verify the oncological impact of the PSM on local and systemic recurrence.

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Table 1

Clinical characteristics of the entire cohort of 800 patients according to SM status.

Preoperative data		**Negative SM (n=761; 95,2%)**		**Positive SM (n=39; 4,8%)**		**P**
Gender, n. %	Male	524	94.9%	28	5.1%	0.70
	Female	237	95.6%	11	4.4%	
Age, year	<65 yrs n %	406	96.4%	15	3.6%	0.07
	≥ 65 yrs n %	355	93.7%	24	6.3%	
	Mean SD	61.8	12.6	66.6	8.8	0.001
BMI, median (IQR)		28.7	24.3-28.5	26.3	23.8-27.7	0.29
Indication, n. %	Elective/Relative	707	95.4%	34	4.6%	0.18
	Absolute	54	91.5%	5	8.5%	
Symptoms at diagnosis, n. %	Asymptomatic	598	95.3%	29	4.7%	0.71
	Symptomatic	163	94.4%	10	5.6%	
ECOG, n. %	0	531	95.7%	24	4.3%	0.28
	≥1	230	93.9%	15	6.1%	
Number of lesions	Single	727	95.0%	38	5.0%	0.57
	Multiple	34	97.1%	1	2.9%	
Clinical diameter, median, IQR		3.3	2.3-4.0	3.2	2.0-3.9	0.60
Clinical T, n. %	T1a	565	95.6%	30	4.4%	0.93
	T1b	176	95.7%	8	4.3%	
	T2	20	95.2%	1	4.8%	
Tumor side, n. %	Right	416	54.7%	19	48.7%	0.35
	Left	345	45.3%	20	51.3%	
Tumor growth pattern, n. %	≥50%Exophytic	577	94.4%	34	5.6%	0.22
	<50%Exophytic	167	97.7%	4	2.3%	
	Entirely endophytic	17	94.4%	1	5.6%	
Tumor site, n. %	Polar sup.	206	90.7%	21	9.3%	0.001
	Mesorenal	303	97.4%	8	2.6%	
	Polar inf.	252	96.2%	10	3.8%	
Tumor localization, n. %	Peri-hilar	38	95.0%	2	5.0%	0.87
	Anterior face	230	94.3%	14	5.7%	
	Posterior face	217	96.0%	9	4.0%	
	Medial margin	68	97.2%	2	2.8%	
	Lateral margin	207	94.5%	12	5.5%	

Table 2

Intra-operative data of the entire cohort of 800 patients according to SM status.

Intraoperative data		**Negative SM (n=761; 95,2%)**		**Positive SM (n=39; 4,8%)**		**P**
Centre volume, n. %	High	559	95.1%	29	4.9%	0.90
	Low	202	95.3%	10	4.7%	
Centre volume, n. %	Very high	322	42.3%	20	51.3%	0.27
	Low	439	57.7%	19	48.7%	
Approach, n. %	Open	442	93.8%	29	6.2%	0.04
	Minimally invasive	319	97.0%	10	3.0%	
Technique, n. %	Simple Enucleation	306	98.4%	5	1.6%	<0.0001
	Standard PN	426	92.6%	34	7.4%	
Operative time, median IQR		130	105-175	147	105-185	0.49
EBL (ml), median IQR		190	100-300	200	100-300	0.77
Hilar clamping, n. %	Not performed	278	94.2%	17	5.8%	0.37
	Performed	483	95.6%	22	4.4%	
Ischemia time, min,median IQR		16	13-20	15	11-21	0.22
Intraoperative complications, n. %	Present	45	93.7%	3	6.3%	0.64
	Absent	716	95.2%	36	4.8%	

Table 3

Pathological characteristics of the entire cohort of 800 patients according to SM status.

Pathological data		**Negative SM (n=761; 95,2%)**		**Positive SM (n=39; 4,8%)**		**P**
Histotype, n %	Clear cell RCC	550	95.3%	27	4.7%	0.75
	Papillary RCC	119	96.7%	4	3.3%	
	Chromophobe RCC	77	96.2%	3	3.8%	
	Unclassified RCC	5	71.4%	2	28.6%	-
	*Other renal tumors**	10	76.9%	3	23.1%	-
Pathological diameter, median IQR		3,0	2.4-4.0	3.0	2.2-4.0	0.84
Nuclear grade, n %	1-2	534	96.9%	17	3.1%	<0.0001
	3-4	134	88.7%	17	11.3%	
Pathologic tumor evaluation, n.%	Intracapsular	702	95.5%	33	4.5%	0.07
	Extracapsular	56	90.3%	6	9.7%	

* Other renal tumors: 8 Multilocular cystic RCC, 1 Sarcomatoid RCC, 2 Translocation carcinoma (MITF/TFE family translocation-associated carcinoma), 1 Mucinous tubular and spindle cell carcinoma, 1 Thyroid-like follicular carcinoma of the kidney

Table 4
Multivariable logistic regression models accounting for the significant predictors of PSM.

Multivariate analysis for PSM	**OR**	**CI 95%**	**P**
Age, year continuous variable	1.04	1.00-1.08	0.01
Tumor site Polar superior lesion vs. others	2.85	1.37-5.87	0.005
Technique Standard PN vs. SE	3.45	1.66-7.19	0.004
Approach Open approach vs. minimally invasive	1.36	0.58-3.19	0.48
Nuclear grade 3-4 vs. 1-2	4.81	1.63-14.16	0.001