ORIGINAL ARTICLE

Open versus robotic-assisted partial nephrectomy: a multicenter comparison study of perioperative results and complications

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Abstract

Purpose To compare surgical results, morbidity and positive surgical margins rate of patients undergoing robotic partial nephrectomy (RPN) versus open partial nephrectomy (OPN).

Methods This is an observational multicenter study promoted by the "Associazione GIovani Laparoscopisti Endoscopisti" (AGILE) no-Profit Foundation, which involved six Italian urologic centers. All clinical, surgical, and pathological variables of patients treated with OPN or RPN for renal tumors were gathered in a prospectively maintained database. Tumor nephrometry was measured with PADUA score, and complications were stratified with modified Clavien system. Differences between RPN and OPN group were assessed with univariate analysis. Perioperative variables independently associated with complications were assessed with multivariate analysis.

Results A total of 198 and 105 patients were enrolled in OPN and RPN group, respectively. Both had similar demographics, indications to surgery, tumor nephrometry, renal function, WIT (18.7 vs. 18.2 min; p = NS), positive margin rate (5.6 vs. 5.7 %; p = NS), intraoperative complications, and postoperative medical complications. Compared to OPN, RPN group was significantly more morbid (p = 0.04), included tumors with smaller size (p = 0.002), had longer operative time (p < 0.001), lower

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blood loss, surgical postoperative complications (5.7 vs. 21.2 %, p < 0.001), Clavien 3–4 surgical complications (1 vs. 9.1 %, p = 0.001), and shorter hospitalization. The surgical approach resulted independently correlated with surgical complications on multivariate analysis.

Conclusion In the present series, RPN was associated with a significant reduction of blood loss, surgical complications, including the reintervention rate for urinary fistula and postoperative bleeding, and with a shorter hospitalization.

Keywords Kidney tumor · Partial nephrectomy · Robotics · Complications

Abbreviations

ADDICVIATIONS	
I postop./III postop.	First/third postoperative day
ASA	American Society of
	Anaesthesiologists
BMI	Body mass index
EBL	Estimated blood loss (during
	surgery)
ECOG	Eastern cooperative oncology group
IQR	Interquartile range
LOS	Length of hospital stay
OPN	Open partial nephrectomy
PB	Postoperative bleeding
PN	Partial nephrectomy
PSM	Positive surgical margins
RPN	Robotic partial nephrectomy
RCC	Renal cell carcinoma
RR	Related risk
SD	Standard deviation
UCS	Urinary collecting system
UF	Urinary fistula
WIT	Warm ischemia time

Introduction

Open partial nephrectomy (OPN) is the standard treatment for renal masses up to 7 cm in major dimensions, if technically feasible [1, 2], since long-term oncological findings resulted comparable to those of radical nephrectomy [3], and the preservation of renal function associated with partial nephrectomy (PN) resulted of crucial importance to prevent all-cause mortality [4, 5]. Laparoscopic partial nephrectomy (LPN) and robotic partial nephrectomy (RPN) are the main mini-invasive alternatives to OPN, aimed at reducing the added morbidity of an open incision and potential rib resection. While bringing excellent results in experienced hands, the diffusion of LPN has been limited by the technical difficulty and is currently performed in a few high-volume centers. At contrary, RPN seemed to be a more reproducible technique, able to bridge the technical difficulties of LPN in favor of a broader diffusion of minimally invasive PN. A few well-designed comparative studies have investigated the perioperative outcomes of RPN versus those of LPN [6-8], while to date no prospective studies comparing RPN and OPN are available, but only few retrospective series with limited cases [9–11]. The aim of the present study is to compare the perioperative results and surgical complications of RPN and OPN.

Patients and methods

This is a two-year observational multicenter study promoted by the "Associazione GIovani Laparoscopisti Endoscopisti" (AGILE) no-profit foundation, which includes a group of urologists performing in daily practice traditional, laparoscopic, and robotic surgery in different hospitals. Between January 2010 and December 2011, the clinical records of all patients consecutively treated with OPN or RPN for clinically localized renal cell carcinoma (RCC) were gathered at six Italian urological centers (Florence, Udine, Brescia, Abano Terme-PD, Novara, Mantova) and included in a prospectively maintained database. The approach selection was based on a chronological criterion, as the robot was available on 4 centers at the beginning of the study and in each center at the end. Additional criteria were patients with preferences for specific approach, or with significant previous transperitoneal surgery, which have been treated with OPN. Approval of study protocol by the local ethical committee was obtained at each center, and informed consent was collected for all patients.

Surgical technique and surgeons experience

The surgical resection was done by standard partial nephrectomy, leaving a minimal tumor-free surgical margin

around RCC. Tachosil[®] or Floseal[®] plus surgical bolsters (Tabotamp[®]) were the hemostatics used in all centers. The surgical approach was chosen according to surgeons and centers preferences as well as to the da Vinci system availability. The surgical complexity and nephrometry score did not represent criteria for the decision. At the beginning of the study, all surgeons performing RPN were within the learning curve (20 cases) [12], but they had previous experience in LPN, while the surgeons performing OPN had a substantial previous experience in open kidney surgery (>50 cases).

Robotic partial nephrectomy was done with da Vinci S/Si Surgical Systems, (Intuitive Surgical, Sunnyvale, USA), all but one center (Abano Terme-Padua) used a transperitoneal approach, because it was the preferred and commonly used access. Patients were placed in flank position. A standard 3-arm approach with a fourth trocar for the assistant and fifth trocar as needed for right-sided cases was used. The renal hilum was identified to locate renal artery and vein. In case of unfavorable position, the kidney was isolated and rotated in order to perform comfortably the demolitive and reconstructive phases. Ischemia, if needed, was obtained with the clamping of renal artery or, according to surgeon's preference, with a selective arterial clamping. Hemostasis in the resection bed was achieved with running sutures (Monocryl 3-0) preloaded with a Hem-o-lok, brought outside through the parenchyma according to the sliding-clip technique. Care was taken to repair all visible opened calices and bleeding sites with these running sutures. Usually, the cortical defect was closed with horizontal interrupted sutures after apposition of hemostatic agents.

Open partial nephrectomy was done using a lateral retroperitoneal approach for all patients. The renal pedicle was usually controlled en bloc with a vascular clamp. Alternatively, manual compression was used in case of polar lesions according to center's preference. Since the warm ischemia time (WIT) was usually under 25 min, cold ischemia was never used in this series. Bleeding vessels and incidentally opened calyces were sutured with 4-0 monofilament running sutures. The parenchymal defect was closed with horizontal interrupted sutures after apposition of hemostatic agents.

Data collection

The following patients characteristics were included in the database: age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, Charlson index, and surgical indication. All patients were staged preoperatively with computed tomography or magnetic resonance imaging. The nephrometry of tumors was assessed by the clinical imaging and measured with PADUA score [13]. The use of pedicle clamping, warm ischemia time (WIT), total operative time, estimated blood loss (EBL), length of hospital stay (LOS), including the date of surgery, was registered. The blood hemoglobin and serum creatinine were recorded preoperatively, in first and third postoperative day. The estimated glomerular filtration rate (eGFR) was calculated with the modification of diet in renal disease equation [14]. Pathological tumor size, 2009 TNM stage [15], Fuhrman nuclear grade [16], surgical margin status, and histological subtypes according to World Health Organization classification [17] were registered. No central pathological slide review was performed. All the intra- and postoperative medical and surgical complications, occurring during surgery and within 30 days, were recorded. The severity of surgical complications was stratified according to the modified Clavien system [18]. Postoperative blood loss was registered in case of reduction >2.5 g/dL in hemoglobin level (grade 1), and the need of blood transfusions (grade 2), superselective embolization of renal artery (grade 3a) or of re-intervention (grade 3b-4) was listed. Urinary fistula was registered if there was persistent leakage from the drainage beyond sixth postoperative day and a biochemical analysis of the drain fluid consistent with urine (drainage fluid-to-serum creatinine ratio greater than 2). Ureteral stenting was limited to urinary fistula with persistent leakage beyond tenth postoperative day.

Statistical analysis

Continuous parametric variables are presented as mean \pm standard deviation (SD), nonparametric variables as median and interquartile range (IQR), and categorical variables with frequencies and proportions. PADUA score was analyzed both as nonparametric continuous (3-13) variable and as a binary with cutoff 10 (<10 vs. \geq 10). Univariate analysis (Pearson's χ^2 test, unpaired t test, and Mann-Whitney U test, as appropriate) was used to assess the differences of preoperative variables, surgical results, and complications between RPN and OPN group. A multivariate logistic regression model tested the ability of the surgical approach, along with the other relevant clinical variables, to predict overall surgical complications and Clavien grade 3-4 surgical complications, analyzed separately. All tests were two-sided, with a statistical significance at p < 0.05. Analyses used all events in Stat view 5.0.1 (SAS Institute Inc. Cary, MC, USA).

Results

Perioperative data are shown in Table 1.

Baseline characteristics

Overall, 302 patients were included. Of them, 198 underwent OPN and 105 RPN. The OPN and RPN groups were significantly different in the following preoperative parameters: clinical tumor size $(3.5 \pm 1.8 \text{ and } 2.8 \pm 1.5; p = 0.002)$ and Charlson index ≥ 2 (5.6 and 25.7 %; p = 0.04), while imperative indications had a trend of difference that did not reach the statistical significance (5 versus 1 %, p = 0.07).

Intra- and postoperative outcomes

Clamping of renal vessels was used in 48 % (95/198) of OPN patients and in 62 % (65/105) of RPN patients. When used, WIT resulted not significantly different in OPN versus RPN group (18.7 and 18.2 min, respectively). In OPN group, the operative time was significantly lower (p < 0.0001) and EBL was higher (p = 0.0004). One robotic procedure was converted to open due to hemorrhage, while the total number of intraoperative complications did not differ between groups. In third postoperative day, the mean change of hemoglobin was higher in OPN group (p = 0.0019), while no significant difference resulted in the mean variation of eGFR. Overall, postoperative complications occurred in 48/198 (24.2 %) patients in OPN group and in 9/105 (8.6 %) in RPN group (p = 0.009). About 3 % of patients had medical complications in each group, thus leaving a higher rate of surgical complications in OPN versus RPN group (21.2 vs. 5.7 %; p < 0.0001). The stratification for severity of surgical complications is summarized in Table 2. Postoperative bleeding (PB) and urinary fistula (UF) were the most frequent; in OPN group, PB occurred in 29/198 (14.6 %) patients; in 21/198 (10.6 %), it was managed with transfusions and in 7/198 (3.5 %) with a second procedure under anesthesia; of these, 4/198 (2 %) were subjected to a superselective embolization and 3/198 (1.5 %) to a reintervention. Nephrectomy was necessary for two patients (1 %), due to the impossibility to stop the bleeding from the resection bed. In OPN group, the UF occurred in 11/198 (5.5 %) patients. Of these, 2/198 (1 %) were treated with expectancy, 8/198 (4%) with the ureteral stent, and one case (0.5%) was complicated with renal abscess and required nephrectomy. Considering the surgical complications of the RPN group, PB occurred in 5/105 (4.8 %) of patients; in 4/105 (3.8 %), it was managed with transfusions only, and one patient (1%) underwent a superselective embolization. In RPN group, UF occurred in 1/105 (1 %) patients and was treated conservatively; no ureteral stenting was needed in robotic group. No Clavien grade 5 complication occurred in either group.

Then, we assessed the preoperative variables associated with surgical complications (Table 3). The clinical tumor size, the Charlson index, the surgical indication, the PADUA score, and the surgical approach were significantly associated with postoperative surgical complications

Table 1 Perioperative data of patients and tumors, stratified according to surgical procedure

	Open partial nephrectomy $N = 198$	Robotic partial nephrectomy $N = 105$	р	
Preoperative variables				
Male gender (%)	62	65.8	Ns	
Age (years) mean \pm SD	63.8 ± 12.4	62.3 ± 11.6	Ns	
Body mass index median (IQR)	26.2 (24.3–29.3)	25.7 (24.0-27.7)	Ns	
ASA score 3 (%)	14.6	14	Ns	
Charlson index ≥ 2 (%)	5.6	25.7	0.04	
Imperative indication (%)	5.05	1	0.07	
Clinical tumor size mean \pm SD	3.5 ± 1.8	2.8 ± 1.5 cm	0.002	
PADUA score median (IQR)	7 (7–8)	7 (6–7)	Ns	
No pts. with PADUA ≥ 10 (%)	7.1	6.7	Ns	
Preoperative Hb (g/dL) mean \pm SD	13.9 ± 1.4	14.1 ± 1.2	Ns	
Preoperative serum creatinine (mg/dL) mean \pm SD	1.0 ± 0.4	0.9 ± 0.2	Ns	
Preoperative eGFR (ml/min) mean \pm SD	79.0 ± 21.1	89 ± 20.8	Ns	
Intraoperative variables				
Warm ischemia time (min) mean \pm SD	18.7 ± 8.1	18.2 ± 7	Ns	
Operative time (min) mean \pm SD	123 ± 43	168 ± 56	< 0.0001	
Estimated blood loss (cc) mean \pm SD	230 ± 208	125 ± 128	0.0004	
Intraoperative complications (%)	5.1	2.9	Ns	
Conversion to open surgery	_	1/105 1 %	_	
Clamping of the renal pedicle	95 (48 %)	65 (62 %)	Ns	
Pedicle en bloc	95 (48 %)			
Artery		53 (50.5 %)		
Selective clamping of artery branch		12 (11.5 %)		
No clamping	103 (52 %)	40 (38 %)		
Surgical results and complications				
Variation Hb (preoperative-III postoperative) (g/dL)	3.1 ± 1.9	2.3 ± 1.5	0.0019	
Variation (III postoperative-preoperative) serum creatinine	0.2 ± 0.3	0.3 ± 0.1	Ns	
Variation eGFR (preoperative-III postoperative) ml/min	8.3	7	Ns	
Overall postoperative complications (pts)	48/198 (24.2) %	9/105 (8.6) %	0.009	
Surgical postoperative complications (pts)	42/198 (21.2) %	6/105 (5.7) %	< 0.0001	
Postoperative bleeding	29 (14.6 %)	5 (4.8 %)		
Urinary fistula	11 (5.6 %)	1 (1 %)		
Intestinal lesions	2 (1 %)	0		
Medical postoperative complications (pts)	6/198 (3.0) %	3/105 (2.9) %	Ns	
Cardiovascular	4 (2 %)	3 (2.9 %)		
Respiratory	2 (1 %)	0		
Clavien grade 3-4 surgical complications (pts)	18/198 (9.1) %	1/105 (1) %	0.001	
Length of hospital stay, including the date of surgery	7 (5–10)	5 (4-6)	0.042	
Days median (IQR)				
Pathological data				
Pathological histotype (%)				
Benign	42 (21.2 %)	14 (13.3 %)	NS	
Malignant	156 (78.8 %)	91 (86.7 %)		
Clear cell	116 (58.6 %)	64 (61.0 %)		
Papillary	18 (9.1 %)	12 (11.4 %)		
Chromophobe	17 (8.6 %)	11 (10.5 %)		
Other malignant	5 (2.5 %)	4 (3.8 %)		

Table 1 continued

	Open partial nephrectomy $N = 198$	Robotic partial nephrectomy $N = 105$	р
рТ 2009			
pTla	112 (56.6 %)	73 (69.5 %)	
pT1b	24 (12.2 %)	7 (6.6 %)	
pT2a–b	8 (4.0 %)	1 (1 %)	
pT3a	12 (6.0 %)	10 (9.6 %)	NS
Fuhrman nuclear grade (%)			
G1	28 (14.2 %)	23 (21.9 %)	
G2	105 (53.0 %)	55 (52.4 %)	
G3–G4	23 (11.6 %)	13 (12.4 %)	
Positive surgical margin	11 (5.6 %)	6 (5.7 %)	NS

Univariate analysis with Pearson's chi-square test, unpaired t test, and Mann-Whitney U test, as appropriate

Table 2 Stratification for severity of postoperative surgical complications of RAPN versus OPN group with modified Clavien system	Postoperative surgical complications	Open partial nephrectomy	Robotic partial nephrectomy
	Clavien-Dindo grade 1	3 (1.5 %)	1 (1 %)
	Drainage leakage treated with expectancy	2 (1 %)	1 (1 %)
	Slight blood loss treated with bedrest	1 (0.5 %)	0
	Clavien-Dindo grade 2	21 (10.6 %)	4 (3.8 %)
	Blood loss treated with homologous blood transfusions	21 (10.6 %)	4 (3.8 %)
	Clavien-Dindo grade 3	15 (7.6 %)	1 (1 %)
	Urinary fistula treated with ureteral stenting	8 (4 %)	0
^a One case of inadvertent lesion of the descendent colon in a kidney extensively attached to the peritoneum. One early strangulated bowel herniation through the lombotomic incision	Blood loss treated with superselective hembolization	4 (2 %)	1 (1 %)
	Reintervention due to hemorrhage	1 (0.5 %)	0
	Intestinal lesions treated with reintervention	$2(1\%)^{a}$	0
	Clavien-Dindo grade 4	3 (1.5 %)	0
	Nephrectomy due to hemorrhage	2 (1 %)	0
	Nephrectomy due to renal abscess	1 (0.5 %)	0
		2	

at the univariate analysis (data not shown), while the avoidance of pedicle clamping was not correlated with postoperative surgical complications (p = 0.59). On the multivariate analysis, only the imperative indication (RR = 3.9; p = 0.050) and the open surgical approach (RR = 3.8; p = 0.005) resulted independently associated with postoperative surgical complications. Finally, surgical approach (RR = 9.4; p = 0.03) was the only variable independently associated with Clavien grade 3–4 surgical complications.

Discussion

In recent years, many papers compared the perioperative results of RPN and LPN, and current evidence suggests that RPN can reproduce the advantages of mini-invasiveness with a shorter learning curve, since it entails excellent perioperative outcomes after about 30 cases [12]. In some studies, it was found that RPN may decrease WIT, operative time and EBL [7, 19, 20], and in a recent series also the incidence of complications, compared to LPN [6].

Ideally, every surgical option for the conservative treatment of renal tumors should be compared to OPN that is the matching standard of treatment and has the robustness of data regarding surgical and oncological results [21]. To our knowledge, this is the second prospectively derived comparative study of perioperative outcomes of RPN and OPN. In accordance with our results, in the previous study, Simhan et al. [9] reported after RPN comparable WIT and eGFR modification, with shorter hospitalization. These data suggest that RPN may replicate the rapidity of the open approach in the more complex phase of intervention, also leading to comparable early functional results.

Preoperative variable	Postoperative surgical complications		Postoperative Clavien-Dindo grade 3-4 surgical complications			
	Risk ratio	p value	95 % CI	Risk ratio	p value	95 % CI
Clinical tumor size	1.15	0.15	0.95-1.4	1.5	0.22	0.9–1.5
Charlson index ≥ 2	0.5	0.1	0.2-1.15	0.6	0.46	0.19-2.13
Imperative indication	3.9	0.050	1.0-16.0	3.1	0.21	0.5-20.1
PADUA score ≥ 10	0.9	0.90	0.25-3.4	1.04	0.96	0.17-6.1
Technique open versus robotic	3.8	0.005	1.5–9.5	9.4	0.03	1.2-72.9
Use of ischemia	0.9	0.78	0.5–1.8	0.9	0.46	0.19–2.13

 Table 3 Multivariate analysis (logistic regression) of preoperative variables to predict surgical complications and Clavien grade 3–4 surgical complications after partial nephrectomy

PADUA preoperative aspects and dimensions used for anatomical classification of renal tumor

However, a previous study on this issue by Lee and colleagues reported a longer WIT in the RPN group (23 vs. 19 min, p < 0.001) [11]. It is not easy to justify this heterogeneity of results. Surely, the increasing surgeons experience in RPN may lead to a progressive reduction in WIT in the most recent series.

Interestingly, in the present series that evaluated all cases of PN regardless the nephrometry score, the robotic approach also resulted in a significant reduction of postoperative surgical morbidity. This is not in agreement with Simhan, which in tumors with moderate-high complexity according to RENAL score reported comparable postoperative complications [9]. This might suggest that benefits in terms of surgical morbidity of RPN are best expressed in tumors of low complexity, although this hypothesis cannot be supported by ourselves. In fact, in a subanalysis of patients with moderate-high nephrometry (PADUA score ≥ 8), not shown in the results section, the advantages of RPN in terms of overall postoperative complications remained significant (8 vs. 29.9 %; p = 0.026). A possible explanation for the reduction of complications might be the better visualization of the resection bed in resulting of a better closure of vessels and/or urinary collecting system. Prospective studies with larger series are needed to further elucidate this issue, and to confirm whether or not RPN has a lower surgical morbidity than OPN, as previously shown in comparison with LPN [6]. In our study, the advantages of RPN regarding the surgical morbidity could have been partially overestimated, due to a not negligible postoperative complications rate in the OPN group (24.2 %) and to a favorable complication rate in the RPN group that are, however, within the ranges reported in the literature (9.6-30.7 and 8-22 % for OPN and RPN, respectively) [22-26]. Also our rate of acute or delayed postoperative hemorrhage requiring reintervention (3 %) and of urinary fistulas (5.5 %) after OPN are within the ranges reported in the literature, 1.3–7.9 % [24, 27, 28] and 1.4–17.4 % [23, 29], respectively. Also Lee et al., in their retrospective study of OPN versus RPN, reported a higher overall postoperative complications rate in the open group (15.4 and 8.7 %, respectively; p = 0.158) although without reaching the statistical significance, possibly due to the relatively low number of patients in RPN group (n = 69). None of the previous comparisons between OPN and RPN subdivided postoperative complications into medical and surgical; in our series, the difference in postoperative complications was solely related to surgical morbidity, while no difference in medical complications was found, although RPN group had an higher Charlson index at baseline.

The oncological outcomes of RPN are usually presented using surrogate endpoints such as the PSM rate. Our PSM rate in RPN group was not higher than OPN, and both were within the range reported in the literature (0-7 %).

We acknowledge some limitations to the present study. First, surgeons experience was higher in the open group. This is an intrinsic bias of studies, which compare a new technique with the standard treatment. Moreover, tumor diameter was higher in OPN group. Nevertheless, tumor nephrometry was homogeneous, and in previous analyses, it resulted a stronger predictor of complications compared to tumor diameter [30]. The strengths of the present study are inherent to the prospective data collection, to the multicenter nature, to the strict definition of any complication that was decided before the data recording, and to the separate analysis of medical and surgical complications. This approach might increase the external validity of the data compared with the single-center, single-surgeon setting, reflecting a "real world" scenario.

The present experience evaluated the perioperative results only; future studies with appropriate follow-up will assess the differences of oncological and long-term functional outcomes between RPN and OPN.

Conclusion

In our analysis, RPN resulted comparable to OPN in terms of WIT and PSM rate, and showed a reduction of bleeding, postoperative surgical complications, and hospitalization. Operative time was significantly higher in RPN group.

Conflict of interest None.

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