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Title:
Strategies for success: a multi-institutional study on robot-assisted partial nephrectomy for complex renal lesions

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Abstract:

Objective

Due to their size, location and proximity to the hilum, some complex renal tumours may preclude a minimally invasive approach to nephron sparing surgery. We describe our technique, illustrated with images and videos, of robotic partial nephrectomy for challenging renal tumours.

Patients and Methods

A study of 249 patients who underwent robotic partial nephrectomy (RPN) in multiple institutions was performed. Patients were identified using prospective RPN databases. A complex renal lesion was defined as a RENAL nephrometry score ≥10. Data was presented as median (interquartile range) and differences between groups were examined.

Results

31 (12.4%) RPN were performed for complex renal tumours. Median age was 57 (50.5 – 70.5) years. 21 (67.7%) were male, 10 (32.3%) were female. American Society of Anesthesiologists score was 2 (2 - 3). Median operative time was 200 (50 – 265) min, median warm ischaemia time was 23 (18.5 – 29) min, and median blood loss was 200 (50 – 265) ml. There were no intraoperative complications. 2 (6.4%) patients had post-operative complications. 1 (3.2%) patient had a positive margin. Length of stay was 3.5 (3 – 5) days. Median follow up was 12.5 (7 – 24) months. There were no recurrences. RPN did result in statistically significant changes in renal function 3 months post RPN compared to preoperative renal function, p=0.0001.

Conclusion

RPN is a safe approach for select patients with complex renal tumours and may facilitate tumour resection and renorrhaphy for challenging cases, offering a minimally invasive surgical option for patients who may otherwise require open surgery

INTRODUCTION

Nephron-sparing surgery (NSS) has been established as the standard of care for localised renal cell carcinoma (RCC) due to equivalent oncological outcomes compared to those of radical nephrectomy and superior functional outcomes and long-term survival [1] [2]. Minimally invasive partial

nephrectomy has been found to be superior to open partial nephrectomy (OPN) with regard to lower rates of perioperative complications, shorter length of hospital stay, reduced pain and less blood loss, while maintaining similar cancer-specific survival [3] [4] [5] [6]. Compared to laparoscopic partial nephrectomy (LPN), robotic partial nephrectomy (RPN) appears to offer favourable rates of conversion to radical nephrectomy, greater preservation of renal function, shorter length of hospital stay and shorter warm ischemia time (WIT) [5].

The RENAL nephrometry scoring system assigns a score to individual tumour characteristics, which are summed to determine an overall score and risk group. This scoring system influences treatment choices, ischaemia time, post-operative renal function, histologic aggressiveness and complications [6] [7]. RENAL is an acronym of the five relevant tumour characteristics; Radius in centimetres, Exophytic nature, Nearness of tumour to the collecting system, Anterior tumour position and Location of tumour relative to polar lines. Scores of 4 to 6 are considered low, 7 to 9 medium and ≥10 considered complex. Several studies have reported that high RENAL score lesions are more likely to undergo OPN or radical nephrectomy [8] [9] [10]. In this study, we describe our approach of RPN for ≥10 RENAL score tumours and discuss the essential steps for a successful outcome. We present the outcomes of our series and also discuss tips and tricks to avoid common pitfalls and increase surgical efficiency.

METHODS AND SURGICAL TECHNIQUE

An analysis of all patients who underwent RPN in three institutions was performed. Patients were identified using an RPN database and/or hospital records. Data was recorded prospectively on each patient in the database, which was completed post-operatively by the operating surgeon. A complex renal tumour was defined as any renal tumour with a RENAL nephrometry score ≥10.

Data obtained included age, gender, tumour side, size, nearness to collecting system and location (anterior or posterior), biopsy results, patient co-morbidities, American Society of Anesthesiologists physical status score (ASA score), Charlson co-morbidity index (CCI) score and pre-operative haemoglobin and creatinine. Intra-operative and post-operative variables measured included operative time, warm ischaemia time (WIT), estimated blood loss (EBL), length of stay and complications. Subjects included in this study were those who underwent RPN for complex renal tumours with a RENAL score ≥10. For example, tumours included in this study will be >4cm in size, <50% exophytic, be within 4mm of collecting system and have >50% of mass across polar lines or mass cross axial renal midline. RENAL scores <10 were excluded from this study.

Post-operative complications ≤30 days of RPN were reported and classified according to the Clavien-Dindo classification [11]. Haemoglobin, creatinine and estimated glomerular filtration rate (eGFR) were assessed three months post RPN.

Unless otherwise stated, data are represented as median (interquartile range) and N represents the number of patients included in the analysis. The median pre- and post-operative serum creatinine levels were compared using the paired-samples *t*-test, and $P<0.05$ was considered statistically significant. Data analysis was carried out with Prism version 5.01 (GraphPad Software, Inc. 2236 Avenida de la Playa La Jolla, CA 92037 USA).

Instruments and equipment

RPN was performed using the da Vinci® SI HD surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA). For each case, three robotic instruments were employed. The Hot Shears™ monopolar curved scissors were used in the dominant hand, the PK forceps in the non-dominant hand and the ProGrasp™ in the third arm. The tips of the PK forceps were useful for blunt dissection of vessels and tumour. The ProGrasp is non-thermal and can be used to lift the kidney and to control the robotic ultrasound (US) probe.

Operative technique

Patient position and trocar placement

For each patient, the case proceeded as follows. After induction of general anaesthesia, a urinary catheter was placed. The patient was positioned in flank position with the affected side up. To increase available abdominal wall space for ports, the patient was positioned over the table fulcrum, which was then pivoted to an angle of approximately 195 degrees, to create lateral lumbar flexion away from the pathological kidney. All pressure points were padded and the patient was secured to the operating table. Pneumoperitoneum was achieved with the Hassan open technique and a laparoscopic balloon port was placed. Insufflation pressures were in the range of 12–16 mmHg. This pressure provided adequate surgical view and did not adversely impact the patient's post-operative pain. Robotic port trocars were placed under direct vision and an AirSeal® iFS port was placed medially to provide stable pneumoperitoneum, constant smoke evacuation, and valve-free access. This port also allowed for more efficient exchange of needles. Figure 1 shows patient and port positioning. We believe that this port arrangement combined with the use of a zero degree lens or 30 degree down lens confers an advantage when removing posterior renal tumours and is versatile enough to facilitate excision of tumours in different locations. No robotic partial nephrectomies were performed with the retroperitoneal approach.

Bowel mobilisation

Using the monopolar curved scissors, the peritoneum was incised sharply along the line of Toldt and the bowel mobilised medially using sharp and blunt dissection. The PK forceps were used to elevate tissues to assist the identification of tissue planes. Dissection was continued to develop the plane between the anterior Gerota's fascia and the posterior mesocolon. Throughout, the surgical assistant aided dissection by maintaining medial counter-traction. Dissection continued superiorly along the upper pole of the kidney to the spleen or liver, depending on side, and inferiorly to the sigmoid colon or caecum, so that the kidney was fully exposed. The gonadal vein, renal vein and

ureter may be visible, particularly in a slim patient. Lateral renal attachments were left in place to aid in counter traction, as excessive mobility of the kidney is disadvantageous.

Splenic mobilisation

The spleen was fully mobilised for any left sided partial nephrectomy. This improves operative space, allows for complete mobilisation of the kidney and reduces the risk of inadvertent splenic injury. Dissection employed the PK forceps to apply gentle medial pressure on the spleen. The monopolar curved scissors were then used to incise the peritoneum towards the diaphragm until the spleen was fully mobilised medially. Care must be taken not to incise the diaphragm.

Renal hilar dissection

Pre-operative imaging should be reviewed to determine the number and location of the renal artery and vein. Intra-operatively, If not initially visible, the left renal vein was identified by tracing the gonadal vein cranially to its insertion or, on the right side, to its insertion in the inferior vena cava near the right renal vein. The ProGrasp™ forceps were used to place the kidney on stretch. The hilar vessels were carefully dissected with the PK forceps and the monopolar curved scissors. As the renal artery typically lies posterior to the renal vein, careful dissection caudally then cranially was found to reliably reveal the artery. The hilar vessels were carefully dissected, being alert to the possibility of multiple renal arteries or early branching. Figure 2 shows the identified hilar vessels. The renal artery must be completely dissected free so that two laparoscopic bulldog clamps may be applied.

Tumour exposure and intraoperative ultrasound

Gerota's fascia was incised to expose the tumour and the surrounding renal capsule. For the complex renal tumours in this series, it was occasionally necessary to completely mobilise the kidney from Gerota's fascia. Complete mobilisation of the kidney from Gerota's fascia can be especially necessary for large renal tumours, posterior tumours and extremely medial tumours. If the fat overlying the tumour required resection to optimise view, this fat should be sent separately to pathological analysis to examine for pT3a disease. To help delineate the tumour, the laparoscopic ultrasound (US) probe was inserted via the AirSeal® port, utilising the ProGrasp™ to guide the probe. As described by Rogers *et al*., the TilePro™ function was used to display the live intraoperative images on the console screen [12]. The ultrasound (US) probe was then used for precise delineation of the position and borders of the tumour as shown in Figure 3. The margin of resection was marked by scoring circumferentially using the monopolar curved scissors.

While not utilised in this series, near-infrared fluorescence (NIRF) imaging with intraoperative administration of indocyanine green (ICG) can improve tumour excision. NIRF allows for the differentiation of renal tumour from normal parenchyma: normal kidney tissue fluoresces green, while the tumour commonly remains hypofluorescent. NIRF can also facilitate selective arterial clamping during RPN, allowing for a regional perfusion deficit in the kidney to be identified [13].

Hilar clamping

To minimise WIT, all sutures for renorrhaphy were prepared in advance (Figure 5). 12.5 grams of mannitol was administered intravenously prior to hilar clamping. A laparoscopic bulldog clamp applier was inserted via the AirSeal port. Two separate Bulldog clamps were placed on the renal artery. Only the renal artery was clamped, and not the vein, unless there was a central hilar tumour. We found this approach gave adequate haemostasis and allowed superior visualisation of the resection margin without any complications. The vascular tourniquet technique is an alternative method that may be used for renal pedicle control that can avoid the potential disadvantage of Bulldog clamp slippage [14].

Tumour resection

The tumour was excised sharply with a rim of normal renal parenchyma along the previously scored margin using cold resection with the robotic Hot Shears. The PK forceps were used to manipulate the tumour away from normal parenchyma to aid dissection. While enucleation and enucleoresection techniques are described and associated with excellent outcomes [15] [16]. It is the preference of the authors to excise the tumour with a clear margin of normal parenchyma. This stage required deft 'duck and weave' movements of the surgical assistant with suction, to maintain visualisation of the resection plane, shown in Figure 4. If large intra-renal vessels were encountered, Hem-o-lok® clips were applied for haemostasis. After complete excision of the tumour, the specimen must be placed with care to prevent loss within the peritoneal cavity.

Renorrhaphy and hilar unclamping

After the tumour specimen was separated from the kidney, the monopolar curved scissors and the PK forceps were replaced with robotic needle-drivers for the renorrhaphy. The pre-prepared sutures were inserted via the AirSeal® port and renorrhaphy was performed in two layers. Compressive sutures across the resection bed using a 15-17cm length of 3-0 V-Loc™ on a V-20 needle (Covidien, Mansfield, MA, USA) were used to achieve haemostasis and repair any previously identified entry into the collecting system. Sutures are shown in Figure 5. Sutures were secured with both regular

knots and the placement of a vascular pledget. Hem-o-lok® clips were used to secure the distal suture in place, shown in Figure 6. After completing the deep layer of renal reconstruction, the bulldog clamps were removed. The artery is unclamped at this stage, as early unclamping may reduce the risk of pseudoaneurysm formation [17]. If significant bleeding was present, a second 3-0 V-Loc™ suture was used on the resection bed. When haemostasis was achieved, the renal parenchymal defects were approximated using two 12-14cm lengths of 2-0 V-Loc™ on a GS-21 needle secured in a Hem-o-lok® clip. Hem-o-lok® clips were used again to secure the distal ends of the suture in place as shown in Figure 6. Gerota's fascia was re-approximated over the defect and a nephropexy performed using a running 3-0 V-Loc™ suture. A large 18 French (Ch) drain was inserted via the fourth arm port and placed in the perinephric space. Figure 7 summarises the key points in the approach towards RPN for complex renal tumours.

Tumour retrieval and port closure

To capture the specimen, the assistant inserted an extraction bag via the AirSeal® port, placed the tumour within it and used the drawstrings to close the bag. These strings were then placed in the peritoneal cavity. Under vision, the AirSeal® port was closed with an Endo Close™ (Covidien, Mansfield, MA, USA). A grasper placed through the balloon port was used to capture the strings of the retrieval bag to remove it and the specimen within. During this step, the balloon port incision was enlarged as needed. The authors prefer this method of specimen extraction as the abdominal wall at the infero-laterally located balloon port was often found to contain less adipose tissue compared with other sites.

RESULTS

Patient characteristics

From to January 2014 to November 2016, a total of 249 patients underwent RPN for renal lesions, 31 patients (12.4%) had a RENAL score of ≥10. Median age was 57 years (IQR 50.5 – 70.5). Twenty-one (67.7%) were male and ten (32.3%) were female. Median ASA score was 2 (IQR 2 – 3). The median Charlson comorbidity index was 3 (IQR 0 – 3.5). Median pre-operative blood variables consisted of haemoglobin 140 g/L (IQR 123 – 147), creatinine 77 g/L (IQR 72 - 101) and eGFR 79 (IQR 63.5 - 88.25). Data is shown in Table 1.

Tumour side and RENAL variables

Seventeen tumours were right sided, and fourteen were left. Median tumour size was 45 mm (IQR 33.5 – 54). Twenty-three (74.2%) were <50% exophytic and eight (25.8%) were completely endophytic. All tumours were within 4mm of the collecting system and all tumours were central and hilar. Sixteen were anteriorly positioned and fifteen were posterior. Data is shown in Table 2.

Intra-operative and post –operative variables

The median operative time was 155 min (IQR 131 – 180). Median warm ischaemia time was 23 min (IQR 18.5 – 29) and median blood loss was 200 ml (IQR 50 – 265). There were two post-operative compilations – a pneumothorax managed conservatively (Clavien-Dindo Grade I) and a patient with haematuria managed with cystoscopy and stent insertion under general anaesthesia (Clavien-Dindo Grade IIIb). The median length of stay was 3.5 days (IQR 3 – 5). Histological analysis revealed twenty-three (74.2%) tumours were clear cell carcinoma, one (3.2%) papillary carcinoma, two (6.4%) chromophobe carcinomas, four (13%) oncocytomas and one (3.2%) angiomyolipoma. Data is shown in Table 3. The positive margin rate was 3.2%. Median post-operative blood variables comprised haemoglobin 120 g/dl (IQR 110.8 – 130.5), creatinine 93 g/dl (IQR 76 - 120) and eGFR 64 (IQR 47 – 75.5). Post-operative haemoglobin was statistically lower than pre-operative (p=0.0001). There were also significant differences seen with post-operative creatinine (p=0.0008) and eGFR (p=0.0003). The median follow up was 12.5 months (IQR 7 – 24) and there were no tumour recurrences in this time. Outcome data is shown in Table 4.

DISCUSSION

Indications for partial nephrectomy (PN) and NSS include patients with synchronous bilateral tumours, tumours in a solitary kidney, or the presence of a poorly functional contralateral renal unit. NSS is also indicated for hereditary papillary RCC and RCC associated with von Hippel-Lindau (VHL) syndrome as these syndromes are associated with multiple and recurrent RCC [18]. Recently, the indications for NSS have expanded to include all lesions up to 7 cm, multiple tumours, hilar masses and tumours that are completely endophytic, even with a normal contralateral kidney [19] [20] [21] [22] [23] [24] [25] [26] [27] [28]. Indeed, partial nephrectomy is the current standard of care for the treatment of small RCC <7 cm [29]. Contraindications for NSS include chronic renal insufficiency. In these patients, OPN with cold ischaemia should be considered [30]. Previous extensive abdominal surgery may also be considered a contraindication, however, RPN may be possible with time given for division of adhesions. Obvious nodal metastasis and the presence of inferior vena cava thrombus could also be considered relative contraindications.

Minimally invasive PN for small renal tumours has been found to be superior to open surgery and studies have shown equivalent-to-favourable outcomes for RPN compared to LPN [31] [32]. This is because LPN requires advanced skills in laparoscopy to accomplish tumour resection and renal reconstruction in a time sensitive manner to minimise WIT. In contrast, robotic technology has reduced the difficulties associated with LPN. RPN employs a magnified 3-dimensional view, which can help to assess and maintain the proper plane of tumour resection. Magnification of the renal resection bed can also aid in the identification of open vessels or openings in the collecting system for closure. The articulating robotic instruments and computer elimination of tremor facilitate precise tumour excision and renorrhaphy, particularly in the setting of difficult surgical angles or adjacent hilar structures. RPN also has a shorter learning curve when compared with other minimally invasive techniques [33] [34].

The definition of surgical complexity of renal tumours has not been clearly standardised but objective anatomical classification systems do exist [26]. Contemporary studies have used scores such as RENAL score ≥10, PADUA score >10 or other anatomical features such as large lesions, endophytic or hilar location as a measure of complexity [20] [21] [22] [23] [24] [25] [26] [27].

The RENAL nephrometry score has been proposed to predict outcomes and complications of PN [35]. The RENAL nephrometry score provides an objective, standardised tool for deciding between

tumours that could be treated by a minimally invasive or open approach. It does this by predicting for increased blood loss and longer ischaemia time when undergoing PN [35]. The PADUA nephrometry score was also introduced as another objective method to describe the anatomical features of a renal mass and, in some ways, is remarkably similar to RENAL score [36].

The safety and feasibility of robotic partial nephrectomy for complex renal lesions has been demonstrated [22] [23] [25] [26] [27] [28]. However, no study to date has reported the outcome and technique for tumours with a RENAL score ≥10. Indeed, this report is one of the largest series of RPN in the literature. Table 5 provides a comparison of contemporary series of robotic partial nephrectomy for complex renal lesions. Despite the selection of challenging renal tumours, our findings compares robustly to other reports of robotic partial nephrectomy. Operative time, WIT and blood loss are similar to other studies, and our positive margin rate is favourable, albeit must be interpreted with caution, given the small sample size. It should also be noted that the favourable outcomes observed in this study may be a reflection of our surgeons' experience in robotic surgery and, therefore, we suggest that less experienced robotic surgeons should develop their expertise with less complex tumours. An alternative, would be the utilisation of patient-specific tissue-like three-dimensional (3D) kidney models. These models can be used in preoperative rehearsals of RPN for complex renal lesions and provide the surgeon with opportunity of a 'dry run' on the renal tumour [37].

Compared with pre-operative values, patients in our study had significantly decreased eGFR three months post-operatively. We feel this reduction in eGFR was unavoidable given the large and central characteristics of the tumours in this series. This study was not designed to compare robotic assistance with other approaches to partial nephrectomy, but rather to describe our surgical technique and outcomes with RPN for a select group of patients with high RENAL scores, which might deter some surgeons from performing minimally invasive surgery in preference of open surgery. The results from our study suggest that robotic assistance may facilitate a minimally invasive approach, offering a potential advantage in select patients with tumours with a high RENAL score.

CONCLUSION

Robotic partial nephrectomy is a safe and feasible approach for select patients with complex renal tumours as defined by RENAL nephrometry score≥10 . These include hilar, endophytic, and large renal tumours. The features of the robotic system can facilitate a successful minimally invasive approach to partial nephrectomy for these difficult cases.

CONCLICTS OF INTEREST

None

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FIGURE LEGENDS

Figure 1: Patient positioning and port placement

Port placement for left sided robotic partial nephrectomy

Figure 2: Dissection of hilum and identification of renal artery and vein

Image shows the two renal arteries (red) and single renal vein (blue) that were identified during hilar dissection.

Figure 3: Intra-operative ultrasound

Intra-operative ultrasound was used to delineate tumour (green) from normal kidney (orange). Renal hilar fat is shown in purple.

Figure 4: Tumour excision

Tumour being excised sharply with a rim of normal renal parenchyma along the previously scored margin using cold resection with the robotic Hot Shears.

Figure 5: Sutures used in renorrhaphy

Suture 1; one 15cm length of 3-0 V-Loc™ on a V-20 needle, with sutures secured by both knots and the placement of a vascular pledget. Suture 2; two 12cm lengths of 2-0 V-Loc™, each on a GS-21 needle, secured to each other with a Hem-o-lok® clip.

Figure 6: Renorrhaphy

Renorrhaphy was performed in two layers. Using a 15-17cm length of 3-0 V-Loc™ on a V-20 needle was used on the renal bed to achieve hemostasis and repair any entry into the collecting system. When haemostasis was achieved, the renal parenchymal defects were approximated using two 12-14cm lengths of 2-0 V-Loc™ on a GS-21 needle secured in a Hem-o-lok® clip.

Figure 7: Key points in successfully RPN for complex renal tumours

RPN; robotic partial nephrectomy.