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Surgery in Motion

Evolution of Robot-assisted Partial Nephrectomy: Techniques and Outcomes from the Transatlantic Robotic Nephron-sparing Surgery Study Group

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Abstract

Background: Robot-assisted partial nephrectomy (RAPN) is considered a feasible minimally invasive alternative to open partial nephrectomy (OPN) for the surgical treatment of renal tumors.
Objective: To provide further evidence supporting the effectiveness of RAPN in a contemporary patient population treated at one of three tertiary care centers for robotic surgery and to describe the evolution of RAPN-based technical improvements.
Design, setting, and participants: The Transatlantic Robotic Nephron-sparing Surgery (TRoNeS) study group prospectively collected data from 635 patients subjected to RAPN for clinically localized kidney cancer between 2010 and 2016 at three high-volume tertiary care centers.
Surgical procedure: RAPN was performed using methods outlined in the supplementary video using either the da Vinci Si or Xi surgical system (Intuitive Surgical, Sunnyvale, CA, USA).
Measurements: Clinical data were collected within a prospectively maintained multi-institutional database. Intra- and postoperative data as well as surgical outcomes were assessed. Descriptive statistical analysis was performed and multivariable logistic regression models were fitted to determine the predictors of surgical outcomes.
Results and limitations: Mean patient age was 60.7 yr and mean preoperative tumor size was 33 mm. According to the PADUA score, 202 (31.8%) patients had a low-, 235 (37.0%) had an intermediate-, and 198 (31.2%) had a high-complexity tumor. In the majority of patients, a transperitoneal approach was used ($n = 447$; 70.4%). Mean operative time was 156.3 min and mean estimated blood loss was 171 ml. Overall, 25 (3.9%) patients experienced a significant (Clavien-Dindo >2) complication after surgery. No statistically significant differences between pre- and postoperative creatinine values were observed ($p \leq 0.823$). Finally, optimal surgical outcomes defined according to the margin, ischemia, and complication score were achieved in 459 (72.3%) individuals. At a mean follow-up of 26 mo, only two local and two distant recurrences of the disease were observed. Finally, in multivariable logistic regression models, tumor complexity was associated with the risk of not achieving optimal surgical outcomes.
Conclusions: RAPN represents an effective minimally invasive alternative to OPN in the treatment of clinically localized renal tumors.
Patient summary: We reported contemporary experience with RAPN for the treatment of kidney cancer. RAPN appears to be a safe and effective procedure, resulting in optimal outcomes in the majority of individuals despite tumor complexity.

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1. Introduction

Robotic-assisted partial nephrectomy (RAPN) was first described in 2004 by Gettman and colleagues [1] and, since its introduction in clinical practice, has progressively gained increasing popularity. To date, RAPN is considered a feasible minimally invasive alternative to open partial nephrectomy (OPN) for the surgical treatment of renal tumors [2]. The main advantages of robotic surgery as compared with the traditional laparoscopic approach have been demonstrated by several studies, and include a three-dimensional magnified view of the surgical field, enhanced dexterity, and greater precision in both dissection and reconstruction. In clinical practice, these advantages translate into a shorter learning curve and broader indications of RAPN as compared with the standard laparoscopic partial nephrectomy (LPN) [3–7]. Consequently, in expert hands, RAPN has become a feasible option for the treatment of complex renal masses [3–7].

Several studies have shown that RAPN may result in comparable, if not better, outcomes relative to OPN [8,9]. These results are attributed to increasing surgical experience as well as the development and application of novel surgical techniques aimed at reducing the morbidity of this procedure. The current study was conceived to provide further evidence supporting the effectiveness of RAPN in a contemporary patient population treated at one of three tertiary care centers for robotic surgery. In addition, we demonstrate the evolution of RAPN-based technical improvements as well as the application of novel technologies that allows the use of RAPN even in patients with highly complex renal tumors.

2. Patients and methods

2.1. Patient population

The Transatlantic Robotic Nephron-sparing Surgery (TRoNeS) study group prospectively collected data from patients subjected to RAPN for clinically localized kidney cancer between 2010 and 2016 at three high-volume tertiary care centers (Humanitas Clinical and Research Center, Milan, Italy; Onze-Lieve-Vrouw Hospital, Aalst, Belgium; and Swedish Medical Center, Seattle, WA, USA). All patients underwent either preoperative computed tomography (CT) scan or magnetic resonance imaging to precisely define the anatomical characteristics of renal masses.

Intra- and postoperative complications, and functional and oncological outcomes were assessed. In addition, the optimal surgical outcome rate, defined according to the margin, ischemia, and complication (MIC) binary system (absence of Clavien-Dindo >2 complications, warm ischemia time [WIT] <20 min, and absence of positive surgical margins), was determined [10,11].

2.2. Surgical technique

2.2.1. Port placement

In all cases, patients were placed in a full-flank position, with the anterior abdomen placed on the lateral edge of the bed to minimize interference with the operative table. All pressure points were padded. When the da Vinci Si (Intuitive Surgical, Sunnyvale, CA, USA) was used and a transperitoneal approach was adopted, port placement was carried out as previously described by Benway et al. [12], with the use of a fourth arm being left to the single surgeon's preference. In case of retroperitoneal RAPN, robotic trocars were placed as previously shown by Hu and colleagues [13]. In most recent years, with the introduction of the da Vinci Xi robotic platform (Intuitive Surgical), port placement was slightly changed as robotic trocars were placed in a linear fashion on the lateral border of the rectus muscle, leaving at least 6 cm between two consecutive ports (Fig. 1). One or two assistant ports were also placed medially as compared with the robotic ports, depending on surgeon's preference and tumor complexity.

2.2.2. Hilar control and tumor identification

The gonadal vein, the ureter, and the psoas muscle are typically identified, and the lower pole of the kidney was elevated to facilitate the identification of the renal hilum. Complete defatting of the renal artery and skeletonization of its major branches are usually performed in order to allow both selective and nonselective artery clamping. Incision of the Gerota's fascia and kidney defatting are then performed to allow for precise identification of the renal mass. The renal mass is then evaluated with laparoscopic ultrasound to confirm tumor size and location, as well as to determine the margin of resection. Subsequently, tumor margins are marked using monopolar scissors, and the renal artery or its branches are then clamped. Hilar clamping is performed using robotic mini-bulldog clamps (Scanlan International, St. Paul, MN, USA), standard laparoscopic bulldog clamps, or tourniquet. As previously described, the renal vein is not routinely clamped, with the exception of selected cases (eg, centrally located or large tumors). For selective arterial clamping, indocyanine green (ICG) is administered, and absence of perfusion to the renal parenchyma surrounding the tumor is confirmed with near-infrared fluorescence (NIRF) imaging and visualized using TilePro technology. In selected cases of small central or hilar masses, a "zero-ischemia" RAPN was performed as previously described by Gill et al. [14]. Three-dimensional reconstruction of the arterial vessels, kidney shape, and tumor characteristics was also adopted in the most recent complex cases using high-resolution CT-scan images to explore the relationship between the renal mass and the surrounding structures.

2.2.3. Tumor excision and renal reconstruction

Once the tumor is correctly identified and its margins marked, robotic scissors are sharply used to dissect the tumor from the surrounding normal parenchyma without using cautery, while the fenestrated bipolar forceps are used to retract the tumor. After tumor excision, the first layer of the renorrhaphy and defect of the collecting system are closed using

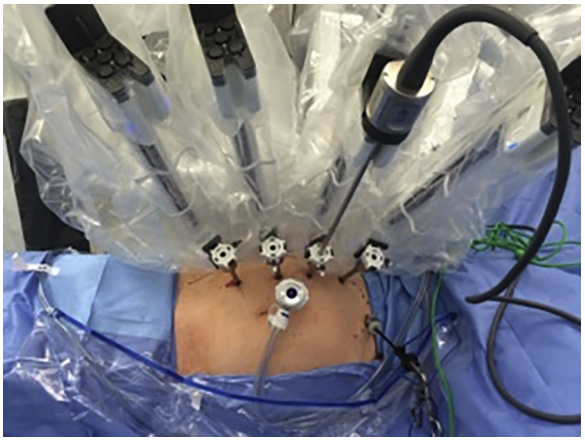

Fig. 1 – Port placement using the da Vinci Xi Robot: trocars are placed in a linear fashion on the lateral border of the rectus muscle, leaving at least 6 cm between two consecutive ports.

either a 3-0 Monocryl suture (Ethicon, Somerville, NJ, USA) or a 3-0 V-Loc suture (Covidien, Mansfield, MA, USA) in a running fashion. One surgeon (J.P.) closes the major vessels and calices with a separate suture. Subsequently, the renorrhaphy is closed externally with the "sliding-clip" technique using a 0 Vicryl CT-1 suture (Ethicon) and Weck Hem-o-lok clips (Teleflex, Research Triangle Park, NC, USA), as previously described by Benway et al. [15].

2.3. Statistical analyses

Demographic and perioperative data were analyzed using descriptive statistics. Counts of frequencies were expressed as percentages, and continuous data were presented as means ± standard deviations. Differences among groups were compared by using either the Student *t* test for continuous variables or the chi-square test for categorical variables. Multivariable logistic regression models (LRMs) were fitted to test the predictors of surgical outcomes. For all statistical analyses, a two-sided $p < 0.05$ was considered statistically significant. All analyses were performed using IBM SPSS version 23 (SPSS Inc., Chicago, IL, USA).

3. Results

Descriptive characteristics of the study cohort are shown in Table 1. Among 737 patients subjected to RAPN within the study period, 635 had complete demographic, perioperative, and pathological information, and were therefore included in the analysis. Of these patients, 399 (62.8%) were males. Mean patient age was 60.7 yr, mean body mass index was 29.4 kg/m^2, mean preoperative tumor size was 33 mm, and mean estimated glomerular filtration rate (eGFR) was 70.4. Right tumors were observed in 324 (51.0%) patients.

According to the PADUA score, 202 (31.8%) patients had a low-, 235 (37.0%) had an intermediate-, and 198 (31.2%) had a high-complexity tumor. Similarly, when stratifying tumor complexity according to the RENAL nephrometry score, 265 (41.7%) individuals had a low-complexity tumor, as compared with 307 (48.3%) and 63 (9.9%) patients with intermediate- and high-complexity tumors, respectively.

In the majority of patients, a transperitoneal approach was used ($n = 447$, 70.4%; Table 2). Mean operative time was 156.3 min and mean estimated blood loss was 171 ml. Overall, 506 (79.7%) patients were subjected to main artery clamping, as compared with selective clamping with intraoperative administration of ICG in 107 (16.9%) individuals. A "zero-ischemia" RAPN was performed in 22 (3.4%) patients with hilar or central renal tumors. Mean WIT was 16.3 min. Overall, 141 (22.2%) patients experienced WIT >20 min, but only in 22 (3.4%) individuals, WIT was ≥30 min. Only eight (1.3%) patients required conversion to open surgery. The mean percentage of change between pre- and postoperative eGFR was −11.3%.

Postoperative variables are shown in Table 2. Malignant tumors were observed in 473 (74.5%) and positive surgical margins in 24 (3.8%) individuals. The overall complication rate was 12.5% ($n = 80$), but only 25 (3.9%) of these patients

Table 1 – Descriptive characteristics of the study population

Preoperative variables	
Patient age (yr), mean ± SD	60.7 ± 12.2
Gender, *n* (%)	
Male	399 (62.8)
BMI (kg/m^2), mean ± SD	29.4 ± 6.8
CCI (age adjusted), *n* (%)	
0	43 (6.8)
1–2	162 (25.5)
≥3	430 (67.7)
Side, *n* (%)	
Right	324 (51.0)
Serum creatinine, preop (mg/dl), mean ± SD	0.96 ± 0.25
Postoperative eGFR, mean ± SD	70.4 ± 21.8
Clinical size (mm), mean ± SD	33.3 ± 16.0
PADUA score categories, *n* (%)	
Low (≤7)	202 (31.8)
Intermediate (8–9)	235 (37.0)
High (≥10)	198 (31.2)
Renal nephrometry score categories, *n* (%)	
Low (≤6)	265 (41.7)
Intermediate (7–9)	307 (48.3)
High (≥10)	63 (9.9)

BMI = body mass index; CCI = Charlson comorbidity index; eGFR = estimated glomerular filtration rate; SD = standard deviation.

Table 2 – Intra- and postoperative variables of the study population

Intraoperative variables	
Surgical approach, *n* (%)	
Transperitoneal	447 (70.4)
Retroperitoneal	188 (29.6)
Operative time (min), mean ± SD	156.3 ± 54.3
Estimated blood loss (ml), mean ± SD	171 ± 193
Type of ischemia, *n* (%)	
Main artery clamping	506 (79.7)
Selective clamping	107 (16.9)
Zero ischemia	22 (3.5)
Warm ischemia time (min)	
Mean ± SD	16.3 ± 6.6
>20, *n* (%)	141 (22.2)
≥30, *n* (%)	22 (3.4)
Conversion to open surgery, *n* (%)	
Yes	8 (1.3)
Postoperative variables	
Pathology results, *n* (%)	
Malignant	473 (74.5)
Benign	162 (25.5)
Postoperative tumor size (mm), mean ± SD	32.1 ± 16.1
Complications (Clavien-Dindo), *n* (%)	
I	21 (3.3)
II	34 (5.3)
IIIa	13 (2.0)
IIIb	12 (1.9)
Complications (CD >2), *n* (%)	
Yes	25 (3.9)
Length of stay (d), mean ± SD	3.2 ± 2.5
Serum creatinine, 1 d after surgery (mg/dl), mean ± SD	1.02 ± 0.33
Serum creatinine, 2 wk after surgery (mg/dl), mean ± SD	1.10 ± 0.32
Serum creatinine, 3 mo after surgery (mg/dl), mean ± SD	1.06 ± 0.29
Preoperative eGFR, mean ± SD	65.9 ± 19.7
% eGFR change, mean ± SD	−11.3 ± 18.8
Positive surgical margins, *n* (%)	
Yes	24 (3.8)
MIC achievement, *n* (%)	
Yes	459 (72.3)

eGFR = estimated glomerular filtration rate; MIC = margin, ischemia, and complication; SD = standard deviation.

experienced a significant complication according to the Clavien-Dindo classification. No statistically significant differences between pre- and postoperative creatinine values were observed ($p \leq 0.823$). Finally, optimal surgical outcomes defined according to the MIC score were achieved in 459 (72.3%) individuals. At a mean follow-up of 26 mo, only two local and two distant recurrences of the disease were observed.

In multivariable LRMs, tumor complexity was associated with the risk of not achieving optimal surgical outcomes (Table 3). More specifically, patients with intermediate- to high-complexity tumors according to the PADUA score experienced, respectively, a 2.1- and 4.7-fold higher risk of not achieving optimal surgical outcomes relative to patients with low-complexity tumors ($p \leq 0.025$). Similar results were observed after stratification according to the RENAL nephrometry score, with patients in the intermediate- and high-complexity tumor groups showing, respectively, a 3.4- and a 12.3-fold higher risk of not achieving optimal outcomes relative to their counterparts in the low-complexity tumor group ($p \leq 0.001$). Besides tumor complexity, gender achieved an independent predictor status, with males showing a three-fold higher risk of not achieving optimal surgical outcomes ($p < 0.001$) relative to their female counterparts.

4. Discussion

The current multi-institutional collaborative study provides further evidence supporting the use of RAPN for the treatment of renal masses. More specifically, in expert hands, RAPN provides optimal surgical and oncological outcomes in the great majority of patients. In addition, we validate the role of both the PADUA and RENAL nephrometry scores in predicting the outcomes of RAPN, therefore supporting their routine use in clinical practice.

According to current guidelines, RAPN is considered an alternative to other surgical techniques (eg, OPN and LPN) in patients with clinical T1 renal tumors, while thermal ablation procedures or active surveillance are suggested only for the elderly and/or comorbid individuals [2]. As shown by previous studies, the advantages of RAPN compared with OPN consist of lower blood loss and surgical complication rates, as well as shorter hospital stay [8,9]. Similarly, when compared with LPN, RAPN is associated with a shorter learning curve and shorter WIT, while sharing the advantages of minimally invasive surgery [3–7].

Further refinement of surgical technique and novel technologies have been implemented progressively in order to maximize the application and improve the outcomes of RAPN. For example, retroperitoneoscopic RAPN has been shown to provide comparable outcomes to those of transperitoneal RAPN and may therefore represent a safe and effective alternative, especially in cases of posterior tumors or in patients with previous abdominal surgeries [13,16–18]. These findings were confirmed in the current series, where no statistically significant differences between the transperitoneal and retroperitoneal approach were observed in terms of both CD >2 complications (3.4% vs 5.3%; $p = 0.245$) and MIC achievement rate (73.6% vs 69.1%, $p = 0.252$). The lack of difference in terms of surgical outcomes between the two approaches was also confirmed in multivariable LRMs, therefore confirming retroperitoneoscopic RAPN as an effective alternative to transperitoneal RAPN.

Similarly, NIRF imaging with ICG administration has shown its feasibility and safety, and is currently widely adopted to intraoperatively confirm the area of targeted ischemia during selective clamping [19–21]. In addition, refinement of the renorrhaphy technique has also been introduced with the aim of minimizing WIT, while

Table 3 – Multivariable logistic regression models evaluating factors associated with the lack of achievement of optimal surgical outcomes (MIC score = 0)

Multivariable logistic regression models				
Variable	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age	0.998 (0.969–1.029)	0.898	0.989 (0.959–1.020)	0.469
BMI	1.016 (0.981–1.052)	0.381	1.013 (0.977–1.050)	0.485
Age-adjusted CCI categories				
CCI 1–2 vs 0	1.367 (0.388–4.817)	0.626	1.470 (0.410–5.273)	0.554
CCI ≥3 vs 0	1.094 (0.252–4.745)	0.904	1.509 (0.338–6.737)	0.590
Gender				
Male vs female	**2.934 (1.761–4.888)**	**<0.001**	**3.007 (1.787–5.062)**	**<0.001**
Tumor side				
Left vs right	1.408 (0.888–2.234)	0.146	1.400 (0.73–2.246)	0.162
Surgical approach				
Retro vs transperitoneal	1.214 (0.761–1.938)	0.416	1.091 (0.674–1.768)	0.723
PADUA score categories				
Intermediate vs low	**2.085 (1.095–3.969)**	**0.025**	–	–
High vs low	**4.710 (2.485–8.926)**	**<0.001**		
RENAL nephrometry score categories				
Intermediate vs low	–	–	**3.446 (1.979–6.001)**	**<0.001**
High vs low			**12.301 (5.319–28.447)**	**<0.001**

Bold values indicate variables that reached statistical significance in multivariable analysis.
BMI = body mass index; CCI = Charlson comorbidity index; CI = confidence interval; MIC = margin, ischemia, and complication; OR = odds ratio.

maximizing the preservation of normal renal parenchyma and ensuring adequate hemostasis [15,22]. Within the current series, 107 (16.9%) individuals were subjected to selective clamping with NIRF imaging and ICG administration. In accordance with previously published articles, no difference in terms of CD >2 complications (4.5% vs 1.9%; $p = 0.203$), MIC score achievement (70.8% vs 75.7%; $p = 0.302$), or mean estimated blood loss (167 vs 155 ml; $p = 0.503$) was observed between patients undergoing either main or selective artery clamping [23,24]. As expected, the mean percentage of decrease between pre- and postoperative eGFR was lower in the selective clamping group (–7.8% vs–11.9%), although this finding did not achieve statistical significance ($p = 0.078$). According to our experience, selective clamping with NIRF imaging and ICG administration represents a feasible alternative to main artery clamping, especially in patients with preoperatively impaired renal function or those with a solitary kidney, where preservation of vital renal tissue is even more critical.

Based on the previous findings, we believe that RAPN should indeed be considered as a feasible and effective alternative to OPN and LPN in the treatment of renal masses. Specifically, in expert hands, RAPN is associated with low complication rates (3.9% of CD >2 complications) and conversion to open surgery rates (1.3%), while ensuring optimal oncological outcomes, as demonstrated by the low (3.8%) positive surgical margin rate and the extremely low recurrence rate. In clinical practice, these results translate into a 72.3% proportion of individuals achieving optimal surgical outcomes according to the MIC score. As shown by our analyses, even in expert hands, tumor complexity represents an effective predictor of surgical outcomes and, in consequence, should always guide the preoperative decision-making process. Besides tumor complexity, male gender also emerged as an independent predictor of worse surgical outcomes, which may be in part explained by the higher proportion of males with adherent perinephric fat [25].

Our study is not devoid of limitations. First, the fact that the study population consisted of contemporary patients with renal tumors translated into a relatively short follow-up that may have positively affected our oncological results. Therefore, further validation of these results with increasing follow-up is required. In addition, the fact that RAPN was performed at three tertiary care robotic-dedicated centers may also limit the generalizability of our findings. As previously shown by other studies, the teaching process and the subsequent learning curve associated with RAPN are indeed shorter relative to OPN or LPN [26,27]. This process may be further accelerated by dedicated teaching programs and the use of the dual console [28,29].

5. Conclusions

The current study provides further evidence supporting the role of RAPN as a viable and effective minimally invasive alternative to OPN in the treatment of clinically localized renal tumors. Despite surgical experience and technological improvements, tumor complexity still represents an independent predictor of optimal surgical outcomes.

Author contributions: James Porter had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Lughezzani, Buffi, Porter, Mottrie.
Acquisition of data: Buffi, Casale, Porter, Mottrie.
Analysis and interpretation of data: Lughezzani, Larcher.
Drafting of the manuscript: Lughezzani, Buffi, Larcher.
Critical revision of the manuscript for important intellectual content: Casale, Saita, Porter, Mottrie.
Statistical analysis: Lughezzani.
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Appendix A. Supplementary data

The Surgery in Motion video accompanying this article can be found in the online version at https://doi.org/10.1016/j.eururo.2018.11.038 and via www.europeanurology.com.

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