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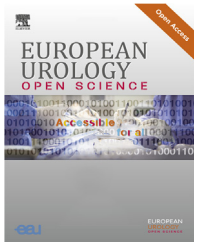

European Association of Urology

Urothelial Cancer

Radical Nephroureterectomy Tetrafecta: A Proposal Reporting Surgical Strategy Quality at Surgery

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Abstract

Background: Standardized methods for reporting surgical quality have been described for all the major urological procedures apart from radical nephroureterectomy (RNU).
Objective: To propose a tetrafecta criterion for assessing the quality of RNU based on a consensus panel within the Young Association of Urology (YAU) Urothelial Group, and to test the impact of this tetrafecta in a multicenter, large contemporary

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cohort of patients treated with RNU for upper tract urothelial carcinoma (UTUC).
Design, setting, and participants: This was a retrospective analysis of 1765 patients with UTUC treated between 2000 and 2021.
Outcome measurements and statistical analysis: We interviewed the YAU Urothelial Group to propose and score a list of items to be included in the "RNU-fecta." A ranking was generated for the criteria with the highest sum score. These criteria were applied to a large multicenter cohort of patients. Kaplan-Meier curves were built to evaluate differences in overall survival (OS) rates between groups, and a multivariable logistic regression model was used to find the predictors of achieving the RNU tetrafecta.
Results and limitations: The criteria with the highest score included three surgical items such as negative soft tissue surgical margins, bladder cuff excision, lymph node dissection according to guideline recommendations, and one oncological item defined by the absence of any recurrence in $\leq$12 mo. These items formed the RNU tetrafecta. Within a median follow-up of 30 mo, 52.6% of patients achieved the RNU tetrafecta. The 5-yr OS rates were significantly higher for patients achieving tetrafecta than for their counterparts (76% vs 51%). Younger age, lower body mass index, and robotic approach were found to be independent predictors of tetrafecta achievement. Conversely, a higher Eastern Cooperative Oncology Group score, higher clinical stage, and bladder cancer history were inversely associated with tetrafecta.
Conclusions: Herein, we present a "tetrafecta" composite endpoint that may serve as a potential tool to assess the overall quality of the RNU procedure. Pending external validation, this tool could allow a comparison between surgical series and may be useful for assessing the learning curve of the procedure as well as for evaluating the impact of new technologies in the field.
Patient summary: In this study, a tetrafecta criterion was developed for assessing the surgical quality of radical nephroureterectomy in patients with upper tract urothelial carcinoma. Patients who achieved tetrafecta had higher 5-yr overall survival rates than those who did not.

1. Introduction

The standard treatment for high-risk upper tract urothelial carcinoma (UTUC) is represented by radical nephroureterectomy (RNU), eventually followed by adjuvant chemotherapy in case of locally advanced or non–organ-confined disease at surgery [1,2]. RNU is a complex surgical procedure in which the technical quality of each step may directly impact oncological outcomes and survival after surgery [1,3,4].

In recent years, composite measures of surgical quality (the so-called "fecta") have been developed aiming to provide standardization for reporting outcomes of surgery. Trifecta and pentafecta have already been used for most major uro-oncology procedures such as radical prostatectomy [5,6], partial nephrectomy [7], and more recently, radical cystectomy [8,9].

For RNU, it is strictly recommended to follow several surgical steps that have been demonstrated to improve oncological outcomes after surgery [1]. Among these are bladder cuff en bloc excision with the ureter and the kidney [3,10], nephrectomy (without entering the urinary tract and avoiding direct contact between instruments and tumor), and lymph node dissection (LND) especially in case of muscle-invasive disease [4]. Although some quality indicators have already been discussed for the management of high-risk UTUC [11], a standardized method for assessing the surgical quality of RNU for UTUC has not yet been validated.

Indeed, nowadays, stakeholders and patients are critically interested in the quality of surgery delivered and are potentially inclined to use imperfect quality measures rather than none. Thus, urologists should develop quality of surgery indicators that can accurately characterize the quality of care rather than have grading based on unclear standards.

Therefore, our study aimed to develop and propose a tetrafecta for assessing the overall surgical quality during RNU for UTUC and to test its oncological impact in a multicenter, large contemporary cohort of patients.

2. Patients and methods

2.1. Study population

We reviewed an initial cohort of 2421 patients with clinically non-metastatic UTUC treated with RNU at 28 international referral centers between 1985 and 2021. Only records complete for surgical, pathological, and oncological outcomes were retained for the purpose of the study. The final cohort included 1765 UTUC patients treated with RNU at 25 academic centers between 2000 and 2021; we excluded patients

treated before 2000 to obtain a final contemporary cohort of patients with adequate follow-up. RNU was performed with an open, a laparoscopic, or a robotic approach. Bladder cuff excision (BCE) technique was not standardized, and LND was performed at the discretion of the surgeon. All RNU specimens were analyzed by experienced uropathologists at each center and were staged based on the TNM classification, while tumor grade was based on the 2004/2016 World Health Organization classification. Owing to the retrospective and multicentric nature of the study, follow-up was not standardized. However, patients were generally followed in accordance with international guidelines [1]. Follow-up usually consisted of physical examination, urinary cytology, abdomen computed tomography scan or abdomen magnetic resonance imaging, and chest radiography every 3–6 mo during the first 12 mo following RNU, every 6 mo between the 2nd and the 5th year after surgery, and yearly thereafter. Bladder cystoscopy was generally performed after 3 and 9 mo from surgery, and yearly thereafter.

2.2. Panel selection and tetrafecta development

We conducted an online interview among a selected panel of experts in urothelial cancer (members of the Young Association of Urology [YAU] Urothelial Cancer Group, $n = 24$).

We asked the panel to propose a list of items (between three and five) to be used as markers of quality of RNU and, therefore, to be included in the "RNU-fecta." The panel had to give 1–5 points, with 5 indicating the most important and 1 the least important criteria for each of the proposed items. Given the results of the interview, a ranking of items was generated based on the highest sum score.

2.3. Statistical analysis

Categorical variables were reported as absolute numbers and percentages. Continuous variables were reported as medians and interquartile ranges (IQRs). Chi-square and Kruskal-Wallis tests were performed for categorical and continuous variables, respectively, to compare the populations. Kaplan-Meyer curves were built to evaluate differences in overall survival (OS) rates between patients who achieved the RNU tetrafecta and those who did not. The log-rank test was used to determine the statistical difference between groups. Univariable and multivariable Cox regression models were built to evaluate the impact of tetrafecta achievement on OS after adjusting for the effect of standard prognosticators such as age, gender, body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) score, preoperative and pathological tumor characteristics, surgical approach, and use of perioperative chemotherapy. Multivariable logistic regression analyses were performed to evaluate the presence of possible predictors of meeting the RNU tetrafecta. Data were analyzed using STATA 16 (Stata Corp., College Station, TX, USA), and a p value of <0.05 was considered statistically significant.

3. Results

According to the experts' panel, the most selected criteria to be used as markers of surgical quality were the following:

1. Negative soft tissue surgical margins (STSMs; median score: 5 points).
2. BCE (median score: 5 points).
3. LND according to guideline recommendations (defined as LND to be performed in case of muscle-invasive disease and optional in case of non–muscle-invasive disease; median score: 4 points).
4. Absence of recurrence (intra- or extravesical) in ≤12 mo (median score: 3 points).
5. Postoperative intravesical instillation (median score: 5 points).

Owing to the long study period (2000–2021) and the fact that the use of postoperative intravesical instillation was recommended starting from 2013 [12,13], this item could not be included in the RNU-fecta. Based on these considerations, negative STSMs, BCE, LND according to guideline recommendations, and absence of any recurrence in ≤12 mo (both intra- and extravesical) formed the final RNU tetrafecta.

Overall, 928 (52.6%) patients met the RNU tetrafecta, with negative STSMs being the most achieved item of the tetrafecta (92.6%), followed by BCE (88.1%), LND according to guideline recommendations (86.9%), and absence of any recurrence in ≤12 mo (70.8%; Fig. 1). Descriptive preoperative patients' characteristics are depicted in Table 1. Patients achieving RNU tetrafecta were younger than their counterparts (median age of 69 vs 72 yr, $p < 0.001$), with lower BMI ($p = 0.004$), American Society of Anesthesiologists score ($p < 0.001$), and ECOG score ($p < 0.001$). Moreover, patients who met the RNU tetrafecta were mostly treated in the first half of the study period ($p = 0.03$) and underwent RNU for organ-confined disease (≤cT2) in a higher proportion of cases ($p < 0.001$). Surgical and pathological characteristics of the enrolled population are reported in Supplementary Table 1. Patients achieving the RNU tetrafecta were mostly treated with a minimally invasive approach ($p < 0.001$), and displayed a lower tumor stage and grade and a lower rate of lymph node involvement at final pathology compared with their counterparts (all $p < 0.001$).

Within a median follow-up of 30 mo (IQR 12–62), 516 (29.2%) patients developed an intravesical recurrence, 354 (20%) experienced an extravesical recurrence, 496 (28.1%) died of any cause, and 417 (23.6%) died due to UTUC. The 5-yr OS rates for patients who achieved the RNU tetrafecta and those who did not were 76% and 51%, respectively ($p < 0.005$; Fig. 2). At both univariable (hazard ratio [HR] 0.41, 95% confidence interval [CI] 0.35–0.50, $p < 0.001$) and multivariable (HR 043, 95% CI 0.28–0.69, $p < 0.001$) Cox-regression analyses that adjusted for the effect of standard prognosticators, tetrafecta achievement was independently associated with OS (Table 2). The inclusion of tetrafecta in a multivariable model for the prediction of OS based on the variables included in Table 2 improved the discrimination of the model (C-index) from 0.76 to 0.78. At multivariable logistic regression analyses that accounted for the effect of standard prognosticators, younger age (odds ratio [OR] 0.97, $p = 0.01$), lower BMI (OR 0.92, $p < 0.001$), and the robotic approach (OR 5.61, $p = 0.013$) were found to be independent predictors of achieving the RNU tetrafecta. Conversely, a history of bladder cancer (OR 0.66, $p = 0.038$), an ECOG score of 3 (OR 0.20, $p = 0.04$), and clinical muscle-invasive disease (cT2-cT4) significantly diminished the probability of meeting the RNU tetrafecta (Table 3).

4. Discussion

Given the rarity of UTUC, its high recurrence rate, and the poor long-term oncological outcomes after RNU, there is

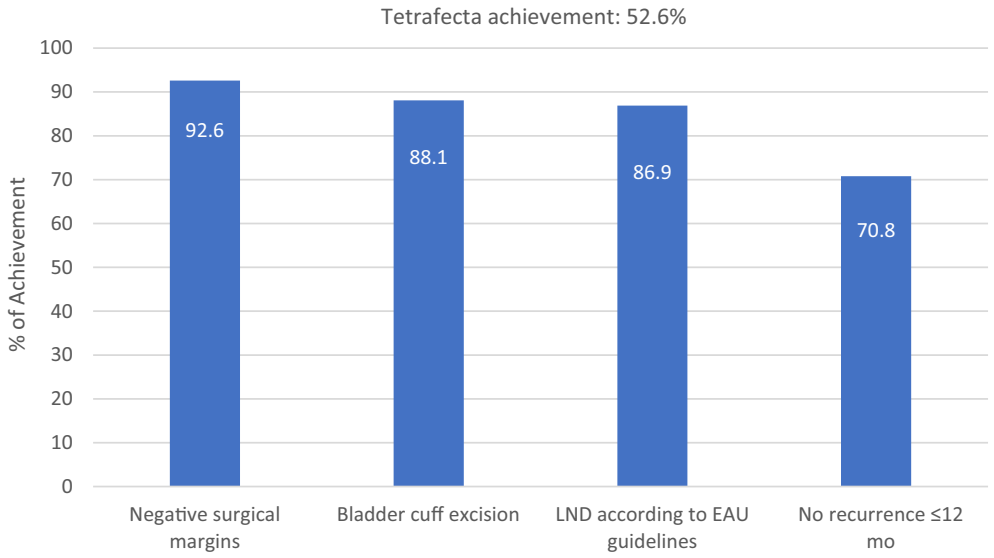

Fig. 1 – Graphical representation of the tetrafecta achievement among 1765 patients with clinical nonmetastatic upper tract urothelial carcinoma treated with radical nephroureterectomy between 2000 and 2021. EAU = European Association of Urology; LND = lymph node dissection.

Table 1 – Descriptive preoperative characteristics of the 1765 patients with clinical nonmetastatic upper tract urothelial carcinoma treated with radical nephroureterectomy between 2000 and 2021

Variables	Total	Tetrafecta achievement		*p* value
		Yes	No	
Number of patients	1765	928 (53)	837 (47)	
Age (yr), median (IQR)	70 (63–77)	69 (61–76)	72 (65–78)	0.0001
Gender, *n* (%)				
Female	510 (28)	269 (29)	241 (29)	0.9
Male	1255 (71)	659 (71)	596 (71)	
Year of surgery, *n* (%)				0.03
2000–2005	118 (7)	67 (7)	51 (6)	
2006–2010	315 (18)	174 (19)	141 (17)	
2011–2015	533 (30)	298 (32)	235 (28)	
2016–2021	799 (45)	389 (42)	410 (49)	
BMI (kg/m^2), median (IQR)	26 (23–28)	25 (23–28)	26 (23–29)	0.004
ASA score, *n* (%)				<0.001
1	122 (9)	91 (13)	31 (4)	
2	686 (48)	372 (51)	314 (45)	
3	550 (39)	247 (34)	303 (44)	
4	62 (4)	16 (2)	46 (7)	
ECOG score, *n* (%)				<0.001
0	630 (50)	349 (55)	281 (45)	
1	441 (35)	198 (31)	243 (39)	
2	158 (13)	78 (12)	80 (13)	
3	27 (2)	7 (1)	20 (3)	
Smoking status, *n* (%)				0.07
Never smoker	554 (37)	298 (37)	256 (37)	
Former smoker	565 (38)	284 (35)	281 (40)	
Current smoker	383 (25)	222 (28)	161 (23)	
Preoperative endoscopic assessment, *n* (%)				0.1
None	976 (59)	522 (60)	454 (57)	
Ureteroscopy	93 (6)	39 (5)	54 (7)	
Ureteroscopy + biopsy	589 (36)	306 (35)	283 (36)	
Preoperative hydronephrosis, *n* (%)	797 (47)	403 (45)	394 (48)	0.2
Tumor localization, *n* (%)				0.02
Pelvicalyceal	751 (49)	392 (51)	359 (47)	
Ureter	517 (33)	263 (34)	254 (33)	
Both	275 (18)	117 (15)	158 (20)	
Tumor multifocality, *n* (%)	290 (19)	143 (19)	147 (20)	0.6
Clinical tumor stage, *n* (%)				<0.001
cTa	189 (17)	102 (21)	87 (14)	
cTis	16 (1)	5 (1)	11 (2)	
cT1	415 (37)	224 (45)	191 (30)	
cT2	289 (25)	88 (18)	201 (31)	
cT3	178 (16)	62 (13)	116 (18)	
cT4	49 (4)	14 (3)	35 (5)	

ASA = American Society of Anesthesiologists; BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; IQR = interquartile range.

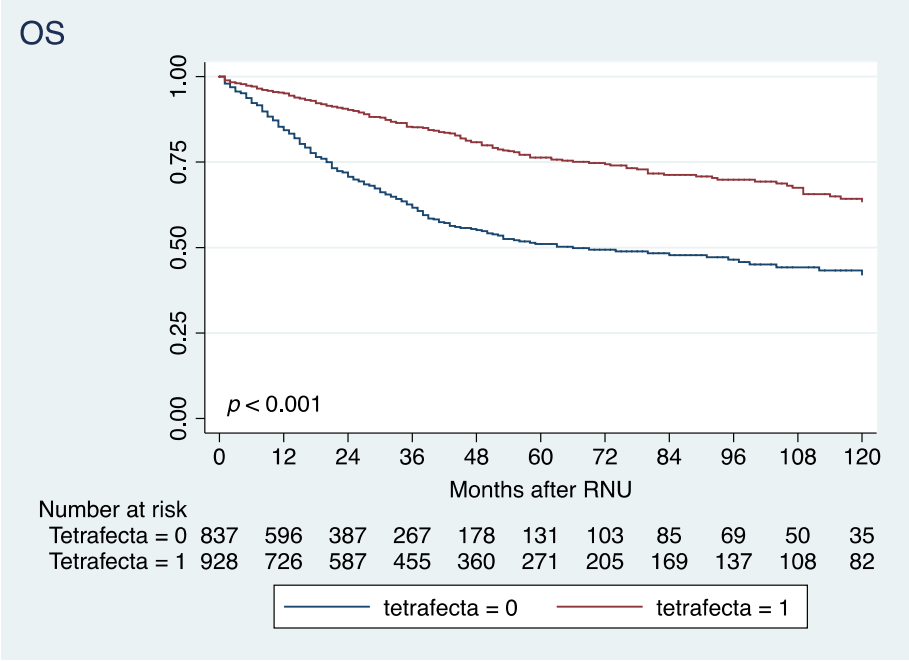

Fig. 2 – Kaplan-Meier estimates overall survival according to tetrafecta achievement in 1765 patients with clinically nonmetastatic upper tract urothelial cancer treated with radical nephroureterectomy. OS = overall survival; RNU = radical nephroureterectomy.

Table 2 – Univariable and multivariable Cox regression analyses for the prediction of overall survival among 1765 patients with clinically nonmetastatic upper tract urothelial carcinoma treated with radical nephroureterectomy

Variable	Univariable			Multivariable		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age (continuous)	1.03	1.02–1.04	<0.001	1.03	1.01–1.05	0.003
Female gender (ref.: male)	1.08	0.89–1.31	0.8	1.12	0.76–1.67	0.6
BMI (continuous)	0.99	0.97–1.02	0.7	1.02	0.97–1.06	0.4
ECOG score (ref.: 0)						
1	1.39	1.10–1.76	0.006	1.02	0.68–1.52	0.9
2	2.10	1.56–2.84	<0.001	1.22	0.71–2.09	0.5
3	4.03	2.47–6.57	<0.001	1.23	0.58–2.62	0.6
Year of surgery (ref.: 2000–2005)						
2006–2010	0.99	0.72–1.36	0.9	1.63	0.51–5.22	0.4
2011–2015	0.87	0.63–1.20	0.4	1.11	0.36–3.47	0.9
2016–2021	1.21	0.86–1.68	0.2	1.15	0.36–3.64	0.8
Previous bladder cancer	1.17	0.96–1.44	0.1	1.35	0.93–1.95	0.1
Preoperative hydronephrosis	1.25	1.04–1.49	0.016	1.02	0.71–1.45	0.7
Multifocal tumor (ref.: single)	1.21	0.96–1.52	0.1	0.90	0.57–1.42	0.7
Type of RNU (ref.: open)						
Laparoscopic	0.87	0.72–1.05	0.1	0.79	0.55–1.14	0.2
Robotic	0.75	0.50–1.13	0.2	0.65	0.09–4.85	0.7
Pathological tumor stage	1.29	1.21–1.37	<0.001	1.28	1.06–1.56	0.01
Pathological tumor grade	2.82	1.65–4.85	<0.001	1.11	0.44–2.80	0.8
Lymphovascular invasion	3.26	2.69–3.96	<0.001	1.41	0.91–2.19	0.1
Carcinoma in situ	1.45	1.13–1.85	0.003	0.91	0.59–1.40	0.7
Pathological lymph node involvement	4.00	3.07–5.21	<0.001	2.41	1.35–4.32	0.003
Neoadjuvant chemotherapy	2.29	1.50–3.53	<0.001	1.62	0.81–3.24	0.2
Adjuvant chemotherapy	2.16	1.71–2.74	<0.001	0.69	0.42–1.14	0.1
Tetrafecta achievement	0.41	0.35–0.50	<0.001	0.43	0.28–0.69	<0.001

BMI = body-mass index; CI = confidence interval; ECOG: Eastern Cooperative Oncology Group; HR = hazard ratio; RNU = radical nephroureterectomy.

an unmet need to standardize and assess the quality of the surgical procedure. In this multicentric retrospective study, we proposed for the first time a RNU tetrafecta that allows assessing of the quality of surgical management during RNU for UTUC.

Indeed, surgeon judgment alone is no longer sufficient to ensure the delivery of quality surgery. A great variability occurs in the outcomes of a wide variety of surgical steps, and a growing body of evidence suggests that the discrepancy between surgical practice in an “ideal world” and the

Table 3 – Multivariable logistic regression analyses for the prediction of tetrafecta achievement among 1765 patients with clinically nonmetastatic upper tract urothelial carcinoma treated with radical nephroureterectomy

Variable	Multivariable		
	OR	95% CI	*p* value
Age (continuous)	0.97	0.96–0.99	0.01
Female gender (ref.: male)	1.17	0.79–1.73	0.4
Smoking status (ref.: never smoker)			
Former smoker	0.87	0.58–1.32	0.5
Current smoker	1.47	0.93–2.32	0.1
BMI (continuous)	0.92	0.88–0.96	<0.001
ECOG score (ref.: 0)			
1	0.87	0.59–1.30	0.5
2	1.30	0.75–2.26	0.40
3	0.20	0.04–0.94	0.042
Year of surgery (ref.: 2000–2005)			
2006–2010	0.51	0.08–3.49	0.5
2011–2015	0.58	0.09–3.79	0.6
2016–2021	0.84	0.13–5.31	0.9
Previous bladder cancer	0.66	0.44–0.98	0.038
Clinical stage (ref.: cTa)			
cTis	0.61	0.09–4.21	0.6
cT1	0.81	0.45–1.46	0.5
cT2	0.24	0.13–0.45	<0.001
cT3	0.37	0.19–0.74	0.005
cT4	0.28	0.11–0.72	0.008
Pre-RNU endoscopic evaluation (ref.: none)			
Ureteroscopy without biopsy	0.51	0.24–1.10	0.09
Ureteroscopy with biopsy	0.82	0.56–1.19	0.3
Preoperative hydronephrosis	1.20	0.81–1.77	0.4
Tumor localization (ref.: pelvicalyceal)			
Ureter	1.05	0.67–1.64	0.8
Both	0.86	0.49–1.49	0.6
Multifocal tumor (ref.: single)	1.16	0.70–1.91	0.6
Type of RNU (ref.: open)			
Laparoscopic	1.26	0.87–1.81	0.2
Robotic	5.61	1.43–22.1	0.013

BMI = body mass index; CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; HR = hazard ratio; RNU = radical nephroureterectomy.

real world, the so-called quality gap, remains substantial [14]. Hence, we found that despite the use of clearly established surgical criteria, the tetrafecta was achieved in only 52% of the cases. These results underlined the need for standardization of the surgical steps and perioperative management of RNU.

After obtaining an experts' consensus, the simultaneous presence of negative STSMs, BCE, LND according to guideline recommendations, and absence of any recurrence within 12 mo from surgery were selected to define the RNU tetrafecta. The status of STSMs is an important marker of surgical quality due to its high impact on patients' survival. Indeed, a systematic review and meta-analysis of 8275 patients who underwent RNU found that positive STSMs were independently associated with intravesical recurrence (HR 1.9) [3]. Similarly, positive STSMs are a strong predictor of long-term oncological outcomes (OS, cancer-specific survival, and metastasis-free survival) [15]. Therefore, it remains crucial to not compromise the integrity of the urinary tract during the nephrectomy to avoid tumor breach and spillage as much as possible.

Resection of the distal ureter and its orifice (BCE) is recommended to reduce the risk of local and intravesical recurrence [1]. Leaving the intramural segment of the ureter significantly increases the risk of both intra- and extravesical recurrence (reported to be as high as 30–65% in the ureteric stump), with detrimental effects on survival [10,16,17]. Despite this evidence, the rate of BCE performance, although increasing, remains unsatisfactory, as reported by a recent analysis of the Surveillance, Epidemiology, and End Results (SEER) database [18]. In our cohort, BCE has been reported in 88% of the cases; this high rate could be explained by the fact that only patients from selected tertiary referral centers were included in this cohort. This is a mandatory step for every RNU, and its rigorous execution remains essential to improve oncological outcomes.

Whether LND should be performed systematically at the time of RNU is still a matter of debate. LND during RNU is performed to improve disease staging, thus providing essential information for decision-making regarding adjuvant treatment, and to improve long-term oncological outcomes, especially in patients with advanced disease [19]. Based on these considerations, and despite the inherent limitation of the unsatisfactory accuracy of preoperative nodal staging, current international guidelines recommend LND in patients with muscle-invasive disease [1]. In our series, LND has been performed following guideline recommendations in 87% of the cases, a proportion significantly higher than that reported in the literature [20]. Nevertheless, as the guidelines also suggest that a template-based LND should be offered to all patients who are scheduled for RNU, an LND was probably performed more often in the tertiary expert centers involved.

Finally, we included 12-mo recurrence-free survival (RFS) in our tetrafecta since this could be considered a proxy of the quality of surgical management, from appropriate patient selection to the quality of surgical excision and judicious perioperative treatment, thereby reflecting the overall quality of the RNU. Seisen et al [3] highlighted how intravesical recurrence after RNU is a consequence not only of patient- or tumor-specific characteristics, but also of treatment-specific features such as surgical approach, STSM status, and bladder cuff removal. Moreover, the absence of early disease recurrence after surgery has previously been included both in the trifecta and pentafecta after radical prostatectomy and radical cystectomy to better reflect the overall surgical management [9,21]. Indeed, the use of early RFS could be considered as a great representative of good overall surgical management and may help evaluate the quality of some other steps that might be hard to obtain from a retrospective cohort (ie, early clipping of the ureter, surgical approach to the bladder cuff, etc.).

We found that younger age at surgery, lower BMI, and a robotic approach independently predicted the RNU tetrafecta achievement. Conversely, a high ECOG score, a history of bladder cancer, and a higher clinical stage were inversely correlated with tetrafecta achievement. While the association between the majority of these predictors and the outcome of interest is easily understandable (ie, for age, BMI, ECOG score, bladder cancer history, and clinical stage), the correlation between surgical approach and tetrafecta achievement deserves further investigations and, to date, remains hypothesis generating. One of the answers might be in the improvement of perioperative management of

patients at the time of robotic RNU, when patients should have received intravesical chemotherapy and/or systemic treatment more often.

The results of our study may have several practical implications. Standardized methods for reporting surgical management during RNU may serve for evaluating surgical quality, thereby allowing comparison between series. Moreover, this tetrafecta may be used for evaluating the learning curve of the procedure and the impact of new advancements and new technologies in the field [22,23]. Indeed, the goal of providing such assessment is to promote changes that will improve patient outcomes and safety, and to identify barriers to high-quality care. Finally, the impact of the tetrafecta achievement on OS could further be explored in future studies as an important factor to adapt the therapeutic strategy and follow-up.

Despite several strengths, our study is not devoid of limitations. Our findings represent a virtual concept based on a survey delivered to experts, and therefore, a selection bias regarding the criteria to be used in the RNU tetrafecta may not be excluded. As previously discussed, we could not add the use of postoperative intravesical instillation to our RNU-fecta, despite certainly representing a marker of treatment quality and despite having been scored by the experts' panel as one of the items to be considered for the purpose of the study. Moreover, despite the exclusion of patients with incomplete data regarding the outcomes of interest, missing data (despite being below average) concerning baseline variables may partially limit the reliability of the results. Surgery was performed in different centers by different surgeons, and the surgical approach was at the discretion of the surgeon; in spite of the fact that the multicentric nature of the trial may contribute toward improving the reproducibility of the results, this may have also introduced unavoidable selection biases. A central pathological review of the specimens was not provided, and postoperative follow-up was not standardized and may have changed along the study period. Despite the non-negligible rate of locally advanced disease and lymph node involvement at final pathology, only a few patients were treated with adjuvant chemotherapy since the majority of patients underwent surgery in a "pre-POUT" era [2]. We were not able to test the impact of early ureteral clipping on oncological outcomes, specifically on RFS. Finally, this first proposal for an RNU quality tool still needs to be validated according to the surgeon's learning curve in order to become a standard for the assessment of surgical skills.

5. Conclusions

Herein, we propose a procedure-specific "tetrafecta" outcome (defined as simultaneous presence of negative STSMs, BCE, LND according to European Association of Urology guidelines, and absence of any recurrence within 12 mo) as a surrogate marker of surgical quality for RNU. The achievement of this composite outcome seems to be associated with better survival outcomes. External validation is needed to confirm our findings. Moreover, this assessment tool could be used to define the learning curve of RNU.

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Study concept and design: Soria, Pradere, Ferro.
Acquisition of data: All authors.
Analysis and interpretation of data: Soria, Pradere.
Drafting of the manuscript: Soria, Pradere, Ferro.
Critical revision of the manuscript for important intellectual content: Pradere, Ferro.
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Appendix A. Supplementary data

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