A narrative review of optimal treatment choices in robot-assisted partial nephrectomy focusing on indication and surgical procedure

Hirohito Naito, Yoichiro Tohi^, Mikio Sugimoto

Department of Urology, Faculty of Medicine, Kagawa University, Kagawa, Japan

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Correspondence to: Yoichiro Tohi, MD. Department of Urology, Faculty of Medicine, Kagawa University, Ikenobe, Miki-cho, Kita-gun, Kagawa 761-0793, Japan. Email: yoto716yotoyoto@gmail.com.

Background and Objective: Recently, robot-assisted partial nephrectomy (RAPN) has emerged as a mainstream technique for PN. However, distinguishing technical feasibility from effective patient outcomes remains debated. This narrative review addresses the surgical precision dilemma by examining patient selection, surgical technique, and postoperative adjuvant therapy.

Methods: We conducted here an unsystematic literature search of PubMed from January 2010 to October 2023 with no restrictions on the study type. The inclusion criteria were full-text articles written in English and published in peer-reviewed journals.

Key Content and Findings: Regarding patient selection for RAPN, available studies show that it is a feasible option for T1b and high-complexity tumors despite potentially longer warm ischemia time. However, limited evidence exists regarding RAPN for T2 tumors, indicating outcomes comparable with those of RN. In elderly patients, RAPN is technically and safely acceptable. However, the outcomes of RAPN and other focal therapies are presumed to be comparable. Multiple ipsilateral renal tumors and solitary a kidney are good indications considering renal function, but a skilled surgeon should perform them. Enucleation may lead to a higher rate of positive surgical margins (PSMs), with more favorable renal function preservation than standard resection, regarding the surgical method selection for RAPN. The transperitoneal and retroperitoneal approaches lead to similar treatment outcomes, and the choice between them should be based on the surgeon's preference and experience, tumor location, and surgical history. The currently available data do not demonstrate a clear advantage of unclamped or super-selective clamping in RAPN over standard clamping regarding short-term renal function preservation,. Minimizing or omitting renorrhaphy may preserve renal function and avoid vascular injury. Regarding adjuvant therapy post-RAPN, PSM is not always indicative of poor outcomes, and patients with PSM may benefit more from close surveillance than from immediate intervention.

Conclusions: This narrative review highlights the effectiveness and adaptability of RAPN across varied patient and tumor profiles while pointing to the need for further research on its optimal surgical techniques. It emphasizes the importance of individualized patient and tumor evaluation in decision-making and indicates areas for clinical and procedural advancements.

Keywords: Outcome; partial nephrectomy (PN); renal cell carcinoma (RCC); robot; treatment choice

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^ ORCID: 0000-0003-3884-8915.

Introduction

Renal cancer reportedly had an estimated 431,288 new cases worldwide in 2020, accounting for approximately 3% of all cancer types (1,2). The frequency of incidental renal cell carcinoma (RCC) detection during health screenings and other disease evaluations using abdominal ultrasound or computed tomography (CT) scans is high. Many of the incidentally detected RCCs are small, early-stage cancers (3,4). Radical nephrectomy (RN) has traditionally been considered the standard surgical approach for RCC. However, in recent years, partial nephrectomy (PN) has become more common, especially for small renal tumors. RN and PN for small renal tumors have equivalent cancer control efficacy regarding their therapeutic outcomes (5). However, when RN is performed, there is a decrease in overall survival (OS) compared with PN because of potential complications related to renal function impairment, such as cardiovascular disorders (6,7).

Several surgical techniques are available for PN, including open, laparoscopic, and robot-assisted surgeries. The treatment of small renal tumors has continued to evolve. In the 2000s, robot-assisted PN (RAPN) was first performed using daVinci robot systems and has been done with new modalities such as HUGO and Hinotori (8-10). In RAPN, highly maneuverable surgical instruments and three-dimensional imaging allow precise and safe surgical procedures. As a result, RAPN is currently a widely spread technique for performing PN because of shorter warm ischemia time (WIT), reduced intraoperative bleeding, and shorter hospital stays (11,12). While RAPN is widely used for tumors with challenging characteristics, such as larger (T1b and T2) and complex tumors and diverse patient backgrounds, it is essential to distinguish between the technical feasibility of the procedure and whether the surgery has been effectively performed.

In this narrative review, we aimed to address this dilemma regarding the surgical precision of RAPN faced by surgeons in choosing the optimal technique. An additional novelty of this review is its focus on postoperative adjuvant therapy. We focused on patient selection, surgical technique, and postoperative adjuvant therapy and discussed the evidence regarding recent advancements in various technologies to provide insights into resolving this dilemma. We present this article in accordance with the Narrative Review reporting checklist (available at https://amj.amegroups.com/article/view/10.21037/amj-23-233/rc).

Methods

We searched PubMed, covering articles published between January 2010 and October 2023, specifically focusing on articles related to RAPN. The search keywords included "T1b", "T2", "complexity", "multiple", "ipsilateral", "solitary", "older", "enucleation", "renorrhaphy", "surgical approach", "clamping", "resection margin" in combination with "robot-assisted partial nephrectomy" (*Table 1*).

Patient selection of RAPN

PN has replaced RN as the gold standard treatment for clinical T1a RCC (13). RAPN is currently the most widely used technique for PN because of the development of robotic technology and its introduction into surgery. Compared with laparoscopic PN (LPN), RAPN offers a shorter WIT, less frequent conversion to laparotomy or RN, better preservation of renal function, and shorter hospital stay (13). RAPN is considered one of the standard treatments and a widely spread treatment for clinical T1a renal tumors because of these advantages. Here, we discuss the indications for RAPN in T1b and T2 tumors. Furthermore, we would like to consider more challenging cases (high-complexity tumors, multiple ipsilateral tumors, tumors in a solitary kidney, and tumors in older patients).

RAPN for T1b tumors

In a retrospective multi-institutional analysis of RAPN for 54 tumors over 4 cm (T1b), the median WIT was 23 min (10–59 min). Median estimated blood loss (EBL) were 180 min (110–425 min) and 100 cc, and three patients had positive surgical margins (PSMs) (14).

A retrospective multi-institutional study (15) comparing T1a (n=1,307) and T1b (n=377) tumors showed longer WIT (15.0 *vs.* 18.8 min; P<0.001), more EBL (100 *vs.* 150 mL; P<0.001). There were no differences in risk of Clavien-Dindo grade III–IV postoperative complications (3.7% *vs.* 3.6%; P=0.917), PSM (3.0% *vs.* 4.6%; P=0.228) or change in estimated glomerular filtration rate (eGFR) (−12.4% *vs.* −8.5%; P=0.156), as other studies have reported similarly (16,17) (*Table 2*).

The above studies indicated that, although EBL and WIT are long in T1b tumors, there is no significant difference between functional and oncological outcomes depending on size. When the tumor location, complexity,

Table 1 The search strategy summary

Item	Specification
Date of search	2023.11.11
Database	PubMed
Search terms used	Robot-assisted partial nephrectomy, T1b, T2, complexity, multiple, ipsilateral, solitary, older, enucleation, renorrhaphy, surgical approach, clamping, resection margin
Timeframe	January 2010 to October 2023
Inclusion criteria	Full-text articles, written in English
Selection process	It was conducted by H.N., Y.T., and M.S.

Table 2 RAPN for T1b tumor

Study	Procedure, n	IT, min, median (IQR)	EBL, mL, median (IQR)	PSM, %	Complications, %	Conversion, %	Change in eGFR, %, median (IQR)	Survival outcome
Petros F, 2012 (15)	T1a 362	17	150	NE	3.9	NE	−3.9	NE
	T1b 83	24	200	NE	8.4	NE	−8.6	NE
Masson-Lecomte A, 2013 (14)	T1b 54	23 (10–59)	180 (110–425)	5.6	Clavien-Dindo grade ≥3, 5.6	NE	−13.0	2-y PFS 90.5%
Reynolds CR, 2017 (16)	T1a 1,307	15.0 (12.0–19.0)	100 (50–150)	4.6	Clavien-Dindo grade ≥3, 3.6	RN 0.5, open surgery 0.1	−8.5 (−19.9 to 3.2)	NE
	T1b 377	18.8 (15.0–23.0)	150 (75–200)	3.0	Clavien-Dindo grade ≥3, 3.8	RN 0.4, open surgery 0.0	−12.4 (−24.7 to 0.9)	NE
Tohi Y, 2019 (17)	T1a 66	14 (9.5–17)	2.5 (0–50)	4.5	Clavien-Dindo grade ≥3, 0.0	0.0	−3.45 (−11.8 to 1.95)	NE
	T1b 34	21 (16–27)	50 (0–200)	11.7	Clavien-Dindo grade ≥3, 8.8	0.0	−5.88 (−17.2 to 0)	NE

RAPN, robot-assisted partial nephrectomy; IT, ischemia time; IQR, interquartile range; EBL, estimated blood loss; PSM, positive surgical margins; change in eGFR, percent change in estimated glomerular filtration rate from baseline; NE, not evaluable; y, year; PFS, progression-free survival; RN, radical nephrectomy.

and general condition of the patient allow for a feasible procedure, RAPN is a sufficient treatment option for T1b tumors.

There are no prospective randomized controlled trials (RCTs) of RAPN for T1b. Although the previous reports are retrospective studies, the number of patients is relatively large, and the quality of evidence is adequate.

RAPN for T2 tumors

There are no RCTs for T2 lesions, only for renal masses up to 5 cm. It shows that survival after RN is higher than survival after PN (5). This RCT is evidence published more than 10 years ago, and there is an urgent need to build the evidence from RCTs about PN for T2 tumors.

There is limited evidence on PN for patients with T2 tumors. Some retrospective comparative studies of PN *vs.* RN for T2 RCC have been published.

In a meta-analysis of 21 studies comparing PN and RN in 11,200 T1b and T2 patients, only four studies reported that they were specific to T2 patients. The four studies compared 212 PN and 1,792 RN. The EBL is reported to be higher for PN groups, as is the likelihood of complications [risk rato (RR) 2.0; P<0.001]. Both the recurrence rate (RR 0.61; P=0.004) and cancer-specific mortality (RR 0.65; P=0.03) were lower for PN (18). A retrospective study compared the survival outcomes of RN (n=122) and PN (n=80) for T2. There was no difference between the RN group and the PN

Table 3 Surgery for T2 tumor

Study	Procedure, n	IT, min, median (IQR)	EBL, mL, median (IQR)	PSM, %	Complications, %	Conversion, %	Change in eGFR, %, median (IQR)	Survival outcome
Kopp RP, 2014 (20)	PN T2 80	29 (25–47)	325 (200–500)	2.9	Clavien-Dindo grade ≥3, 17.5	NE	NE	5-y PFS 69.8%, 5-y OS 80.0%
	RN T2 122	NE	225 (100–400)	1.7	Clavien-Dindo grade ≥3, 2.5	NE	NE	5-y PFS 79.9%, 5-y OS 83.3%
Delto JC, 2018 (22)	RAPN T1a 1,358	15.0 (12.0–19.2)	100 (50–150)	4.5	Clavien-Dindo grade ≥3, 3.5	RN 0.29	−11.3 (−22.7 to 1.0)	1-y PFS 99.6%
	RAPN T1b 379	18.1 (15.0–23.0)	150 (75–200)	3.3	Clavien-Dindo grade ≥3, 3.5	RN 0.26	−18.9 (−30.8 to −6.8)	1-y PFS 100%
	RAPN T2a 41	19.7 (15.3–25.0)	200 (100–400)	4.5	Clavien-Dindo grade ≥3, 4.9	0.0	−26.4 (−31.6 to −14.7)	1-y PFS 91.7%
Bertolo R, 2018 (23)	RAPN T2a 298	25.0 (20.0–32.0)	150 (100–300)	8.0	Clavien-Dindo grade ≥3, 5.0	RN 0.3	−15.6 (−20.0 to −11.0)	PFS 90%, OS 96.7% (median follow-up 12 mo)

IT, ischemia time; IQR, interquartile range; EBL, estimated blood loss; PSM, positive surgical margins; change in eGFR, percent change in estimated glomerular filtration rate from baseline; PN, partial nephrectomy; NE, not evaluable; y, year; PFS, progression-free survival; OS, overall survival; RN, radical nephrectomy; RAPN, robot-assisted partial nephrectomy; mo, months.

group in survival. For RN and PN, the 5-year progression-free survival (PFS) was 69.8% and 79.9% (P=0.115), cancer-specific survival (CSS) was 82.5% and 86.7% (P=0.407), and OS was 80% and 83.3% (P=0.291). However, there was a significant difference between the two groups in Clavien ≥3 complications (PN, 17.5% *vs.* RN, 2.5%; P<0.001) (19,20).

The guidelines mentioned the indications for T2 tumors as follows: the risks and benefits of PN should be discussed with patients with T2 tumors. In this setting, if technically feasible, PN should be considered in patients with a solitary kidney, bilateral renal tumors, or chronic kidney disease (CKD) with sufficient parenchymal volume preserved to allow sufficient postoperative renal function (21).

Evidence for RAPN for T2 tumors has been even more lacking, but one retrospective study compared RAPN for renal tumors in patients with T1a (n=1,358), T1b (n=379), and T2a (n=41) tumors (22). T2a tumors were associated with greater EBL and IT. However, compared with the T1 tumor, the T2a tumor was not associated with a greater rate of complications (T1a for 10.4%, T1b for 13.2%, T2a for 7.3%) or PSM (T1a for 4.5%, T1b for 3.3%, T2a for 4.5%). Recurrence-free survival at 12 months was significantly lower in the T2a group (T1a for 99.6%, T1b for 100%, T2a for 91.7%). In another retrospective study of RAPN for T2a patients (n=298), the median WIT was 25 min [interquartile range (IQR), 20–32 min], and the median EBL was 150 mL (IQR, 100–300 mL). Sixteen patients had intraoperative complications (5.4%), whereas 66 (22%) had postoperative complications (5% were Clavien grade ≥3). Twenty patients (8%) had PSMs. Ten deaths and 25 recurrences/metastases occurred at a median follow-up of 12 months (IQR, 5–35 months) (23) (*Table 3*).

These retrospective studies indicated that RAPN could be a feasible treatment option for T2 tumors in a selected patient population. In the future, prospective studies comparing the outcome of robot-assisted RN (RARN) and RAPN for T2 tumors should be conducted. However, because of the lack of evidence, the indication of RAPN for T2 tumors must be cautious.

In T2 renal masses cases, the indication for systemic neoadjuvant therapy is discussed. Several small studies (24,25) have demonstrated a potential benefit of systemic neoadjuvant therapy (mostly with VEGFR-TKIs), including a modest reduction in tumor size and possible facilitation of locally advanced tumor resection and complex PN. However, no RCTs support the use of neoadjuvant therapy. At this point, there is no indication for neoadjuvant therapy before planned surgical resection of the primary kidney tumor outside the context of a clinical trial (26).

Table 4 RAPN for high-complexity tumor

Study	Procedure, n	Complexity	IT, min, median (IQR)	EBL, mL, median (IQR)	PSM, %	Complications, %	Conversion, %	Change in eGFR, %, median (IQR)	Survival outcome
Abdel Raheem A, 2016 (31)	72	PADUA 6–7	23.0 (18.0–27.0)	200 (100–332)	4.1	Clavien-Dindo grade ≥3, 2.8	RN 0.0	−6 (−15 to 3)	PFS 95.8%, OS 98.6%
	102	PADUA 8–9	24.0 (18.0–30.0)	275 (130–563)	5.8	Clavien-Dindo grade ≥3, 7.9	RN 1.0	−1 (−16 to 13)	PFS 94.1%, OS 94.1%
	121	PADUA ≥10	26.0 (22.0–32.0)	360 (200–550)	9.9	Clavien-Dindo grade ≥3, 5.0	RN 5.9	−2 (−15 to 8)	PFS 97.5%, OS 97.5%
									Follow-up 48.5 mo
Buffi NM, 2020 (29)	255	PADUA ≥10	18.0 (15.0–23.0)	150 (100–250)	1.9	Clavien-Dindo grade ≥3, 5.1	Open surgery 1.6	NE	NE
							RN 1.9		
Koukourikis P, 2021 (32)	155	PADUA ≥10	26.0 (23.0–32.0)	250 (100–500)	10.5	Clavien-Dindo grade ≥3, 2.3	RN 5.2	NE	RFS 93.6%, OS 96.7% (median follow-up 58 mo)

RAPN, robot-assisted partial nephrectomy; IT, ischemia time; IQR, interquartile range; EBL, estimated blood loss; PSM, positive surgical margins; change in eGFR, percent change in estimated glomerular filtration rate from baseline; RN, radical nephrectomy; PFS, progression-free survival; OS, overall survival; mo, months; NE, not evaluable; RFS, recurrence-free survival.

RAPN for high-complexity tumors

Not only tumor size but also tumor location is important for RAPN indication. Several standardized anatomical classification scoring systems exist, such as the RENAL nephrometry (27) and PADUA scores (28). PADUA and RENAL score of 10 or higher is considered a high-complexity tumor.

In the retrospective study compared the results of RAPN for PADUA scores 6–7 (n=72), PADUA scores 8–9 (n=102), and PADUA scores ≥10 (n=121), PADUA scores ≥10 tumors are associated with a lower rate of trifecta achievement [PADUA scores 6–7, scores 8–9, and scores ≥10 tumors of trifecta achievement: 65.3%, 56.9%, and 45% (P<0.001)]. There was no group difference in WIT >25 and overall complication (P=0.12, 0.62) and a significant difference in PSM (P<0.001). Significantly, WIT was longer, EBL was more, and PSM was higher in PADUA scores ≥10 tumors. There was no statistically significant difference between groups in the postoperative eGFR values at all intervals (P>0.05). Generally, the PFS and OS rates at 46.5 months were 96.6%, 91.3%, and 90.2%, respectively, and no significant difference was found between groups for PFS and OS. There was no group difference in overall complication. However, intraoperative complications resulted in a statistically higher rate of conversion to RN in PADUA scores ≥10 (5.9%, P=0.02) (29).

Also, in the studies including 255 and 155 patients with PADUA ≥10 tumors, conversion to RN (1.9–5.2%) or open surgery (1.6%) were reported (30,31). Another study for RENAL ≥10 reported that Clavien-Dindo grade ≥3 was 16.3% (22). However, the survival outcome of RAPN for high-complexity tumors was acceptable. These studies (29,31,32) reported that PFS was 93.6–97.5% at 4–5 year follow-up (*Table 4*). RAPN may be a feasible treatment option for high-complexity tumors. However, there have been reports of conversion to nephrectomy, and caution should be required. Patients should be informed of the possibility of conversion to nephrectomy or to open surgery, for example, kidney auto-transplantation.

In RAPN for high-complexity tumors, WIT tends to be longer. Therefore, a unique surgical technique was reported to provide a solution to long WIT and to protect renal function. After incising the renal artery and vein, 4 ℃ heparinized saline is administered intravascularly through a Fogarty catheter to maintain renal hypothermia while

Table 5 RAPN for multiple ipsilateral tumor

Study	Procedure, n	Tumors per patients	IT, min, median (IQR)	EBL, mL, median (IQR)	PSM, %	Complications, %	Conversion, %	Change in eGFR, %, median (IQR)	Survival outcome
Boris R, 2009 (34)	9	Median 2.7 (IQR, 2–4)	17.6 (0–45.0)	360 (100–500)	NE	Clavien-Dindo grade ≥3, 10.0	RN 10.0 Open surgery 10.0	−7.4	NE
Yang J, 2019 (35)	12	2 tumors: 9 cases 3 tumors: 3 cases	37.5 (32.0–52.0)	150.0 (50–350)	0.0	Clavien-Dindo grade ≥3, 0.0	0.0	−9.3	PFS 100% (mean follow-up 5.4 mo)
Buffi N, 2023 (36)	61	Mean 2.32	17.0 (12.0–24.0)	200 (100–400)	6.56	Clavien-Dindo grade ≥3, 3.2	0.0	NE	NE
Biebel MG, 2023 (37)	50	Multiple ipsilateral renal masses	17.0 (mean)	137.6 (mean)	NE	Clavien-Dindo grade ≥2, 10.2	NE	−6.4	NE
	146	Single renal mass	15.3 (mean)	117.8 (mean)	NE	Clavien-Dindo grade ≥2, 11.3	NE	−8.7	NE

RAPN, robot-assisted partial nephrectomy; IT, ischemia time; IQR, interquartile range; EBL, estimated blood loss; PSM, positive surgical margins; change in eGFR, percent change in estimated glomerular filtration rate from baseline; NE, not evaluable; RN, radical nephrectomy; PFS, progression-free survival; mo, months.

performing RAPN. The median warm and cold ischemia times (ITs) were 4 min (IQR, 3–7 min) and 60 min (IQR, 33–75 min), respectively. The median rewarming IT was 10.5 min (IQR, 6.5–23.75 min). The median pre- and postoperative eGFR values at least 1 mo after surgery were 90 mL/min (IQR, 78.35–90 mL/min) and 86.9 mL/min (IQR, 62.08–90 mL/min), respectively (33).

An attempt to expand the feasibility of minimally invasive nephron-sparing surgery for highly complex renal masses has been made in this way.

RAPN for multiple ipsilateral tumors

Reports of RAPN for multiple ipsilateral renal tumors have been seen since around 2009 (34). The feasibility of the unique clamping technique of sequentially blocking segmental renal arteries for multiple ipsilateral renal tumors in 11 patients was demonstrated (35). There were reported good results with renal function preservation or oncological outcomes [insignificant reduction of postoperative eGFR (9.3%), no PSM, and no recurrence or metastasis during a follow-up period of 5.4 months]. A study of 61 patients with multiple ipsilateral renal masses reported acceptable results concerning complications, WIT, EBL, and PSM by preoperative simulation for hilum management using 3D construction from images and intraoperative use of TilePro (Life360; San Francisco, CA, USA), indocyanine green fluorescence and intraoperative ultrasound [3 (4.8%) intraoperative complications occurred, all classified as grade-1 according to EAUiaiC]. Postoperative complications were reported in 14 (22.9%) cases with 2 Clavien-Dindo grade >2 complications. The median WIT was 17 min (12–24 min), the median EBL was 200 mL (100–400 mL), and PSM was 6.56% (36).

In a study in which 50 patients who underwent RAPN for ipsilateral multiple renal masses (mRAPN) were matched with 146 patients who underwent RAPN for a single renal mass (sRAPN), there were no significant differences in complications, renal function outcomes, and EBL. However, ipsilateral multiple renal masses were associated with increased median operative time (mPN 174.6 *vs.* sPN 156.4 min, P=0.008) and median WIT (mPN 17.0 *vs.* sPN 15.3 min, P=0.032) (37) (*Table 5*).

mRAPN is more challenging than sRAPN because the optimal anatomic approach for each tumor is different. Limitations in the range of motion and rotation of the kidney during RAPN also contribute to the difficulty. It has been reported that mRAPN increases operative time and WIT (37). Inexperienced surgeons, with the employment of the currently available technologies (3D construction from images and intraoperative ultrasound) and surgical techniques, mRAPN may guarantee optimal outcomes.

RAPN for tumors in a solitary kidney

Nephron-sparing surgery is a good indication for tumors in solitary kidney patients. When performed by an expert, LPN is minimally invasive, and the WIT will not be prolonged. However, open PN (OPN) would be the first choice. if the surgeon lacks expertise and is considering renal function-sparing

In a study for tumors in solitary kidneys comparing 169 OPN cases with 30 LPN cases, there was no difference in renal function at 3 months postoperatively between LPN and OPN. The WIT of LPN was 9 min longer than OPN (P<0.0001), and the chance of postoperative complications of LPN was 2.54-fold higher than OPN (P<0.05). OPN might be the preferred nephron-sparing approach at this time for these patients at high risk for chronic kidney disease (38). However, the above was a long time ago, and with the rise of robotic surgery, RAPN has replaced OPN.

One study reported that RAPN for solitary kidneys is a feasible treatment option because it preserves renal function, has few complications, and better oncological outcomes [WIT: 17 min; no significant change in percentage of eGFR after surgery (P=0.13); intraoperative complication rate: 7.7%; postoperative complication rate: 11.5%; recurrence rate: 3.8%] (39). Another study demonstrated that RAPN is a safe and effective treatment option for solitary kidneys, as it showed good trifecta outcomes in solitary kidneys (40); 38 of 66 patients (57.6%) achieved trifecta outcomes (WIT: 15.5 min; overall complication rate: 24.1%; rate of Clavien-Dindo grade ≤ II complications: 16.3%; PSM: 5.4%) (40).

In a retrospective comparison study for tumors in solitary kidneys between RAPN and OPN on perioperative and functional outcomes, 68 (45%) patients in the RAPN group and 82 (55%) in the OPN group were included. It was reported that postoperative renal function was comparable between the two groups (P=0.45). Trifecta was achieved in 40% of the patients in the RAPN group and 33% in the OPN group (P=0.42). A significant difference was observed for the length of stay, 5 days for the robot group *vs.* 9 days for the open surgery group (P<0.0001). The surgical approach did not modify functional results, and RAPN is a safe and efficient method for managing tumors in solitary kidneys (41). In another retrospective study compared oncological and renal functional outcomes between OPN (n=15) and RAPN (n=20) in patients with a pT2-pT3 renal tumor in a solitary kidney, OPN group had a longer IT (48.9 *vs.* 27.3 min, P<0.001), a higher major complication rate (38.5% *vs.* 11.1%, P=0.009), and a higher length of stay (5 *vs.* 3.5 days, P=0.023). The PSM rate was comparable (20% OPN *vs.* 15% RAPN; P=1.000) (42). The above two studies showed the robotic approach for tumors with solitary kidneys is a reasonable alternative to OPN in selected cases and with skilled hands (*Table 6*).

Focal therapy (FT) has emerged, as well as RAPN. However, studies of FT for tumors in the solitary kidney are limited. A study comparing cryotherapy with PN for tumors in solitary kidneys showed no significant differences concerning postoperative renal function and OS. However, the recurrence rate was higher with cryotherapy (29% *vs.* 3.2%, P=0.005) (43). As mentioned above, there is a lack of evidence about FT for tumors in a solitary kidney. RAPN is less invasive than OPN, and tumors in solitary kidneys are considered to be a good indication of RAPN at the moment.

RAPN for older patients

In a study evaluating OS with propensity score matching of 4,457 patients with T1a aged 70 years or older who underwent PN or non-surgical treatment (NST; treatment details unknown), the PN group had better OS than the NST group in both patients aged 70–79 years and 80 years or older (70–79 years old; PN 158 months *vs.* NST 75 months. Over 80 years old; PN 158 months *vs.* NST 59 months). In multivariate analysis, treatment (PN *vs.* NST) and age (70–79 *vs.* 80 years) were independent prognostic factors. Although there may be patient selection bias, this study demonstrates the benefit of PN for elderly patients with T1a. However, age is a prognostic factor, and the indication for PN in older people should be carefully considered (44).

RAPN is known to have fewer complications and better operative outcomes than OPN or laparoscopic PN (45). If PN is the procedure of choice in older patients, RAPN is preferred. In a retrospective study evaluating trifecta in PN for patients aged 75 years or older, patients who underwent RAPN (n=152) had a higher mean age than those who underwent OPN (n=325) and LPN (n=176). There were no significant differences in PSM rates, complication rates, or renal function among the three groups, but RAPN had better results among the three groups in terms of IT, EBL, and length of hospital stay (46).

In one study, the median patient age was 74 years (IQR, 72–76.5 years), and most of the patients (67.3%) had low

Table 6 Surgery for tumor in a solitary kidney

Study	Procedure, n	IT, min, median (IQR)	EBL, mL, median (IQR)	PSM, %	Complications, %	Conversion, %	Baseline eGFR/ postoperative eGFR	Change in eGFR, %	Survival outcome
Hillyer SP, 2013 (39)	RAPN 26	17.0 (12.0–28.0)	225 (100–437)	3.8	Clavien-Dindo grade ≥3, 3.8	0.0	58.9 (43.6–73.2) 43.9 (37.1–58.7)	−15.8 (median)	Recurrence 1 case (3.8%)
Arora S, 2018 (40)	RAPN 74	15.5 (8.75–20.0)	150 (100–350)	5.4	Clavien-Dindo grade ≥3, 8.4	RN 1.35 Open surgery 0.0	61.0 (50.0–72.0) 53.0 (35.0–62.0)	−11.0 (median)	None of recurrence (median follow-up 10.5 mo)
Beksac AT, 2022 (43)	RAPN T2–3 20	27.3 (mean)	325 (200–1,000)	15	Clavien-Dindo grade ≥2 11.1	NA	61.1 (mean) NA	−20.9 (mean)	Recurrence 15.0%
	OPN T2–3 15	48.9 (mean)	300 (200–600)	20	Clavien-Dindo grade ≥2 38.5	NA	54.9 (mean) NA	−24.8 (mean)	Recurrence 26.7%
Benichou Y, 2023 (41)	RAPN 82	16.2 (mean)	329 (mean)	10.8	Clavien-Dindo grade ≥3, 3.6	NE	66.9 (mean) Baseline 13.4	−20.0 (mean)	NA
	OPN 68	19.6 (mean)	510 (mean)	9.1	Clavien-Dindo grade ≥3, 8.8	0.0	57.0 (mean) Baseline 9.3	−16.3 (mean)	NA

IT, ischemia time; IQR, interquartile range; EBL, estimated blood loss; PSM, positive surgical margins; change in eGFR, percent change in estimated glomerular filtration rate from baseline; RAPN, robot-assisted partial nephrectomy; RN, radical nephrectomy; mo, months; NA, not available; OPN, open partial nephrectomy; NE, not evaluable.

PADUA scores (47). The complication rate was 15.4%, and the trifecta achievement rate was 71.2%. The disease-free survival, OS, and CSS were 89.33%, 90.06%, and 94.4%, respectively. These results demonstrated that RAPN is a feasible and safe treatment option for older patients with good oncological outcomes.

In another study comparing RAPN with RARN in older patients with large renal masses, the mean ages were 71.3 and 73.0 years, and the mean RENAL scores were 9.6 and 8.6 points for the RARN and RAPN groups, respectively. EBL (200 *vs.* 100 mL; P<0.001) and rate of overall complications (38% *vs.* 23%; P=0.05) were higher in the RAPN group (48). There was no significant difference in major complications between the groups (P=0.678). Higher eGFR levels (55.4±22.6 *vs.* 45.7±15.7 mL/min; P=0.016) and lower eGFR variation (9.7 *vs.* 23.0 mL/min; P<0.001) at the final follow-up were observed for RAPN. The procedure type was not associated with PFS [hazard ratio (HR), 0.47; P=0.152] or OS (HR, 0.22; P=0.084). These results demonstrate that RAPN was a feasible and safe treatment for elderly patients with acceptable oncological outcomes. However, minimally invasive treatments [cryotherapy and radiofrequency ablation (RFA), etc.] other than RAPN for older people should also be discussed.

In a meta-analysis of minimally invasive PN (MIPN; RAPN and LPN) and FT [RFA, microwave ablation (MWA), cryoablation (CA), irreversible electroporation (IRE), non-thermal IRE ablation, and stereotactic body radiation therapy (SBRT)] for 4,420 patients with small renal masses (SRMs), Renal function of FT was significantly lower decrease and FT possessed lower risk in minor complications (Clavien I–II) (P=0.023) and overall complications (P=0.008).

Finally, there is no obvious difference between FT and MIPN in local recurrence, distant metastasis, and major complications (49). In another study comparing perioperative, oncological, and renal outcomes of cryotherapy and RAPN in elderly patients (>75 years) using propensity score matching, the overall complications rate was higher for RAPN (31% *vs.* 9%; P=0.007), but no difference was found in major (Clavien III–IV) complications (6% *vs.* 1.5%). No significant differences were found in cancer-specific and OS, but recurrence-free survival was higher for RAPN (RAPN *vs.* CA, 100% *vs.* 83%, P=0.02). Renal function was comparable between the groups (50) (*Table* 7).

Table 7 Treatment for elderly patients

Study	Procedure, n	Age, y, median (IQR)	CCI (mean)/ ASA (≥3, %)	Ischemia time, min	EBL, mL, median (IQR)	PSM, %	Complications, %	Length of hospital stays, days, median (IQR)	Renal function	Survival outcome
Bindayi A, 2020 (46)	OPN 325	78.4 (mean)	CCI 3.5	23.1 (mean)	351.9 (mean)	3.4	Clavien-Dindo grade ≥3, 5.8	7.6 (mean)	≥90% eGFR rate recovery 42.8%	NA
	LPN 176	77.7 (mean)	CCI 3.5	25.4 (mean)	192.9 (mean)	2.9	Clavien-Dindo grade ≥3, 5.1	6.0 (mean)	≥90% eGFR rate recovery 49.4%	NA
	RAPN 152	79.4 (mean)	CCI 3.4	19.3 (mean)	157.6 (mean)	5.3	Clavien-Dindo grade ≥3, 7.2	5.6 (mean)	≥90% eGFR rate recovery 48.0%	NA
Vartolomei MD, 2019 (47)	RAPN 52	74 (72.0–76.5)	ASA 15.4%	Median 14.5 (IQR, 4–21)	100 (50–200)	1.9	Clavien-Dindo grade ≥3, 7.6	5 (4–6)	Baseline eGFR 73.4 Postoperative eGFR 71.8	5-y DFS: 89.3% 5-y OS: 90.06%
Veccia A, 2020 (48)	RARN 74	71.3 (67.7–77.0)	ASA 47%	NA	100 (50–150)	14	Clavien-Dindo grade ≥3, 4.1	3.0 (2.0–5.5)	Baseline eGFR 65.8 Postoperative eGFR 46.2	NA
	RAPN 73	73.0 (68.0–77.0)	ASA 52%	NA	200 (100–475)	9	Clavien-Dindo grade ≥3, 5.4	5.0 (4.0–7.0)	Baseline eGFR 66.1 Postoperative eGFR 51.9	NA
Bertolo R, 2019 (50)	RAPN 65	79.3 (mean)	CCI 2.0	NA	195 (mean)	NA	Clavien-Dindo grade ≥3, 6.0	4 (mean)	eGFR difference 1.2 (cryoablation *vs.* RAPN)	5-y RFS: 100% 5-y CSS:100%
	Cryoablation 65	79.3 (mean)	CCI 2.3	NA	140 (mean)	NA	Clavien-Dindo grade ≥3, 1.5	1 (mean)		5-y RFS: 83.0% 5-y CSS: 95%

Y, years; IQR, interquartile range; CCI, Charlson's Comorbidity Index; ASA, American Society of Anesthesiologists score; EBL, estimated blood loss; PSM, positive surgical margins; OPN, open partial nephrectomy; eGFR, estimated glomerular filtration rate; NA, not available; LPN, laparoscopic partial nephrectomy; RAPN, robot-assisted partial nephrectomy; DFS, disease-free survival; OS, overall survival; RARN, robot-assisted radical nephrectomy; RFS, recurrence-free survival; CSS, cancer-specific survival.

Considering the above literature, RAPN for older people is technically sound and has an acceptable safety profile. However, the outcomes of RAPN and other focal therapies are presumed to be comparable. Especially for small renal tumors, the choice of treatment should be carefully considered depending on the patient's comorbidities and general condition.

Surgical method selection of RAPN

Standard resection vs. enucleation

In standard resection, a section of the peritumoral tissue is routinely removed to ensure the presence of negative margins (51). In contrast, enucleation was established to avoid the removal of healthy parenchymal tissue, resulting in the preservation of renal function and preventing violation of the urinary collecting system, the renal sinus, or both (52). Enucleation, characterized by the removal of the tumor with no surrounding healthy parenchyma and a relatively avascular dissection plane, can simplify renal reconstruction and offer advantages such as the preservation of renal function and reduction of perioperative complications (53). Enucleoresection involves the removal of the tumor and a thin rim of healthy peritumoral parenchyma.

Minervini *et al.* conducted a prospective multicenter study to assess the influence of different resection techniques (enucleation *vs.* enucleoresection *vs.* resection) on PN outcomes, including perioperative outcomes, acute kidney injury, and PSM. They demonstrated that the median WIT was 17 *vs.* 18 *vs.* 17 min, median EBL was 200 *vs.* 150 *vs.* 175 mL, eGFR loss (mL/min/1.73 m^2) at discharge was 4.1 *vs.* 8.9 *vs.* 7.3, and PSM 13% *vs.* 15% *vs.* 2% for enucleation, enucleoresection, and standard resection, respectively; the choice of resection technique significantly affected PSM and early renal functional outcomes (54). A systematic review and pooled analysis of comparative studies have provided an overview of the different resection techniques for RAPN, identifying two main resection techniques: resection (non-anatomic) and enucleation (anatomic) (55). The study found no significant differences in the operative time, WIT, EBL, transfusions, or PSM between these two techniques. However, enucleation was found to have an advantage in avoiding arterial clamping, overall/major complications, length of hospital stay, and renal function (55). Regarding nucleation to avoid arterial clamping, the concept of nucleation by tumor-specific devascularization aimed at eliminating global ischemia with a renal remnant, according to Satkunasivam *et al.* (56).

In other words, the dilemma in the choice of surgical procedure between standard resection and enucleation is that enucleation involves cutting the interface between the parenchyma and pseudo-capsule. However, a systematic review supported that enucleation does not contribute to increased PSM (55).

Transperitoneal vs. retroperitoneal approach

The choice of surgical access, whether transperitoneal or retroperitoneal, is a critical factor in kidney surgery as it may significantly affect the ease of the procedure and perioperative outcomes (57). The transperitoneal approach usually benefits from familiarity with anatomical structures and adequate working space (58). The retroperitoneal approach, by contrast, is a viable alternative, particularly for renal masses in the posterolateral region. This approach offers direct access to the renal artery without colonic mobilization (59). That is, the decision between transperitoneal and retroperitoneal approaches has traditionally been influenced by factors related to the tumor, such as its location and surgical complexity, as well as patient-specific characteristics, such as a history of abdominal surgery and excess abdominal fat.

The RECORD 2 project, an Italian multi-institutional prospective observational project, aimed to compare perioperative outcomes between transperitoneal and retroperitoneal approaches in MIPN for clinical T1 renal tumors (59). A total of 1,669 patients were included, of whom 1,256 underwent the transperitoneal approach, and 413 underwent the retroperitoneal approach. Following propensity score matching, 413 patients from each group were compared. The intraoperative variables showed no significant differences, except for shorter operative times in the transperitoneal group. The transperitoneal group had higher overall rates of intraoperative and surgical complications. Postoperatively, complications and renal function were similar. However, the retroperitoneal group had a shorter drainage duration and hospital stay. This prospective study concluded that both approaches are feasible; however, the retroperitoneal approach may offer quicker postoperative recovery despite longer operative times (59). A systematic review compared the outcomes of retroperitoneal RAPN and transperitoneal RAPN for localized renal tumors (60). Seventeen studies published between 2013 and 2021, with 6,266 patients, were included in the analysis. Retroperitoneal RAPN was associated with a lower EBL, shorter operative time, and shorter hospital stay than transperitoneal RAPN. The overall complication rate was slightly lower in the retroperitoneal RAPN group, but there were no significant differences in major complications or PSM rates. The results of matched-pair studies were similar. This systematic review concluded that retroperitoneal RAPN offers surgical outcomes comparable to transperitoneal RAPN, with the potential advantages of shorter operative time and hospital stay. However, more randomized clinical trials are needed for conclusive evidence (60). The reason why the operative time varied depending on the reports may be because of surgical skills. However, the retroperitoneal approach generally reduces operative time because the time required to secure the renal artery is reduced, and steps such as avoiding bowel mobilization are no longer necessary.

Robotic surgery simplifies the execution of complex surgical procedures using both transperitoneal and retroperitoneal approaches. This is achieved through enhanced ergonomic positioning for the surgeon, a three-dimensional view of the operative area, and increased instrument maneuverability facilitated by the EndoWrist® technology (61). In other words, robotic surgery is feasible for PN irrespective of surgical access, which has helped alleviate the dilemma of choosing optimal surgical access. Therefore, when making decisions regarding surgical access, a balance between the surgeon's preferences and experience remains crucial.

Clamping vs. no-clamping

Ideally, PN should prioritize optimizing both functional and oncological outcomes while minimizing the complications associated with the procedure. It is crucial to preserve the maximum possible parenchymal volume and minimize nephron damage caused by ischemia to optimize functional outcomes (62,63). In the era of open surgery, surgeons used techniques such as ice slush to fill the renal surgical field and introduce hypothermic conditions to lower kidney metabolism. As PN becomes less invasive, hypothermic techniques are becoming less common. Surgeons performing RAPN should ideally aim to limit WIT by clamping for 20–25 min, as indicated in previous reports (64). Surgical techniques for minimizing ischemic renal injury, such as off-clamp and selective clamping approaches, have also been reported (63,65). However, the off-clamping technique raises concerns regarding poor visibility owing to bleeding during tumor resection.

The CLOCK RCT aimed to compare the functional outcomes of on- and off-clamp RAPN (66). The trial included patients with normal baseline kidney function and specific mass characteristics. Both groups required renal defatting and hilum isolation; however, the on-clamp group developed renal ischemia, whereas the off-clamp group did not. The primary endpoint was the 6-month change in eGFR, and the secondary endpoints included eGFR changes at different time points and other renal function measures. The crossover was observed in 14% and 43% of the on- and off-clamp arms. The study found no significant differences between the two groups regarding renal function outcomes despite a crossover, indicating that both approaches were comparable in patients with normal kidney function and two kidneys (66). A systematic review and meta-analysis of 156 studies aimed to analyze the outcomes of different ischemic techniques (cold, warm, and zero ischemia) for PN for renal masses (67). There were no significant differences in the EBL between the techniques. Postoperative complication rates were 14.1%, 11.1%, and 9.7% for cold, warm, and zero ischemia, respectively. PSMs were 4.8%, 4.0%, and 5.6%; local recurrence rates were 3.2% and 3.1% for warm and zero ischemia. However, their effects on renal function varied slightly. No ischemia technique can be definitively recommended over other techniques (67).

Selective clamping aims to block the vasculature specific to the tumor selectively to minimize global ischemia further. The EMERALD RCT aimed to assess the impact of selective clamping in RAPN compared with early renal artery unclamping on long-term renal function (68). This randomized trial included patients with single renal tumors who underwent RAPN. The primary endpoint was the change in eGFR of the operated kidney after 6 months, and the secondary endpoints were the feasibility and safety of the technique. This study found that selective RAPN did not significantly differ from early unclamping regarding eGFR reduction, blood loss, complications, or other factors. The trial was terminated early because there was no evidence supporting the superiority of selective RAPN in preserving renal function (68).

The currently available data do not demonstrate a clear advantage of unclamped or selective RAPN clamping over standard renal function preservation. Therefore, it may be said that there is no dilemma regarding clamping during RAPN. Clinical studies on selective clamping or off-clamping presented were conducted on patients with bilateral kidneys, small renal tumors (little to no T1b-T2), and good renal function. Thus, caution is required in interpreting the results.

Renorrhaphy vs. without renorrhaphy

Urologists aim to minimize complications and preserve renal function during RAPN. Renorrhaphy, a reconstructive technique following tumor removal, is performed to prevent postoperative bleeding and urinary leakage. Conventional renorrhaphy techniques are typically performed by suturing separate medullary and cortical layers using a two-layer approach with running or interrupted sutures. Single-layer renorrhaphy is generally a technique in which medullary and cortical layers are sutured together in one layer. However, double-layer renorrhaphy is a technique in which medullary and cortical layers are sutured separately in two layers. In contrast, renorrhaphy has been indicated as a potential factor affecting the amount of vascularized parenchyma, resulting in decreased eGFR or pseudoaneurysm (64,69). Therefore, urologists face dilemmas regarding renorrhaphy during RAPN.

A systematic review was conducted on the first pooled analysis of the impact of suture techniques on renal function after PN (70). It included three studies comparing interrupted *vs.* running sutures and three studies comparing single- and double-layer renorrhaphy. The results showed no significant differences in pre- and postoperative eGFR between the interrupted and running suture techniques. However, the single-layer renorrhaphy technique demonstrated a benefit regarding renal functional outcomes compared with the double-layer technique. This analysis indicates that the single-layer closure technique may offer better renal function outcomes in PN (70).

Instead of the renorrhaphy technique, there have also been reports of using hemostatic agents on the resection surface during PN to achieve hemostasis (71,72). A meta-analysis examined six studies involving 1,066 patients to assess the role of hemostatic agents in PN. The results showed that hemostatic agents in PN significantly reduced WIT, operative time, and EBL without increasing postoperative complications (72). Available data show the potential for preserving renal function and avoiding vascular injury by minimizing or omitting renorrhaphy during RAPN. However, its applicability largely depends on the surgeon's judgment.

After RAPN

PSMs

PSMs are found in approximately 2–8% of PN cases (11). Retrospective analyses reported to date indicate that PSM does not lead to an increased risk of metastasis or decreased CSS (73,74). In contrast, one retrospective study showed that PSMs are an independent PFS predictor (75). However, only a few patients with uncertain margins have residual malignancy (76). Local tumor bed recurrence was observed in 16% of patients with PSM compared with 3% of those with negative margins (77). Thus, RN or re-resection of the margins may often lead to overtreatment. Patients with PSM should be informed that they need to be followed up with more intense surveillance (imaging) and that they are at a high risk of secondary local or systemic therapy (73,78).

Adjuvant therapy

Several clinical trials have been conducted but failed to demonstrate the benefit of postoperative adjuvant therapy (79,80). The KEYNOTE 564 phase 3 trial demonstrated the efficacy of pembrolizumab as adjuvant therapy for clear cell RCC (81). In this trial, most of the cohort (more than 80%) was in the M0 intermediate-to-high-risk group. Long-term results are unavailable. However, at the 30-month follow-up in the M0 intermediate-to-high-risk group, the disease-free survival rates for the placebo and pembrolizumab groups were approximately 70% and 80%, respectively (82). Pembrolizumab was less effective in the M0 intermediate-to-high-risk group than in the other risk groups (M0 high-risk and M1 with no evidence of disease).

Therefore, not all patients in this group should receive pembrolizumab, and those who require it should be selected carefully. There are several useful recurrence scoring systems (83-85). In 2018, Leibovich's scoring system (84) investigated postoperative recurrence in over 3,600 patients with RCC, including 2,700 patients with clear cell RCC targeted for pembrolizumab. Pembrolizumab should be considered for patients with a high recurrence rate in such scoring systems.

These findings may be useful in selecting patients for adjuvant therapy. In addition, although nuclear grade and tumor size are often focused on as prognostic factors, tumor necrosis has been reported to be a poor prognostic factor (86,87). A recent study has shown that all three variables [World Health Organization/International Society of Urological Pathology (WHO/ISUP) grade, pathological tumor stage, and tumor necrosis] are independently associated with poor oncological outcomes (86). In another study, nuclear grade was reported as insignificant when incorporated with tumor necrosis and stage in a multivariate analysis. In contrast, tumor necrosis and pathological tumor staging were independent predictors of poor outcomes for clear cell RCC (87). It is important to select patients with a high risk of recurrence rather than providing adjuvant therapy indiscriminately.

Currently, there are no comprehensive reports on adjuvant therapy after RAPN. However, evidence from a phase 3 trial indicates that pembrolizumab administration is possible. Careful patient selection should be performed, considering the risk of recurrence.

Estimation of renal function

Concerning postoperative renal function, there is a trade-off between PN and RN. Therefore, estimating postoperative renal function may provide clinicians with insights into whether it is worth accepting the potentially higher surgical risks associated with complex PN compared to RN. The Fundació Puigvert model, using machine learning and data from 568 patients undergoing minimally invasive PN between 2005 and 2022, identified key predictors of chronic kidney disease progression post-surgery. A c-index of 0.75 highlights the importance of perioperative renal function in recovery, offering a tool to improve patient management and minimize renal function decline post-operation (88). A systematic review of available prediction models for estimating postoperative renal function, 21 prediction models were assessed from 18 studies on estimating mid- to long-term postoperative renal function after surgery for renal masses, focusing on preoperative or modifiable intraoperative factors. Patient-, kidney-, surgery-, tumor-, and provider-related factors were included among the predictors in 95%, 86%, 100%, 61%, and 0% of the models, respectively. However, most were not yet suitable for routine clinical use, indicating a need for further validation and assessment of clinical utility (89). Thus, at this time, there is no robust predictive model of postoperative renal function, which is an unmet clinical need.

Conclusions

While RAPN is a viable treatment option for various patient populations and tumors, there are still ongoing debates regarding the optimal techniques and procedures, highlighting room for further refinements. The decision to opt for RAPN should be made following careful consideration of the patient profile and tumor characteristics. Clamping techniques do not demonstrate superior renal function preservation, and renorrhaphy omission may be beneficial. In cases with PSMs, close surveillance may be a prudent approach rather than immediate intervention. As long as proper patient selection and surgical techniques are considered, RAPN will continue to be a flexible resource for urologists.

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Footnote

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