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Review

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Laparoscopic and Robotic-Assisted Partial Nephrectomy: An Overview of Hot Issues

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Abstract
Laparoscopic partial nephrectomy and robot-assisted partial nephrectomy are attracting increased attention from urologists. They can achieve the same effect of oncology control as radical nephrectomy; moreover, they can offer better preservation of renal function, thus obtaining long-term living benefits. The indications are also expanding, making it possible for larger and more difficult tumors. Laparoscopic partial nephrectomy and robot-assisted partial nephrectomy can be performed by transperitoneal and retroperitoneal approaches, with their individual advantages and limitations. In addition, the renal tumor scoring systems have been widely used and studied in laparoscopic partial nephrectomy and robot-assisted partial nephrectomy. In order to better preserve renal function, the zero-ischemia technique is widely used. The application of intraoperative imaging technology provides convenience and greater benefits. Besides, whether minimal invasive partial nephrectomy can be performed without stop antiplatelet treatment is still disputed. Clinicians perform substantial exploration and practice to achieve the "trifecta" of surgery: complete resection of the tumor, maximum protection of renal function, and no complications.

Introduction

Laparoscopic partial nephrectomy (LPN) was initially carried out in 1993 [1]. The development of this procedure has gradually been refined over the past 2 decades. Partial nephrectomy (PN) has become the gold standard of surgical management for T1 renal cell carcinoma over the last decade [2]. PN has comparable oncologic outcomes with radical nephrectomy (RN), which has been

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reported to be associated with higher mortality and a greater likelihood of renal failure [3]. Although technically challenging, LPN and, more recently, robot-assisted partial nephrectomy (RAPN) have obtained wide application.

In this review, we systematically described the current state of hot LPN and RAPN issues, particularly indications, transperitoneum and retroperitoneum approaches, preoperative score systems, zero-ischemia PN, intraoperative images that could assist operation and outcomes, and patients with oral antiplatelet drug treatment and complications.

Expansion of the Size Boundary

Minimal invasive partial nephrectomy (MIPN) has become a gold standard treatment strategy for small renal mass. For tumors larger than cT1a, MIPN has emerged as an optional treatment method because it provides better renal function preservation, without increasing positive surgical margin (PSM) rate [4].

Recently, more and more complex renal tumors are managed though MIPN; although technically challenging, complete tumor resection can be achieved [5]. Pavan et al. [4] conducted a systematic review and meta-analysis, including 13 case-control studies, to compare the data of MIPN for tumors >4 cm (n = 4,441) and for tumors <4 cm (n = 1,024). Warm ischemia time (WIT) was longer for the >4 cm group. No significant differences were found in postoperative estimated glomerular filtration rate (eGFR) and onset of postoperative chronic kidney disease. Moreover, there was no difference in the PSM rate [4]. RAPN also achieved satisfactory results for renal tumors larger than cT1b, and complications were acceptable. Long-term oncological control and renal function outcomes need to be further observed, but from the data on open partial nephrectomy and LNP, long-term outcomes should be acceptable [6]. With the development of technique for LNP, imaging technology and renal anatomy, more and more technically challenging tumors such as hilar [7] and central or large lesions [8] are treated. MIPN is also technically possible in patients with totally intrarenal tumors [9], kidney stones [10], ureteropelvic junction stenoses [10], and renal venous tumor thrombi [11]. But for clinical stage >T1b tumors, large-sample, randomized control studies are expected for the evaluation and comparison of long-term oncological outcomes of MIPN with minimal invasive radical nephrectomy.

RAPN versus LPN

Comparative studies have shown that LPN is more economically effective than RAPN. Recently, Zhang X and their group evaluated LPN and RAPN in completely endophytic renal tumors and reported that no significant differences were found in operation time, estimated blood loss (EBL), WIT, rates of PSM RATE, and postoperative complications; however, LNP was correlated with a lower cost [9]. Froghi et al. [12] performed a meta-analysis, which included 6 nonrandomized controlled studies, containing 256 patients with stage T1a renal tumors. The results showed that LPN and RAPN were similar in terms of perioperative outcomes such as WIT and complications. Aboumarzouk et al. [13] conducted a similar study, evaluating 7 nonrandomized observational studies of RAPN (>300) and LPN (>400) patients. Ultimately, RAPN showed a significantly shorter WIT, but there were no significant differences in terms of EBL, operative times, conversion rates, complication rates, and length of stay (LOS). On the other hand, Choi and colleagues [14] performed a meta-analysis which included 2,240 patients. No differences were found in complications, renal function change, operative time, EBL, and PSM between the RAPN and LPN groups. However, the RAPN group showed a significantly better outcome in conversion to open surgery and RN, WIT, eGFR change, and LOS. These benefits may be attributed to advantages of the robot including superior image magnification, 3D imaging, 7-degree-of-freedom wristed devices, and tremor filtering [15].

Transperitoneum Approach versus Retroperitoneum Approach

PN can be performed through a transperitoneum or retroperitoneum approach. Both approaches have advantages and disadvantages, which are summarized in Table 1.

Pavan et al. [16] conducted a systematic review to evaluate the perioperative outcomes of transperitoneal and retroperitoneal approaches for RAPN in 886 and 513 patients, respectively. The tumors were found to be a little bit larger for the retroperitoneal group and more frequently posteriorly or laterally located. Posterior tumors were included in only 2 studies. Significantly shorter operating times and lower EBL were found with the retroperitoneal approach. Moreover, the retroperitoneal approach achieved a significantly shorter LOS. There were

Table 1. The advantages and disadvantages of different approaches of MIPN in nephron-sparing surgery

Approaches	Strengths	Weaknesses	References
Transperitoneal	Convenient for tumors with an anterior location	Difficult for tumors in posterior locations	[6]
	Greater operating space	Difficult to access the renal artery	
Retroperitoneal	Convenient for tumors with posterolateral locations	Limited amount of operative space	[6]
	Reduce the risk of bowel injury	Limited range of motion	
	Suitable for patients with prior abdominal procedures	Suboptimal visualization	
	Shorter operative time		[16, 17]
	Lower EBL		[16–18]
	A shorter duration of hospital stay		[16–18]
	A faster return of bowel function		[18]
	Avoid colonic mobilization; reduce the risk of bowel injury		[49]
	Ensure a more direct access to the kidney and renal hilum	Limited land marks	[17]
	Easier to access the renal artery		[18]

MIPN, minimal invasive partial nephrectomy; EBL, estimate blood loss.

no differences in overall complications, major postoperative complications, WIT, and PSM (p values were 0.67, 0.82, 0.96, and 0.95, respectively). Arora et al. [17] evaluated retroperitoneal and transperitoneal RAPN in a multi-institutional study; 394 patients were in the transperitoneal group and 99 patients were in the retroperitoneal group. Median LOS of transperitoneal and retroperitoneal approaches was 3 days and 1 day, respectively ($p < 0.001$). EBL was significantly lower in the retroperitoneal setting, with 100 versus 125 mL, respectively ($p = 0.007$). No differences were found in terms of operative time, WIT, PSM RATE, intraoperative complications, conversion to RN, postoperative major complications, and change in eGFR (p values >0.05). Mittakanti and colleagues [18] reviewed 281 cases of patients treated by robotic retroperitoneal PN and 263 cases of transperitoneal PN from 2006 to 2016. They conducted a matched paired study on 166 pairs of cases. No differences were found in terms of complexity, WIT, PSM rates, pathology, complications, and renal function change. But, significantly shorter operation time and lesser EBL were observed in the retroperitoneal PN group.

Retroperitoneal LPN can achieve the same results as the transabdominal approach in appropriate patients. Moreover, it may be more suitable for tumors in the posterior/upper position and around the renal hilum, with reducing surgical time and hospital stay [16]. Doctors should master operation techniques of both approaches, in order to choose the most suitable pathway depending on tumor location and size and whether the patient has undergone abdominal surgery.

Renal Nephrometry Scoring Systems

For the purpose of standardizing tumor assessment, standardizing tumor assessment bias, complication prevention, predicting ischemia time, and improving clinical outcomes and clinical decision making, many preoperative scoring systems for renal tumors have been developed. Some of the frequently used renal nephrometry scoring systems are discussed below.

RENAL nephrometry score (RNS) is an anatomical classification system for renal masses. It is first proposed by Kutikov and Uzzo in 2009 [19] and is widely recognized and used in clinical practice (Fig. 1). Many studies have shown that RNS is significantly associated with perioperative outcomes and complications [20–25]. Another study by Satasivam et al. [26] showed that an increase in RNS is associated with histological features of tumor aggressiveness. Ficarra et al. [27] developed the PAUA score, which integrates the tumor size and anatomical features of renal mass. In 2010, Simmons et al. [28] published the c-index renal tumor scoring system, which re-

	1 pt	2 pts	3 pts
(R)adius (maximal diameter in cm)	≤4	>4 but <7	≥7
(E)xophytic/endophytic properties	≥50%	<50%	Entirely endophytic
(N)earness of the tumor to the collecting system or sinus, mm	≥7	>4 but <7	≤4
(A)nterior/posterior	No points given. Mass assigned a descriptor of a, p, or x		
(L)ocation relative to the polar lines* *Suffix "h" assigned if the tumor touches the main renal artery or vein	Entirely above the upper or below the lower polar line	Lesion crosses polar line	>50% of mass is across polar line (a) or mass crosses the axial renal midline (b) or mass is entirely between the polar lines (c)

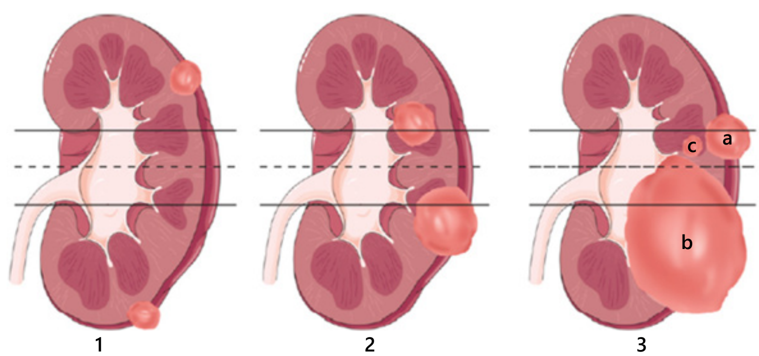

Fig. 1. RENAL is the abbreviation of (R)adius (scores tumor size as maximal diameter), (E)xophytic/endophytic properties of the tumor, (N)earness of the deepest portion of the tumor to the collecting system or sinus, (A)nterior (a)/posterior (p) descriptor, and the (L)ocation relative to the polar line. Of the 5 components, 4 (R.E.N.L.) are scored on a 1, 2, or 3-point scale. The fifth descriptor (A) is a suffix which describes the mass as primarily located anterior (a) or posterior (p) to the coronal plane of the kidney. The suffix x is assigned to the tumor if an anterior or posterior designation is not possible. Polar lines (solid lines) and axial renal midline (broken line) are depicted on each sagittal view of the kidney. Numbers 1–3 represent points attributed to each category of tumor [19].

quires calculation and was, to a certain degree, complex for clinical practice. Later, Simmons et al. [29] further designed a Diameter-Axial-Polar (DAP) nephrometry scoring system in 2011, integrating three aspects of tumor features associated with the kidney: diameter, axial distance, and polar distance. In 2016, Spaliviero et al. [30] developed the ABC scoring system, which could assess the complexity of renal tumor surgery including the relationship between renal tumor aggressiveness and renal artery anatomy, especially the arterial branches to be dissected in PN. The scoring system did not directly include the proximity between the renal tumor and the collecting system, but the collecting system is anatomically parallel to the renal artery system, so it was indirectly included in the collecting system [30].

Many studies of determining different nephrometry score systems and their clinical significance in MIPN have been carried out. Different renal nephrometry scores and associated clinical significances are summarized in Table 2. There are newly developed renal score systems and parameters we do not mention; the stability and clinical value of some of the novel systems and parameters are still in an initial stage and need further verification.

Although these image-based scoring systems can assist to predict the difficulty of PN, they only focus on tumor-specific factors. The Mayo adhesive probability score,

Table 2. Different renal nephrometry scores and associated clinical significance [21–25, 27, 29–31]

Renal nephrometry scores	Clinical significance	References
RENAL nephrometry	Correlations with WIT, ORT, and percent change in eGFR	[21, 23, 25]
	Predict the perioperative and postoperative complications; indicate ischemia time	[22, 25]
	Predict collecting system entry	[23]
	Associated with the type of surgical approach (open vs. laparoscopic/robotic) and urine leak	[24]
PADUA	Correlated with WIT, ORT, blood loss, and UCS repair	[25]
	Independent predictors of WIT and overall complications	[25, 27]
	Predict the perioperative and postoperative complications; indicate ischemia time	[22, 25, 27]
Centrality index score	Correlations between complexity categories and WIT, ORT, and EBL	[21]
	Associated with WIT	[21]
Diameter-axial-polar score	Estimate the complexity of tumor characteristics better than the RENAL score	[29]
	Associated with kidney volume preservation	[31]
ABC	Associated with EBL, warm and cold ischemia time, and urinary fistula	[30]

WIT, warm ischemia time; ORT, operation time; eGFR, estimated glomerular filtration rate; EBL, estimated blood loss; UCS, urinary collecting system.

which is easy to calculate, can accurately predict perirenal attached fat encountered during RAPN [32]. This system can predict whether perinephric fat is adherent or its characteristics, which may predict the difficulty of PN. It is a promising risk score that needs to be validated in a larger patient population and applied in different forms of PN in the future.

Zero-Ischemia PN

The zero-ischemia technique was initially used to avoid the hot ischemic injury, which is caused by the blocking of the renal hilum to preserve maximal renal function. Recently, selective occlusion of renal arteries or veins and their branches is also included in the "zero-ischemia" technique.

Off-Clamp PN

Liu et al. [33] performed a meta-analysis which included 10 retrospective studies of 728 off-clamp (OC) PN cases and 1,267 on-clamp (ON) PN cases. No significant differences were detected in gender, age, body mass index, tumor volume, and pre-eGFR in the 2 groups, except for location of the mass. The OC group had a higher blood transfusion rate, but lower postoperative complication rate and lower PSM rate than the ON group. Importantly, OC could offer a better renal function preservation than ON ($p = 0.005$). In a meta-analysis of 14 studies, no significant differences were detected in size of tumor, operation time, EBL, PSM rates, LOS, transfusion rates, overall complications, as well as urinary leaks between OC PN and ON PN. There was, however, a trend of increased blood loss and transfusion rates in the OC group, which is not statistically significant ($p = 0.12$ and 0.07, respectively). The OC group had a significantly better renal functional outcome than the ON group [34]. Kavoussi and colleagues [35] retrospectively reviewed a series of 390 cases consisting of stages cT1a (313), cT1b (62), and cT2 (15). The OC LPN group had 126 patients, and the ON LPN group had 264; the OC group had a higher EBL, but no significant difference was found in perioperative blood transfusion rates. No difference was observed in terms of operative time or LOS between OC and ON groups by stage. After a systematic review of almost 50 published articles, Simone and his colleagues [36] concluded that patients with peripheral kidney cancer or small tumors could benefit more from the use of OC PN, while those with hilar kidney cancer or medially located tumors would be good candidates for minimally ischemic

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Table 3. Overview of imaging techniques that can be used during MIPN [42]

	Application	Strengths	Weaknesses	References
In vivo US	Tumor localization and delineation	Widely available	Probe has to stay in contact with tissue, not practical for real-time guidance during resection	[42]
	Margin assessment of resected specimens	No contrast agent needed	In vivo assessment of surgical margins may slightly prolong ischemia time	
	Guide selective ischemia when Doppler or CE-US is used	High tissue penetration depth		
Ex vivo US	Margin assessment of resected specimens	Quick and simple assessment of surgical specimens	No real-time guidance	[42]
			A PSM would require re-entering the abdomen and reclamping the kidney	
Fluorescence/ dual-modality imaging	Tumor localization and delineation	Real-time imaging before, during, and after tumor resection	Fluorescence has a limited tissue penetration depth, therefore not suitable for endophytic tumors	[42]
	Real-time guidance during tumor resection	Dual modality imaging: radiolabel has high tissue penetration depth	Contrast agent needed	
	Assessment of the surgical cavity	Targeted imaging approaches: high and specific accumulation in tumor tissue	Interval required between tracer injection and imaging time point depending on pharmacokinetics of the tracer (ICG quick vs. antibodies slow)	
	Margin assessment of resected specimens			
	Guide selective ischemia (ICG)			
AR	Tumor localization and delineation	Accurate visualization of tumor localization and vital structures	Tissue deformation currently limits it use during tumor resection	[42]
		No contrast agent needed		

MIPN, minimal invasive partial nephrectomy; AR, augmented reality; CE-US, contrast-enhanced ultrasound; ICG, indocyanine green; PSM, positive surgical margin; US, ultrasonography.

PN. Perioperative blood loss and transfusion rates increased with such approaches, compared to those of ON PN. For cases with longer ischemia time or patients with poor renal function, minimally ischemic or OC PN would be the optimal choice. After 5 years of follow-up, the researchers failed to find any significant difference between the OC and ON groups in regard to eGFR or the incidence of chronic kidney disease. In this case, the elimination of intransient ischemia seems to yield no clinical benefit [37].

Selective Arterial Clamping

Gill et al. [38] applied the technique of zero ischemia in MIPN, and the goal was to eliminate ischemia to the remaining part of the renal except the tumor. This technique requires microdissection of selective renal artery or vein branches and clamping and, at the same time, transitory pharmacologically induced decreasing of blood pressure, coinciding with resection of the deep part of the tumor. Preliminary results are favorable. Long-term evaluation and further experience are needed. They also found a lower postoperative hemorrhage rate in the selective arterial clamping cases, which may be due to bleeding and is more likely to be detected compared with hilar clamping. This method may be more suitable for renal mass patients with chronic kidney disease or solitary kidney. Recently, another study used fluorescence to guide selective arterial clamping during RAPN, which offered better early functional outcomes compared with standard clamping based on renal scan [39].

Table 4. Studies on MIPN without ceasing antiplatelet drugs

Studies	Patients (no-stop group/stop group/no chronic antiplatelet therapy group), *n*	Drugs used	Operation methods	Outcomes and conclusions
Althaus et al. [43]	4/–/–	Aspirin, clopidogrel	RAPN	RAPN is safe and feasible in patients without discontinuation of antiplatelet who underwent severe screening
Leavitt et al. [44]	17/84/329	Aspirin	LPN	1 case developed postoperative bleeding, and vascular embolization was used to treated hemorrhage in the aspirin-taking group; 1 case developed myocardial infarction in the no-stop group; no significant difference in main complications, EBL, transfusion rates, and rehospitalization rates
Benjamin et al. [45]	9/61/463	Aspirin	RAPN	Higher risk of bleeding complications was found in the aspirin-taking group; no difference was found in EBL between 2 groups
Timothy et al. [46]	67/254/776	Aspirin, clopidogrel	PN	The no-stop group was older and had greater comorbidity, with a higher rate of bleeding complications and transfusions. Increasing bleeding complications and transfusion rates were due to the use of clopidogrel; use of aspirin alone was not associated with bleeding complications

MIPN, minimal invasive partial nephrectomy; RAPN, robot-assisted partial nephrectomy; LNP, laparoscopic partial nephrectomy; PN, partial nephrectomy; EBL, estimate blood loss.

Intraoperative Imaging Techniques

Intraoperative imaging techniques have been used to optimize the operation of RAPN and LPN for decades. The most well-used technique is ultrasonography. A study from New York University showed ultrasonography can confirm hilar structure and renal ischemia followed by renal artery occlusion [40]. At the same time, laparoscopic Doppler ultrasound can reduce time of renal hilar isolation and improve the detection of renal hilar vessels [41]. On the other hand, the application of fluorescence imaging during MIPN has been widely studied, and this technique can assist in the identification of tumors and provide real-time guidance during resection as well as guiding selective ischemia and assessing the margin [42]. The augmented reality technique provides clinicians subsurface structures through overlaying preoperative image data on the living surgery video [42]. Different intraoperative imaging techniques have their individual applications, as well as strengths and weaknesses, which are summarized in Table 3 [42].

PN in Patients on Chronic Oral Antiplatelet Therapy

With increasing incidence of cardiovascular and cerebrovascular diseases, tumor patients often need to take long-term antiplatelet drugs because of stent indentation. For renal cancer patients who have been taking antiplatelet drugs for a long time, there is no consensus on whether to stop antiplatelet drugs before MIPN (Table 4) [43–46]. When to stop and how long still need further exploration. Not discontinuing use of antiplatelet drugs may increase the potential risk of perioperative bleeding complications, while discontinuation of antiplatelet drugs may increase the probability of cardiovascular and cerebrovascular accidents and stent thrombosis.

Complications

A series of studies have been conducted and found a high RENAL or PADUA score is correlated with an increased risk of complications [22, 25, 27]. Hemorrhage is a common complication during RAPN and LPN. Kavoussi and colleagues [47] retrospectively analyzed 335 LPN cases to determine the relationship of clinicopathologic factors with hemorrhagic complications. They found that among smokers the incidence of bleeding complications was 3.5 folds that of nonsmokers and 2.9 folds that of ASA class 3 or higher. Complication of hemorrhage did not affect LOS significantly, but age and operative time were correlated with longer LOS. Conversion is also an unfavorable complication for MIPN. With increasing use of PN to treat larger and more complicated tumors, there is a greater risk of conversion to RN. One study shows that increased tumor size and RENAL score were correlated with a higher risk of conversion. Poor preoperative renal function, large tumor size, and higher RENAL score were independent predictors of conversion [48]. Richstone et al. [49] reported a conversion rate of 4.32% from LPN to open PN in a cohort of 347 patients. Gill et al. [50] described open conversion in 16 LPN patients (2.1%) including 15 cases that underwent LPN and 1 case that required open RN in their earlier experience in an 800-patient cohort. But, the pattern of conversion of open PN or LRN should be studied further. The experience of the clinician, the disease, and the patient characteristics may affect the occurrence and degree of perioperative complications. The most important thing for us is to try our best to prevent the occurrence of complications; moreover, once there are complications, we should promptly identify and handle them properly.

Conclusions

LPN and RAPN are becoming the standard treatment for patients eligible for nephron-sparing surgery, and more complicated cases have been included. MIPN can be performed through either a transperitoneum approach or a retroperitoneum approach with advantages and limitations; surgeons should master both approaches to adapt the tumor location and optimize the procedure and outcomes. With the development of technology, RAPN seems to have improved perioperative outcomes associated with LPN. For the purpose of standardizing tumor assessment, standardizing tumor assessment bias, and so on, many preoperative scoring systems for renal tumors have been developed, which have been greatly evaluated in the perioperative outcomes of MIPN. To maximize the preservation of kidney function, zero-ischemia technology is widely used during MIPN. In addition, intraoperative imaging techniques, such as ultrasonography, fluorescence imaging, and augmented reality, have been used with MIPN to refine the procedure and outcomes. On the other hand, there is no consensus on whether to stop antiplatelet drugs before MIPN, when to stop, and how long. Surgeons have performed substantial research and practice to achieve the "trifecta" of MIPN, which is complete tumor removal with maximum preservation of renal function and no complications.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

Ming Li: project development, data collection, and manuscript writing and editing. Liang Cheng: manuscript writing and editing. Hongxian Zhang: manuscript writing and editing. Lulin Ma: project development. Ying Wang: data collection. Wanting Niu: data collection. Zeqi Liu: data collection. Yan Song: manuscript writing and editing. Peihe Liang: manuscript writing and editing. Guoan Zhao: manuscript writing and editing. Bin Wu: project development. Yongsheng Song: project development. Renge Bu: project development, data collection, and manuscript writing and editing.

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