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ORIGINAL ARTICLE – UROLOGIC ONCOLOGY

First Comparison of Retroperitoneal Versus Transperitoneal Robot-Assisted Nephroureterectomy with Bladder Cuff: A Single Center Study

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ABSTRACT

Introduction. After recent presentation of the first complete robot-assisted retroperitoneal nephroureterectomy with bladder cuff (RRNU) for patients with upper tract urothelial cancer (UTUC), we aimed to compare this new surgical technique with robot-assisted transperitoneal nephroureterectomy (TRNU) representing the current standard of care.

Methods. Robot-assisted nephroureterectomies (NUs) were retrospectively analyzed and compared based on two groups: transperitoneal versus retroperitoneal approach. Baseline data were collected for patient demographics, tumor characteristics, intra- (EAUiaiC) and postoperative (Clavien-Dindo) complications, and perioperative variables. Tumor characteristics included grade of malignancy, clinical stage, and surgical margin status. Short-term follow-up data including 30-day readmission rates were collected. Statistical analyses were performed assuming a significant p-value of < 0.05.

Results. The analysis includes perioperative patient data after proven UTUC of 24 TRNU versus 12 RRNU (mean age: 70 versus 71 years; BMI: 25.9 versus 26.1 kg/m^2; CCI score $\geq$ 4: 83% versus 75%; ASA score $\geq$ 3: 37% vs 33%). Intraoperative (16.4% vs 0%, $p = 0.35$) and postoperative (25% vs 12.5%, $p = 0.64$) complications demonstrated no significant discrepancy. Notably, RRNU demonstrated significantly shorter surgery time ($p < 0.05$) and length of stay ($p < 0.05$). There was no significant difference in histopathological tumor characteristics, whereas significantly more lymph nodes were removed through RRNU (11.0±3.3 vs. 6.4±5.1, $p < 0.05$). Finally, no statistical difference was shown in short-term follow-up.

Conclusion. We report the first head-to-head comparison between RRNU and TRNU. RRNU proves to be a safe and feasible approach which appears to be non-inferior to TRNU. RRNU expands the spectrum of minimally invasive treatment options, particularly for patients with major previous abdominal surgery.

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Due to demographic changes, the incidence of upper tract urothelial cancer (UTUC) increases continuously year by year. Currently, 5–10% of all urothelial carcinomas primarily manifest in the upper tract,[1] whereas 7.5% of all patients with non-muscle invasive tumors of the bladder develop a UTUC over the years. While bladder cancer is mostly detected as localized disease, UTUC is often discovered as an invasive stage due to the absence of the muscularis propria layer in upper urinary tract,[1] making it a life-threatening condition. For years, radical NU has been the standard of care for most UTUC, whether it is located in the ureter or kidney. While open surgery for NU is often still performed for UTUC, minimally invasive procedures have gained increasing attention. Laparoscopic NU was introduced in 1991 by Clayman et al.[2] Since then, several approaches for robot-assisted surgery have been described, progressively replacing open and laparoscopic surgery.[3] Several transperitoneal and retroperitoneal approaches for robot-assisted NU have been reported so far. The main challenge in robot-assisted surgery for NU is to create a port placement that allows one to simultaneously accomplish surgery of the nephrectomy portion in the upper abdomen, and excision of the bladder cuff in the pelvis. More common for robot-assisted NU is the transperitoneal approach, for which several different strategies for port placement have been described. Whereas Patel and Zagar et al. proposed a port placement in a straight line to the linea semilunaris, lateral to the rectus abdominis muscle,[4,5] Darwiche et al. set up an oblique line for port positioning (Fig. 2) beginning from the subcostal space and ending near to the linea alba in the lower abdomen.[6] All the abovementioned transperitoneal techniques allow access to the nephrectomy and bladder portion at once. Of note, after completing the nephrectomy portion, most retroperitoneal approaches for robot-assisted NU need an intraoperative switch to either conventional laparoscopic surgery or even open surgery for the management of the bladder cuff,[7,8] thus either making the surgery more sophisticated or reducing the benefits of minimally invasive procedures. In 2022, our study group described a complete retroperitoneal robot-assisted NU[9] for the first time where all steps, including bladder cuff excision, were performed robotically and through a unique retroperitoneal approach using the DaVinci^{R} Xi robotic platform. This robot-assisted approach uses a singular trocar placement and two-step docking without the need to relocate the surgical robot.

Based on experience from partial nephrectomies, several study groups identified advantages in favor of retroperitoneal compared with transperitoneal approaches. A strict retroperitoneal approach might have several positive impacts, e.g., on hilar control, blood loss reduction, operative time, and hospital stay.[7,10] Furthermore, postoperative discomfort might be reduced by decreasing pain and intestinal atony, resulting in a shorter hospital stay. Finally, even patients with previous major abdominal surgery can be judged feasible for minimally invasive surgery by avoiding intraperitoneal adhesions and occasionally time-consuming adhesiolysis.[9]

We aimed to assess this novel strict retroperitoneal surgical approach for robot-assisted NU by comparing it with the most common transperitoneal approach.

METHODS

Study Population

Demographics, surgical, and postoperative outcomes of RRNU were compared with those of TRNU. For comparison of both NU techniques, we included the last 24 consecutive TRNU and all 12 RRNU performed so far. All patients treated with robot-assisted NU after diagnosis of nonmetastatic UTUC at our institution (single-center design) were included. While data from TRNU were retrospectively evaluated (period from March 2017 until October 2021), data for RRNU were prospectively enrolled (period February 2021 until July 2022). Trocar placement (Fig. 2) for TRNU was performed according to Darwiche et al.[6] and for RRNU according to Sparwasser et al.[9] RRNU was executed through one single surgeon and TRNU through three different surgeons. Depending on previous ureterorenoscopy, a ureteral stent was placed in some patients of both groups, while the indication for ureteral stent placement was either biopsy or clinically relevant hydronephrosis. All patients signed an informed consent for transperitoneal or retroperitoneal surgical approach after discussion with a physician.

Surgical Technique

Patient Position, Port Placement, and Docking for RRNU As already described by our study group,[9] for RRNU the patient is placed in a 90° full-flank position (Fig. 1), that is well known in open kidney surgery. To enable retroperitoneal trocar placement, both arms are positioned perpendicular to the body, while a slight table flexion between 15° and 20° is induced in the torso. This also facilitates trocar placement by enlarging the space between the iliac crest and the costal arch (Fig. 1). Thereafter, the modified trocar placement for a four-arm configuration using the DaVinci^{R} Xi robotic platform (Intuitive^{R}, Sunnyvale, USA) is performed (Fig. 2). Creation of the retroperitoneal space is enabled through insufflation of a balloon-dilatator after sharp and blunt preparation for the first port incision in the midaxillary line (12-mm Hasson trocar). After this, medialization of the peritoneum is executed laparoscopically, and the remaining ports are placed in a curved line parallel to the costal arch. This allows the patient cart to be docked ventrally or dorsally, depending on the capability of the operation theater. For bladder cuff excision re-docking is necessary by a simple 180° rotation of the boom, while no relocation of the robot is needed. The three most medial trocars are connected to the patient cart, enabling bladder cuff excision with a three-arm configuration, while the 12-mm Hasson trocar now serves as an additional assistant port. A 0° camera is used for all surgical steps. A detailed description is available in Sparwasser et al.[9]

Patient Position, Port Placement, and Docking for TRNU Several techniques for transperitoneal approaches for robot-assisted NU have been described. In our institution we prefer the abovementioned trocar placement by Darwiche et al.[6] For TRNU the patient is placed in a 70° flank position (Fig. 1), basically the most common patient position for transperitoneal approaches for robotic-assisted kidney surgeries. While the contralateral arm is positioned perpendicular to the body, the arm of the surgery side is fixed to the torso. Moderate table flexion between 15° and 20° is induced but is less important than for RRNU. For port placement, a

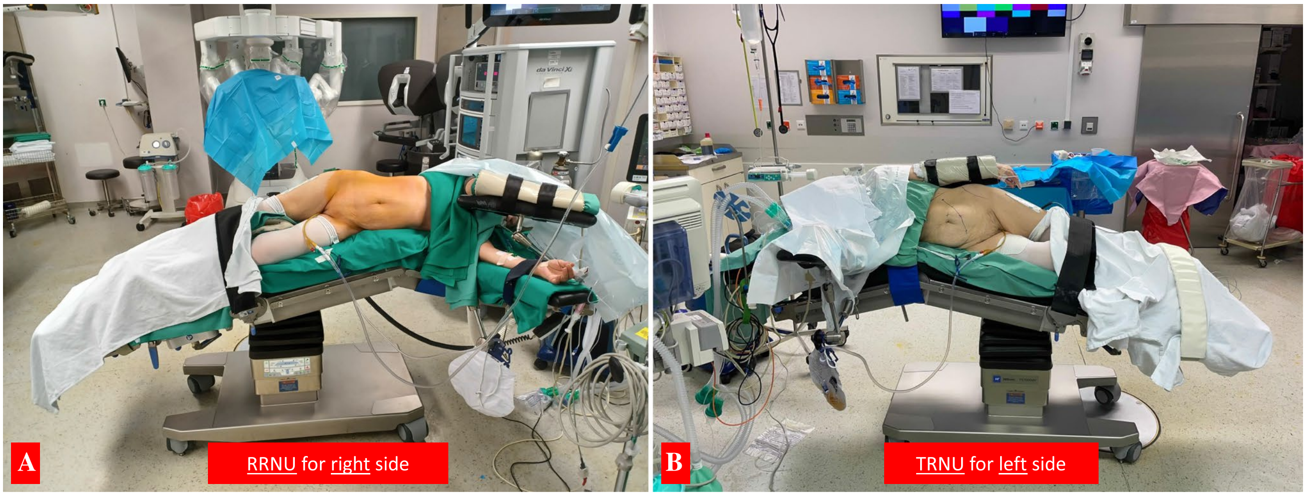

FIG. 1 Patient position for RRNU and TRNU Illustration of patients position for right side RRNU (**A**) and left side TRNU (**B**): For RRNU patients are placed in a 90° full flank position and both arms are positioned perpendicular to the body to enable retroperitoneal access (**A**). In case of TRNU patients are placed in a 70° flank position and while the contralateral arm is positioned perpendicular to the body the arm of surgery side is fixed to the torso. For both approaches we induce a moderate table flexion between 15° and 20°. The patient cart (DaVinci Xi) always is located from the back of the patient for TRNU, while for RRNU the patient cart can be placed ventraly or dorsaly dependig on capability of the operation theater

four-arm configuration using the DaVinci^{R} Xi robotic platform, an oblique line starting at the costal arch and ending near to the linea alba in the lower abdomen, is also set up (Fig. 2). After placement of the first port and insufflation of the abdominal cavity, there is no general need for manually creating an intraperitoneal space before placement of the remaining ports by eye, except if intra-abdominal adhesions are present. For TRNU, four 8-mm robotic ports, a single 12-mm assistant port and a 30° camera are used for all surgical steps (Fig. 2). For the bladder cuff excision, re-docking might sometimes be necessary by shifting the camera port one trocar more medio-caudally than the basic position.

Nephrectomy and Management of Bladder Cuff for RRNU and TRNU

Nephrectomy portion For transperitoneal approaches, mobilization of the bowel by paracolic incision of the dorsal peritoneum is initially utilized to access the retroperitoneal space. Due to intraperitoneal adhesions this step might occasionally be difficult. In case of RRNU we directly try to identify the vessels from a dorsal position. This step is facilitated by elevation of the kidney ventro-medially to the abdominal wall using the ProGrasp Forceps (Intuitive^{R}). In both approaches the first major step is control of the renal hilum. In case of TRNU of the right side, an extra assistant port for liver retraction is sometimes additionally placed to provide a better visualization of the renal hilum. Once the hilar anatomy is clearly defined, the renal vessels are sealed by Hem-o-lok clips and then transected. Now, in both procedures, mobilization of the kidney is performed by releasing the superior and lateral attachments of the kidney under protection of the adrenal gland until the kidney is fully mobile in the renal fossa. Particularly during RRNU, this step needs a good anatomical understanding to discriminate the adrenal gland from perirenal fat.

Dissection of the ureter is now performed for TRNU and RRNU by following the ureter on the psoas muscle from proximal downwards by using sharp and blunt dissection. In the case of TRNU this step can be performed continuously to the bladder orifice. During RNNU, preparation of the ureter is only possible up to its middle section. Thereafter, re-docking as described above is necessary. However, re-docking results here in a very practical arrangement of the robotic arms parallel to the ureter, allowing a good view of the ureteral orifice for a precise bladder cuff excision. In both approaches we clip the ureter distally to the tumor burden to prevent cell spreading.

Lymph node dissection This step is performed for RRNU right before re-docking, whereas lymph node dissection for TRNU can be performed before or after bladder cuff excision. For RRNU and TRNU, retroperitoneal lymph nodes are selectively removed according to preoperative radiological findings, while over the study period a transition to template-based lymph node dissection occurred.[22] This disparity refers to the former vague recommendations for lymph node dissection by expert panels. The resection boarders for

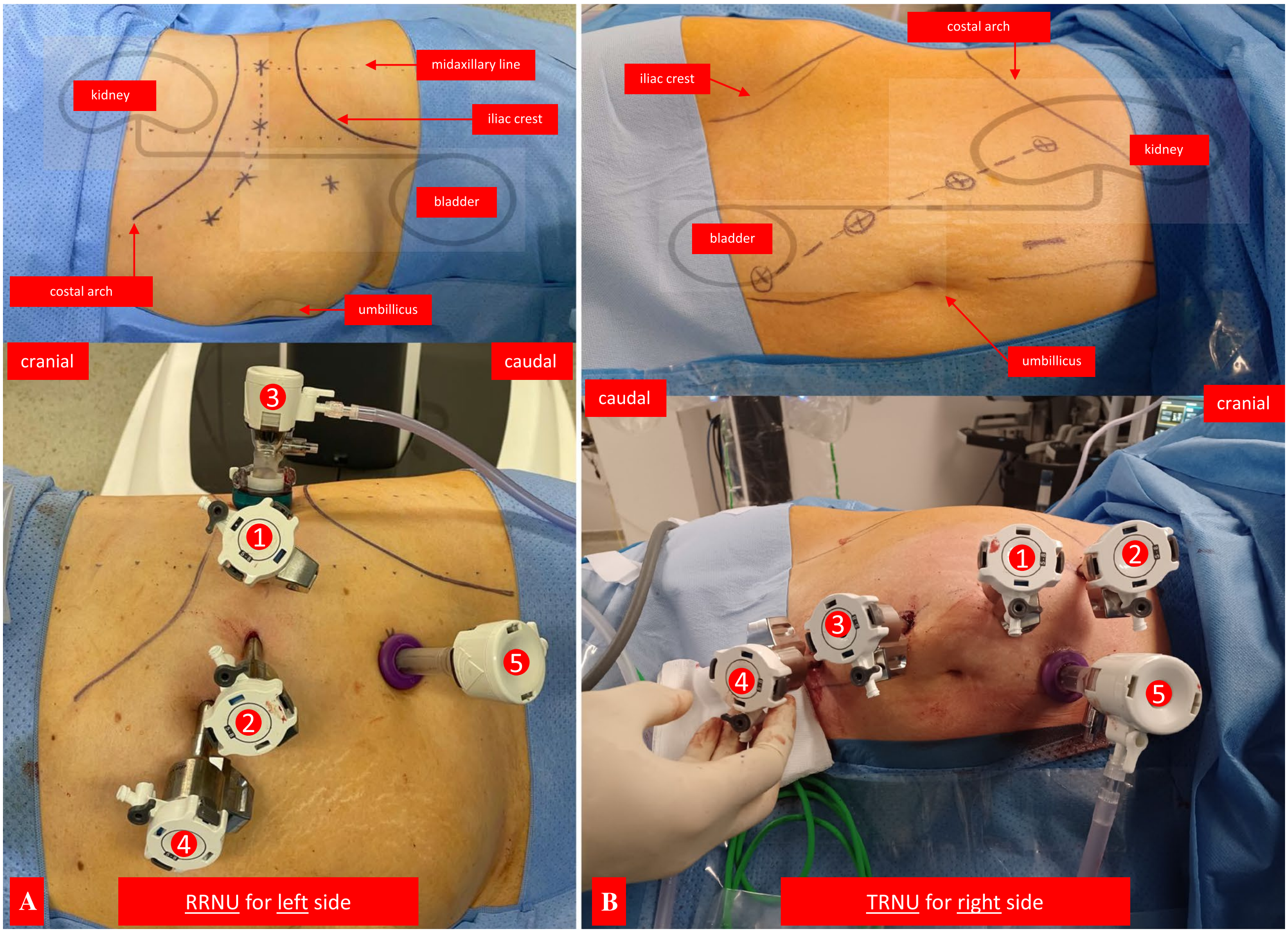

FIG. 2 Portplacement for RRNU and TRNU Illustration for initial portplacement for left side RRNU (**A**) and right side TRNU (**B**): Both approaches starting in fourarm- configuration (1 = cam; 2 = right robotic arm; 3 = left robotic arm; 4 = ProGrasp; 5 = 12mm assistant port). For RRNU after nephrectomy re-dockingwithout relocation of the DaVinci Xi for bladder cuff excision is necessary. Bladder excision is then conducted in 3- arm configuration

lymph node dissection were the renal hilum to the iliac vessels, while larger lymphatics were clipped.

Bladder cuff excision The bladder is filled with 200 ml saline through the Foley catheter to identify exact borders of the ureteral orifice in both approaches. The detrusor muscle fibers are then dissected until the bladder mucosa is visible. In the case of RRNU, a stich (V-Loc 3-0, Covidien^{R}, Dublin) is placed at the medial dissection margin to prevent retraction of the bladder wall just before entire dissection of the bladder cuff is executed. This step is not generally performed for TRNU. Finally, a circumferential en bloc excision is then executed, including the complete orifice. The bladder defect is closed with a running suture line, whereas in RRNU we use the previously attached V-Loc suture. Watertightness testing by irrigating the Foley catheter with saline approves the efficiency of the suture line. A laparoscopic entrapment sac is introduced by the assistant port, and before the entrapment sac is retrieved, a Robinson drain is placed at the renal hilum through one of the 8-mm ports.

Data Analysis

We used descriptive statistics, using means ± standard deviation (SD) for continuous variables and frequencies and proportions for categorical variables. All clinical data was set up in a database including patient age, sex, body mass index (BMI), health status, American Society of Anesthesiologists score (ASA), Charlson Comorbidity Index (CIC), length of hospital stay, postoperative transfusion rate, surgery time, tumor size, positive margins, tumor stage, all kinds of relevant histopathological information, as well as the count and grade of intraoperative and postoperative complications using a proper grading system with the EAU Intraoperative Adverse Incident Classification (EAUiaiC)[11] and Clavien classification (Clavien-Dindo).[12] Comparisons were performed statistically using a chi-square test with Yates' correction for homogeneous groups, Fisher's exact test for small sample sizes and a Mann-Whitney *U*-test for nonparametric groups. A statistical significance level was set up at $p < 0.05$.

RESULTS

Overall, we collected and analyzed the data of 36 patients with a ratio of 2:1 (24 TRNU vs. 12 RRNU). All these patients were treated according to the EAU-Guidelines[1] because of initial diagnosis of UTUC with radical robot-assisted NU using a retroperitoneal or transperitoneal approach.

Baseline Characteristics

Clinical, demographic, and tumor characteristics are depicted in Table 1. Overall, demographics showed no substantial differences between the groups. The mean age was 71 versus 70 years with mean BMI of 26.1 vs. 25.9 kg/m^2 (RRNU vs. TRNU) and, according to CCI and ASA, with a comparable but at best moderate health status on average. Some patients had several previous major abdominal surgeries in the RRNU group (e.g., cholecystectomy, appendectomy, prostatectomy, hysterectomy, bowel resection etc.), as well as in the TRNU group (e.g., cholecystectomy, appendectomy, adnexectomy, prostatectomy, bowel resection, partial nephrectomy etc.). Comparing both groups, there were statistically no significant ($p > 0.05$) differences for demographics or tumor characteristics.

Outcomes

Main surgical outcomes and histopathological characteristics are summarized in Table 2. RRNU reported statistically significant ($p < 0.05$) shorter surgery time, 192 vs. 219 min, as well as a shorter length of stay with hospital discharge after 5.75 vs. 6.5 days. No statistically significant differences were found for intraoperative or postoperative complications. Overall, there were no major intraoperative complications (EAUiaiC grade ≥ 2) for RRNU and four (16.4%) were reported for TRNU ($p = 0.35$), including 2

TABLE 1 Patient characteristics for those treated with RRNU or TRNU

Demographics and perioperative data	RRNU	TRNU	*p*-value
Patients, no.	n = 12	n = 24	
Age, years, mean (SD)	71 (±12.0)	70 (±10.1)	0.51
Sex, no. (%)			0.81
Female	5 (41.7)	9 (37.5)	
Male	7 (58.3)	15 (62.5)	
BMI, kg/m^2, mean (SD)	26.1 (±3.8)	25.9 (±3.1)	0.58
ASA score ≥3, no. (%)	4 (33.3)	9 (37.5)	0.81
Charlson Comorbidity Index score (CCI) ≥4, no. (%)	9 (75.0)	20 (83.3%)	0.88
Side, no. (%)			0.71
Right	3 (25.0)	9 (37.5)	
Left	9 (75.0)	15 (62.5)	
Lymph node dissection, no. (%)	5 (41.7)	9 (37.5)	0.81
Operative time, min, mean (SD)	192 (±33.5)	219 (±53.4)	**< 0.05**
EAUiaiC (intraoperative complications) ≥ 2, no. (%)	0 (0.0)	4 (16.4)	0.35
Conversion to open surgery, no. (%)	0 (0.0)	2 (8.3)	0.80
Clavien-Dindo grade (postoperative complication) ≥ 2, no. (%)	3 (25.0)	3 (12.5)	0.64
Blood transfusion, no. (%)	1 (8.3)	1 (4.2)	0.61
Creatinine in drain fluid, no. (%)	0 (0.0)	0 (0.0) *	
Sufficient cystography, no. (%)	12 (100)	24 (100)	
Foley catheter removal, days, mean (SD)	5.2 (±0.6)	5.6 (±1.1)	0.23
Mitomycin instillation postoperative, no. (%)	12 (100)	16 (66.7)	0.07
Length of stay, days, mean (SD)	5.75 (±2.0)	6.5 (±1.2)	**< 0.05**
30-day readmission, no. (%)	0 (0)	3 (12.5)	0.52

Bold values indicate significant level with *p*-value of < 0.05

ASA American Society of Anesthesiologists; *BMI* body mass index; *CCI* Charlson Comorbidity Index score; *EAUiaiC* Intraoperative Adverse Incident Classification by European Association of Urology; *SD* standard deviation; *data of 16 patients available

TABLE 2 Pathology findings and follow-up data for patients treated with RRNU or TRNU

Pathology findings and follow-up data	RRNU	TRNU	*p*-value
Location of tumor, no. (%)			0.81
Kidney	5 (41.7)	11 (45.8)	
Proximal	3 (25.0)	7 (29.2)	
Mid	2 (16.7)	3 (12.5)	
Distal	2 (16.7)	3 (12.5)	
Tumor stage UTUC, no. (%)			
Ta	3 (25.0)	14 (58.3)	0.13
T1	4 (33.0)	1 (4.2)	0.06
T2	0 (0.0)	2 (8.4)	0.80
T3	5 (41.6)	7 (29.1)	0.71
T4	0 (0.0)	0 (0.0)	
Size UTUC, cm, mean (± SD)	3.6 (±1,7)	4.1 (±2.5) *	0.70
Grade, no. (%)			0.51
High	10 (83.3)	16 (66.7)	
Low	2 (16.7)	8 (33.3)	
Positive surgical margin, no. (%)	0 (0.0)	1 (4.2)	0.47
LN status, no.			0.36
Positive LN, no. (%)	1 (20.0)	0 (0.0)	
Negative LN, no. (%)	4 (80.0)	9 (100)	
LN removed per procedure, no. mean (±SD)	11 (±3.3)	6.4 (±5.1)	**<0.05**
Intravesical bladder cancer recurrence			
Within 6 month, no. (%)	2 (16.6)	3 (12.5)	0.73
Progression-free within 6-month follow-up, no. (%)	12 (100)	23 (95.8)	0.47

Bold value indicates significant level with *p*-value of < 0.05

UTUC upper tract urothelial carcinoma; *LN* lymph node; *SD* standard deviation; *data of 22 patients available

conversions to open NU in the TRNU group. Postoperative complications (Clavien-Dindo grade ≥ 2) were recorded for RRNU in 25% (n = 3; blood transfusion, hypertensive lung edema, chylascites) and TRNU in 12.5% (n = 3; blood transfusion, ileus, stroke) of cases. Foley catheter removal was not significantly earlier in the RRNU compared with the TRNU group [5.2 vs. 5.6 days; ($p = 0.23$)], whereas 30-day readmission was observed for minor reasons (e.g., pain, hematuria) for TRNU in 12.5% of cases. As mentioned above, tumor characteristics demonstrated no major significant differences beside the fact that more lymph nodes per patient (11.0 vs. 6.4) were removed during RRNU.

DISCUSSION

To date, many different techniques have been presented for radical NU, while none have been demonstrated to be superior to others. With growing adoption of robot-assisted surgery, robotic NU increasingly becomes the first treatment option for patients with UTUC, replacing laparoscopic and open surgery,[3,13] with some evidence for better postoperative convalescence including short-term morbidity,[14] length of stay,[13] and complication rates.

Whereas the transperitoneal approach for entirely robot-assisted NU has been nearly brought to perfection, an intraoperative switch to either conventional laparoscopic or even open surgery was necessary for the retroperitoneal approach[7,8] for completion of bladder cuff excision until the presentation of the RRNU approach.[9] Beside the above-mentioned benefits of a robot-assisted approach, an entirely retroperitoneal approach might additionally intensify these positive observations. As reported for robot-assisted partial nephrectomy, a complete retroperitoneal approach might be associated with a reduction in surgery time,[15–17] intraoperative blood loss,[7] and length of stay,[16] whereas major intra- and postoperative complications are almost the same.[16,18] Since other retroperitoneal approaches for NU are only partly performed under robot guidance, we focused on a direct comparison of both completely robotically executed approaches — TRNU versus RRNU.

Regarding the safety of RRNU and TRNU, we rarely observed intra- or postoperative complications. While no conversion to open or laparoscopic surgery was observed in the RRNU group, two patients in the TRNU group needed conversion to open surgery. Notably, one of these two patients had distinct periureteral adhesions due to prior aorto-iliacal prothesis, necessitating conversion. According to the Clavien-Dindo classification, we recorded one major postoperative complication (grade 3b) after extended lymph node dissection with postoperative chylascites, and the need for surgical revision with open ligature of the open lymphatic vessel in the RRNU group. In comparison, TRNU also showed a single major postoperative complication (grade 4; stroke) leading to admission to the intensive care unit.

Furthermore, we observed a significantly shorter surgery time for RRNU (192 vs. 219 min). For TRNU, Patel et al., Darwiche et al., and Bae et al. demonstrated mean surgery times of 152, 184, and 189 min, respectively.[3,4,6] Importantly, more sophisticated trocar placement for our retroperitoneal approach does not lead to major delay and justifies the initial effort. Interestingly, Veccia et al. reported in their meta-analyses the shortest surgery time (225 min) for open NU.[13] In addition, surgery time is significantly dependent on the duration of lymphadenectomy, making comparison with external data difficult.

RRNU was associated with a significantly shorter length of stay of 5.75 days (vs. 6.5 for TRNU). This observation is in line with Veccia et al. who demonstrated a length of stay for robot-assisted NU of 5.35 days,[13] while several other groups reported discharging between 2 and 7 days.[4–6,9] This significant benefit of RRNU might be related to better postoperative convalescence including reduced pain, earlier bowel movement, and earlier patient mobilization, while we are clear that general studies comparing these topics for retroperitoneal versus transperitoneal approaches are yet missing.

In terms of histopathological outcomes, no major differences between the techniques were evident. UTUC was distributed in both groups equally to the complete upper urinary tract, while approximately two thirds of cases were high-grade tumors.[1] No T4 tumors were encountered, while surgical treatment for T3 tumors was successful in 42% and 30% of all RRNU and TRNU, demonstrating precise oncological feasibility for both techniques, even in locally advanced disease. This is underpinned by further histological examination reporting no positive surgical margin for RRNU (0%) and only one for TRNU (4.2%). Here, several studies with larger cohorts noted positive margins in 2–23%[9] of patients.

Unfortunately, the impact of lymphadenectomy during NU on survival of patients with UTUC is still a matter for debate, likewise for its anatomical resection boundaries.[24] Prospective evidence is hence urgently warranted in this field in order to tailor surgical treatment and optimize outcomes. According to the EAU guidelines, lymph node dissection should be performed in high-risk UTUC. High-risk UTUC is thereby defined in cases with clinical evidence for multifocal diseases, high-grade cytology/biopsy, tumor size ≥ 2 cm, hydronephrosis, local invasion etc.[1] Furthermore, a template-based lymphadenectomy is recommended for all patients with high-grade non-metastatic UTUC scheduled for robot-assisted NU.[1] Thereby, templates are composed based on tumor origin in the upper urinary tract. During our study period, whether and how lymph node dissection should be performed systematically at the time of NU was still a matter of debate. We performed lymph node dissection in both groups for 42% versus 37% of patients (RRNU vs. TRNU), which is in conflict with the literature reporting on considerably higher rates of lymphadenectomy.[19] As mentioned previously, this refers to incoherent guideline recommendations over the years, while the decision for lymphadenectomy was based especially on radiological findings of enlarged and/or metastasis-suspicious lymph nodes. The higher number of retrieved lymph nodes per patient in the RRNU compared with the TRNU population may be attributable to the growing adoption of the template-based approach of lymphadenectomy over recent years. In fact, rigorously and systematically performed lymph node dissection as opposed to selective “cherry-picking” of clinically abnormal lymph nodes inevitably results in a higher lymph node yield per patient and may provide therapeutic advantages due to the removal of undetected lymph node micrometastases and a subsequent improvement in recurrence rate and cancer-specific survival.[24] Thus, Roscigno et al. reported, for therapeutic benefits, removal of a minimum of 6[20] respectively 8 lymph nodes[21] per patient. Interestingly, according to the EAU guidelines, a greater impact on patient survival is expected for a template-based strategy than for totally dissected lymph nodes,[1,22] resulting in an improvement in survival even for clinically and pathologically lymph node-negative patients.[1] Speculatively, there might be a benefit in favor of RRNU to retrieve retrocaval and retroaortic lymph nodes due to the more feasible angle of their visualization compared with TRNU. However, further research is needed to elucidate this issue. Overall, we believe that RRNU allows adequate lymphadenectomy, while adoption of a general template-based lymphadenectomy for high-risk UTUC is advisable.[1]

Importantly, considering the high recurrence rate in cases with incomplete bladder cuff removal, proper dissection of the bladder cuff was possible in all cases for RRNU and TRNU. According to “Tetrafecta”,[19] sufficient bladder cuff excision is one of the four major achievements to guarantee surgical quality of a radical NU in patients with nonmetastatic UTUC. In addition, negative surgical margins, performance of template-based lymphadenectomy, and no recurrence within the first 12 months are of crucial importance.[19]

"Tetrafecta" was established to optimize comparison between surgical series of NU and to evaluate the impact of novel surgical techniques.[19] According to "Tetrafecta" criteria, we demonstrated very rare positive surgical margins and sufficient bladder cuff excision for all patients, while lymphadenectomies were performed irregularly, and a minor recurrence rate was observed. Unfortunately, our follow-up period includes only the first 6 instead of 12 months as required for "Tetrafecta" outcomes. Therefore, RRNU and TRNU have been demonstrated to be feasible, while adoption of the template-based lymph node removal is necessary. Addressing future studies for assessment of long-term cancer-specific survival rates of RRNU, observation should consider "Pentafecta" criteria including negative surgical margin, a complete bladder-cuff resection, the absence of hematological complications, the absence of major complications, and the absence of 12-month postoperative recurrence.[23]

Some limitations of our study need to be addressed. While surgery for RRNU was always carried out by the same operation staff, TRNU was performed by three different surgeons from a single center. In addition, the fact that we are still the only institution performing RRNU may also lead to some sort of bias. Furthermore, the cohort size was small, and regarding long-term follow-up, especially including recurrence rate, overall, and progression-free survival, we covered only a short period. Nevertheless, we provide the first comparative data supporting non-inferiority of RRNU compared with TRNU, fostering further research activity.

CONCLUSIONS

We present the first comparison of RRNU versus TRNU with bladder cuff. RRNU was demonstrated to be non-inferior to TRNU. Further prospective studies with longer follow-up and larger patient cohorts are warranted to finally classify the significance of RRNU in surgical management of UTUC.

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ETHICAL APPROVAL All ethical standards were ensured. Ethical board number 2021-16269 for "Robot-assisted retroperitoneal versus transperitoneal Nephroureterectomy".

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