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Robot-Assisted Partial Nephrectomy for Complex Renal Tumors

Deepansh Dalela and Craig Rogers

Abstract

Partial nephrectomy (PN), whether using open or robotic approach, is an oncologically safe alternative for radical nephrectomy (RN) in appropriately selected patients with renal cell cancer (RCC). As urologists become increasingly facile with the robotic platform, robot-assisted partial nephrectomy (RAPN) will be increasingly performed in patients with complex renal tumors. These include tumors that are completely endophytic or hilar in location, ≥cT1b, tumors with a high RENAL nephrometry score, multiple tumors, or tumors in patients with solitary kidney or significant chronic kidney disease (CKD). While the "trifecta" of negative surgical margins, minimal renal functional decline and no urologic complications remains the ideal goal for any PN, its attainment may pose unique surgical challenges in patients with complex renal tumors. In this chapter, we describe some of the approaches for such patients, tailored to the specific clinical presentation. General considerations to optimize outcomes in such cases include additional assistant ports, judicious use of the 4th robotic arm, and use of pre-clamp check lists. Specific technical maneuvers include use of intraoperative ultrasound probes (for endophytic tumors), tumor enucleation/enucleoresection and modified renorrhaphy techniques (for hilar tumors), cutting wide and deep without excess traction (in cases of cystic/≥cT1b tumors), and minimizing warm ischemia ('on-demand' ischemia and early unclamping of the main renal artery, selective clamping of tumor specific arteries, or regional hypothermia) in patients with multiple renal tumors, solitary kidney or pre-existing CKD.

Keywords

Robot-assisted partial nephrectomy · Complex tumors · Renal cell cancer · Hilar tumors · Endophytic tumors · cT1b tumors

Introduction

Surgical extirpation of the renal cell cancer (RCC), either by a partial (PN) or radical nephrectomy (RN), has been the mainstay of treatment of localized disease [1–3]. According to current guidelines, partial nephrectomy is the standard treatment for clinical T1a renal tumors and the preferred treatment for clinical T1b renal tumors [1, 2].

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A growing evidence base suggests that while PN offers equivalent cancer control outcomes as RN [4], it is associated with significantly lesser risk of chronic kidney disease (CKD) [5], which may translate into lower cardiovascular events, hospitalizations and all-cause mortality [6–8]. With the advent of minimally invasive surgery, robot-assisted partial nephrectomy (RAPN) has become an increasingly common approach for performing PN [9].

An ideal PN is characterized by the “trifecta” of negative surgical margins, minimal renal functional (RF) decline and no urologic complications, and these outcomes are intrinsically determined by tumor specific, patient specific and surgeon specific factors (Fig. 41.1). As urologists become increasingly facile with the robotic platform, they are likely to confront more complex tumors for RAPN. These include tumors that are completely endophytic or hilar in location, ≥cT1b, tumors with a high RENAL nephrometry score, multiple tumors, or tumors in patients with solitary kidney or significant CKD. While reports from centers of excellence have described the feasibility of performing RAPN in such patients [10–20], RAPN in these conditions remains challenging.

In this chapter, we highlight some of the technical maneuvers and summarize the contemporary outcomes of patients undergoing RAPN for complex renal tumors.

Port Placement

RAPN for complex tumors may require additional port placement to improve access to the tumor (Fig. 41.2). An additional assistant port may be used to introduce a Satinsky clamp for ‘en-bloc’ clamping of the renal hilum in cases such as hilar tumors in which visibility or access to the hilum could be compromised. For right sided tumors, passive liver retraction may be performed using a locking grasper through a 5-mm sub-xiphoid port placed under the liver and secured to the diaphragm. The 4th arm may be useful to provide additional autonomy in complex tumors or vascular anatomy, obese patients or abundant perinephric fat.

Exposure and 4th Robotic Arm

As with any oncological surgery, adequate exposure is of paramount importance in complex renal tumor surgery. The goal is wide mobilization of bowel and kidney, such that the tumor/s directly face the surgeon. This may be facilitated by use of the 4th robotic arm, extra assistant ports, or use of lap sponges.

The situations where the 4th arm and extra assistant ports may be useful include:

- Bowel mobilization: Following peritoneal incision along the line of Toldt and medial mobilization of the bowel, the bedside assistant maintains medial countertraction on the bowel initially. The 4th arm can be used at this stage to grasp the anterior Gerota’s fascia and retract the kidney anteriorly to facilitate further bowel mobilization (Fig. 41.3a). This can be particularly useful in obese patients with abundant perinephric fat.
- Hilar dissection and clamping: Once a window is created between the ureter and the psoas muscle and a psoas plane is developed to the lateral side wall, the 4th arm can be placed under the ureter to provide upward lift to the kidney and put the renal hilum on stretch (Fig. 41.3b). This allows the surgeon to have both arms free for hilar dissection. Robotic bulldog clamps can be placed to occlude the renal hilum by the surgeon (using the 4th arm), or by a skilled bedside assistant through the assistant ports.
- Tumor exposure and excision: The 4th arm can also be used to mobilize and retract the kidney during dissection of the Gerota’s fascia and perinephric fat for optimal tumor exposure (Fig. 41.3c). The primary assistant port may be used to introduce the ultrasound probe, which can then be grasped by the

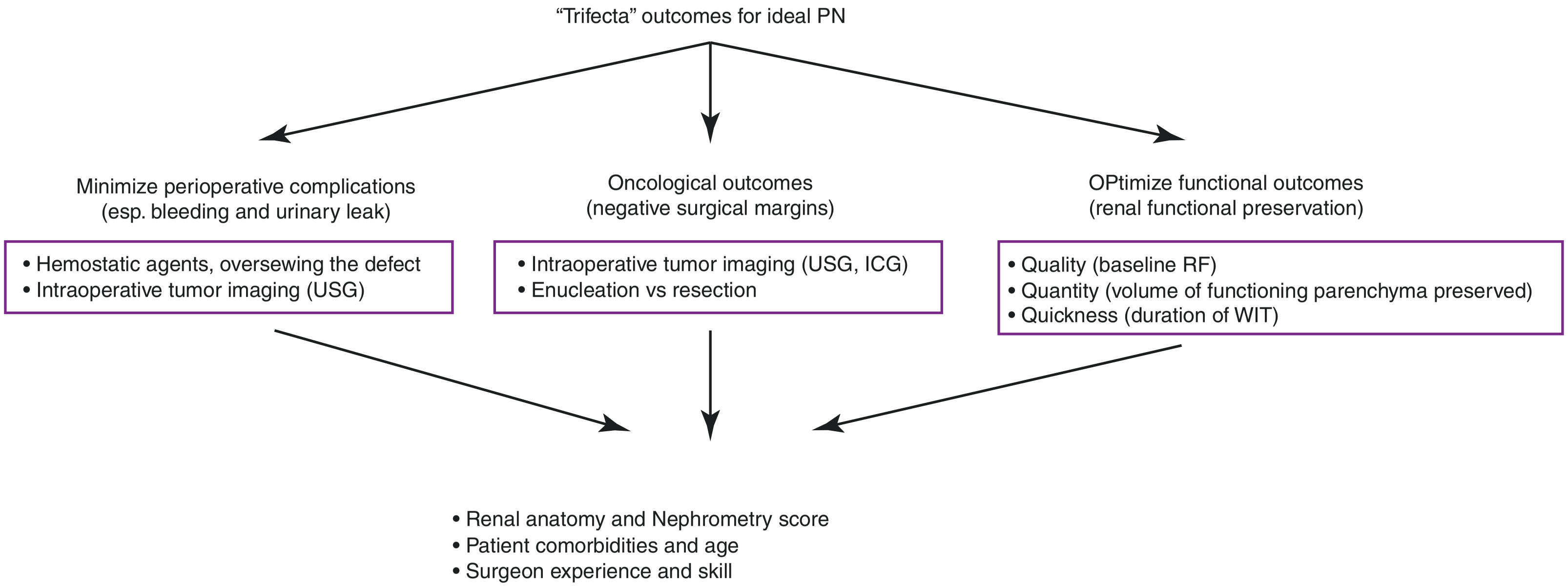


Fig. 41.1 Achieving optimal outcomes in partial nephrectomy (PN). *USG* ultrasonography, *ICG* indocyanine green, *RF* renal function, *WIT* warm ischemia time

4thw arm and moved over the kidney/tumor surface to demarcate tumor margins and borders of resection for more endophytic tumors. Posterior, upper pole tumors require medial mobilization of the kidney for adequate tumor exposure in a transperitoneal approach. In such cases, placement of a lap sponge behind the kidney prevents the kidney from springing back into its normal anatomical position.

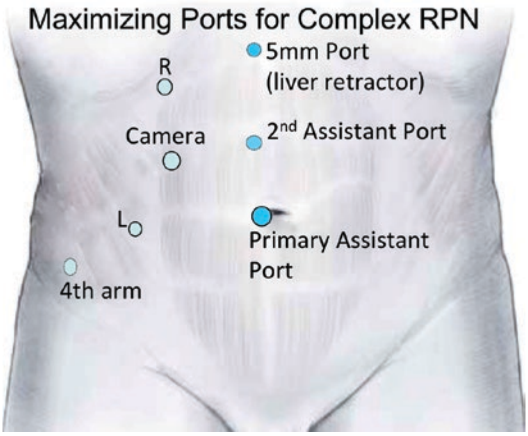


Fig. 41.2 Port placement for complex robotic partial nephrectomy (RPN). Dotted lines represent optional ports

Preparation and Pre-clamp Time Out

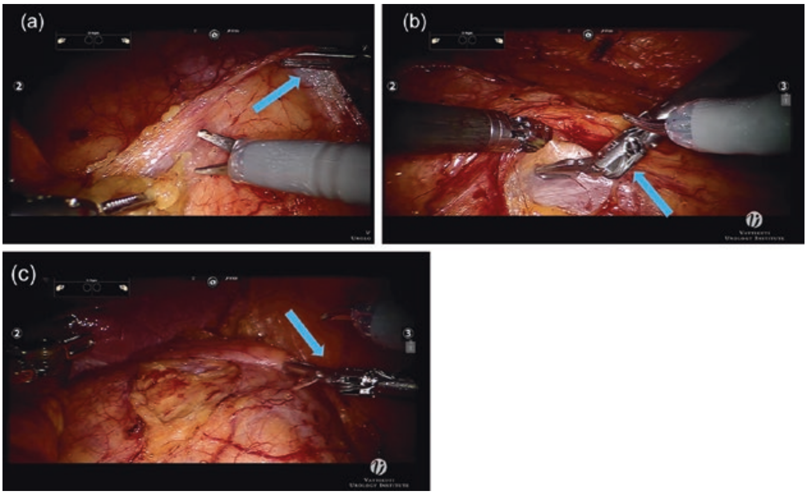
It is important to have all the necessary equipment available for complex tumors for any potential occurrences while the kidney is on-clamp and tumor excision is being performed. An example of a pre-clamp checklist includes the following:

- All sutures and hemostatic agents (Floseal, Surgicel) ready and visually confirmed
- Adequate CO_2 for insufflation
- Clean camera and instruments, test needle drivers
- Hydration and mannitol
- Bulldog clamps, Satinsky clamp, GIA stapler, and open tray available
- Robotic/laparoscopic ultrasound probe, indocyanine green (ICG) for near-infrared fluorescence imaging (NIRF)
- No breaks around clamp time

Endophytic Tumors

Renal tumors that are mostly (>50%) or entirely endophytic pose additional surgical challenges for PN (Fig. 41.4). These cases are associated

Fig. 41.3 Use of the 4th robotic arm to optimize exposure. (**a**) anterior retraction of kidney to facilitate bowel mobilization in an obese patient with abundant perinephric fat; (**b**) 4th arm under ureter to place renal hilum on stretch for hilar dissection; (**c**) kidney retraction for optimal tumor exposure. Blue arrows represent 4th robotic arm



with poor recognition of mass extension to the collecting system, higher risk of inadvertent vascular or pelvicalyceal system injury, potential for positive surgical margin, difficulty in performing renorrhaphy as well as higher perioperative complication rates from bleeding or urine leak. Use of intraoperative ultrasound can facilitate surgery for endophytic tumors. Important aims of surgery in these cases include wide and deep resection (up to the level of sinus fat or collecting system) based on preoperative imaging and/or intraoperative ultrasound to help ensure an adequate tumor margin.

Intraoperative ultrasound is used to delineate tumor margins and boundaries of resection, to screen for additional small lesions, and assist in obtaining negative resection margins during RAPN. Both robotic and laparoscopic probes can be used for this purpose. Robotic ultrasound probes offer comparable perioperative outcomes and surgical margin rates, with the added advantage of surgeon autonomy [21]. The ultrasound probe is connected to the da Vinci system, allowing the ultrasound view to be displayed on the console screen using the TilePro® system (Fig. 41.5a). Once the tumor margins are identified, the renal capsule can be scored circumferentially (Fig. 41.5b) with an adequate margin around the tumor to serve as a guide for resection.

Fig. 41.4 Representative case of endophytic tumor (*red arrow*)

Hilar Tumors

Similar to endophytic tumors, hilar tumors necessitate careful surgical planning owing to their proximity to the renal vessels and the pelvicalyceal system (Fig. 41.6). The feasibility of RAPN in the setting of hilar tumors has been previously demonstrated [10, 13, 17–19]. It is essential to dissect distal arterial branches supplying the tumor and the sinus plane to minimize inadvertent vascular and/or collecting system injury. Tumor enucleation and enucleoresection techniques (Fig. 41.7a, b) have been proposed to protect critical hilar structures [22, 23]. During enucleative PN, tumor excision is performed immediately adjacent to the tumor edge. The radially oriented renal parenchyma and pyramids lend themselves favorably to developing a cleavage plane for enucleation/enucleoresection

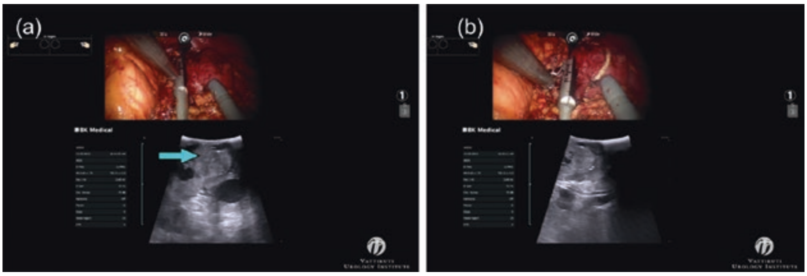


Fig. 41.5 Intraoperative ultrasound using robotic ultrasound probe for (**a**) delineation of tumor (blue arrow), and (**b**) scoring margins of resection

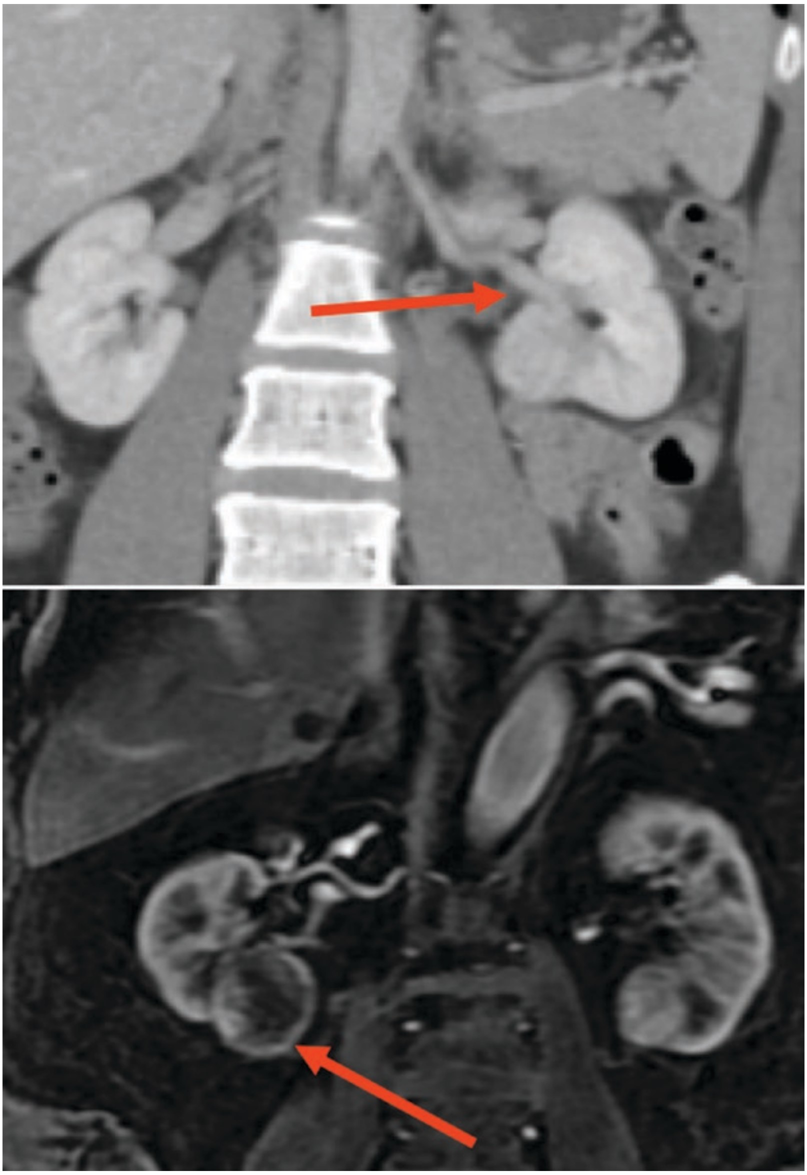


Fig. 41.6 Representative examples for hilar tumors (*red arrows*)

by atraumatic blunt separation rather than sharp cutting. Oncologically, the tumor-parenchyma interface is often marked by a 'pseudocapsule' (consisting of inflammatory and sclerotic tissue at the tumor margin), which forms a surgically favorable plane for enucleative PN. Even when there is pseudocapsular penetration into normal renal parenchyma, a thin rim of renal tissue is generally sufficient for a negative surgical margin when tumor enucleation is performed [1, 2, 23]. Functionally, enucleation helps preserve healthy parenchyma, which is an important determinant of maintaining renal function post-RAPN [24–27].

Following resection of hilar tumors, a careful renorrhaphy is key to minimize vascular and collecting system injury. Kaouk and colleagues [28] proposed a technique of V-hilar suture renorrhaphy for complex hilar tumors (Fig. 41.8). This was performed by using inner

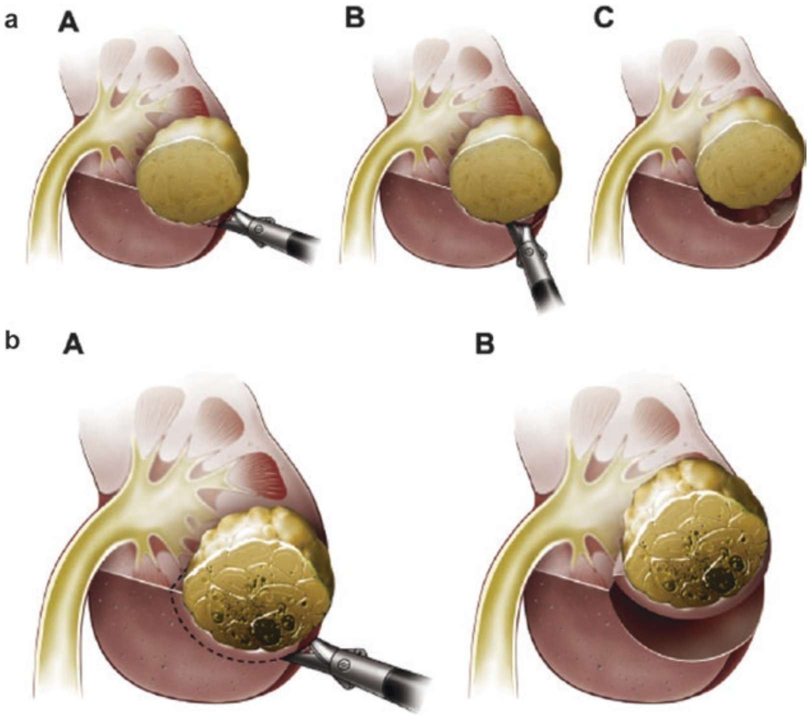


Fig. 41.7 Comparison of enucleoresection (upper panel) and tumor excision (lower panel) approaches for hilar tumors. (**a**) Schematic diagram of enucleation for small renal tumor (left kidney is depicted from anterior aspect, with the anterior half and the lower third removed). In part A, the initial incision is made into normal renal parenchyma close to the margin of the tumor. In part B, the incision is carefully advanced until the enucleation plane adjacent to the tumor pseudocapsule is entered. In part C, the tumor can then be gently separated from the renal parenchyma along this plane. (**b**) Schematic diagram of sharp excision for small renal tumor (left kidney is depicted from anterior aspect, with the anterior half and the lower third removed). The tumor is excised sharply with cold scissors (A), with a thin rim of normal parenchyma surrounding the entire excision (B). Adapted from Urology, 83(6), Anudeep Mukkamala, Christopher L. Allam, Jonathan S. Ellison, Khaled S. Hafez, David C. Miller, Jeffrey S. Montgomery, et al., Tumor Enucleation vs Sharp Excision in Minimally Invasive Partial Nephrectomy: Technical Benefit Without Impact on Functional or Oncologic Outcomes, 1294–1299, Copyright 2014, with permission from Elsevier

layer sutures to reshape the renal parenchymal defect, followed by a continuous horizontal mattress suture to reapproximate the renal capsule.

Cystic/≥cT1b Tumors

Oncological challenges associated with a cystic and ≥cT1b (>4 cm; Fig. 41.9) tumors include the risk of positive surgical margin, pathological upstaging, and, in some cases, greater likelihood of postoperative complications [29]. Important technical points to keep in mind during RAPN in such patients include the need for wider surgical margins (given their high likelihood of pathological upstaging [11] and pseudocapsular invasion [23]) and avoiding excess traction (to minimize the potential for tumor spillage). The first RAPN series comparing outcomes of renal tumors >4 cm to those ≤4 cm was reported by Patel et al. [14]. While patients with larger tumors had longer WIT (25 vs. 20 min, $p = 0.01$), there were no significant differences in estimated blood loss, total operative time, hospital stay, complication rates, and

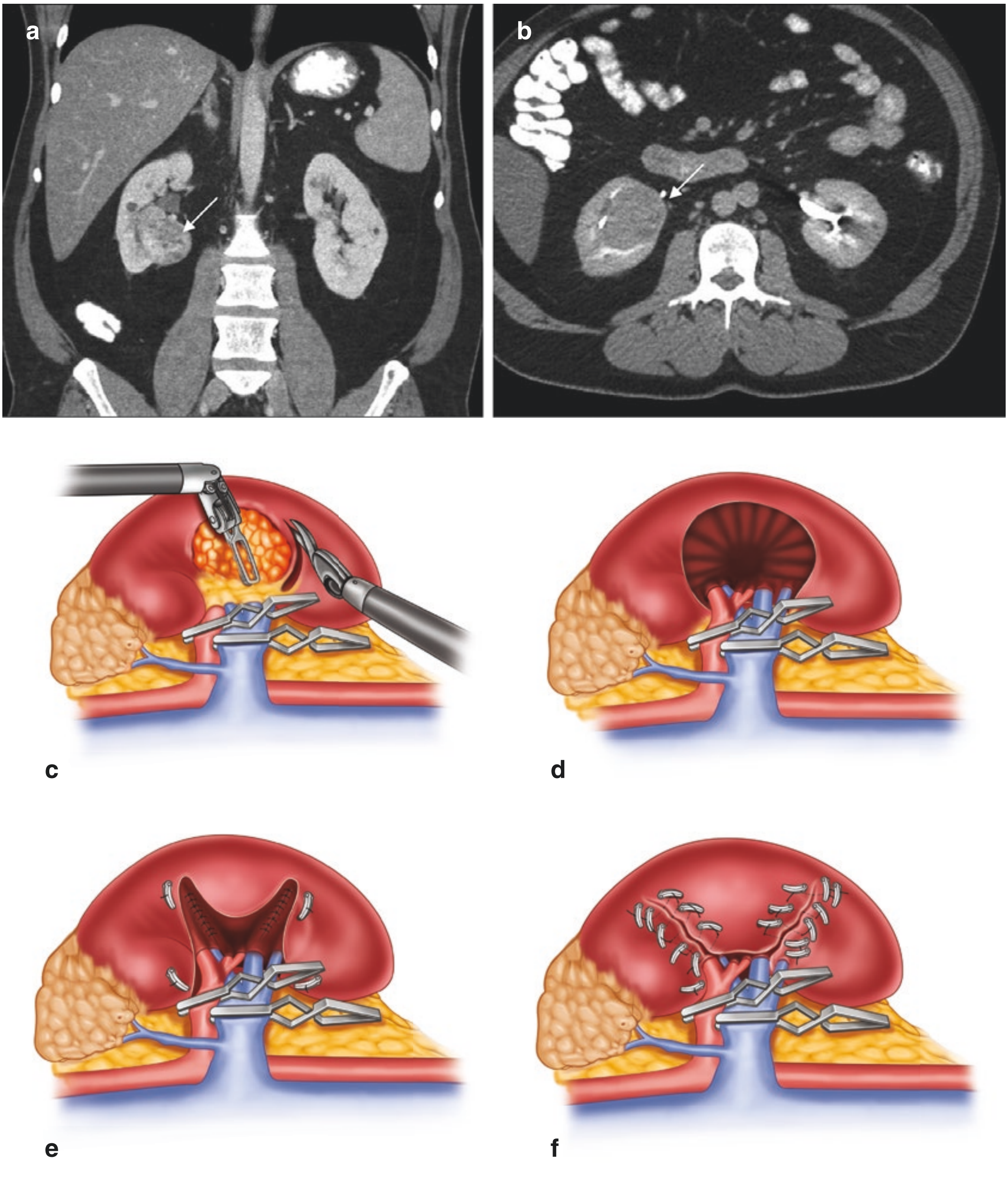


Fig. 41.8 V-stitch renorrhaphy technique (lower panel) for hilar tumors (upper panel, white arrows). Adapted from Urology, 80(2), Ali Khalifeh, Riccardo Autorino, Shahab P. Hillyer, Jihad H. Kaouk, Vhilar Suture Renorrhaphy During Robotic Partial Nephrectomy for Renal Hilar Tumors: Preliminary Outcomes of a Novel Surgical Technique, 466–473, Copyright 2012, with permission from Elsevier

change in estimated glomerular filtration rate between the two groups. Similar results were highlighted in a recent meta-analysis [30] and by Tiu et al. in patients undergoing robotic laparoendoscopic single-site PN, with no increase in the rates of adverse outcomes [31]. Nonetheless, these reports have been confined to centers of excellence with high surgical volume, and it is reasonable to contemplate radical nephrectomy in renal tumors >4 cm that are either likely to be technically challenging or associated with a healthy contralateral kidney.

Renal Tumors in Patients with Pre-existing CKD, Solitary Kidney or Multiple Tumors: Minimizing Ischemia Time

Renal functional (RF) preservation assumes key importance in patients with renal tumors and either pre-existing renal compromise (such as CKD stage 3 [eGFR <60 ml/min/m^2] or greater [12]) or greater likelihood of postoperative RF decline (solitary kidney [32] or multiple tumors). In such a setting, volume preservation and minimizing/attenuating the impact of warm ischemia time are (partially) modifiable, surgeon specific factors to optimize postoperative RF. Figure 41.10 is a schematic representation of factors determining postoperative RF in patients undergoing PN.

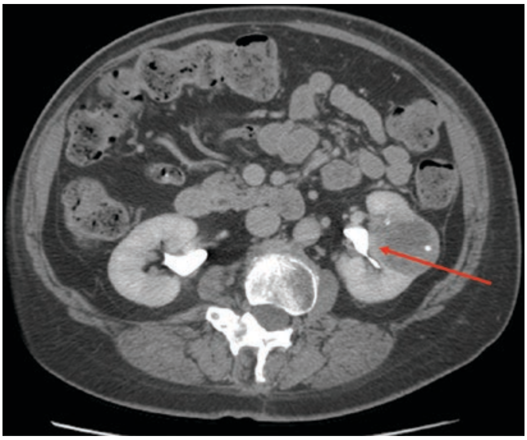


Fig. 41.9 Representative tumor >4 cm with deep extension to the collection system (red arrow)

The definition of the ideal ischemia time threshold during PN is still debated [25, 33, 34]. However, given that duration and type of ischemia are perhaps the only surgeon-specific, directly modifiable risk factors [34], strategies to mitigate the impact and/or duration of warm ischemia have evolved over the last decade [35]. These include "on-demand" ischemia, early unclamping, selective clamping, off-clamp PN, and regional hypothermia.

One approach to decreasing the duration of WIT is "on-demand ischemia": tumor excision is started with cold scissors and the renal pedicle is clamped only when bleeding obscures the surgical

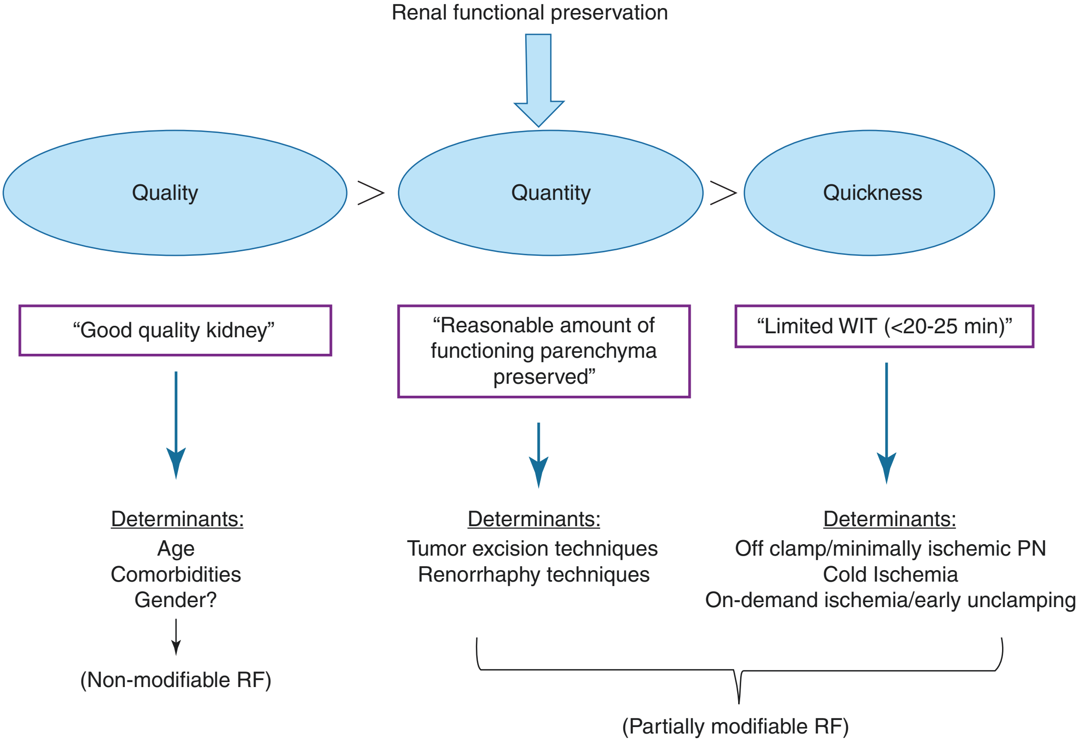


Fig. 41.10 Factors determining renal function in patients undergoing PN. *RF* risk factor, *WIT* warm ischemia time, *PN* partial nephrectomy

field and visualization of tumor [36]. While this approach was initially described for smaller tumors (median size 2.3 cm), it may have utility even for larger tumors that would otherwise necessitate a greater duration of on-clamp resection. Similar to this approach of decreasing global ischemia time, Baumert et al. suggested unclamping of the renal artery immediately following the initial central running suture or inner-layer renorrhaphy ("early" unclamping [37]). The second hemostatic running suture (usually with 2-0 Vicryl) is then performed off-clamp (Fig. 41.11). In case of ongoing bleeding from the tumor bed, additional hemostatic sutures and hemostatic agents may be considered. Peyronnet and colleagues [38] showed that despite larger (mean 3.6 vs. 3.2 cm) and more complex tumors (mean RENAL score 6.9 vs 6.1), patients undergoing early unclamping had shorter WIT (16.7 vs. 22.3 min), higher blood loss (369.5 vs. 240 ml) and no statistically significant difference in transfusion rates. Similar reductions in WIT were noted by other groups (from 31.1 to 13.9 min [39] and 28 to 18.5 min [40]).

Selective clamping of the segmental artery(ies) supplying the tumor (in an effort to spare global renal ischemia) has been demonstrated in OPN [41] and LPN [42] series. After isolation of the renal artery, further dissection is performed to expose multiple segmental renal arteries, and those segmental arteries that appear to supply the tumor are clamped. The region of ischemia (which includes the tumor and surrounding renal parenchyma) can be identified by visual inspection, intraoperative ultrasound with Doppler mode, or near-infrared fluorescence (NIRF) imaging with indocyanine green (ICG) dye (Fig. 41.12). While most tumors <3.5 cm could be resected by clamping one single segmental artery, larger (cT1b) tumors may require clamping of two or three segmental arteries [43] without converting to main renal artery clamping or adversely affecting perioperative complications.

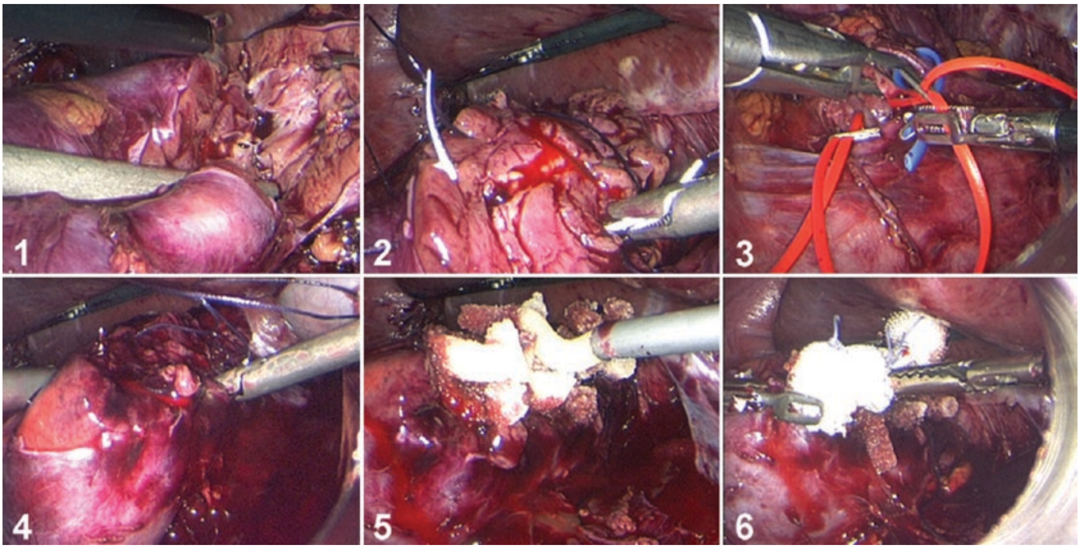


Fig. 41.11 Technique of early unclamping. (1) Upper pole partial nephrectomy, for a 3-cm tumor, using cold scissors. (2) First 2-0 Vicryl running suture to close the collecting system and achieve hemostasis in the same time. (3) Removal of the bulldog clamp, in this case after 10 min of warm ischemia time. (4) Second 2-0 Vicryl runnning suture to improve hemostasis on the vascularized kidney. Note the slight bleeding during this step. In this case, estimated blood loss was 100 cc. If necessary, extra sutures can be applied to visibly bleeding vessels before parenchyma closure. (5) FloSealis applied to improve hemostasis. (6) Closure of the parenchyma over a surgical bolster. Adapted from European Urology, 52(4), Hervé Baumert, Andrew Ballaro, Nimish Shah, Dhouha Mansouri, Nauman Zafar, Vincent Molinié, David Neal, Reducing Warm Ischaemia Time During Laparoscopic Partial Nephrectomy: A Prospective Comparison of Two Renal Closure, 1164–1169, Copyright 2007, with permission from Elsevier

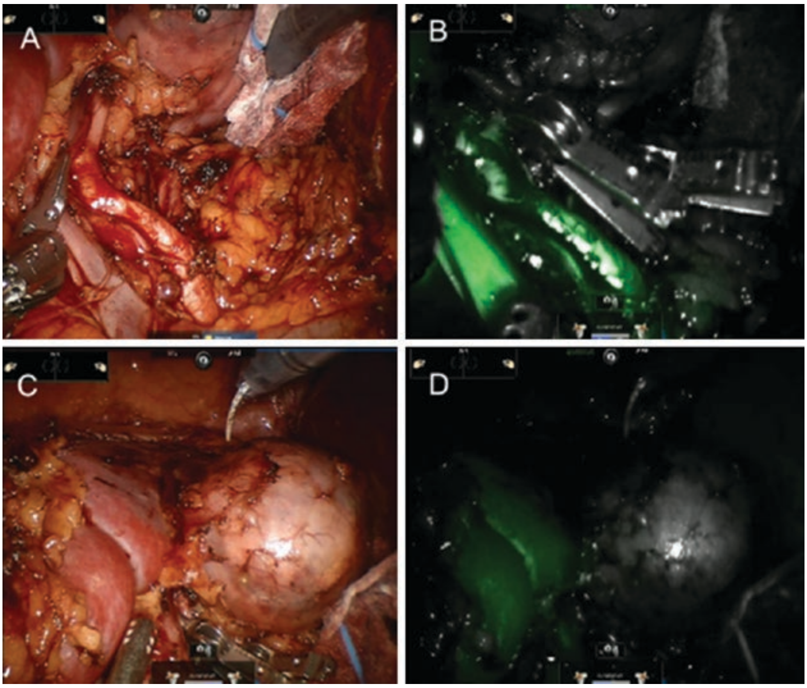


Fig. 41.12 Selective clamping technique using near infrared fluorescence imaging (NIRF) with indocyanine green (ICG) dye. (**a**) Renal hilum exposed to show multiple arterial branches. (**b**) Vascular phase of ICG dye, showing blood flow via multiple vessels (green fluorescence). (**c**) Clamping of the tumor specific arterial branch for cause 'selective ischemia'. (**d**) Parenchymal phase of ICG dye, confirming absence of blood flow to the tumor (hypofluoroscent region) and preserved blood flow to the rest of the kidney (green fluorescence). Reprinted from Current Urology Reports, Near Infrared Fluorescence Imaging with Intraoperative Administration of Indocyanine Green for Robotic Partial Nephrectomy, 16(4), 2015, Marc A. Bjurlin. With permission of Springer

Further refinement of the selective clamp approach resulted in description of the anatomical "zero-ischemia" concept by Gill and colleagues [44, 45]: super-selective clamping of the tumor-specific tertiary or higher-order arterial branches to exclusively devascularize the tumor without compromising perfusion of the surrounding normal parenchyma. The use of selective clamping may be facilitated by NIRF imaging with intraoperative administration of ICG dye [46]. ICG is a water-soluble dye that fluoresces bright green when viewed under near-infrared light (700–1000 nm). ICG binds to albumin when intravenously injected and therefore remains primarily in the vasculature. Following application of bulldog clamps on the secondary, tertiary or quaternary level arterial branches, ICG is administered at a dose of 5–10 mg intravenously (IC-Green, Akorn, Lake Forest, IL, USA). Well-perfused renal parenchyma appears fluorescent green under NIRF imaging, while ischemic tissue and tumor do not (Fig. 41.12), verifying the correct arterial branch has been controlled. The surgeon can toggle between standard white light vision and near-infrared vision on the console view to confirm the plane of excision between tumor and parenchyma, thereby avoiding entry into the tumor.

While off clamp techniques may be a surgical tour-de-force, these techniques require use of advanced preoperative imaging to visualize the arterial anatomy (such as 3-D CT scan, with its higher doses of contrast), are associated with an increased risk of bleeding, and require a technically skilled surgeon and bedside assistant. The beneficial impact of these approaches on estimated GFR has yet to be demonstrated over long term, where volume preservation continues to be a significant prognosticator of outcomes.

Fig. 41.13 Regional hypothermia during robotic partial nephrectomy using application of ice slush over the kidney. (**a**) Modified syringes prefilled with ice slush for cold ischemia. (**b**) Internal view of kidney with ice slush while renal artery is clamped with robotic bulldog clamp. Inset picture demonstrated the external view of injection of the ice slush through the Gelpoint. (**c**) Introduction of ice slush through ice plunger. (**d**) Renal surface temperature (8.8 °C in this figure) can be measured using a temperature probe. Adapted from European Urology, 63(3), Craig G. Rogers, Khurshid R. Ghani, Ramesh K. Kumar, Wooju Jeong, Mani Menon, Robotic Partial Nephrectomy with Cold Ischemia and Onclamp Tumor Extraction: Recapitulating the Open Approach, 573–578, Copyright 2013, with permission from Elsevier

Finally, a number of studies have suggested techniques for intracorporeal (regional) hypothermia to cool the kidney, in an effort to alter the oxygen demand-supply ratio [16, 47–50]. Lane et al. showed that patients with median WIT of 22 min had comparable decline in GFR 3 months after surgery to those with cold ischemia time of 45 min [34], suggesting the potential mitigating impact of the latter technique in patient with complex tumors and longer durations of expected WIT. At our center, we evolved a technique for intra-corporeal cooling and extraction (ICE) [16]: following hilar clamping, ice slush was introduced through the GelPoint™ (via modified Toomey syringes, rigid sigmoidoscopes or dedicated ice plungers) and applied all over the kidney surface (Fig. 41.13), with mean cold ischemia time of 19.6 min. This allowed renal parenchymal temperatures <16 degrees C without significantly affecting the core body temperature. Importantly, the median RENAL score in this series was 8, suggesting tumors of significant complexity may be amenable to ice slush cooling. Additionally, this approach allows immediate extraction of the excised tumor through the GelPoint, allowing gross margin assessment by pathology during the renorrhaphy.

Renal Tumors in Patients with Abdominal Surgery

Patients with extensive abdominal surgery may pose a challenge due to high risk of intra-abdominal adhesions and injury to abdominal structures during transperitoneal PN. One option in such cases is utilization of retroperitoneal approach, the technique for which has been described elsewhere in the book.

Conclusions

RAPN for complex tumors is feasible, however more challenging and associated with a greater risk of complications. Good judgement is needed to determine which surgical approach will optimize the goals of trifecta achievement.

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