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Robot-assisted partial nephrectomy for renal tumors larger than 4 cm: results of a multicenter, international series

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Abstract

Backgrounds Limited data are available for the use of robot-assisted partial nephrectomy (RAPN) in tumors >4 cm. The objectives of this study were to report the perioperative outcomes of a series of patients who underwent RAPN for suspicious >4 cm renal tumors and to compare these results with those observed in a group of patients with ≤4 cm tumors.

Methods We analyzed retrospectively the clinical records of 49 patients who underwent RAPN for suspicious of renal cell carcinoma (RCC) >4 cm in size at four centers from September 2008 to September 2010. All patients underwent da Vinci RAPN. The results were compared with those observed in a group of patients undergoing RAPN for ≤4 cm renal tumors.

Results The median warm ischemia time (WIT) was 22 min (Interquartile range [IQR] 18–28). The median console time was 145 min (median IQR 112–177). The median blood loss was 120 mL (IQR 62–237). In two cases, we observed intraoperative renal vein injury (4 %). Postoperative complications were reported in 13 (26.5 %) patients. Major complications were observed in 4 (8.2 %) cases. Patients with large tumors showed perioperative outcomes worse than those received the RAPN for ≤4 cm tumors. Conversely, no significant difference was observed in positive surgical margin (PSM) rates.

Conclusions These outcomes support the use of RAPN as possible alternative to open PN for the treatment for patients with suspicious renal masses >4 cm. Positive surgical margin rates demonstrated RAPN is an oncologically safe procedure for tumors >4 cm.

Keywords Partial nephrectomy · Robotic surgery · Kidney tumor

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Introduction

International guidelines have recently supported the use of partial nephrectomy (PN) in patients with tumors greater than 4 cm and a normal contralateral kidney. The American Urological Association (AUA) guidelines recommend that PN should be considered as an alternative to radical nephrectomy in T1b cases, especially when there is a need to preserve renal function [1]. The European Association of Urology (EAU) guidelines consider PN the standard procedure for solitary T1b tumors whenever technical feasible [2]. These recommendations are based on the results of available comparative, non-randomized studies reporting overlapping oncologic outcomes between open PN and open or laparoscopic RN in T1b tumors [3–5].

Recently, robot-assisted partial nephrectomy (RAPN) has become an alternative to OPN with promising perioperative and early oncologic results reported in the literature, for the treatment for renal tumors ≤4 cm in size [6, 7]. The use of RAPN is considered in the latest version of the NCCN guidelines [8]. Preliminary data confirm the feasibility and safety of RAPN for tumors greater than 4 cm [9, 10]. However, only a limited number of cases of RAPN for large tumors are reported in the literature [6, 11].

The objective of the present study was to analyze the perioperative outcomes of a large number of patients who underwent RAPN for tumors >4 cm and suspicious renal cell carcinoma (RCC) and compare these data with those observed in cT1a category.

Patients and Methods

From the initial 347 cases included in the international, multicenter RAPN databases, we selected the clinical records of 49 patients who underwent the RAPN for tumors greater than 4 cm in size. All patients were treated in four Centers (Aalst, Belgium; Milan San Raffaele, Italy; Washington University School of Medicine, Saint Louis; and Swedish Urology Group, Seattle, WA, USA) between September 2008 and September 2010.

Prior to surgery, all patients underwent MRI or three-dimensional CT scans to define clinical stage and anatomical characteristics of the tumors.

For every patient, we extracted from the database the following variables: age, gender, clinical tumor size, anatomical tumors' parameters according to PADUA classification [12], warm ischemia time, upper collecting system (UCS) repair, console time, blood loss, intra-, and postoperative complication rates. Specifically, according to the PADUA score, tumors were stratified in low (score 6–7), intermediate (score 8–9), and high-risk groups (score ≥ 10) [12]. Three-month postoperative complications were classified according to the Dindo modification of the Clavien system [13]. We also extracted from the databases the following pathological variables: tumor size, extension of the primary tumor according to 2009 version of TNM classification [14], histological subtypes according to the World Health Organization (WHO) classification [15], nuclear grade according to the Fuhrman classification [16], and surgical margin status. Positive surgical margin was defined as cancer cells at the level of inked parenchymal excision surface.

Statistical analysis

Continuous variables were reported as median and interquartile range (IQR). Mann–Whitney U test and Pearson chi-square test were used to compare continuous and categorical variables, as appropriate. Preoperative and postoperative eGFR values were compared using the Wilcoxon test. Perioperative outcomes observed in the study group were compared with those reported in a contemporary series of patients who underwent RAPN for tumor ≤4 cm.

For all statistical analyses, a two-sided $p < 0.05$ was considered statistically significant. All data were analyzed with the Statistical Package for Social Sciences software, v.16.0 (SPSS Inc., Chicago, IL, USA).

Results

Patients characteristics

The median age of selected patients was 60 years (IQR 52–66). The median clinical tumor size was 5 cm (IQR 4.4–5.5). The tumors were located at right side in 20 (40.8 %) cases and at left in 29 (59.2 %). The median PADUA score was 10 (IQR 8–10). According to PADUA risk stratification, 5 (10.2 %) cases were classified as low-risk, 15 (30.6 %) as intermediate risk, and 29 (59.2 %) as high risk. Table 1 summarizes the anatomical characteristics of tumors included in this analysis (Table 1).

Perioperative outcomes

The median WIT was 22 min (IQR 18–28). WIT longer than 20 min was reported in 28 (57 %) cases. In only 8 (16 %) patients, the WIT was higher than 30 min. The median console time was 145 min (median IQR 112–177). The median overall operative time was 177 min (IQR 138–200). The median blood loss was 120 mL (IQR 62–237). During the surgical procedure, the upper collecting system (UCS) was repaired in 28 cases (57 %). In two cases, a renal vein injury occurred during exposure of the renal hilum (4 %). Postoperative complications were reported in 13 (26.5 %) patients. Specifically, we observed a single (2 %) grade 1; 8 (16.3 %) grade 2, and 4 (8.2 %) grade 3 complications. One patient (2 %) received prolonged antibiotic therapy for fever (grade 1); 7 patients (14.2 %) required blood transfusion, and one (2 %) medical therapy for cardiovascular disease (grade 2); 2 patients had ureteral stent for urine leakage, and 2 received selective arterial embolization for bleeding (grade 3). Therefore, minor complications were observed in 9 (18.3 %) cases (Grade 1–2) and major complications in 4 (8.2 %) cases (Grade 3).

Pathological and oncologic outcomes

The final histopathological examination showed benign tumors in 10 (20.4 %) cases, clear cell RCC in 25 (51 %),

Table 1 Tumors anatomical characteristics according to the PADUA classification

Variable	Cases (%)
Longitudinal (polar) location	
Upper pole	14 (28.6)
Middle pole	23 (46.9)
Inferior pole	12 (24.5)
Exophytic rate	
≥50 %	18 (36.7)
<50 %	26 (53.1)
Endophytic	5 (10.2)
Renal rim	
Lateral	41 (83.7)
Medial	8 (16.3)
Renal sinus	
Not involved	26 (53.1)
Involved	23 (46.9)
Urinary collecting system (UCS)	
Not involved	19 (38.8)
Involved	30 (61.2)
Face	
Anterior	23 (46.9)
Posterior	26 (53.1)

papillary RCC in 7 (14.3 %), chromophobe RCC in 6 (12.2 %), and unclassified RCC in 1 (2 %) case, respectively. Considering the 39 malignant tumors, the pathological stage was pT1a in 3 (7.7 %), pT1b in 30 (76.9 %), pT2 in 2 (5.1 %), and pT3a in 4 (10.3 %). Fuhrman nuclear grade was 1 in 9 (23 %) cases, 2 in 17 (47.2 %), 3 in 12 (33.3 %), and 4 in 1 (2.8 %) case, respectively. Positive surgical margins were detected in 2 (5.1 %) cases. All patients underwent a strict cancer surveillance program and at a mean follow-up of 12 months were alive and disease-free.

Functional outcomes

All the patients reported a preoperative estimated glomerular filtrate rate >60 mL/min/1.73 m^2 (eGFR). The median baseline eGFR value was 91 mL/min/1.73 m^2 (IQR 77–104). Three months after surgery, the median eGFR value was 84 mL/min/1.73 m^2 (IQR 64–103) ($p < 0.01$). Only 5 (10.2 %) cases reported a eGFR value lower than 60 mL/min/1.73 m^2. In this subgroup of patients, the median postoperative eGFR was 55 mL/min/1.73 m^2 (IQR 47–58).

Comparison between large and small tumors

Table 2 shows the comparison between large and small tumors (Table 2). WIT ($p < 0.001$), console time ($p = 0.004$), blood loss ($p = 0.001$), percentage of UCS repair ($p = 0.02$), and postoperative complications rates ($p = 0.001$) reported in the large tumors group were significantly greater than those reported in patients with tumor size ≤4 cm. Positive surgical margin rates were similar in the two groups ($p = 0.37$).

Discussion

This international, multicenter study demonstrated that RAPN is a safe procedure for tumors greater than 4 cm. The reported perioperative outcomes allow us to consider this procedure as an alternative to open partial nephrectomy (OPN) for the treatment for cT1b tumors.

Currently, most of the perioperative, oncologic, and functional data supporting the use of RAPN comes from single-center or multicenter studies analyzing patients with suspicious renal cancer ≤4 cm in size [6, 7, 11]. Less than 15 % of tumors treated in these series were larger than 4 cm. Only a few papers analyzed RAPN data in larger tumors [9, 10].

Prolonged WIT, the higher risk of perioperative complications, and positive surgical margins represent the most important concerns potentially limiting the diffusion of RAPN in tumors larger than 4 cm. In 2009, for the first time, Patel et al. showed the feasibility of the RAPN in a single-center series including 15 renal tumors larger than 4 cm. In that study, RAPN for tumors >4 cm showed comparable outcomes to RPN for smaller tumors, although with longer warm ischemia times (25 vs. 20 min). Interestingly, in this preliminary experience, the authors reported an overall complication rate of 26 % with 3 major complications (19.8 %). Of note, neither intraoperative complications nor positive surgical margins were reported [9]. More recently, Gupta published the results of a single-center series analyzing 19 procedures performed in 17 patients with tumors greater than 4 cm. In this series, the median WIT was 36 min and the median blood loss 500 mL. However, no patient received blood transfusion during the perioperative period and the unique complication reported was a case of urine leakage and ureteropelvic junction obstruction requiring postoperative stenting. Three procedures required conversion to OPN due to excessive bleeding, and there were no positive surgical margins were reported [10]. Both previous studies did not show any significant impairment of kidney function comparing preoperative and postoperative (3 and 12 months) creatinine and eGFR values [9, 10]. Table 3 compares data reported in the literature and those observed in the present study (Table 3).

The present multicenter study is the largest series available in the literature evaluating tumors greater than 4 cm. A high percentage of patients were classified into the

Table 2 Perioperative outcomes observed in 49 cases who underwent RAPN for cT1b-2 tumors were compared with data observed in a contemporary series of 298 cases who underwent RAPN for cT1a tumors

Variable	Tumor ≤ 4 cm (n = 298)	Tumor > 4 cm (n = 49)	p value
Median clinical tumor size (cm) (IQR)	2.5 (1.9–3.1)	5 (4.4–5.5)	<0.001
Median WIT (min) (IQR)	17 (14–22)	22 (18–28)	<0.001
UCS repair (%)			
Not performed	178 (59.7 %)	21 (43 %)	0.02
Performed	120 (40.3 %)	28 (57 %)	
Median console time (min) (IQR)	105 (90–150)	145 (112–177)	0.004
Median blood loss (mL) (IQR)	100 (50–150)	120 (62–237)	0.001
Intraoperative complications (%)	9 (3)	2 (4)	0.87
Postoperative complications (%)	28 (9.4)	13 (26.5)	0.001
Positive surgical margins (%)	6 (2.5)[a]	2 (5.1)[b]	0.37

[a] Frequency calculated on 236 RCC

[b] Frequency calculated on 39 RCC

Table 3 Perioperative outcomes in patients performing RAPN for tumors greater than 4 cm

Variable	Patel [9]	Gupta [10]	Present study
Cases (n)	15	16/19[a]	49
Anatomical characteristics			
Intermediate risk	Not assessable	12 (63.1 %)[b]	15 (30.6 %)[c]
High risk		6 (31.6 %)[b]	29 (59.2 %)[c]
Median WIT (min) (IQR)	25 (20–30)	36 (17–61)	22 (18–28)
UCS repair (%)	4 (27 %)	8 (50 %)	28 (57 %)
Median console time (min) (IQR)	275 (229–344)	390 (220–535)	145 (112–177)
Median blood loss (mL) (IQR)	100 (75–200)	500 (100–1600)	120 (62–237)
Conversion rate (%)	0	3 (16 %)	0
Intraoperative complication rate (%)	0	0	2 (4 %)
Postoperative complication rate (%)	4 (26.6 %)	1 (6 %)	13 (26.5 %)
Dindo-Clavien ≥3 grade complications (%)	3 (19.8 %)	1 (6 %)	4 (8 %)
Positive surgical margin rates (%)	0	0	2 (5.1 %)[d]

Literature data

[a] 16 patients/19 procedures

[b] RENAL nephrometry stratification

[c] PADUA score stratification

[d] Frequency calculated on 39 RCC

high-risk group according to PADUA score, and the median WIT for our group was significantly less than that observed in the Bethesda series [10]. Moreover, only 8 (16 %) patients experienced a WIT >30 min and were potentially exposed to a higher risk of kidney injury [17]. We found that WIT in tumors >4 cm was significantly higher in comparison with tumors ≤4 cm. Our findings are similar to those previously reported in another comparative study [9]. The results of RAPN are different from those previously reported in a large series of OPN by Patard et al. [18]. In that multicenter study, the authors reported similar WIT between tumor >4 cm and ≤4 cm in size, with a

mean WIT of 17 min for the first group and 19 min for the latter [18]. In 2010, Porpiglia et al. reported the results of a European study including 63 cases treated with traditional laparoscopic partial nephrectomy for renal tumors larger than 4 cm. In that series, the authors reported a mean WIT of 25.7 min [19]. Worse results were reported by Simmons et al. [20] in patients with tumors larger than 4 cm, where they reported WIT as long as 38 min [21]. Obviously, the difference in terms of WIT should be adjusted for anatomical and topographic tumor characteristics. Unfortunately, that data were not available in the previous papers evaluating LPN cases.

Our results differ from those reported in the other studies in terms of intra- and postoperative complications. We observed 2 intraoperative complications characterized by renal vein injury performed during the hilum isolation. Both injuries were immediately repaired without consequences. No intraoperative complications were reported in the other two studies [9, 10]. However, Gupta et al. reported 3 conversions to OPN due to significant bleeding. Looking at the major complications, we reported complication rates similar to those of Gupta et al. [10] but significantly lower in comparison with the Patel series [9]. Urine leakages requiring stenting and bleeding needing selective embolization were the most common major postoperative complications. Specifically, the percentage of urinary fistula was 4 % in our experience, 6 % in the Gupta experience, and 13 % in the Patel series [9, 10]. Looking at the European LPN survey, the authors reported major postoperative complications in 9.5 % of cases. Also in this series, the most frequent complications were represented by acute bleeding and urinary fistula [19].

In the present series, we observed positive surgical margins in 2 patients (5.1 %). This percentage overlapped that reported in the subgroup of patients with tumors ≤4 cm. No PSMs were reported in the other series analyzing the role of RAPN in tumors larger than 4 cm [9, 10]. This difference could be due to the higher complexity of cases included in our series in comparison with the initial experiences of the other studies where they were more selective.

Few studies compared RAPN with OPN in the subgroup of patients with large and/or complex cases. Recently, Sprenkle et al. showed that in patients with tumors >4–7 cm, minimally invasive technique including both traditional and robot-assisted laparoscopic partial nephrectomy offers acceptable and comparable perioperative and functional results in comparison with open approach [21]. Similarly, Simhan et al. in a recent paper comparing RAPN and OPN in moderately and highly complex tumors concluded that RAPN offered comparable perioperative and functional outcomes to OPN [22]. The retrospective study design is the main limitation of the present study. Therefore, some variable of potential relevance such as patient comorbidity were not collected in our dataset. Moreover, minor complications were not routinely collected by the participant centers.

Conclusions

The reported perioperative outcomes support the use of RAPN as an alternative to OPN for the treatment for patients with suspicious renal masses larger than 4 cm. However, patients in this subgroup are likely to experience longer WIT and an increased risk of perioperative complications. RAPN is an oncologic safe procedure for tumors greater than 4 cm in size based on a low PSM rate. Further studies evaluating intermediate and long-term oncologic outcomes are needed. Moreover, further investigations comparing RAPN to open or traditional laparoscopy approaches are awaited.

Conflict of interest None.

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