Review Article

Technologic advances in robot-assisted nephron sparing surgery: a narrative review

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Background and Objective: Nephron sparing surgery (NSS) is the preferred management for clinical stage T1 (cT1) renal masses. In recent years, indications have expanded to larger and more complex renal tumors. In an effort to provide optimal patient outcomes, urologists strive to achieve the pentafecta when performing partial nephrectomy. This has led to the continuous technologic advancement and technique refinement including the use of augmented reality, ultrasound techniques, changes in surgical approach and reconstruction, uses of novel fluorescence marker guided imaging, and implementation of early recovery after surgery (ERAS) protocols. The aim of this narrative review is to provide an overview of the recent advances in pre-, intra-, and post-operative management and approaches to managing patients with renal masses undergoing NSS.

Methods: We performed a non-systematic literature search of PubMed and MEDLINE for the most relevant articles pertaining to the outlined topics from 2010 to 2022 without limitation on study design. We included only full-text English articles published in peer-reviewed journals.

Key Content and Findings: Partial nephrectomy is currently prioritized for cT1a renal masses; however, indications have been expanding due to a greater understanding of anatomy and technologic advances. Recent studies have demonstrated that improvements in imaging techniques utilizing cross-sectional imaging with three-dimensional (3D) reconstruction, use of color doppler intraoperative ultrasound, and newer studies emerging using contrast enhanced ultrasound play important roles in certain subsets of patients. While indocyanine green administration is commonly used, novel fluorescence-guided imaging including folate receptor-targeting fluorescence molecules are being investigated to better delineate tumor-parenchyma margins. Augmented reality has a developing role in patient and surgical trainee education. While pre-and intra-operative imaging have shown to be promising, near infrared guided segmental and sub-segmental vessel clamping has yet to show significant benefit in patient outcomes. Studies regarding reconstructive techniques and replacement of reconstruction with sealing agents have a promising future. Finally, ERAS protocols have allowed earlier discharge of patients without increasing complications while improving cost burden.

Conclusions: Advances in NSS have ranged from pre-operative imaging techniques to ERAS protocols Further prospective investigations are required to determine the impact of novel imaging, *in-vivo* fluorescence biomarker use, and reconstructive techniques on achieving the pentafecta of NSS.

Keywords: Urologic surgery; partial nephrectomy; pentafecta; augmented reality (AR); contrast-enhanced ultrasound (CEUS)

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Introduction

In 2020, renal malignancies compromised 2.4% of cancer diagnoses with an incidence of over 431,000 cases, worldwide (1). The prevalence is highest in the United States and Western Europe; however, the incidence is projected to rise in Asia, Africa and Latin America as these countries continue to transition to a Western lifestyle. The management of renal masses has continued to evolve over time. Open partial nephrectomy (PN) was first performed in 1887 but since the advent of minimally invasive surgery in urology, this approach has been favored for many renal tumors (2,3). The first laparoscopic partial nephrectomy (LPN) was performed in 1990 with the robot-assisted approach following approximately a decade later (4-6). Currently, AUA guidelines recommend PN for cT1a tumors; however, with advances in the understanding of vascular anatomy and development of advanced techniques, PN has been performed on complex, unfavorably located, larger tumors, and in solitary kidneys (7-16).

The principles of robotic-assisted partial nephrectomy (RPN) have also changed over time. Initially, the concept of the "trifecta" was used to evaluate the success of RPN. However, as surgeons have progressively performed more complex RPN, an understanding of the functional ramifications of surgery have become better delineated. This ultimately resulted in the expansion of the trifecta to the so-called "pentafecta" (17). In order to achieve the RPN pentafecta while removing larger and more complex renal masses, a more detailed understanding of renal anatomy and its vasculature has been investigated. Through concepts such as selective vascular clamping, three-dimensional (3D) modeling, and intraoperative imaging techniques, great strides have been made in the oncologic outcomes and preservation of renal function in those with renal masses. In this narrative review, we discuss the many recent technological advances that have been implemented in the ever-changing landscape of RPN. We present this article in accordance with the Narrative Review reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-23-107/rc).

Methods

We performed a non-systematic literature search of PubMed and MEDLINE on November 1, 2022 to identify and select manuscripts from January 2010 to September 2022 (*Table 1*). The search keywords included "augmented reality", "fluorescence markers", "renorrhaphy", "ultrasound", "surgical approach", "clamping" and "early recover after surgery" in combination with "partial nephrectomy" and "nephron sparing surgery". We manually reviewed all resulting manuscripts relevant to the topic that were written in English. We also reviewed the references lists of review articles to include other papers relevant to the topic.

Striving for pentafecta achievement

In an attempt to standardize post-operative outcomes following RPN, the term "pentafecta" emerged from the initial concept of the "trifecta". The "pentafecta" is now the gold standard when comparing long-term success of nephron sparing surgery (NSS). This concept includes achieving (I) negative surgical margins, (II) warm ischemia time (WIT) ≤25 minutes, (III) no major complications, (IV) >90% preservation of baseline estimated glomerular filtration rate (eGFR), and (V) no upgrading of chronic kidney disease (CKD) stage. During partial nephrectomy, optimized oncologic outcomes are sought while simultaneously minimizing reciprocal damage from surgery and preservation of renal function. Optimization of factors including pre-operative imaging to minimize the risk of surgery for benign lesions, decreasing WIT by implementing artery-only clamping or totally clampless RPN, utilizing intraoperative models, fluorescence markers, ultrasound to minimize excision of normal parenchyma, decreasing ischemic suturing techniques and utilization of percutaneous ablation have been published. Great strides have been made since the advent of RPN and their relative contributions towards pentafecta achievement will be explored in this narrative review (18).

Pre-operative planning

Imaging

Cross-sectional imaging

The incidence of localized renal masses continues to rise with almost 70% of renal tumors being identified incidentally as the use of cross-sectional imaging has increased (19,20). While traditionally, contrast-enhanced computed tomography (CT) has been used to characterize renal masses, other imaging modalities have been implemented in recent years to better characterize malignant renal lesions. Magnetic resonance imaging (MRI) has been utilized as an alternative to CT without associated patient irradiation. Diffusion-weighted imaging (DWI) had a sensitivity of 86% and a specificity of 78%

Table 1 Search strategy summary

Items	Specification
Date of search	November 01, 2022
Databases and other sources searched	PubMed, MEDLINE
Search terms used	Partial nephrectomy, nephron sparing surgery, augmented reality, fluorescence markers, renorrhaphy, ultrasound, surgical approach, clamping, early recovery after surgery
Timeframe	January 2010–September 2022
Inclusion and exclusion criteria	Exclusion: non-English text
Selection process	Independent article selection

in differentiating between malignant and non-malignant lesions in a recent meta-analysis, and was moderately accurate in distinguishing low- and high-grade lesions which was comparable to CT findings (21). Perfusion levels based on perfusion MRI and in particular, arterial spin labeling (ASL) has been shown to vary among renal mass histology type with oncocytoma having higher perfusion levels than renal cell carcinoma (RCC) (22). In additional to traditional MRI, positron emission tomography (PET)-CT based molecular and nuclear imaging have been developed and studied as biomarkers in RCC. ^{18}F-fluorodeoxyglucose (FDG) PET/CT is the most common radiotracer used; however, its use in RCC is limited due to physiologic uptake in normal parenchyma (23). However, it may have use in determining the aggressiveness of renal masses. Higher ^{18}F-FDG PET/CT activity has been correlated with a higher Fuhrman grade, tumor-node-metastasis (TNM) stage, and identifying sarcomatoid features and thus may have utility in predicting aggressiveness and risk of progression (24-27). Girentuximab is a carbonic anhydrase IX binding protein that has been evaluated in combination with PET/CT to evaluate indeterminant renal lesions. In the multicenter, phase III REDECT trial, imaging with contrast enhanced CT and girentuximab-PET/CT prior to surgical resection was conducted in 195 patients to identify clear-cell *vs.* non-clear-cell RCC. The imaging results were compared surgical pathology at time of excision. Girentuximab-PET/CT had a sensitivity and specificity of 86.2% and 85.9%, respectively and contrast-enhanced CT had a sensitivity and specificity of 75.5% and 46.8%, respectively (28). Currently, the ZIRCON trial is underway, investigating the ability of girentuximab PET/CT to distinguish clear-cell RCC from other renal lesions, and preliminary results have been promising (29). Other radiotracers including ^{11}C-acetate PET/CT and prostate-specific membrane antigen (PSMA)-targeted PET/CT as well as imaging-based radiomics have been studied (30). Though some potential is evident in using novel markers to distinguish benign *vs.* malignant lesions and predict renal mass histopathology, there is insufficient evidence to suggest their use in clinical practice at this time. There is significant promise for these markers to guide patient counselling; however, further validation is required.

Contrast-enhanced ultrasound (CEUS)

Ultrasound remains a highly sensitive tool in detecting renal masses although it is limited in its characterization of anatomical factors related to surgery, including number and location of renal arteries and veins. Though traditionally not used for pre-operative surgical planning, it is particularly useful in those with pre-existing renal insufficiency or contrast allergy. Duplex ultrasound is readily available at most centers; however, the granular detail regarding malignant potential is not easily obtained using this modality. CEUS is an evolving imaging technique that maintains the cost-effectiveness, lack of radiation exposure, and reliability of duplex ultrasound while utilizing sonovue contrast to obtain enhancement patterns of indeterminant renal masses (31). The malignant potential of renal masses remains a difficult area to navigate for the urologist as 25% of resected renal masses have benign pathology (32). A recent study by Tufano *et al.* demonstrated that when using a combination of qualitative and quantitative parameters to distinguish between benign and malignant lesions, sensitivity was 93% and specificity was 100% (33). Another study has also demonstrated the ability of CEUS to distinguish between RCC and specific benign lesions including angiomyolipoma (AML) with one study correctly identifying lesions in 80% of patients, though 20% of patients with lipid poor AMLs had incorrectly identified lesions (34).

When focusing on oncocytoma in particular, a study by Wei *et al.* incorrectly identified 100% of oncocytomas as malignant lesions resulting in surgical excision of these masses (35).

A variety of CEUS based characteristics have been investigated to delineate benign and malignant lesions including: heterogenous enhancement, late washout, fast wash-in, and rim-like enhancement; however, there is a significant degree of overlap between these characteristics in malignant and benign lesions. There remains a paucity of literature supporting the use of any given imaging characteristic, mandating further investigations before CEUS is widely implemented in the delineation of malignant lesions. Though CEUS is a promising imaging modality, contrast-enhanced cross-sectional imaging remains the imaging of choice for characterization of these masses without larger prospective studies (36).

3D models

3D models and their application to renal masses have been a critical development. The concept of individualized precision surgery is embodied by its use. Currently, the majority of pre-operative planning for RPN is based on conventional two-dimensional (2D) imaging. Intraoperative ultrasound is commonly used for the resection of renal masses. Issues with this method arise primarily when attempting selective clamping and teaching surgeons-in-training (37). A solution to this may be using 3D-printed models to guide surgeon decision-making and to augment trainee and patient understanding. The question of 3D-printed model accuracy continues to be investigated. Michiels *et al.* demonstrated an 87.5% validity of their 3D-printed model compared to CT imaging; however, this study did not evaluate upper urinary tract-tumor contact (38).

Selective or super-selective clamping is thought to decrease global renal ischemia by clamping only necessary vessels associated with the renal mass to be excised. This is a tedious process and is difficult with only 2D imaging. Though super-selective clamping has not shown benefit *vs.* main artery clamping alone, selective artery clamping has demonstrated improvements in post-operative renal function recovery (39,40). A recent study demonstrated that 3D-printed reconstruction of renal vasculature allows for improved surgeon confidence in selective clamping as well as occasional changes in surgical planning (41). Another study by Fan *et al.* demonstrated that the use of 3D models in LPN for T1-T2b renal masses with a R.E.N.A.L. (tumor radius, exophytic/endophytic properties, nearness to collecting system, anterior/posterior, location to polar line) score ≥8, reduced overall WIT and intraoperative blood loss though no short-term differences in renal function were noted (42).

Perhaps the most important role of 3D models is on trainee education and pre-operative patient education. As the prevalence of robotic surgery has increased, trainees have as a consequence become more involved in the surgical steps than in the past (43). Complex intra-renal anatomy particularly when combined with endophytic tumors makes pre-operative planning difficult for trainees to fully grasp. These models allow for trainees to understand this complex tumor-kidney interface and may improve confidence and procedural understanding. Monda *et al.* conducted a study including participants across all levels of urologic training and demonstrated significant usefulness of 3D models for pre-operative training (44). Furthermore, the use of 3D models has been shown to improve patient understanding in regards to the disease process and treatment plan as well as comfort level with surgery (45). Cost analysis of these models ranges between $1–1,000 USD based on the type of printer used and time required for printing and processing ranges from 1.5 hours to 4 days (46). Ultimately, the utility of these models lies primarily in patient education and surgical trainee education; however, the widespread use of 3D models will clearly be inhibited by cost and time. Acquisition of 3D printers with shorter printing and processing times may allow for the ubiquitous use of these models.

Intra-operative considerations

Surgical approach

Transperitoneal *vs.* retroperitoneal approach

The transperitoneal approach to RPN may be favored for anterior and medial tumors (47,48). For patients with hostile abdomens or with posterior or peri-hilar tumors, a retroperitoneal approach may be preferable. The advantages of the retroperitoneal approach also include direct hilar access and reduction in renal pedicle injury (49). Arora *et al.* demonstrated equivalent perioperative outcomes with the exception of longer length of stay and increased blood loss for the transperitoneal approach (50). A larger study by Porpiglia *et al.* demonstrated shorter operative time by 35 minutes in the transperitoneal group which came at a cost of a 3% increase in the overall complication rate (51). These results have been corroborated by several other groups, indicating the retroperitoneal approach may provide some benefits while maintaining oncologic outcomes in larger or completely endophytic masses (52-56). Furthermore, Ghani *et al.* demonstrated decreased time to normal diet, shorter catheter durations, and a reduction in post-operative opioid needs for those undergoing retroperitoneal RPN (57). The transperitoneal approach is widely considered the standard surgical technique and larger-scale adoption of retroperitoneal RPN is limited by lack of utilization and demonstration for surgical trainees across all programs.

While many surgeons are proponents of the retroperitoneal approach in the appropriately selected patient, many comparative studies have presented mixed results. A recent study by Choi *et al.* demonstrated that while retroperitoneal RPN resulted in shorter operative times, less blood loss, and less WIT, when comparing pentafecta rates for masses ≥4 cm, no differences were seen. Furthermore, they demonstrated that at 1 year, those who underwent a retroperitoneal approach were noted to have a greater reduction in eGFR than the transperitoneal approach. This was attributed to decreased working space resulting in excision of larger amounts of non-diseased parenchyma (58). Likewise, Mittakanti *et al.* demonstrated no differences in the trifecta categories of WIT, positive surgical margins (PSM), and complication rates between the two groups (59). Based on existing literature, retroperitoneal RPN may reduce hospital costs, catheter times, and opioid consumption at the cost of excision of greater non-diseased renal parenchyma and longer operative times. Ultimately, long-term outcomes are lacking and peri- and post-operative outcomes are likely highly dependent on surgeon comfort with the retroperitoneal approach, requiring up to 300 cases for the transperitoneal approach (57,60). Thus, surgical approach to RPN should be individually tailored to each patient and outcomes associated with retroperitoneal RPN will likely improve as surgeons become more facile with the technical aspects of the retroperitoneal approach.

Single-port (SP) *vs.* multi-port (MP) approach

MP RPN has facilitated the widespread adoption of minimally invasive partial nephrectomy. The da Vinci SP robotic surgical system was more recently introduced in 2017 and continues to develop its place in the urologist's armamentarium (61). Within urological surgery, the SP robot has been utilized for perineal prostatectomy, radical cystectomy, urinary diversion, ureteroneocystostomy, pyeloplasty, and partial as well as radical nephrectomy (62-67). While still in its youth, the use of the SP system for RPN has been studied, albeit mainly in single-center experiences, case series, and retrospective studies. A report of three patients by Kaouk *et al.* in 2019 initially demonstrated the feasibility SP RPN. All patients had negative surgical margins with an average WIT of 25 minutes though one patient required angioembolization in this study (68). While an SP system could theoretically reduce post-operative opioid consumption, a comparative, retrospective study from 2021 demonstrated similar short-term perioperative outcomes as well as similar inpatient and outpatient morphine equivalent consumption between the MP and SP study arms. Likewise, this study demonstrated no significant peri-operative differences between the SP and MP systems (69). Similarly, a recent prospective cohort study of 292 patients showed that the SP system resulted in longer WIT; however, all other peri-operative outcomes were similar between the groups (70). Ultimately, the SP system has not been widely investigated; however, retrospective and small cohort studies have demonstrated equivalent oncologic, peri-operative and pain-related outcomes to the MP system. Longer WIT may be attributed to surgeon comfort with the SP system and thus may be expected to improve over time. As outcome measures appear to be equivalent to MP, an SP system can be implemented if available and based on surgeon preference. There does not appear to be sufficient evidence to support the healthcare expenditure of acquiring an SP surgical system solely for RPN.

Fluorescence-guided therapy

Indocyanine green (ICG)

ICG is a fluorescent molecule that emits light when excited with near-infrared light (71). When injected intravenously, ICG binds to bilitranslocase and healthy, well-vascularized tissue appears isofluorescent (72). Applied to the surgical management of renal masses, tumors have lower expression of bilitranslocase and thus tumors appear hypofluorescent (73,74). This hypofluorescence has been demonstrated to have an 84% sensitivity and 87% of positive predictive value for malignant lesions in 100 cases, providing a reliable intraoperative method of identifying the oncologic potential of a renal mass (75). Furthermore, ICG is used to guide arterial clamping during RPN (76). The da Vinci platform has improved visualization and improved dexterity which has allowed for dissection of segmental and sub-segmental vasculature to ultimately decrease global renal ischemia (77). In combination with ICG these advances have allowed for super-selective arterial clamping which was initially demonstrated to reduce loss of post-operative eGFR 10-fold (74). Further studies have demonstrated a more modest reduction in eGFR post-operatively and at near 2 years follow-up (78-80). Conversely, a study by McClintock *et al.* demonstrated a reduced loss in eGFR with ICG-assisted segmental renal artery clamping in short-term follow-up, these results did not hold at 3 months (81). A more recent study by Takahara *et al.* comparing ICG-assisted full and selective clamping found increased blood loss with selective clamping with no benefit in eGFR at 6 and 12 months (82). While ICG-assisted RPN may not improve long-term compromise in renal function, it allows for rapid identification of the renal malignancy and may improve overall WIT and thus can be used to rapidly identify the tumor and normal renal parenchyma (83,84).

Folate receptor-targeting agents

The folate receptor is a widely abundant receptor with a difference in expression in normal and malignant renal tissue. Folate-linked ligands have previously been used as drug deliver agents into human cancer cells (85). Folate-receptor targeted near infrared (NIR) dye have been implemented in patients ovarian malignancy undergoing cytoreductive surgery, allowing surgeons to resect 29% greater malignant lesions than those not receiving dye (86). Since then, these dyes have been used for endometrial carcinoma, pulmonary adenocarcinoma, pituitary adenocarcinoma, metastatectomy for osteosarcoma, and for partial nephrectomy (87-91). While a paucity of literature is available for its application in RPN, a preliminary case report of three patients demonstrated tumor hypofluorescence with a good delineation between normal parenchyma and tumor. Furthermore, the authors were able to correlate patterns of intraoperative fluorescence to immunohistochemistry (92). A more recent study, similarly found excellent demarcation between normal parenchyma and tumor. Immunohistochemistry demonstrated staining limited to the proximal renal tubules which was significantly greater in normal parenchyma compared to tumor cells (93). While functional studies including a phase 2 clinical trial are underway, the benefits of folate receptor-targeted agents are not yet available.

Intra-operative imaging

Intra-operative ultrasound

The accurate identification and delineation between tumor and normal renal parenchyma is the primary goal when performing RPN. The tumor-parenchyma interface is difficult to precisely ascertain based on pre-operative 2D imaging and direct vision alone. Intraoperative ultrasound using a laparoscopic probe, when initially introduced, was cumbersome due to lack of surgeon (94). Drop-in ultrasound probes have since been introduced and controlled robotically by the surgeon to help identify this interface and depth of extension particularly for large, endophytic tumors or hilar tumors (95,96). Intraoperative ultrasound has also been used to identify renal vasculature for selective clamping and determine the distance between tumor and segmental vessels (97). In cases with renal vein and inferior vena cava thrombi, ultrasound can help localize the proximal extent of thrombus. Achieving negative surgical margins and preservation of as much normal parenchyma as possible are tenants of RPN; however, lower WIT have also been associated with decreased global kidney function, particularly in those with chronic pre-existing conditions (98-101). In an effort to reduce global ischemia and WIT, selective clamping in combination with CEUS has been used to reduce eGFR decrease after RPN (102-104). While intraoperative CEUS is not widely available, intraoperative drop-in ultrasound with assistance of TilePro technology will continue to play a critical role in all RPN cases.

Intra-operative use of augmented reality (AR)

While AR and 3D models have proven to be useful and trainee education and pre-operative patient education, its use intraoperatively as a replacement for ultrasound is emerging. This concept was first described by Porpiglia *et al.* (105). A retrospective study compared traditional intraoperative 2D ultrasound to AR-assisted RPN. These models developed pre-operatively were used intra-operatively during tumor resection and reconstruction phases. The use of intra-operative on-lay of pre-operative AR models resulted in lower rates of global ischemia and lower reduction in estimated renal plasma flow at 3 months (−12.38% in 3D AR group *vs.* −18.14% in 2D ultrasound group) by depicting detailed tumor, contact with collecting system, and vasculature (106,107). This study suffers from short-term follow-up; however, it provides promising support for the use intra-operative 3D on-lay technology.

Clamping technique

In an effort to eGFR after RPN, urologists have attempted to reduce WIT. Theorized to reduce ischemia to normal renal parenchyma distant from the tumor, selective clamping has been employed. These techniques have ranged from selective, super-selective, and clampless approaches to renal artery clamping alone (108,109). Clampless or "off-clamp" partial nephrectomy, as demonstrated by recent studies, have not been advantageous in preservation of renal function in patients with two functional renal units (109-111). There was also no difference in change in renal function at 9 months with those undergoing renal artery clamping alone *vs.* those undergoing renal artery and vein clamping (112). In combination with pre-operative CT imaging, segmental vessel clamping with ICG and near-infrared fluorescence (NIRF) was suggested to reduce the ischemic zone while reducing the risk of PSM and reduce the impact on eGFR after RPN (113). A retrospective study by Takahara *et al.* demonstrated that selective clamping resulted in greater blood loss with no benefit in preservation of eGFR (92.0% *vs.* 91.6% at 12 months) (82). Another study by Badani *et al.* demonstrated neither benefit nor harm in selective clamping, though this study had extremely short WIT (<15 minutes) (114). These findings have been corroborated by another retrospective cohort study (115).

The use of super-selective clamping strives to clamp tumor-specific vasculature in hopes to further reduce global ischemia. Super-selective clamping has been demonstrated to improve reductions in eGFR after partial nephrectomy at up to 6 months in follow-up compared to conventional RPN with early unclamping (116). Conversely, the recently published EMERALD trial demonstrated no benefit at 6 months in the conventional partial nephrectomy group compared to those undergoing super-selective clamping group. Though blood loss and complication rates were no different between the groups, this study was prematurely stopped due to lack of benefit for super-selective clamping (117). Combined, the current available data suggests that selective and super-selective clamping may lead to increased blood loss while providing limited benefit in preservation of renal function after NSS.

Reconstruction following tumor excision

Renorrhaphy technique

As a tenant of the pentafecta for RPN, urologists strive to minimize complications and preserve renal function. After tumor excision, reconstructive techniques have been postulated to impact eGFR and the risk of complications such as urine leak (118,119). Renorrhaphy techniques include single *vs.* a double layer closure and running *vs.* interrupted closure. While few studies existing comparing long-term eGFR as a function of reconstruction method, some studies have reported short-term results. When comparing running *vs.* interrupted renorrhaphy, a recent systematic review conducted by Bertolo *et al.* found no differences in peri-operative or functional outcomes. While WIT was higher in the interrupted group due to longer suturing time, this was though to be offset by greater tissue necrosis resulting from the running technique (120,121). Ultimately, WIT does not appear to impact eGFR in the short term, underlying the developing understanding of the relationship between renal ischemia and function (118).

Convention dictates closure of the renal defect in distinct medullary and cortical layers. However, in recent years this dogma has been challenged insofar as single-layer closure has been reported to have decreased reduction in eGFR at the risk of a small increase in urinary fistula rate (120). A study by Bahler *et al.* investigated the possibility of an isolated, medullary closure alone and found no differences in post-operative outcomes and a decreased loss in ipsilateral renal mass with exclusion of the cortical layer (122). Williams *et al.* excluded the collecting system closure and closed only the cortical layer using a sliding-clip technique and found no differences in perioperative outcomes or differences in eGFR at 2-year follow-up (123). A more novel study in this regard by Hidas *et al.* omitted the defect altogether and implemented tissue sealant (CoSeal or BioGlue) in a subset of patients and found improved functional outcomes measured by quantitative dimercaptosuccinic acid (DMSA) scanning (124). A recent meta-analysis of this technique which incorporated six studies demonstrated a reduction in WIT, operative time, and blood loss for those patients in whom suture closure of the defect was substituted by hemostatic agents without any increase in complication rates (125). As such, implementing single-layer renorrhaphy or substituting closure with tissue sealing agents may help to achieve the pentafecta of NSS. Ultimately, reconstruction technique will vary by surgeon; however, many options are available to minimize collateral damage during RPN.

Post-operative drain placement

Partial nephrectomy has a high risk of complications due to its technical complexity (126). As such, many surgeons performing RPN elect to leave a post-operative, closed suction drain as a surgical principle, especially in cases where there is entry into the collecting system, though little evidence to support this is present in the literature. While drains potentially increase patient discomfort and pain, they may allow for earlier detection of post operative hemorrhage and urine leak (127). Contrary to surgeon dogma regarding post-operative drains, a retrospective study of 636 patients from 8 academic centers showed similar complication rates between patients with and without a drain (128). These findings were supported by Beksac *et al.* who found that reserving drain placement to non-routine cases only, was better than routinely placing drains (129).

While drain placement appears to be unnecessary, many consider drains to have relatively few consequences. Several reports from other surgical fields have reported drain-related complications including retained drain fragments, patient discomfort, and post-operative small bowel obstruction due to drain placement (130,131). Drain placement has also been demonstrated to reduce post-operative length of stay after RPN. Therefore, given the body of evidence it appears routine drain placement can be omitted in routine RPN to prevent patient discomfort and minimize risk of drain related complications while potentially reducing patient length of stay.

Post-operative management

Early recovery after surgery (ERAS)

Advancements in perioperative protocols, including ERAS protocols, have been designed to improve patient outcomes, reduce hospital stays, and reduce post-operative complications. While commonly implemented for major abdominal operations, recently ERAS protocols have been developed for minimally invasive partial nephrectomy. An early study investigated fast-track programs for patients undergoing laparoscopic nephrectomy. The authors found a reduction in length of stay, pain and nausea scores, inpatient morphine equivalent consumption, and improved patient satisfaction scores (132). A recent prospective randomized trial in patients undergoing laparoscopic partial nephrectomy focused on improving pre-operative education, reducing pre-operative fasting, omitting bowel preparation, decreasing intraoperative fluid resuscitation, and early catheter removal as well as early ambulation and feeding. This study demonstrated that patients on an ERAS protocol had fewer complications, earlier return of bowel function, and shorter length of stay compared to controls (133). This has been demonstrated by Sentell *et al.* in a multi-institutional study which showed single overnight stay did not lead to increased complication rates compared to >1 day stay (134). While ERAS protocols are typically applied to major abdominal cases where longer length of stay and higher post-operative complication rates are expected, the importance of ERAS principals to robotic surgery cannot be overstated. For RPN, practice patterns vary widely; however, the general principals of ERAS seem to improve patient outcomes and increase patient satisfaction. Thus, in patients undergoing RPN, surgeons should focus on minimizing pre-operative fasting, limiting intra-operative fluid resuscitation, utilization of local anesthetics and nerve blocks, and early discontinuation of surgical drains and urethral catheters.

Complications following robotic partial nephrectomy

Robotic partial nephrectomy has advantages over the open approach in several categories; however, many of the same complications are seen with an incidence of up to 33%. Potential complications include injury to other visceral organs, diaphragm injury, small bowel obstruction, fistulae, development of arteriovenous malformation and the more common complications including urinary leak and hemorrhage. Urinary leakage after minimally invasive partial nephrectomy has been reported in up to 1% of patients which is four-fold lower than in open nephrectomy. With increasing experience and use of sliding clip renorrhaphy, urine leakage after RPN can be minimized though the index of suspicion must remain high in patients with persistently elevated surgical drain output or delayed ileus. Post-operative hemorrhage, seen in up to 10% of patients, may be seen acutely or in a delayed fashion associated with pseudoaneurysms. These can be managed with re-exploration or selective angioembolization if needed. Ultimately, these complications can be avoided with meticulous robotic port placement, visualization of instruments during the operation, careful dissection in initial phases of the operation, and optimally placed sliding-clip renorrhaphy sutures (135).

Impact of PSM

As surgeons have successfully performed RPN on T1b and T2 renal masses, the evaluation of PSM rate is critical to examine. While PSM after RPN is relatively uncommon, their presence poses a risk of recurrence. A recent study by Rothberg *et al.* demonstrated 6.7% of patients in a cohort of 432 patients had PSM after RPN and only 0.6% of patients had disease recurrence after upfront RPN. Survival analysis between those with PSM and negative surgical margins showed no difference in recurrence free survival (136). A multi-institutional analysis demonstrated a similarly low PSM rate of 5.1% and no association between PSM and overall survival (137). As such, PSM after RPN in and of itself does not appear to warrant adjuvant therapy; however, attentive post-operative surveillance should be pursued in lieu of these findings.

Conclusions

Partial nephrectomy remains one of the most commonly performed robotic surgeries and is the recommended management for cT1 renal masses where technically feasible. Technical innovations within urological surgery have led to progressive expansion of the indications for RPN including more hilar and T1b renal masses. In order to perform partial nephrectomy and strive for pentafecta achievement, a variety of pre- and intra-operative imaging techniques including fluorescence marker implementation, and post-operative patient management protocols have been implemented. CEUS has emerged as a promising technique for pre-operative imaging; however, its ability to distinguish many benign from malignant tumors remains uncertain. AR and 3D reconstructions have not been demonstrated to improve reductions in eGFR; however, their usefulness for surgical trainee education cannot be overstated. Intra-operative imaging with ICG and drop-in ultrasound with TilePro technology allow for rapid tumor-parenchyma identification and reductions in WIT leading to shorter operative times and higher rates of negative surgical margins. Newer fluorescence techniques are emerging including folate receptor targeting agents to allow for better tumor-parenchyma delineation; however, head-to-head comparisons are lacking. Optimized renorrhaphy technique and, in particular, substitution of renorrhaphy with sealing agents, may represent the future of renal defect reconstruction after partial nephrectomy. Furthermore, development in post-operative management has led to earlier patient discharge with decreased post-operative complications. While head-to-head studies and randomized controlled trials (RCTs) are lacking, advancements in partial nephrectomy have allowed urologists to decrease WIT, operative time, and time to discharge while achieving the pentafecta of partial nephrectomy. The need for RCTs and cost analysis of these technique merit further investigation.

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Footnote

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