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New Trends in Robotic Retroperitoneal Partial Nephrectomy

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Abstract: Robotic technology and new surgical adjuncts are continually evolving to aid the operating surgeon and improve patient outcomes. Retroperitoneal access in renal surgery has clear benefits over traditional transperitoneal surgery with robotics augmenting the surgeon's ability to operate in this anatomically confined space. Traditionally, the retroperitoneal approach was reserved for patients with posterior or laterally located tumors, or in patients with hostile abdomens; however, more streamlined surgical robots, improvements in port placement and increased utilization of the retroperitoneal approach has meant that the vast majority of small renal masses can be safely accessed via the retroperitoneum. This chapter aims to explore this paradigm shift further, while also exploring the use of added technologies and variations in surgical techniques.

Keywords: nephron sparing surgery for small renal mass; retroperitoneal approach to nephrectomy; robotic assisted partial nephrectomy; robotic retroperitoneal partial nephrectomy; transperitoneal approach to nephrectomy

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INTRODUCTION

Representing 2–3% of cancers, kidney cancer is in the top ten most prevalent cancers in the Western Society (1), with an annual increase of 2% in incidence worldwide (2). Most of these renal cancers are found incidentally, with this rise in incidence partly due to the increased use of cross-sectional imaging (1). Renal cell carcinoma is the most common solid lesion within the kidney comprising approximately 90% of all kidney malignancies. Robotic assisted partial nephrectomy (RAPN) is increasingly becoming the gold standard for the treatment of the small renal mass. With an ageing general population and increases in Chronic Kidney Disease (CKD), nephron sparing surgery will become increasingly important in the management of renal tumors (3). RAPN has historically been performed via the transperitoneal approach (T-RAPN), however the use of a retroperitoneal approach may especially aid the treatment of posterior and laterally placed tumors without compromising oncological or patient outcomes. Here we aim to review the evolution of nephron sparing surgery and describe the recent consensus and updates surrounding the use of a retroperitoneal approach in the context of evolving robotic technology and innovative surgical techniques.

THE SMALL RENAL MASS: EVOLUTION OF TREATMENTS

Small renal mass (SRM) is defined as a solid enhancing renal tumor of less than 4 cm in maximal diameter. Small renal masses comprise >40% of new renal cancer diagnoses (4) . Approximately 80% of small renal masses are malignant, while the other 20% usually represent benign masses with the rate of malignancy increasing with increasing tumor size (3). The majority of SRMs exhibit a slow growth rate and possess low metastatic potential. The most common solid lesion in the kidney is renal cell carcinoma and this makes up over 90% of all kidney cancers. Historically, the gold standard of treatment for any solid renal lesions was surgery with a radical nephrectomy, which resulted in patients losing a large portion of nephrons and resultant negative impact upon renal function.

With evolving technology and research, we now know that the cancer specific outcomes for partial and radical nephrectomy are equivalent. Partial nephrectomy has the added benefit of preservation of renal function and potentially limiting the incidence of cardiovascular disease and its health implications (5). Open partial nephrectomy is a very morbid operation with a prolonged length of hospital stay, large incision, and complications that are associated with major open abdominal surgery. With the evolution of technology with laparoscopy, and now robotic assisted, partial nephrectomy has become the gold standard surgical treatment for most SRMs. The evidence favors partial nephrectomy for T1 tumors; however, there is limited evidence on the optimal surgical treatment for patients with large renal masses. Partial nephrectomies have been reported on much larger tumors, however the feasibility is dependent on tumor factors such as size, location, proximity to renal hilum or collecting system and patient factors including tissue types, body habitus, previous interventions (5). With increasing experience we can perform increasingly complex partial nephrectomies, preserving renal function whilst still not compromising cancer outcomes (6).

With advancements in early diagnosis and development of minimally invasive procedures, there has been a paradigm shift in the management of SRMs to favor nephron sparing surgery. Some institutions have coined terms such as the "trifecta"—relating to negative surgical margins, and nephron sparing procedure with no post-op urological complications (7), and more recently the evolution towards a "pentafecta" to also include ischemia time <25 minutes and return of renal function to within 90% of pre-operative levels with no upstaging of CKD (8). All of these factors are achievable with traditional nephron sparing surgery in the form of an open partial nephrectomy; however, the morbidity of a large flank incision is a difficult to justify to patients when removing a T1a, localized low risk disease.

Progression of nephron sparing surgery

In the last two decades, the preferred techniques for partial nephrectomy have transitioned from open to minimally invasive. Because conventional laparoscopic partial nephrectomy remains a technically challenging procedure, the increased accessibility to robotics has emerged as an alternate minimally invasive option for surgeons willing to adopt a new technique. Compared to traditional laparoscopy, robotics has a comparable learning curve, but increased dexterity, improved vision, and enhanced surgical precision. With regards to partial nephrectomy, this allows operators to both dissect and reconstruct with more precision and speed. Controversy regarding the optimal surgical approach for achieving the "trifecta" in minimally invasive partial nephrectomy still exists. This chapter aims to highlight the retroperitoneal approach and the issues/ benefits this technique delivers.

Partial nephrectomy remains the standard of care for T1 tumors, with its utility still being explored in the management of T2 tumors (6). Increased utilization of laparoscopic and robotic nephron sparing surgeries allow for a minimally invasive surgery, however, require an additional level of surgical training and experience to achieve equivalent oncological outcomes when compared to open surgery. In the laparoscopic era, partial nephrectomy was a difficult surgical procedure due to the difficulties associated with laparoscopic suturing, however robotic assisted surgery has revolutionized this and is now the standard of care for small renal masses in institutions where robotic platforms are available. Recent studies have shown that oncological outcomes are comparable between open and minimally invasive partial nephrectomy (9, 10); however, variability in intra-operative ischemic time and post-operative complications were often proportional to the operating surgeon's experience (11). Interestingly, in patients who were found to have positive surgical margins post nephron sparing surgery, salvage nephrectomy often does not reveal residual carcinoma in the final specimen (12), raising questions as to what degree of positive margin should be respected.

There has since been a shift towards enucleation of tumors, which aims to further preserve normal renal parenchyma without compromising oncological outcomes. Tumor enucleation is defined as the dissection along the peritumoral pseudocapsule without additional renal parenchyma (13, 14). Enucleation of renal tumors during partial nephrectomy can be performed without negatively impacting disease recurrence or long term survival (15). A study by Ishiyama et al in 2021 compared the outcomes for 704 patients with T1 renal tumors who underwent RAPN either using the enucleation or standard resection technique. Their data showed that enucleation contributed to early preservation of renal function as measured by eGFR, without compromising oncological margins or patient outcomes (16). Interestingly, trifecta attainment was emphasized in patients with more complex renal tumors, whereby preservation of renal functions when compared to standard resection was most pronounced in the complex tumor group (16).

Transperitoneal vs. retroperitoneal approach

Traditionally the transperitoneal approach to laparoscopic kidney surgery is taught. The advantages of increased working space and more familiar landmarks makes this technique accessible. Due to the approach vector to the kidney, this technique still remains the standard for very anterior and medial tumors (17, 18). Retroperitoneal access is familiar to Urologists, however, development of the retroperitoneal space remains a meticulous and crucial step that requires surgeon familiarity with anatomical landmarks and an ability to maximize retroperitoneal working space without breaching the peritoneum (18, 19). Once gained, retroperitoneal access gives visualization of posterior, lateral and a significant proportion of anterior renal lesions and provides direct access to the renal hilum and reduces the risk of renal pedicle injury during its isolation (20).

Recently, a large multi-institutional Italian cohort study named the RECORD 2 Project compared perioperative outcomes of transperitoneal and retroperitoneal approaches in minimally invasive partial nephrectomy patients (21). Overall, 1669 patients were sampled, and included both laparoscopic and robotic techniques, with the majority (1256) being transperitoneal approach. In this study, the transperitoneal approach resulted in shorter operative time, on average by 35 minutes, however exhibited a modest increase in both intraoperative overall complications (3%) and intraoperative surgical complications (3.6%) when compared to the retroperitoneal approach. Postoperatively, the trifecta outcomes were comparable between the groups, with the retroperitoneal group showing an added reduction in both length of surgical drain time and length of stay (21). Similar results have been reported previously by Fan et al (22), Ren et al (23), and Xia et al (24).

Benefits of retroperitoneal approach

Retroperitoneal access permits direct access to the hilum and renal artery without the need for colon mobilization and gives optimal visualization of posteriorly and laterally located tumors (25). It also allows for direct access and isolation of the artery within minutes of commencing the dissection. Not entering the peritoneal cavity avoids bowel mobilization and provides a virgin approach in patients who have had previous abdominal surgery. This reduces the risk of iatrogenic damage, ileus, peritoneal irritation by surgical procedure (26), and intraoperative tumor spillage throughout the peritoneum. Some surgeons feel more comfortable with a transperitoneal approach due to familiarity and increased working space, however more standardized methods to gaining retroperitoneal access, and improved retroperitoneal dilatation techniques are making this approach less challenging (27). Previous multicenter comparison studies have reported that the retroperitoneal approach was often performed in higher volume centers, in units which were highly motivated to perform nephron sparing surgery (21).

Traditionally, RAPN continues to gain popularity as the minimally invasive surgical technique of choice for T1 renal tumors. Traditional RAPN has been taught and performed in a transperitoneal fashion, however the retroperitoneal approach provides an attractive alternative with practical advantages. Retroperitoneal approach is particularly advantageous for posterior tumors or peri-hilar tumors due to the anatomical relations to this approach (28) and is particularly attractive in patients who have had previous abdominal surgery (25). Furthermore, high volume units may employ the retroperitoneal approach for all but the most anterior and hilar of tumors. A recent study by Malki et al. compared the outcomes of 127 patients with a body mass index (BMI) of >30 kg/m^2 who underwent a RAPN (29) . Of these 127 patients, only 17 patients were treated via the transperitoneal approach due to anterior-hilar renal tumors. In this cohort, 86% of tumors were accessible via the retroperitoneal approach, including 25% of renal lesions that were located anteriorly (29) . Additionally, the group reported significantly shorter operative time, fewer postoperative complications, a shorter hospital stay, less blood loss and lower rates of transfusion in this obese cohort, without oncological compromise (29). With epidemiological data suggesting an ever more obese society with higher rates of renal cancer diagnoses, the ability to be competent in R-RAPN will be paramount for future Urologists.

Using robotic assisted technology appears to augment the surgeons ability to work in this confined space (28,30), where traditional laparoscopy has limited maneuverability of the straight instruments and especially difficulty with the renorrhaphy (31). Additionally due to articulating robotic arms, the relative lack of retroperitoneal space becomes less of an issue (32). The improved technology with the DaVinci robot allows increased accessibility within the retroperitoneum with the articulating arms and the decreased need for space between the arms, thus making it more conducive to operating in the small retroperitoneal space (23, 24). With regards to operative comparison, Retroperitoneal Robotic-Assisted Partial Nephrectomy (R-RAPN) has shown reduced operative time, significantly reduced blood loss (33), and overall reduced length of stay when compared to transperitoneal surgery (28). With regards to the trifecta, there has been no difference in warm ischemia time, oncological margins or 30-day post operative complications between the two approaches (33). Additionally, the retroperitoneal approach is associated with a shorter time to normal diet, less time with an Indwelling Catheter (IDC) and reduced need for opioid medications in the recovery period (26).

So whilst R-RAPN offers comparative surgical outcomes when compared to its transperitoneal counterpart, it carries additional benefits in shorter operative time and patient length of stay (17). Shorter length of stay is largely attributed to earlier return of bowel function and drain removal (21). Laviana et al. showed that T-RAPN added $2337 in cost when incorporating disposables, extra length of stay and staffing required (21). Where increased variability in warm ischemia time and post-operative complications are documented for RAPN, they strongly correlate to the operating surgeons procedural experience (25). All this provides advantage to both patient, surgeon and healthcare institution alike, potentially meaning more cases on an operating list, i.e., greater efficiency, shorter in-patient bed occupancy and fewer complications. Although there remains no consensus on the optimal approach for RAPN, tumor location and surgeon experience with the approach should dictate the decision.

ADVANCES IN ROBOTIC ASSISTED PARTIAL NEPHRECTOMY

With equivalent oncological outcomes with improved surgical morbidity, the paradigm has shifted to favor minimally invasive nephron sparing surgery for localized kidney masses. Subsequently, increasing familiarity with these procedures means that Urologic surgeons are taking on more challenging cases. Continued advancements in robotic surgery and novel adjuncts aim to further improve patient and oncological outcomes, while minimizing risk and renal impairment. Intraoperative administration of indocyanine green (ICG) is one such advancement, which has been proposed to help surgeons assess kidney and tumor perfusion intraoperatively. Selective clamping and off-clamp partial nephrectomy is another change to the traditional partial nephrectomy procedure. The use of intraoperative ultrasound is now routinely employed for endophytic tumors and is a useful adjunct for difficult to identify tumors and for minimising loss of normal parenchyma.

Indocyanine green and ICG-fluorescence

The use of ICG and near-infrared fluorescence (NIRF) have been proposed to help surgeons assess both tumor margins and kidney perfusion intraoperatively (34, 35). ICG acts as a fluorescent tracer which can be visualized by NIRF intraoperatively. ICG-fluorescence imaging intraoperatively allows surgeons to ensure that the arterial supply to the tumor and necessary part of the kidney are isolated prior to excision of the tumor. This allows for minimizing bleeding from missed renal arteries during warm ischemia. It also allows for selective and super-selective clamping of renal arteries, minimizing the ischemia to normal renal parenchyma. Conventional pre-operative imaging with CT angiography helps describe individual patient's anatomy; however, it fails to describe the nuance of intrarenal vascular distribution. Modern three-dimensional image rendering and the use of holographic technologies detail the anatomy more comprehensively, but none of these modalities can confirm downstream tissue ischemia intraoperatively (36, 37). By using NIRF imaging- real time confirmatory devascularization can be achieved. If tumor devascularization is inadequate or healthy parenchymal margins are poorly delineated, ICG can be used to help identify further segmental arterial branches to aid devascularization and help the surgeon achieve selective regional control (38).

Clamping techniques in nephron-sparing surgery

Maximizing nephron sparing during partial nephrectomy involves minimizing resection of healthy parenchyma and judicious use of renal ischemic time. Variation in arterial clamping techniques including off-clamp and selective clamping were developed in an attempt to improve post-operative renal function following nephron sparing surgery. Early studies suggest that selective and super-selective clamping, enabled by NIRF-ICG more precisely defines the surgical margin; leading to earlier recovery of renal function in the short term when compared to started whole- clamping RAPN. A systematic review by Veccia compared the renal function outcomes of 369 patients who underwent RAPN either with or without NIRF-ICG. Analysis revealed a higher overall eGFR in the short-term period of

1–3 months post RAPN plus higher split differential function on renal imaging during the same period. Interestingly, there was no statistical difference in eGFR between the groups at the time of discharge, implying that the effects of renal ischemia are delayed. Whether or not this translates into a clinical benefit for the patients in the long term is yet to be elucidated (38) Selective and super-selective arterial clamping aims to reduce global renal ischemia and continues to emerge as a technique for providing selective regional ischemia (39).

Renal function at the short and intermediate terms are described as being superior in these off clamp and selective clamp groups, however multiple studies have shown no difference in renal function at the 6 month mark (40). Antonelli et al compared the oncological and functional outcomes of 2075 patients following T-RAPN and R-RAPN undertaken either on or off-clamp. This meta-analysis revealed that renal function as measured by eGFR at 6, 12, and last available follow up were not statistically different, in the context of equivalent oncological outcomes (41). Although the off-clamp group led to higher blood loss, transfusion rates were equivalent between the groups with an added benefit of less major complications (41). Although patient's age at the time of surgery plays a significant role in post-operative renal function (42), in patients with normal baseline renal function and healthy contralateral kidney, the impact and significance of warm ischemia time appears negligible. With this in mind, patient safety and oncological outcomes remain paramount, whereby current recommendations continue to endorse the main artery clamp technique as the gold standard for complex renal tumors (40).

Airseal

The addition of 'airseal' has revolutionized laparoscopic surgery by enabling a stable pneumoperitoneum (or retroperitoneal space) with continuous smoke evacuation and gas recirculation throughout surgery. This allows surgeons to operate in a stable environment even when suctioning is required. This enables more streamlined faster surgery and a constant environment which improves vision and space, especially beneficial in the small retroperitoneal space. Prior to this, suction of blood and smoke meant loss of the space and impaired vision of the tumor margins during excision or renorrhaphy, potentially compromising patient care and leading to an increase in operative time (43, 44). For this reason, AirSeal is often preferred, especially in complex procedures where a stable working environment is essential. This effect is likely compounded while using the retroperitoneal approach compared to transperitoneal due to the already limited space.

A recent single surgeon, prospective randomized trial conducted by Feng et al aimed to compare pneumoperitoneum related complications with standard vs valve-less insufflation systems (45). Although no difference was seen with regards to post-operative analgesia use or length of hospital stay, a significant reduction in mean pain scores at 12 hours post-operatively was seen. Furthermore, there was a significant reduction in subcutaneous emphysema, particularly amongst the AirSeal group, while operating at pressures of 12 mmHg. These findings were reflected by Desroches et al., showing comparable rates of pneumothorax with significant reduction in surgical emphysema and pneumomediastinum while using AirSeal at 12 mmHg (46).

TilePro and endoscopic ultrasound

The role of intraoperative ultrasonography in partial nephrectomy has been well described. It augments the surgeons tactile feedback and helps to localize tumors, delineate tumor margins, identify multifocal disease and, with the aid of color doppler, assess vascular supply to renal tumors including location of accessory renal arteries (45, 46). These features are useful in difficult to see, endophytic tumors or those with unclear margins or poorly defined arterial supply (47). Through the use of TilePro software, the operating surgeon can view the ultrasound picture on the robotic console screen in real time while they move the probe over the kidney. This allows for improved ability to identify tumors that are endophytic or poorly defined and thus minimizing unnecessary kidney mobilization or excess excision of normal kidney margins (48). The use of the laparoscopic ultrasound probe is more difficult in the confined space of the retroperitoneum, but it remains a useful tool.

Developments in robotic technology

The intuitive DaVinci surgical system continues to dominate the robotic surgical market with an estimated current instillation base of 5764 units worldwide as of June 2020, however the competition is increasing (investigative and clinical urology). It is an exciting time for the technology of robotic surgical devices in partial nephrectomy with multiple other *new* robotic platforms evolving in this sphere. This is largely due to the expiration on multiple key robotic device patents in 2019, opening the door for competing companies to develop and implement robotic technology. The CMR Surgical Versius robot has initial experience with partial nephrectomy. The feasibility of this platform for partial nephrectomy continues to be explored and the technology continues to be refined to better facilitate this procedure. Medtronics Hugo robotic surgical system, the Korean system Revo-I, and Elementall Healthcare Distalmotion Dexter, amongst many others systems, are under early evaluation and clinical investigation (investigative and clinical urology) (49).

The Intuitive DaVinci robotic surgical systems have revolutionized minimally invasive nephron sparing surgery. With the most updated technology, the Xi allows for better articulation of wrists and arms, narrower profile which allows instruments to be closer together and thus allows more precise work in the limited space of the retroperitoneum. Previous issues with difficult instrument triangulation, robotic arm clashes and limited working space may be truncated with the help of this new technology and are particularly advantageous in the retroperitoneal approach.

The use of the fourth arm is a known adjunct for transperitoneal renal surgery, however its utility in the retroperitoneal approach was previously limited due to crowding of robotic arms and difficult triangulation. Use of the fourth arm in retroperitoneal RAPN was first described by Felicano et al in 2012 (32). The team described the use of the fourth arm as a method for keeping the renal hilum on gentle but constant traction, which in doing so, allows the operating surgeon to use both left and right arms to meticulously dissect the hilum (32). It can also be used throughout later dissection to retract perinephric fat, tissues, or peritoneum. Improved counter-traction, target exposure and ability for the surgeon to operate with both arms can all be achieved with selective deployment of the fourth arm. Hence, during critical parts of the procedure such a hilar dissection, tumor excision and renorrhaphy, the benefits of a fourth arm appear compelling. Other studies describe the benefit of using the fourth arm, particularly for optimizing tissue exposure (33), however the benefits in operative time, blood loss and oncological outcomes using this technique have yet to be described.

CONCLUSION

With increasing diagnosis of T1 renal tumors and the concurrent issues of ageing general population, obesity, and record rates of CKD, the need for nephron sparing surgery in the future will continue to rise. The transition from open to minimally invasive surgery has paved the way for robotic technologies to become the gold standard of care. Equivalent oncological outcomes with significantly reduced patient morbidity makes minimally invasive renal surgery the obvious choice, however the optimal surgical approach including port placements is still being developed. This current review advocates for the use of robotic assisted partial nephrectomy, and the retroperitoneal approach for patients with posterior or laterally located tumours, or in patients with hostile abdomens from previous intraperitoneal surgery.

Ongoing advancements in robotic technology aim to negate the impact of the confined retroperitoneal space; however, further development is required. The use of adjuncts such as ICG-NIRF and Airseal systems continues to improve the procedure and anecdotally improve patient outcomes; however, their lack of routine use means their impact is yet to be elucidated on a larger scale in the literature. The use of selective renal clamping technique and tumor enucleation appear to preserve renal function in the short-term; however, the long-term benefits of this are yet to be proven in trials. Overall, the use of a retroperitoneal approach needs to be considered in the context of the patient's disease and the surgeon's experience with this approach. In appropriately selected patients and confident operators, retroperitoneal robotic assisted partial nephrectomy provides an oncologically equivalent surgical approach for treating small renal tumors whilst reducing patient length of stay and overall morbidity. In our experience, more than 90% of patients undergoing RAPN can benefit from these advantages by the use of the retroperitoneal approach.

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