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Abbreviations

EBL	Estimated blood loss
eGFR	Estimated glomerular filtration rate
LPN	Laparoscopic partial nephrectomy
PN	Partial nephrectomy
RAPN	Robot-assisted partial nephrectomy
WIT	Warm ischaemic time

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Key Messages

- RAPN in the hands of expert surgeons is associated with excellent outcomes in terms of perioperative complications and functional results.
- RAPN could also be indicated in complex tumours, including hilar lesions, bilateral tumours, tumours in solitary kidney, or tumours in kidneys previously treated with partial nephrectomy.
- Special complex indications must be reserved to very experienced surgeons.
- The natural history of the small renal masses typically treated with RAPN as well as the short-term follow-up available in the published studies due to the relatively recent development of the procedure prevent definitive conclusions on the oncological outcomes.

10.1 Introduction

Historically, radical nephrectomy has been considered the gold standard for localised renal carcinoma. Partial nephrectomy was initially limited to absolute indications such as patients with bilateral RCC or a solitary kidney and relative indications such as impaired renal function in the contralateral kidney. With growing experience in the surgical technique, the procedure has been

subsequently adopted in elective indications, i.e. patients with a single tumour in one of the kidney with contralateral healthy kidney, with the purpose to preserve healthy renal parenchyma and maintain good renal function. Currently, according to all the urological guidelines, elective partial nephrectomy is indicated in tumours smaller than 4 cm, whenever it is technically feasible, in the presence of a healthy contralateral kidney [1].

Initially, partial nephrectomy (PN) was predominantly performed with an open approach. More recently, minimally invasive approaches (i.e. pure laparoscopy or robot-assisted laparoscopy) have gained widespread popularity and have been increasingly applied to PN. However, pure laparoscopic partial nephrectomy (LPN) is a challenging procedure with a long learning curve. The procedure requires delicate extirpative and reconstructive oncological surgery, with negative surgical margins, in one of the most vascularized human organs and in the shortest time possible in order to reduce warm ischemia time [2]. The dissemination of the da Vinci surgical system has allowed increased adoption of robot-assisted partial nephrectomy (RAPN) in the treatment of small renal tumours. This chapter highlights the main data concerning the different surgical steps of RAPN and the main results available in the literature.

10.2 Surgical Technique

10.2.1 Conventional Multiport vs. Single-Site Robot-Assisted Partial Nephrectomy

Single-site surgery has been developed in the last few years in order to provide less port-related complications, quicker recovery time, less pain and better cosmesis, due to the minimization of skin incisions to gain access to the abdominal or pelvic cavities [3]. Although the technique has been applied to RAPN only in selected cases and by experienced surgeons with promising results [4], a recent comparative study evaluating multiport vs. single-port RAPN demonstrated significantly better outcomes for standard multiport

RAPN in terms of operative time, warm ischemia time (WIT) and postoperative estimated glomerular filtration rate as well as in achieving the trifecta outcomes (defined as WIT less than 25 min, negative surgical margins and no intraoperative or postoperative complications) [5]. Hence at the present time and with the currently available da Vinci platform, there is only a limited role for single site in RAPN.

10.2.2 Transperitoneal vs. Retroperitoneal Approach

RAPN is more commonly performed through a transperitoneal approach. However, the retroperitoneal approach has been described in several surgical series [6]. The main advantages of retroperitoneal approach include avoiding bowel mobilisation, more direct access to kidney and renal hilum as well as potentially easier dissection of posterior tumours, with the potential to decrease operating time. Conversely, the main disadvantages are characterised by the small working space and the presence of restrictive landmarks. Although comparative studies with transperitoneal and retroperitoneal RAPN are sparse, a recent systematic review and meta-analysis on LPN demonstrated shorter operating time (weight mean difference 48.85 min; $p < 0.001$) and shorter length of hospital stay (weight mean difference 1.01 days; $p = 0.001$) in favour of the retroperitoneal approach [7]. The validity of those figures for RAPN remains unclear, and the selection between the two approaches is mainly based of surgeon preference and tumour location.

10.2.3 Hilar Control

The classic approach to RAPN includes clamping of the main renal artery in order to reduce blood loss and allow tumour resection in a bloodless field. The vascular clamp is typically removed at the end of the cortical renorrhaphy. More recently, Gill et al. reported an early unclamping technique, whereby artery clamps

are removed after closure of the inner medullary defect, allowing significantly reduced WIT [8].

Due to the increased relevance of WIT as modifiable factor to reduce kidney injury and loss of renal function, alternative approaches have been reported. Off-clamp RAPN has been described in selected cases with of non-complex tumours and large exophytic growth (e.g. low RENAL nephrometry or PADUA scores), demonstrating good perioperative results and preservation of the renal function [9]. More recently, a super-selective clamping of tertiary or higher-order arterial branches has been described by Gill et al. in order to provide ischemia of the tumour without compromising blood flow in the remaining parenchyma in complex tumours not suitable for off-clamp techniques [10, 11]. Specifically, a detailed preoperative 3D reconstruction of triphasic CT images of the kidneys with 0.5-mm thickness slice acquisition is performed to evaluate tumour and vascular anatomy accurately. Intraoperative vascular microdissection of secondary, tertiary and quaternary branches is performed in order to identify specific vascular branches directly supplying the tumour, which are clip-ligated and divided. Conversely, tertiary or quaternary branches supplying the peri-tumoural parenchyma are selectively and transiently controlled with a neurosurgical micro-bulldog clamp during tumour excision. Intraoperative colour Doppler ultrasound is performed before tumour resection to confirm the absence of blood flow within the tumour as well as a reduction in peri-tumoural blood flow [8, 9]. Alternatively near-infrared fluorescence imaging can also be adopted to demonstrate the efficacy of the super-selective clamping before tumour resection [12].

In the most recent publication by the same group comparing such sophisticated technique with the standard artery clamping, the authors demonstrated that super-selective clamping was associated with longer median operative time ($p < 0.001$) and higher transfusion rates (24% vs. 6%, $p < 0.01$) but comparative perioperative complications (15% vs. 13%) and hospital stay. However, patients receiving super-selective clamping experienced significantly less reduction in estimated glomerular filtration rate at

discharge (0% vs. 11%, $p = 0.01$) and at last follow-up (11% vs. 17%, $p = 0.03$) as well as greater parenchymal preservation on postoperative CT volumetrics [13]. Although extremely appealing, vascular microdissection and super-selective clamping are extremely complex surgical techniques, whose reproducibility outside of the centre which initially promoted has not been extensively tested.

As an alternative technique to performing minimally invasive partial nephrectomy without artery clamping in complex tumours, preoperative super-selective transarterial embolization or intraoperative controlled hypotension have been reported [14, 15], but the use of either techniques remains limited. Finally, cold ischemia has been also adopted during RAPN either by transarterial cold perfusion of the kidney, by retrograde ureteral cooling or, more recently, by the use of ice slush to cover the kidney during ischemia time [16].

10.2.4 Tumour Identification and Excision

Although not mandatory in the presence of predominantly exophytic tumours, margin identification and marking by intraoperative ultrasound are of particular use in case of neoplasms with large endophytic components and/or proximity to the hilum (Fig. 10.1). Robotic ultrasound probes

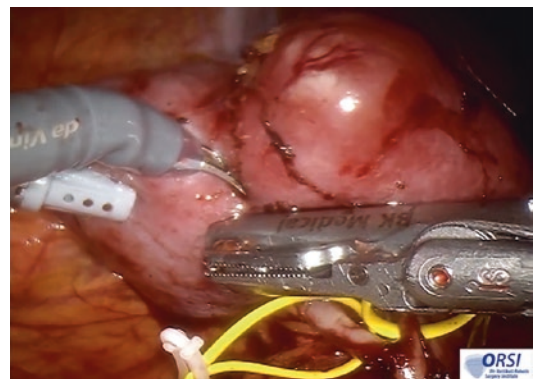


Fig. 10.1 Demarcation of the tumour (cT1b, >50% exophytic, PADUA score 8 lesion) by intraoperative ultrasound

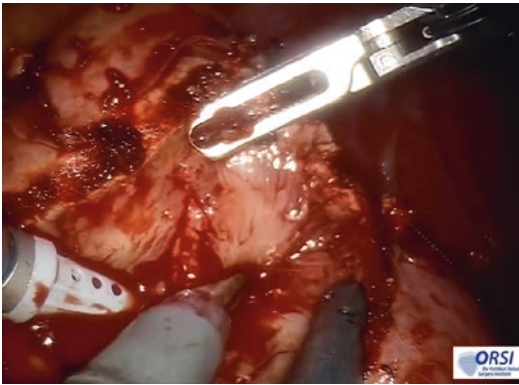


Fig. 10.2 Sharp dissection preserving a rim of healthy parenchyma on the tumour margin free of any cautery. Note the robotic suction device adopted in the dual console system in order to improve suction and countertraction during resection of the tumour (same case as Fig. 10.1)

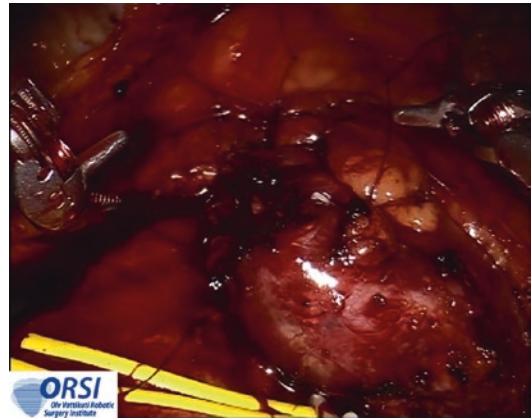


Fig. 10.3 Resection bed after inner renorrhaphy and early unclamping. A running Monocryl 3-0 suture preloaded with a Hem-o-lok clip is brought outside through the parenchyma and secured with a Hem-o-lok clip at the end of the renorrhaphy

are available, allowing direct control of the probe by the console surgeon [17].

Tumour excision should be ideally performed sharply with a rim of normal renal parenchyma, mainly using cold scissors, in order to better visualise the healthy surrounding parenchyma and minimise the risk of positive surgical margins (Fig. 10.2). In order to allow off-clamping dissection, a variety of lasers have been tested in tumour excision, including thulium, CO₂, Green Light and diode lasers [18–20]. Although promising, laser excision is not currently regarded as a standard technique, likely due to the lack of the ideal laser.

10.2.5 Renorrhaphy

Renorrhaphy is typically performed according to the sliding clip technique, originally described by Benway et al. [21]. Specifically, the inner medullary defect is closed with a running Monocryl 3-0 suture preloaded with a Hem-o-lok clip, taking all retracted calices and vessels in the running suture. On closing the Monocryl is brought out through the parenchyma and secured with a Hem-o-lok clip. The sliding clip technique allows the right tension and can be brought onto the suture (Fig. 10.3).

Various fibrinogen coagulation enhancers and tissue sealants (e.g. Floseal) can be used on the defect, together with bolsters. However, their usefulness is questionable (Fig. 10.4). Monopolar or bipolar cautery can be applied on the cortex of the resection bed. The borders of the defect are closed with polyfilament 1-0 sutures. According to the surgeon's preferences, either interrupted sutures or, more commonly and quicker, a running suture secured with a Hem-o-lok clip at each bite can be used and proper tension applied to the tissue. Subsequent tension readjustments can be made [21, 22] (Fig. 10.5). Notably, some surgeons have advocated avoiding cortical renorrhaphy in order to reduce the risk of renal function loss. However, clinical data on the benefits and risks of this technique are still awaited.

10.3 Results

LPN remains a challenging procedure. In a single surgeon series of 800 cases performed by one of the pioneers of LPN who also has the largest experience in the field, Gill et al. demonstrated mean WIT of about 32 min over the first 500 cases performed, with WIT shorter than 20 min in only 15% of cases [8]. Moreover, complication rates were as high as 24% in the first 275 cases



Fig. 10.4 Application of a haemostatic agent (PerClot®) at the end of the cortical renorrhaphy (same case as Fig. 10.1)

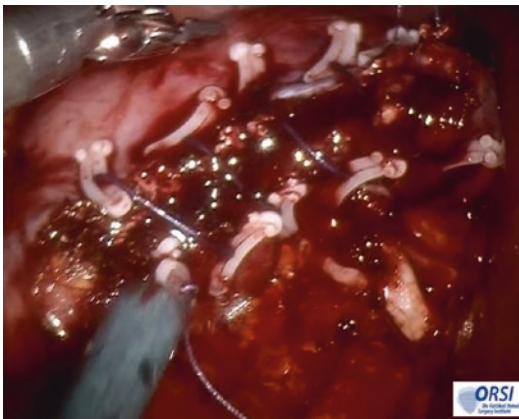


Fig. 10.5 Appearance of the kidney at the end of the cortical renorrhaphy (same case as Fig. 10.1)

and only decreased to 15% in the subsequent 289 cases [8]. Taken together, these data suggest that, even with an overwhelming surgical volume which is impossible to achieve for most laparoscopic surgeons, the procedure is associated with a high risk of complications and a long WIT. Consequently, it is not surprising that population-based studies suggest that the adoption of LPN is not widespread, being used in only 9% of all the partial nephrectomy cases performed in the USA from 2008 to 2010, as reported in the Nationwide Inpatient Sample dataset [23].

Due to the da Vinci surgical system, RAPN may offer significant advantages over conventional LPN. Two recently reported systematic reviews and meta-analyses compared the

outcome of LPN and RAPN. Froghi et al. [24] reported a meta-analysis of six non-randomised comparative studies [25–30] evaluating RAPN and LPN in the treatment of T1a small renal mass. Two hundred fifty-six patients were included in analysis which demonstrated that all the perioperative outcomes, including WIT and complication rates, were similar between LPN and RAPN [24]. Subsequently, Aboumarzouk et al. [31] reported a study with similar methodology, evaluating seven non-randomised observational studies [26, 29, 30, 32–35] and included more than 300 RAPN and 400 LPN cases. RAPN was found to be associated with significantly lower WIT (mean difference 2.7 min; 95% confidence interval 1.1–4.3 min; $p = 0.0008$). Conversely, operative times, estimated blood loss, conversion rates, complication rates and postoperative length of hospital stay were similar in the two groups [31]. Notably, despite similar inclusion criteria and designs, the two systematic reviews identified different studies, with only three papers [26, 29, 30] being included in both analyses. This clearly suggests that the systematic searches at the bases of both reviews were not sufficiently sensitive. Nevertheless, virtually all included studies were of poor methodology, due to lack of randomisation and small sample sizes which prevented definitive conclusions to be made (Table 10.1). For example, most of the studies included in the meta-analyses included patients treated by surgeons in the initial phase of their RAPN learning curves, as demonstrated by the limited volume of RAPN cases included in analyses. It is well known and accepted that, even for surgeons with previous robotic experience, RAPN outcomes over the course of at least the first 50 cases [22]. Consequently, clinically speaking, the only concept which can be derived from both reviews is that, even during the learning curve, RAPN already resulted in equal perioperative outcomes to LPN performed by more experienced laparoscopic surgeons [36].

Mature series of RAPN have provided more insights on the huge potentiality of this surgical approach. In a multicentre series of almost 350 cases of RAPN performed in four European and US high-volume referral centres, Ficarra et al.

Table 10.1 Comparative studies reporting outcomes of RAPN and LPN

Authors	Study design	Cases	Tumour size (cm)	Mean operative time (minutes)	Median/ Mean blood loss (mL)	Mean warm ischemia time (minutes)	Overall complication rate (%)	In-hospital stay (days)	Positive surgical margins (%)
Aron et al. 2008 [25]	Retrospective	RAPN 12	2.4	242	329	23	—	4.7	0
		LPN 12	2.9	256	300	22		4.4	0
Jeon et al. 2009 [34]	Retrospective	RAPN 31	3.4	170	198	20.9	—	5.2	3
		LPN 26	2.4	139	208	17.2		5.3	0
Kural et al. 2009 [26]	Retrospective	RAPN 11	3.2	185	286	27	—	3.9	0
		LPN 20	3.1	226	387	36		4.2	5
Haber et al. 2010 [33]	Retrospective	RAPN 75	2.7	200	323	18	16	4.2	0
		LPN 186	2.5	197	222	20	13	4.1	0
Hillyer et al. 2011 [27]	Prospective	RAPN 9	2.8	—	225	19	22	4	0
		LPN 17	2.7	—	175	37	23	4.5	0
Lavery et al. 2011 [28]	Retrospective	RAPN 20	2.5	189	93	23	15	2.6	0
		LPN 18	2.3	180	140	25	11	2.9	0
Pierorazio 2011 [35]	Retrospective	RAPN 48	2.2	152	122	14	10	2	4
		LPN 102	2.5	193	245	18	17	2	1
Seo et al. 2011 [30]	Retrospective	RAPN 13	2.7	153	284	35	15	6.2	0
		LPN 14	2	117	264	36	0	5.3	0
Williams et al. 2011 [29]	Prospective	RAPN 27	2.5	233	180	18	18	2.5	4
		LPN 59	3	221	146	28	20	2.7	12
Ellison et al. 2012 [32]	Prospective	RAPN 145	2.9	215	368	25	33	2.7	7
		LPN 204	2.7	162	400	19	20	2.2	7

Modified from [24, 31]

demonstrated that WIT <20 min was achievable in 64% of the cases (with median WIT of only 18 min) and overall complication rates as low as 12% (and only 3% of high-grade complications) [37]. In another multicentre series, comprising 450 cases from 4 institutions, Spana et al. demonstrated an overall prevalence of complications of 15.8%, with most of the complications being of Clavien grades 1 or 2 and only 3.8% major complications [38].

Dulabon et al. analyses a large multicentre series from four high-volume, US referral centres evaluating the outcome of RAPN in hilar tumours [39]. In this cohort of complex tumours, with a mean diameter of 3.6 cm, RAPN as performed by experienced surgeons was associated with mean WIT of 26 min, no risk of conversion to open or laparoscopic partial nephrectomy, no loss of

renal unit, low risk of complications (2.4% of Clavien grade 2 complications) and very low risk of positive surgical margins (2%) [39].

Moreover, in two other large multicentre series, Ficarra et al. [40] and Petros et al. [41] demonstrated that RAPN was feasible in cT1b tumours, with acceptable mean WIT (22 and 24 minutes in the two studies, respectively) and low risk of intraoperative (4% and 0%, respectively) and postoperative high-grade complications (about 8%) [40, 41]. Notably conflicting results have been reported in other series [42–44] (Table 10.2).

Finally, the accuracy of RAPN makes the procedure feasible with good perioperative and functional results even in patients with baseline chronic kidney disease. In another multi-institutional collaboration, Kumar et al.

Table 10.2 RAPN surgical series for cT1b renal mass

Authors	Cases	Tumour size (cm)	Mean operative time (minutes)	Median/Mean blood loss (mL)	Mean warm ischemia time (minutes)	Overall complication rate (%)	Positive surgical margins (%)	Estimated glomerular filtration rate decrease
Ficarra et al. 2012 [41]	49	5	177	120	22	26	5	7
Petros et al. 2012 [42]	83	5	194	200	24	8	0	9
Patel et al. 2010 [43]	15	5	275	100	25	27	0	12
Gupta et al. 2013 [44]	17	5	390	500	36	6	0	5

Modified from [44]

demonstrated that RAPN in patients with baseline chronic kidney disease was associated with a higher risk of complications as compared to a matched population of patients with normal renal function undergoing the same procedure [45]. However, patients with pre-existing chronic kidney disease experienced a more limited decline of glomerular filtration rate [45].

Few studies evaluated the efficacy of RAPN in very challenging cases, such as hilar tumours, totally endophytic lesions, large tumours (≥ 4 cm), tumours in solitary kidney, multiple unilateral or bilateral tumours and local recurrences after previous PN.

With regard to hilar tumours, Dulabon et al. compared 41 patients with hilar renal masses with 405 patients without hilar masses. They demonstrated that RAPN is a safe, effective and feasible option in such a complex category of tumours. Specifically, only WIT was significantly longer in hilar tumours than in the non-hilar group (26.3 min vs. 19.6 min; $p < 0.0001$), whereas no other differences in other perioperative or postoperative outcomes and pathologic surgical margin rate were found [39]. In 2013, Eyraud et al. compared 294 non-hilar tumours and 70 hilar ones treated with RAPN by an expert surgeon. In this series, hilar location for patients undergoing RAPN in a high-volume institution seems not to be associated with an increased risk of transfusions, major complications or decline of early postoperative renal function. Specifically, the authors reported longer operative time, longer WIT and increased estimated blood loss (EBL) in

hilar tumours. Conversely, no differences were noted in terms of complications and positive margins as well as in postoperative eGFR at last follow-up. WIT was the only perioperative outcome influenced by hilar location in multivariable analysis [46]. Recently, in a single centre study evaluating 44 cases with a PADUA score ≥ 10 performed by an expert robotic surgeon, the authors reconfirmed the feasibility of RAPN for complex cases, showing short WIT, acceptable major complication rate and good long-term renal functional outcomes. Specifically, median operative time, EBL and WIT were 120 min, 150 mL and 16 min, respectively. Two intraoperative complications occurred (4.5%): one inferior vena cava injury and one bleeding from the renal bed, which were both managed robotically. Postoperative complications were observed in 10 cases (22.7%), of whom 4 (9.1%) were high Clavien grade, including two bleeds that required percutaneous embolization, one urinoma that resolved with ureteral stenting, and one bowel occlusion managed with laparoscopic adhesiolysis. Two patients (4.5%) had positive surgical margins and were managed expectantly with no radiological recurrence at a follow-up of 23 months. Interestingly, in this study the authors reported no decline in serum creatinine and eGFR 6 months after surgery [47].

With regard to RAPN in solitary kidney, RAPN is rarely used for tumour in solitary kidneys and only by expert robotic surgeons. In 2013, Hillyer et al. reported the results of 26 (2.9% of the whole cohort) patients with a solitary

kidney treated at five academic institutions from May 2007 to May 2012. The study showed that RAPN was a feasible treatment option in this specific population by offering reliable preservation of renal function, low surgical morbidity and early oncologic safety in the hands of experienced robotic surgeons. Specifically, the authors reported a median WIT of 17 min and only two intraoperative complications. Postoperative complication rate was 11.5%, and, at median follow-up of 6 months, postoperative eGFR did not decline significantly [48]. In 2013, Panumatrassamee et al. compared 52 LPN and 15 RAPN robotic ones performed in a single institution between June 2000 and April 2012 for tumours in solitary kidney [49]. The study showed that RAPN offers a significant benefit over LPN in terms of operative time, WIT and hospital stay. Conversely, no significant differences were found in terms of EBL, transfusions, complications, pathological results, margin status and postoperative renal function [49].

A minimally invasive PN in the setting of multifocal renal masses is challenging but can be performed in experienced hands. Both LPN and RAPN have been described. Although both procedures are feasible, patients must be appropriately informed about the risk of open conversion [50]. For synchronous, bilateral renal tumours that require intervention, the timing of surgery remains under debate. Surgical strategies can be concomitant, bilateral PN, staged PN with the larger/more complex side first or, conversely, staged PN with the smaller/less complex side first. Performing bilateral concomitant LPN or RAPN is difficult due to patient positioning changes and is often not feasible [50]. For staged LPN or RAPN, the strategy to start from more complex or less complex side is no different from open PN. In 2009, Boris et al. reported the results of initial experience with RAPN for multiple renal masses demonstrating the feasibility of this procedure. Specifically, a total of 24 tumours in nine patients were removed with robot assistance [51]. In 2013, Abreu et al. evaluated perioperative outcomes in a series of patients who underwent minimally invasive PN

for multiple renal tumours. They performed a matched pair-analysis comparing 33 patients who underwent RAPN for multiple tumours with 33 who received the same treatment for a single tumour. EBL and WIT were similar in both groups. Conversely, median operative time and hospital stay were longer in the patients with multiple tumours. There were two conversions to laparoscopic RN per group. Overall, complications developed in 33 and 21% of the patients treated for multiple vs. single tumours. Median eGFR at discharge was similar in the two groups [52].

Very few reports are available in the literature concerning RAPN for treatment of a new or recurrent tumour in a kidney previously treated with PN. In 2008, Turna et al. reported the first experience with repeat LPN. They included in analysis 25 cases initially treated with open PN. WIT and EBL were 35.8 min and 215 mL, respectively. No intraoperative complications were reported, and postoperative complication rate was 12% [53]. Recently, Autorino et al. reported the results of the first series of repeat RAPN. They described the perioperative outcomes of nine patients previously treated with open, laparoscopic or robot-assisted PN. In three cases the surgeon performed an unclamping technique. In the remaining cases, WIT was 17.5 min. The EBL was 150 mL, and no intraoperative complications were reported. Postoperative complications were observed only in two cases [54].

Conclusions

The results of the available studies indicate that RAPN in the hands of expert surgeons is associated with excellent outcomes in terms of perioperative complications and functional results. RAPN may also be indicated in complex tumours, including hilar lesions, bilateral tumours, tumours in solitary kidney or tumours in kidneys previously treated with partial nephrectomy. Such special indications require the expertise of very experienced surgeons. The natural history of the small renal masses typically treated with RAPN as well as

the short-term follow-up available in the published studies due to the relatively recent development of the procedure prevent from drawing definitive conclusions on the oncological outcomes.

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