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Peri-operative and Pathologic Outcomes of Minimally Invasive Partial Nephrectomy (MIPN)

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Abstract

Aim

In this paper we assess the peri-operative, functional and early oncological outcomes of patients undergoing minimally invasive partial nephrectomy (MIPN) for the management of renal masses and investigate the influence of tumour complexity on these parameters.

Methods

We prospectively followed up all patients undergoing MIPN for the management of renal masses, by a fellowship-trained laparoscopic and robotic surgeon.

Results

One hundred and fifty patients were included (60.7% male); 64 underwent laparoscopic and 86 underwent robotic partial nephrectomy. Median age was 55.8±12.75 years.

Nephrometry Score was <6 in 37.2%, 7-9 in 55.4% and >9 in 7.4%.

Mean ischaemia-time was 24±1 minutes. There were 3 conversions to Open PN, and 8 to radical nephrectomy. Median bloods loss was 100mls (20–1600mls).

Tumour Stage was pT1a (68.7%), pT1b (14%), pT2a (0.67%), T3a (5.3%), benign/not applicable (10.6%). Five patients (3.3%) had positive margins.

Mean serum Creatinine (ng/ml) was 85.5±23 pre-op, 100.2±31.9 at 6 weeks and 94.2±25.1 at 3 months post-op.

Significant complications (>Clavien-Dindo 2) occurred in 7 patients. There was no association between nephrometry group (p=0.67) or stage (p=0.11) and complications.

Conclusion

In this series, we demonstrate that MIPN has excellent peri-operative and pathological outcomes, with a low overall complication rate.

Introduction

Partial nephrectomy has emerged as the treatment modality of choice for small renal masses, as it affords equivalent oncological outcomes to radical nephrectomy[1], while preserving greater renal function[2]. When performed using a minimally invasive approach (laparoscopically or robotically), improvements in post-operative pain, length of stay and blood loss can be achieved[3,4]. Both the EAU[5] and AUA[6] recommend MIPN as a treatment option for small renal tumours. We present our early experience with minimally invasive partial nephrectomy in 150 patients and aim to demonstrate the excellent peri-operative outcomes associated with this approach.

Materials and Methods

We prospectively followed up all patients undergoing MIPN for the management of renal masses, by a single fellowship-trained laparoscopic and robotic surgeon. All consecutive patients were included on an intention to treat basis.

Tumour complexity is expressed by RENAL nephrometry scores, calculated from pre-operative cross-sectional imaging (CT or MRI). RENAL scores of <6 were deemed Low Complexity, 7-9 Intermediate Complexity and >10 High Complexity. For patients with multiple tumours the nephrometry score of the most complex tumour is reported.

Renal function (Serum Creatinine and eGFR) and Haemoglobin (g/dl) were recorded pre-operatively and on Day one, Day two and three-months post operatively.

Surgery was performed across 4 centres, only 2 of which offered robotic surgery. As such, the choice of laparoscopy v robotics was not made by randomisation but rather by the operative modality which was available. Pre-operative work up, peri-operative care and post-discharge follow-up was identical for both operative modalities.

Robotic Surgery was performed using the Da Vinci Xi robot in a side-docked configuration with four robotic ports and a standard assistant port, while laparoscopic surgery routinely utilised three ports, with placement of an additional fourth port for liver retraction if required. All patients were placed in a lateral position with 45 degrees flexion centered on the umbilicus.

Most cases (93.3%) were performed via a transperitoneal approach, but in selected cases a retroperitoneal approach was utilized.

Depending on the tumour characteristics, a combination of off-clamp, segmental ischaemia and hilar clamping was utilized. Tumours were excised using a cold scissors, and an enucleation technique, followed by Sliding Clip renhorraphy using a continuous 3-0 V-Lock suture and Haemolock clips. Specimen extraction was through an extended port site incision.

A Ready-Vac drain was placed in the perinephric space, which was removed day one post-op if drain fluid creatinine measurement showed no evidence of urine leak.

Data was collected from patient medical notes, laboratory records and radiology databases, and compiled and analysed using Stata/IC 12.1 (StataCorp, 4905 Lakeway Dr, College Station, TX, USA 77845). Data collected was identical for each group and only data routinely collected in patient's peri-operative course was recorded. Results are presented as means and standard deviations, or medians and ranges. Mean comparison was performed using t-tests and categorical variable comparison using Chi-Squared or Fisher's Exact Tests. All reported p-values are 2-tailed.

Results

Demographics

One hundred and fifty consecutive patients were included in the study, 91 (60.7%) males and 59 (39.3%) females. Sixty-four patients underwent LPN (42.7%) and 86 underwent RAPN (57.3%). Mean age at time of surgery was 55.8 ± 12.75 years.

Demographics	**N (%)**
Sex	
• Male	91 (60.7%)
• Female	59 (39.3%)
Age (mean + SD)	55.8 ± 12.75 years
Operation (ITT)	
• Laparoscopic	64 (43.7%)
• Robotic	86 (57.3%)

Table 1: Demographic Details.

Tumour Characteristics

Nephrometry score was <6 in 56 patients (37.3%), 7-9 in 82 patients (54.7%) and >9 in 11 patients (7.3%). Nephrometry data was unavailable for one patient (0.7%). Fourteen tumours were hilar in location.

Pre-operative biopsy was performed in 50 patients (33.1%). Biopsy result was Clear Cell RCC (n=32), Papillary RCC (n=3), Cystic RCC (n=1), Chromophobe RCC (n=4), Oncocytoma (n=2), Oncocytic neoplasm/Chromophobe (n=1), , Inflammatory (n=1) and indeterminate (n=4). Biopsy histology was concordant with final histology for tumour type in 91.4%, and concordant for grade (where applicable) in 55.2%.

Operative Details

Actual procedure performed was partial nephrectomy (n=127), partial nephrectomy for multiple lesions (n=4), radical nephrectomy (n=8) and heminephrectomy (n=11). Three patients required conversion to open surgery due to difficulty with closure of renal defect post tumour resection (n=2) and toxic fat adherent to tumour and renal pelvis (n=1). One patient was converted from robotic partial nephrectomy to laparoscopic radical nephrectomy in order to obtain tactile sensation due to dense hilar reaction. Indications for conversion from partial to radical nephrectomy were adherent toxic fat (n=4), dense perihilar desmoplastic reaction (n=1), complex anatomy and adhesions (n=1) and retro-hilar location precluding safe excision and reconstruction (n=1).

A transperitoneal approach was employed in 140 (93.3%), retroperitoneal in 9 (6%) and 1 case (0.67%) was commenced retroperitoneal but converted to transperitoneal for technical reasons. Three patients (2%) had tumours excised from a solitary kidney.

One hundred and four patients (69.3%%) had a drain inserted, which was removed on Day 1 post-op in 78.8% (n=82) and Day two post-op in 11.5% (n=12).

Where vessel clamping was utilised, mean ischaemia time was 24.1 ± 8.2 minutes. Fifteen patients underwent zero-ischaemia surgery (10.5% of patients receiving PN), while 1 had selective vessel clamping.

Median blood loss was 100mls (Range: 20 – 1600mls). Blood transfusion was required in 6% (n=9).

Length of Stay

Median length of stay was three days (Range: 1-26) (Figure 1). Ten patients (6.67%) had prolonged admissions in excess of 7 days, due to open conversion (n=1), AV fistula requiring embolisation (n=1), decompensated pre-existing liver failure (n=1), urinoma and iatrogenic PUJ obstruction (n=1), urine leak requiring stent (n=1) ileus and prolonged atelectasis (n=2), new diagnosis of brain metastases (n=1) and severe respiratory failure requiring ICU support (n=1). (Table 1).

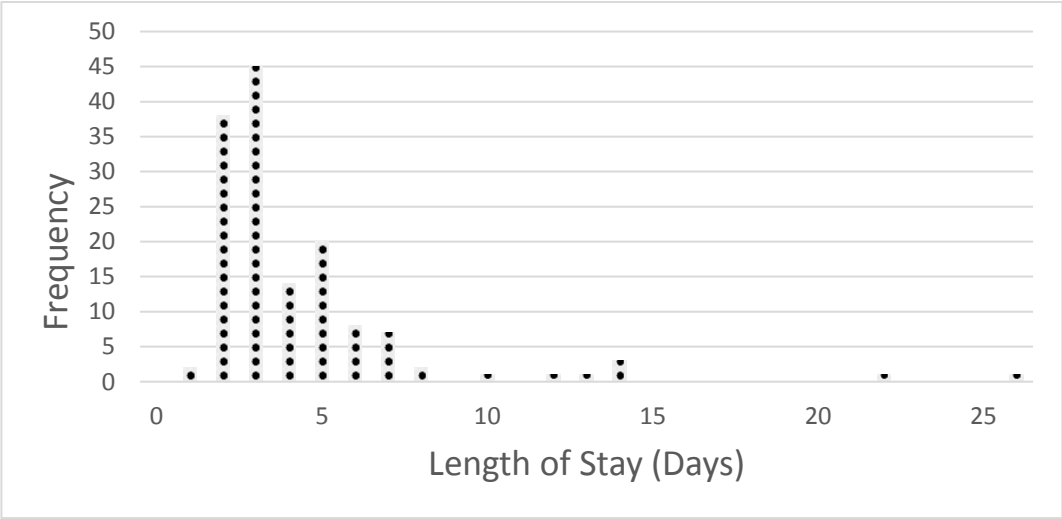

Figure 1: Distribution Dot Plot of Length of Stay.

Complications

Complications occurred in 46 patients (30.7%). Grade of complications using the Clavien-Dindo Classification was Grade 1 (n=4), Grade 2 (n=37), Grade 3b (n=6) and Grade 4 (n=1). There were no Grade 3a or Grade 5 complications. Overall rate of significant complications (>Clavien-Dindo 2) was 4.67%. Procedures required for those with Grade 3b complications were embolization of AV fistula (n=1), open insertion of drain for ascites due to decompensated liver failure (n=1), cardioversion for atrial fibrillation (n=1), re=exploration for bleeding and completion nephrectomy (n=1), JJ Stent insertion for urinoma (n=1) and rendez-vous procedure for iatrogenic PUJ obstruction (n=1). One patient required admission to the intensive care unit (Clavien-Dindo 4) owing to pneumonia, pleural effusion and respiratory failure. He recovered well and was discharged home on day 26.

Complications were noted more frequently in patients in the High Nephrometry Score group (45%) than in the Low (32.7%) and Intermediate (27.5%) groups (p=0.01).

Histological Findings

Mean tumour size was 32 ± 15.2mm. Histology demonstrated Clear Cell RCC (n=102), Papillary RCC (n=11) , Chromophobe RCC (n= 7), Oncocytoma (n=10), Cystic RCC (n=5), RCC not otherwise specified (n=1), RCC Unclassified (n=2), Angiomyolipoma (n=4), MEST (n=2), Multilocular Cystic Neoplasm of Low Malignant Potential (n=2), Metanephric Adenoma (n=1), Mucinous Tubular and Spindle Cell Tumour (n=1), Benign Cyst (n=1) and inflammation/sclerosis (n=1). (Table 2).

Histology	**N**	**%**
Clear Cell	102	68%
Papillary	11	7.33%
Chromophobe	7	4.67%
Oncocytoma	10	6.67%
Angiomyolipoma	4	2.67%
Other	16	10.67%

Table 2: Tumour Histology from resected specimen.

Five patients (3.3%) had positive margins.

Tumour Stage was pT1a (n=103, 68.7%), pT1b (n=21, 14%), pT2a (n=1, 0.67%), T3a (n=8, 5.3%) and benign/not applicable (n=16, 10.6%). Stage data was unavailable for one patient (0.67%). Positive surgical margins occurred in 5 patients (3.3%) (one focal), all of whom underwent robotic surgery. None of these patients with positive margins have had either local or distant recurrence to date.

Haematologic and Renal Function Outcomes

Mean serum Creatinine (ng/ml) was 85.5 ± 23 pre-op, 107.1 ± 29.6 Day 1, 109.2 ± 36.0 Day 2, 100.2 ± 31.9 at 6 weeks post op and 94.2 ± 25.1 at 3 months post op. There was a statistically significant difference between serum creatinine pre-operatively and at all follow up time points post op ($p<0.0001$ Day 1 and Day 2 post op, $p=0.029$ at 2-6 weeks, $p=0.0013$ at 3-6 months) .

Mean Haemoglobin (g/dl) was 13.8 ± 1.6 pre-op, 12.2 ±1.4 Day 1, 11.8 ± 1.4 Day 2, and 13.3 ± 1.6 at 3 months post op.

Comparison of Laparoscopic vs Robotic PN

We identified no significant differences between the laparoscopic and robotic approach, in terms of tumour nephrometry group ($p= 0.365$), ischaemia times ($p=0.98$), length of stay ($p=0.71$) or incidence of complications ($p=0.56$) (Table 3). There was no statistical difference in serum Creatinine pre-operatively or at any time period post op, although there was a trend towards lower levels at 3-6 months in the robotic group (87.8 v 100.4ng/ml, $p=0.06$). We did identify a statistical reduction in blood loss in the robotic group (210.5 ± 260.4mls v 276.5 ± 313.33mls, $p=0.037$), but no difference in transfusion rates ($p=0.3$).

Variable	**Laparoscopic**	**Robotic**	**P-Value**
Ischaemia Time (mins)	24.2 ± 8.2	24.1 ± 0.96	*0.98*
Complications	18/64 (28.1%)	28/86 (32.5%)	*0.56*
Mean Length of Stay	4.3 ± 3.7	4.1 ± 3.1	*0.71*
Blood Loss (mls)	276.5 ± 313.33	210.5 ± 260.4	*0.038*
Blood Transfusion	2/64 (3.1%)	7/86 (8.1%)	*0.3*

Table 3: Comparison of Laparoscopic and Robotic Surgery.

Discussion

The guiding principle of nephron sparing surgery is the ability to achieve equivalent oncologic control to radical nephrectomy for patients with renal tumours[1], while maintaining the maximum possible renal function, through preservation of nephron mass[2]. Central to this is the recognition that renal dysfunction is an independent risk factor for cardiovascular disease and death[7]. What remains to be clearly elucidated however, is whether surgically created chronic kidney disease (CKD) (ie. eGFR decline following nephrectomy), carries the same overall health risk as CKD from chronic medical disease, and whether nephron sparing surgery confers an overall survival benefit over radical nephrectomy[1].

Both the EAU[5] and AUA[6] advocate partial nephrectomy as a treatment option for T1 tumours, based on the current AJCC staging system.

However, the complexity of nephron sparing surgery is not solely based on the size of the mass to be excised, but rather on a number of tumour characteristics, including distance from the collecting system, polarity and whether it is endo or exophytic. These features are quantified using nephrometry scores, such as the RENAL[8] or Padua Scores[9], which have been shown to predict peri-operative outcomes including ischaemia times[10,11], conversion to radical nephrectomy[10] and incidence of high grade complications[11,12].

Partial nephrectomy also carries a number of imperative indications, including bilateral renal masses and tumours in solitary kidneys.

Laparoscopic partial nephrectomy has been shown to achieve equivalent oncologic outcomes as open partial nephrectomy, while achieving a shorter operative time, shorter length of stay and lower blood loss[3]. There was however an increase in ischaemia times and overall complication rates with the laparoscopic approach.

When compared to open PN, robotic PN results in lower complication rates, blood loss and length of stay, with similar operative time, warm ischaemia time, change in creatinine and rates of positive surgical margins[4].

Robotic PN is associated with similar operative time, blood loss, positive margins and complication rates to laparoscopic PN, while affording lower rates of conversion to open or radical surgery, shorter ischaemia times and shorter length of stay[13]. Owing to the increased dexterity offered it may permit surgeons to take on tumours of higher complexity than the standard laparoscopic approach.

Our data demonstrate excellent peri-operative outcomes, with low blood loss and transfusion rates, as well as short length of stay, in line with those reported in the international literature, and summarised in the meta-analysis by Choi et al[13]. Length of stay data in out series is skewed by a small number of outliers who required prolonged admissions owing to medical co-morbidities (Figure 1).

While the overall complication rate initially appears high at 32.8%, 85% of these were minor Grade one and two complications. A large proportion of these patients suffered from atelectasis and post-operative respiratory infection related to the procedure. Our rate of significant complications (Clavien-Dindo Grade 3 and above) at 4.6% compares favourably with those studies analysed by Choi et al (Range 2-12.2%, Pooled 6.86%)[13].

While we observed a statistical increase in mean serum creatinine at 3-6 month follow up compared to pre-op levels (85 ± 22.5 v 94 ± 55.4,p =0.013), this is not considered to be of clinical consequence.

We did not identify any association between length of stay or complications and tumour complexity or stage.

Owing to the short follow up of this cohort, we are presenting only peri-operative data, with margin status serving as a surrogate of oncologic control. While this has not been shown to predict recurrence for low risk disease (HR 0.62, p=0.64), Shah et al demonstrated an increased risk in those with high risk disease (>T2 or Fuhrman Grade 3 and 4) (HR 7.48, p<0.001)[14]. The same authors reported positive margin rates of 7.8% in their cohort[14], which is higher than we report in this series (3.3%). We acknowledge higher rates of positive margins in the robotic group (5.8% v 0%), but attribute this to taking on higher complexity cases robotically than would have been attempted laparoscopically.

While this study was not formally randomized, operative modality was selected based on that which was available in the unit at the time, rather than on patient or tumour factors. As such we expect bias to be minimal with regard to modality. We acknowledge the short duration of follow-up as a limitation of this paper, but plan to follow-up these patients and examine medium and long-term oncologic and functional outcomes.

In conclusion, we advocate minimally invasive PN as a safe and effective management strategy for the management of selected renal masses, whether performed by a laparoscopic or robotic approach. It affords excellent oncologic outcomes, as well as short length of stay, low blood loss and minimal deterioration in renal function. The choice of LPN versus RAPN should be made based on local availability and expertise, with largely equivalent functional outcomes achievable with each approach. Nephrometry scores may be helpful in identification of patients in whom the operative risks and probability of conversion to RN are high, to facilitate informed counselling and decision making.

Declaration of Conflicts of Interest:
The authors confirm that there are no conflicts of interest to be declared.

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