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后腹膜机器人与腹腔镜肾肿瘤部分切除术：一项单一外科医生围手术期疗效的配对比较

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摘　要　目的：应用 R.E.N.A.L. 肾功能评分系统进行配对分析，比较腹膜后腹腔镜肾部分切除术（Laparoscopic Partial Nephrectomy，LPN）与机器人肾部分切除术（Robot-assisted Partial Nephrectomy，RPN）的围手术期疗效。方法：对 2016 年 1 月—2020 年 3 月 543 例于浙江大学医学院附属第一医院泌尿外科行腹腔镜及机器人辅助肾部分切除术患者的相关临床资料进行分析。根据 R.E.N.A.L. 肾功能评分、性别和年龄进行 1：1 配对（112 对配对），通过统计分析对围手术期结果进行比较。结果：LPN 组和 RPN 组在年龄、性别、体重指数（Body Mass Index，BMI）、肿瘤大小、美国麻醉学家协会（American Society of Anesthesiologists，ASA）评分和术前估算肾小球滤过率（Estimated Glomerular Filtration Rate，eGFR）方面均无显著差异。接受 LPN 的患者左侧肿瘤所占比例略高（51.7% Vs 42.9%，P=0.032）。两组在手术时间、术中出血量、术后住院时间（Length of Stay，LOS）、术后 eGFR、输血量和 / 或术后并发症等方面均无显著差异。RPN 组热缺血时间（Warm Ischemia Time，WIT）明显比 LPN 组短（18.9 min Vs 22.6 min，P=0.032）。以复杂性为特点的亚集分析显示，复杂肿瘤 RPN 的 WIT 显著短于 LPN（21.1 min Vs 26.3 min，P=0.012），而单纯性肿瘤 RPN 与 LPN 的 WIT 差异无统计学意义（16.4 min Vs 18.3 min，P=0.085）。结论：经腹膜后 RPN 手术时间较经腹膜后 LPN 短，但二者围手术期效果基本相同。在有限的腹膜后工作空间内进行复杂的肿瘤切除和修补，机器人辅助手术可能比传统的腹腔镜术更具优势。

关键词　肾细胞癌；肾部分切除术；腹腔镜手术；机器人辅助手术

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Retroperitoneal robotic versus laparoscopic partial nephrectomy for renal tumors: a matched comparison of perioperative outcomes of a single surgeon

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Abstract Objective: To compare the perioperative outcomes of patients undergoing retroperitoneal laparoscopic partial nephrectomy(LPN) and retroperitoneal robot-assisted partial nephrectomy (RPN) by matched analysis using R.E.N.A.L. nephrometry scoring system. Methods: Relevant clinical data of 543 case of laparoscopic and robot-assisted partial nephrectomy performed by a single surgeon via the RP approach from January 2016 to March 2020 from our database were screened and analyzed. Two groups were matched 1:1 (112 matched pairs) by R.E.N.A.L. nephrometry score, gender, and age. Statistical analysis was done to compare perioperative outcomes. Results: There was no significant difference between the LPN group and RPN group in terms of age, gender, body mass index (BMI), tumor size, American Society of Anesthesiologists (ASA) score or preoperative estimated glomerular filtration rate (eGFR). Patients undergoing LPN had a slightly higher proportion of the left side tumor (51.7% Vs 42.9%, P=0.032). No significant differences regarding to operative time, estimated blood loss, postoperative LOS, postoperative eGFR, transfusion or postoperative complications were found between the two groups. However, Warm ischemia times (WIT) in the RPN group were significantly shorter than that in the LPN group (18.9 min Vs 22.6 min, P=0.032). Subset analysis based on complexity indicated that WIT of complex tumors in the RPN group was significantly shorter than that in the LPN group (21.1 min Vs 26.3 min, P=0.012), but no difference of WIT was found on simple tumors between the RPN group and LPN group (16.4 min Vs 18.3 min, P=0.085). Conclusion: Retroperitoneal RPN showed shorter WIT and generally equivalent perioperative results to retroperitoneal LPN. Robotic surgery may have advantages over the traditional laparoscopic surgery on complex tumor excision and renorrhaphy in the limited retroperitoneal space.

Key words Renal cell cancer; Partial nephrectomy; Laparoscopic surgery; Robot-assisted surgery

Partial nephrectomy (PN) currently represents the standard of care for small renal tumors, as it can provide oncologic outcomes equivalent to those of radical nephrectomy (RN)[1]. Although open PN (OPN) is an efficacious procedure, progress in technology has recently led to effective minimally invasive surgical approaches for PN, including laparoscopic PN (LPN) and robot-assisted PN (RPN)[2].

LPN or RPN may be performed via a transperitoneal (TP) or retroperitoneal (RP) approach. Compared with TP approach, the main advantage of the RP approach is that it could pass renal artery directly and quickly. However, due to the smaller and limited working space, the RP approach may be more technically challenging[3].The Da Vinci Surgical System mitigates the disadvantages of the retroperitoneal laparoscopic approach because of increased degrees of freedom of movement and enhanced reconstructive capabilities, which make it possible to operate easily in confined spaces[3–4]. However, as so far, few studies on comparison of surgical outcomes between retroperitoneal LPN and retroperitoneal RPN. In this article, perioperative outcomes for retroperitoneal LPN and retroperitoneal RPN performed by a single experienced laparoscopic surgeon using R.E.N.A.L. nephrometry scoring were compared and reported[5].

1 Materials and Methods

1.1 Study population

All patients treated with LPN and RPN via retroperitoneal approach by a single surgeon (WANG S) for renal tumor from January 2016 to March 2020 were identified in our institution and were maintained prospectively in a database approved by the Institutional Review Board. Patients who had solitary kidneys, multifocal tumors, or radiological evidence of locally advanced disease or metastases were excluded. Medial renal masses were also not included in this study since they are very difficult to remove via the retroperitoneal approach. For our RPN cases, the 15 initial cases were excluded to avoid the influence on learning curve. RPN was performed using the da Vinci® SiTM Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). All patients underwent computed tomography angiogram (CTA) prior to surgery to determine tumor characteristics, renal vascular anatomy and R.E.N.A.L nephrometry score.

Patient demographics, tumor characteristics, perioperative information and pathologic findings were abstracted from the database. The R.E.N.A.L nephrometry score was determined as previously described by Kutikov A and Uzzo R G[5]. The complex tumor was defined as the tumor with R.E.N.A.L score ≥ 7, the simple tumor was defined as the tumor with R.E.N.A.L score<7. The operative time was considered to be started from the initial carbon dioxide insufflation to gas discharge, which could avoid biases caused by setup time or anesthesia time. Renal function was assessed by the estimated glomerular filtration rate (eGFR), which was calculated using the modification of diet in renal disease (MDRD) formula[6]. The eGFR results was obtained preoperatively, and the last available value (obtained at least 3 months before surgery) was used to calculate the change in renal function. Preservation of eGFR was defined as a ratio of postoperative eGFR to preoperative eGFR. Surgical complications were graded according to the Clavien classification system[7]. Hemorrhagic complications were defined as those requiring blood transfusion for intraoperative or postoperative bleeding, or those involving clinically significant bleeding requiring further management, such as false aneurysm, arteriovenous fistula, hematuria et al. One-to-one matching was done between the LPN and RPN groups based on R.E.N.A.L. nephrometry score, gender, and age (within 10 years).

1.2 Surgical techniques

Patients were placed in full flank position with the ipsilateral side up. Retroperitoneal working space establishment and Trocar placement for LPN has been described previously[8]. Trocar placement for RPN was performed according to UCLA mode[9]. The fourth robotic arm was not used due to the limited retroperitoneal working space. Intracorporeal operation of RPN was similar to LPN. Generally, the Gerota fascia paralleled to the psoas major was incised after the paranephric fat being cleared. The ureter could be easily identified anterior to the psoas major and dissection towards to the hilum was then performed. The renal artery is skeletonized to allow for adequate closing pressure with bulldog clamps. The renal vein is rarely clamped and only if a tumor in a very central location encroaching on the venous vasculature. The capsular borders of the tumor were defatted circumferentially to obtain clear visualization of the dissection margin and provide a clear view of the capsule for subsequent reconstruction. The fat overlying the tumor was left and attached to the capsule for retraction. The laparoscopic ultrasound probe was used to identify and confirm tumor location and resection margins scored by electrocautery. Tumor excision was performed by cold scissors dissection in all cases. Renorrhaphy was performed in 2 layers, 3–0 V-Loc suture was used on the deep layer for the closure of vascular structures and any collecting system injury, and 2–0 V-Loc suture was used for the closure of the outer cortical layer. All tumors were sent to pathology for frozen section analysis.

1.3 Statistical analysis

Patient demographics, perioperative parameters and complications were compared using SPSS version 19. Continuous variables were presented as mean ± standard deviation (SD), nonparametric variables were presented as median and interquartile range (IQR), and categorical variables were reported as frequencies and proportions. The Student's t test and Mann-Whitney U-test were used to compare continuous variables, as appropriate. Categorical variables were compared using the Chi-square (χ^2) test. All tests were considered statistically significant at $P<0.05$.

2 Results

A total of 365 cases of retroperitoneal LPN and 178 cases of retroperitoneal RPN were performed by a single surgeon (Wang S) at our institution from January 2016 to February 2020, of which 16 cases of LPN and 3 cases of RPN were excluded from this study due to incomplete clinical or image data. 2 cases of LPN converted to nephrectomy for oncological control were also excluded. Acceptable matches were obtained for the remaining 112 patients in each group.

There was no difference in terms of age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, tumor size, tumor location, nephrometry score and preoperative eGFR between the LPN and RPN groups (Table 1). Left side tumors were more common in the LPN group while more right tumors in the RPN group. No patient with solitary kidney was found in either group.

Operative time, estimated blood loss (EBL), oral resumption, postoperative length of hospital stay (LOS) and Transfusion were not significantly different between the two groups (Table 2). Warm ischemia time (WIT) was significantly shorter in the RPN group than that in the LPN group[(22.6 ± 5.2)min Vs (18.9 ± 4.1) min, P= 0.032]. However, no significant difference for postop eGFR [(71.3 ± 21.5) mL/min/1.73 m^2 Vs (72.2 ± 20.2) mL/min/1.73 m^2, P= 0.096), postoperative drainage time, change of eGFR and eGFR reserved (85.2% Vs 86.6%, P=0.205) was found between the RPN group and the LPN group.

In terms of subset analysis based on tumor complexity, as defined by the R.E.N.A.L score, there were 54 simple and 58 complex tumors in both the LPN group and RPN group (Table 3). After further analysis, we found that the tumor complexity had a rather significant effect on WIT. The WIT of complex tumors in the LPN group was longer than that in the RPN group (26.3 min Vs 21.1 min, P=0.012).

Table 1 Patient baseline characteristics

Variables	LPN (*n*=112)	RPN (*n*=112)	*P* value
Age, yr, mean (SD)	54.1(13.6)	56.2 (12.8)	0.078
Gender, *n* (%)			0.082
M	68(60.7)	71(63.4)	
F	44(39.3)	41(36.6)	
BMI, kg/m^2, mean (SD)	24.5 ± 4.8	23.9 ± 4.2	0.187
ASA score, *n* (%)			0.058
1–2	40(35.7)	45(40.2)	
3–4	72(64.3)	67(59.8)	
Tumor size, cm, mean (SD)	3.1 (1.5)	3.2(1.4)	0.206
Tumor side, *n* (%)			0.032
Left	58(51.7)	48(42.9)	
Right	54(48.3)	64(57.1)	
Tumor location, *n* (%)			0.185
Anterior	32(28.6)	31(27.7)	
Posterior	46(41.1)	49(43.8)	
Neither anterior nor posterior	34(30.4)	32(28.6)	
eGFR, ml/min/1.73 m^2, mean (SD)	84.2(20.2)	83.7(19.8)	0.126
Nephrometry score, *n* (%)			
4–6	54(48.2)	54(48.2)	1
7–9	51(45.5)	51(45.5)	
10–12	7(6.3)	7(6.3)	

Table 2 Perioperative outcomes

Variables	LPN (*n*=112)	RPN (*n*=112)	*P* value
Operative time, min, mean(SD)	125 (42)	132 (47)	0.065
WIT, mins, mean(SD)	22.6 (5.2)	18.9 (4.1)	0.032[a]
EBL, ml, mean(SD)	90 (70)	110 (130)	0.122
Oral resumption, d, median(IQR)	2 (1–3)	2 (1–4)	0.635
Postop LOS, d, median(IQR)	7 (5–10)	7 (5–9)	0.800
Postoperative bed time, d, median(IQR)	3 (2–4)	3(2–4)	0.905
Postoperative drainage time, d, median(IQR)	4 (3–5)	4(3–5)	0.972
Postop eGFR, ml/min/1.73 m^2, mean(SD)	71.3 (21.5)	72.2(20.2)	0.096
Change of eGFR, ml/min/1.73m^2, mean(SD)	−12.9 (14.5)	−11.5(13.6)	0.157
eGFR reserved, % (SD)	85.2% (16.1)	86.6%(15.2)	0.205
Transfusion, n(%)	1 (0.9)	2(1.8)	0.360

Note: [a]$P<0.05$

However, the WIT for simple tumors in the LPN group and RPN group was not significantly different (18.3 min Vs 16.4 min, P=0.085). With respect to renal function outcomes, there were no significant differences on postop eGFR, change of eGFR and preservation of eGFR between the LPN group and RPN group for both simple and complex tumors.

Postoperative complications were graded by the Clavien classification system (Table 4). There were no significant differences on overall, minor (Clavien grade 1 and 2) and major (Clavien grade 3 and 4) postoperative complications between the LPN group and RPN group. Postoperative complications occurred in 19 patients who underwent LPN (17.0%), including 2 major complications, of which 1 case of bleeding(false aneurysm) was managed by super-selective angioembolization. There were 17 (15.2%) complications in the RPN group, including 3 major complications, of which 2 cases of bleeding (1 arteriovenous fistula and 1 false aneurysm) were also managed by angioembolization.

The definitive pathological examination showed 11(9.8%) benign tumors (oncocytomas or angiomyolipomas) in the LPN group and 9 (8.0%) in the RPN group (P=0.312)(Table 5). There were no significant differences on Fuhrman nuclear grade and pathological stage between the two groups.

PSM (Positive surgical margin, PSM) was found in 1(0.9%) patient in the LPN group and 2 (1.8%) patients in the RPN group (Table 6). Clear cell renal cell carcinoma was found in 2 cases of patients with PSM and chromophobe cancer in 1 patient with PSM by final pathological diagnosis. All patients with PSM were managed with active surveillance. With a mean follow-up of 32 months for the LPN grou and 12.5 months for the RPN group, no local recurrence or distant metastasis were found during the follow-up.

3 Discussion

The majority of published reports on less-invasive nephron-sparing surgery described the transperitoneal approach, which probably be due to larger working space and more anatomic landmarks provided by the transperitoneal laparoscopic approach. Retroperitoneal LPN or RPN is less commonly used, although it has advantages on early exposure and renal vasculature isolation, which could reach posteriorly located tumors directly with less manipulation of abdominal organs and quicker recovery.

Table 3 Warm ischemia times and renal functional outcomes in simple tumor and complex tumor groups

	Simple tumor (n=108)			Complex tumor(n=116)		
	LPN(n=54)	RPN(n=54)	p value	LPN(n=58)	RPN(n=58)	p value
WIT, min, mean (SD)	18.3 (3.7)	16.4 (3.9)	0.085	26.3 (2.9)	21.1 (2.9)	0.012[a]
Preoperative eGFR, ml/min per 1.73 m^2, mean (SD)	83.8 (20.9)	84.1 (20.2)	0.920	84.6 (19.8)	83.3 (19.6)	0.254
Postoperative eGFR, mL/min/1.73 m^2, mean (SD)	73.5 (20.6)	74.1 (19.5)	0.875	69.2 (21.9)	70.4 (21.0)	0.362
Change of eGFR, mL/min/1.73 m^2, mean (SD)	−10.3 (14.2)	−10.0 (13.3)	0.922	−15.4 (14.7)	−12.9 (13.8)	0.057
eGFR preservation, % (IQR)	87.2 (15.7)	87.9 (14.8)	0.908	83.3 (16.5)	85.4 (15.7)	0.161

Note: [a]P<0.05

Table 4 Postoperative complications according to the Clavien system

	LPN (*n*=112)	RPN (*n*=112)	*P* value
Over complications, *n* (%)	19 (17.0)	17 (15.2)	0.192
Minor complications, *n* (%)	17 (15.2)	14(12.5)	0.078
(Clavien grade 1 and 2)	wound infection(2)	wound infection (3),	
	bleeding/transfusion(4)	bleeding/transfusion(3)	
	acute heart failure(1)	pulmonary atelectasis(1)	
	[a]urine leak (1)	pneumonia(3)	
	pneumonia (4)	atrial fibrillation(2)	
	atrial fibrillation(3)	acute heart failure(2)	
	deep vein thrombosis(1)		
	supraventricular tachycardia (1)		
Major complications, *n* (%)	2(1.8)	3(2.7)	0.205
(Clavien grade 3 and 4)	[b]bleeding (1)	[b]bleeding (2)	
	[c]pneumonia(1)	[d]wound infection(1)	

Note: [a]Conservative management; [b]Superselective angioembolization; [c]Acute care ; [d]Incision and rainage

Table 5 Pathological characteristics based on different surgical approaches

	LPN (*n*=112)	RPN (*n*=112)	*P* value
Pathological histotype, *n* (%)			
Benign	11 (9.8)	9(8.0)	0.312
Oncocytoma	3 (2.7)	4(3.6)	
Angiomyolipomas	8 (7.1)	5(4.4)	
Malignant	101 (90.2)	103(92.0)	0.560
Clear cell	76 (67.9)	82(73.2)	
Papillary	15 (13.4)	13(11.6)	
Chromophobe	10 (8.9)	8(7.1)	
Furhman grade, *n* (%)			0.782
Low (1–2)	74 (81.3)	75(78.9)	
High (3–4)	17 (18.7)	20 (21.1)	
Pathological stage, *n* (%)			0.638
T_{1a}	88 (87.1)	91(88.3)	
T_{1b}	12 (11.9)	10(9.7)	
T_{2a}	1 (1.0)	2(1.9)	
Margin status, *n* (%)			0.760
Neg	101 (100)	102(99.0)	
Pos	0(0)	1(1.0)	

Table 6 Clinical characteristics of patients with positive surgical margins

	Tumor size (cm)	R.E.N.A.L score	Pathology	Fuhrman grade	Stage	Management	Follow-up (month)
LPN:							
1	3.2	7P	Clear cell	2	T1aNxMx	Surveillance	32
RPN:							
2	2.5	9P	Clear cell	2	T1aNxMx	Surveillance	7
3	4.2	9A	Chromophobe	–	T1bNxMx	Surveillance	18

Because the traditional LPN remains technically challenging, RPN has emerged as an attractive option for both naive and experienced laparoscopic surgeons[10].To date, although several studies on retroperitoneal RPN have been reported[9, 11-17], no study on the comparison of surgical outcomes between retroperitoneal LPN and retroperitoneal RPN has been reported. Thus, our study aims to evaluate of the outcomes of retroperitoneal LPN and retroperitoneal RPN in treating renal tumor.

A study on the comparison of LPN and RPN shows that RPN is a safe and viable alternative to LPN, and RPN appears to decrease LOS, significantly reduce intraoperative EBL and shorten WIT[10]. In a similar analysis, 102 cases of comparison study between LPN and RPN for the treatment of suspected RCC of a single-surgeon experience was reported by WANG S[18], whose results showed that the mean operative time (140 min Vs 156 min, P=0.04), WIT (19 min Vs 25 min, P=0.03), and LOS (2.5 d Vs 2.9 d, P=0.03) of RPN were significantly shorter than LPN. However, these studies mentioned above were performed through the transperitoneal laparoscopic approach.

In this study, a matched-pair analysis with R.E.N.A.L. nephrometry scores was used to compare retroperitoneal LPN and retroperitoneal RPN performed by a single surgeon. No significant difference was found between the retroperitoneal RPN and the retroperitoneal LPN group in terms of operative parameters, except that the RPN group had significantly less WIT. Then, renal tumors in our study were divided into simple tumors (< 7) and complex tumors (⩾ 7) according to the R.E.N.A.L. nephrometry score[5]. The results showed that WIT of the retroperitoneal LPN and retroperitoneal RPN both increased with increasing complexity of tumors. Furthermore, WIT was not significantly different between the LPN and RPN in the excision of simple tumor (18.3 min Vs 16.4 min, P=0.085), however, the WIT of the RPN group was significantly less than the LPN group in the excision of complex tumor (26.3 min Vs 21.1 min, P=0.012). This result is different with the study reported by Long J A et al, who retrospectively compared the LPN and RPN in treating single renal mass with moderate or high complexity[19], and the results showed that there was no difference in WIT between moderate and high R.E.N.A.L. score subgroups. We believe that surgeon experience and tumor anatomical characteristics are important factors influencing WIT. Furthermore, a large working space is greatly facilitated to intracorporeal suturing, but robotic technology make it possible to perform renorrhaphy within confined retroperitoneal space.

One of the most important aims of NSS (Nephron Sparing Surgery, NSS) is to preserve renal function. Declining renal function after PN is usually caused by 2 independent factors: WIT[20] and the percentage of functional volume preservation[21]. The importance of WIT is well known, every minute matters was proposed by Eggener S E, who emphasized that the shorter WIT, the higher possibility of better recovery of renal function after PN[22]. However, some researchers believe that limited WIT in minimally invasive PN has only a marginal impact on postoperative renal functional outcomes, despite the clear cutoff value still being debatable[23–24]. In our study, the RPN group had a shorter WIT comparing with the LPN group, but the decreasing of eGFR was not statistically significant. There are several reasons that might explain this result. Firstly, the GFR was estimated based on the measurement of serum creatinine, which may not accurately reflect the degree of renal dysfunction in the clamped kidney. Secondly, in our unilateral minimally invasive PN study, WIT occurs unilaterally and the real function could be compensated by improving the function of the normal contralateral kidney. In addition, Simmons M N et al[21] reported that the degree of renal volume reduction was the primary determinants of the long-term functional outcome in patients who had acceptable ischemia time. Unfortunately, the volume of resected renal was not calculated for our patients in our study.

Despite a PSM rarely progressing to local recurrence[25], every effort should be taken to ensure complete gross and microscopic removal of the tumor in PN. Based on different surgical approaches, PSM rates are 0 to 7% after open PN, 0.7% to 4% after LPN, and 3.9% to 5.7% after RPN[26]. PSMs were detected in 1 (0.99%) patient after LPN and in 2 (1.94%) after RPN, the PSM rate was lower in our study than that in the other reported studies[25–26]. In our experience, less intraoperative blood loss could provide a clear operative field, which could help us to improve visualization of the resection margin. In our study, all patients underwent CTA examination to understand the variations exactly in renal vascular anatomy preoperatively. The variations in the origin of renal arteries are very common, such as accessory renal arteries, double renal arteries and early dividing renal artery. During resection the tumor, we underline the role of complete vascular occlusion to improve visualization of the resection margin.

The limitations of our study must be noted. This study was not a randomized trial, which may lead to possible bias. Moreover, surgeon experience was higher in the LPN group. The initial 15 RPN cases were excluded to minimize the effect of a learning curve, but it was impossible to adequately control for variable surgeon experience. Additionally, we also could not evaluate the oncologic outcomes duo to limited time of follow-up, especially in the RPN group.

4 Conclusion

Robotic surgical systems help to overcome the obstacles caused by the limited retroperitoneal working space in LPN. Our study indicates that retroperitoneal RPN could bring equivalent perioperative outcomes to the retroperitoneal LPN with a significantly shorter WIT. In terms of subset analysis based on tumor complexity, RPN has shorter WIT than LPN in the excision of complex tumors. However, the WITs of RPN and LPN in treating simple tumors are equivalent.

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