ORIGINAL ARTICLE

Transperitoneal laparoscopic nephrectomy for renal tumour disease versus non-tumour disease: What are the differences in outcomes?

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ABSTRACT

Introduction: Laparoscopic nephrectomy is the standard of care for the removal of both non-functioning and tumour-bearing kidneys. This study was conducted to compare the characteristics and outcomes follow-ing laparoscopic transperitoneal nephrectomy (TP) for tumour and non-tumour disease.

Methods: We retro-spectively reviewed all TP nephrectomies performed in the Hospital Sultanah Bahiyah Alor Setar, Kedah between January 2016 and July 2017.

Results: A total of 36 eligible cases were identified, 10 of which were for renal tumours and the others for non-functioning kidneys. There were no statistically significant differ-ences between the two groups in terms of demographics and comorbidities. We also did not identify any sta-tistically significant differences between the two groups in terms of operating time, blood loss, need for transfusion, septic complications and postoperative recovery. The only significant difference between the groups was the postoperative rise in serum creatinine, which was higher in the tumour disease group (mean rise 23.4 vs 5.35µmol/l; p = 0.012).

Conclusions: Our study showed that laparoscopic nephrectomy is both feasible and safe for the treatment of tumour and non-tumour renal disease with low complication rates in both groups.

KEY WORDS:
Renal tumor, renal cell carcinoma, non-tumor, non-functioning kidney, laparoscopic transperitoneal nephrectomy

INTRODUCTION

Since the advent of laparoscopic nephrectomy (LN) in the 1990s, the procedure has evolved into the gold standard procedure for the surgical extirpation of kidneys afflicted by both malignant and non-malignant conditions. As experience with LN increased over the years, associated perioperative outcomes have im-proved as well. In the early 2000s operating times averaged over 4 hours per case, with blood loss exceeding 300cc;[1] by the 2010s most cases required around 2 hours for completion, with blood losses falling below 200cc and with conversion rates of less than 10%.[2,3]

In line with this growth in experience in the procedure in various clinical settings, there is increasing appre-ciation of the differences between malignant and non-malignant disease in terms of perioperative outcomes. In many centres, the terms 'simple' LN and 'radical' LN are used to denote surgery for benign and malignant renal conditions respectively, with radical LN being perceived as the more technically demanding procedure. Such denominations are, however, increasingly being disputed as it has been found that a simple LN may be more challenging than its radical counterpart due to the presence of perirenal fibrosis and adhesions resulting from chronic infection and obstruction.[4] As illustrated by Keeley and Tolley in 1998,[5] LN in the setting of inflammatory conditions can be wrought with difficulties and may result in unacceptably high complication rates; so much so that such conditions were once considered relative contraindications to LN. Xanthogranu-lomatous pyelonephritis is a particularly vexing inflammatory condition in which hilar abnormalities and perihilar adhesions are present in the great majority of operated cases (71% and 86% respectively as reported by Manohar et al).[6] In a case series by Hsiao and colleagues involving 42 completed cases of LN for non-malignant disease, a complication rate of 21.4% was reported with nearly two-thirds of these being classified as major complications.[7] However, with advancements in surgical technology, including energy devices, haemostatic techniques and laparoscopic systems, as well as improved experience on the part of laparoscopic surgeons, benign inflammatory renal lesions are increasingly being managed through LN, with progressively encouraging results and outcomes.[8]

The aim of our study was to compare patient characteristics and perioperative outcomes of laparoscopic transperitoneal nephrectomy for renal tumour disease and non-tumour disease.

MATERIALS AND METHODS

Data of all laparoscopic nephrectomies performed at the done at Urology Department, Sultanah Bahiyah Hospital Kedah, over a period of 19 months between January, 2016 and July, 2017.were collected from the central operating database. Informed consent was obtained from all patients involved in the study prior to surgery. All cases were examined retrospectively based on electronic patient records.

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Eligible cases were divided into two groups, namely tumour (all malignancies) and non-tumour groups (all non-functional, non-cancerous kidneys). All cases were performed by one consultant urological surgeon.

Pre-operatively, CT imaging, complete blood count, renal function test and urine analysis were performed, with additional liver function test for tumour cases. One dose of intravenous Unasyn 1.5g (sulbactam-ampicillin) was given during induction of anaesthesia for tumour cases, while for patients with non-functioning kidneys intravenous antibiotics were started the day before surgery and continued until the day of discharge.

Following induction of anaesthesia, bladder catheterisation was performed, and the patient was then posi-tioned in a lateral position with extension at the ipsilateral loin to open up the renal angle. Firstly, a 12 mm paraumbilical port was inserted with open technique. Once diagnostic laparoscopy was performed, two addi-tional 12 mm ports were inserted under direct visualisation; one at the medial hypochondrium and the other at the iliac fossa. Adhesions were then released. Medial mobilisation of the colon, at the level of the hepatic flexure and splenic flexure for right and left nephrectomies respectively, was performed. Dissection of kid-ney was then carried out in caudal direction until the ureter and gonadal veins were identified. The ureter was then traced and dissected cranially towards the hilum. The renal artery and vein was dissected and divid-ed in sequence after hemostatic lock application. Following that the kidney was mobilised completely, and the ureter divided between clips. The kidney was then removed via the enlarged iliac fossa wound within a specimen removal bag. Closure of the extirpation wound was performed in two layers with polyglactin su-tures. A final laparoscopic inspection of the renal bed was performed; a drain would be inserted if deemed necessary by the surgeon. Lastly, port site closure was done with polyglactin sutures.

Postoperatively, patients were encouraged to ambulate and resume oral intake the same day. Analgesics, thromboprophylaxis and antibiotics were administered as required.

Parametric data was statistically tested with the student t-test, whereas for non-parametric data, the chi square test was used. With respect to statistical significance, a p-value of less than 0.05 was considered as statistically significant.

This study was registered under the National Medical Research Registry of Malaysia bearing the registration number 45974.

RESULTS

Within the planned study period a total of 42 nephrectomies were performed laparoscopically, but six cases were eventually excluded from the study. Three of these were for extraperitoneal approach to surgery (our study intentionally included only transperitoneal LN cases to ensure standardisation of the surgical tech-nique), while three cases were excluded due to conversion to open surgery. Of the cases involving conver-sion, one was due to the intraoperative discovery of a previously unsuspected renal vein tumour thrombus which required open extirpation. The two other cases that were converted to open surgery were due to the presence xanthogranulamatous pyelonephritis with severe dense adhesions, thus rendering further laparo-scopic surgery hazardous. All three conversions were deemed necessary by the operating surgeon at the time of surgery.

Demographically, there was no statistical significance in terms of gender distribution (p=0.102), in spite of the finding that there were eight male patients in tumour group, and for non-tumour group there were 13 male and female patients each. Laterality distribution was not statistically significant (p=0.836). The mean patient age for the tumour group was 55.00±11.52 years and for the non-tumour group, 58.53±9.87 years; for this there was no statistical significance (p=0.426) (Table I).

Regarding patient co-morbidities, the prevalence of diabetes mellitus (p=0.667) and hypertension (p=0.792) among our study population were all not statistically significant. Two out of 10 (20%) patients in tumour group were diabetics, while 7 out of 26 (26.92%) patients in non-tumour group were diabetics. Both groups had a high prevalence of hypertension. In all 70% (7 out of 10) of patients in tumour group were hyperten-sive, whereas 65.38% (17 out 26) of patients in non-tumour group were hypertensive. There were more pa-tients (10 out of 26, 38.46%) in the non-tumour group had previous transperitoneal abdominal surgery or ipsilateral percutaneous renal surgery, as compare to the tumour group (1 out of 10, 10%). However, this was not statistically significant, p=0.100 (Table IV).

Ten patients were in the tumour group. Nine had clear cell renal cell carcinoma, while one had acquired cyst-ic renal cell carcinoma. The mean tumour size was 73.90±22.0mm. Two patients had stage T1 tumour, two cases had stage T2 disease, five patients had stage T3 tumour and one case was reported as stage T4 disease post-operatively on histological examination. One out of the 10 cases showed positive lymph nodes spread on histological examination and distant metastatic spread on pre-operative imaging (Table II).

In the non-functioning kidney (non-tumour group), there were 26 cases. One patient had xanthogranuloma-tous pathology, and 25 had chronic pyelonephritis. Three patients had an atrophic kidney, whereas 23 had a hydronephrotic kidney. The majority had stone as the underlying aetiology (24 cases), while two cases were due to stricture disease. The mean kidney size among these cases was 128.70±49.42mm (Table III).

Mean operative time for tumour and non-tumour groups were 139.70±33.57 minutes and 165.62±57.45 minutes respectively. Although longer operating times were experienced in the non-functioning kidney group, there was no statistical significance (p=0.118). There was also no statistical difference in the usage of abdominal drain (p=0.676) between both groups. One patient in the tumour group had required an abdominal drain, while there were 4

Table I: Demographic properties

	Tumour, n=10	Non-tumour, n=26	P value
Sex			
Male	8	13	0.102
Female	2	13	
Side			
Right	5	12	0.836
Left	5	14	
Age, years			
Mean ± SD	55.00 ± 11.52	58.53 ± 9.87	0.426
Range	32-72	38-75	
Median	57	59	

SD = standard deviation

Table II: Tumour pathology

	Total, n=10
Type of renal cell carcinoma	
Clear cell	9
Acquired cystic	1
Tumour size, mm	
Mean ± SD	73.9 ± 22.0
Range	54-130
Median	66
pT stage	
T1	2
T2	2
T3	5
T4	1
pN stage	
N0	9
N1	1
M stage	
M0	9
M1	1

SD = standard deviation
Staging of cancer is based on the American Joint Committee on Cancer (AJCC) staging system, 8th edition
pT = pathological staging of primary tumour
pN = pathological staging of regional lymph nodes
M = distant metastases

Table III: Characteristics of non-functioning kidneys

	Total, n=26
CT findings	
Atrophic kidney	3
Hydronephrotic kidney	23
Etiology	
Stone	24
Stricture	2
Histology	
Chronic pyelonephritis	25
Xanthogranulomatous pyelonephritis	1
Kidney size, mm	
Mean ± SD	128.7 ± 49.42
Range	60-247
Median	121

CT = computerised tomography
SD = standard deviation

Table IV: Comorbidity variables

Comorbidities	Tumour, n=10	Non-tumour, n=26	P value
Diabetes mellitus			
Diabetic	2 (20%)	7 (26.92%)	0.667
Non-diabetic	8 (80%)	19 (73.08%)	
Hypertension			
Hypertensive	7 (70%)	17 (65.38%)	0.792
Non-hypertensive	3 (30%)	9 (34.62%)	
Previous transperitoneal abdominal surgery or ipsilateral percutaneous renal surgery			
Ýes	1 (10%)	10 (38.46%)	0.100
No	9 (90%)	16 (61.54%)	

Table V: Operative variables

	Tumour, n=10	Non-tumour, n=26	P value
Operation time (minutes), mean ± SD	139.70±33.57	165.62±57.45	0.118
Abdominal drain insertion			
Yes	1	4	0.676
No	9	22	
Hemoglobin drop (g/dl), mean ± SD	1.20 ± 1.03	0.74 ± 0.69	0.240
Blood transfusion			
Yes	2	1	0.116
No	8	25	
Creatinine increase (μmol/l), mean ± SD	23.40 ± 17.21	5.35 ± 6.26	0.012

SD = standard deviation

such patients in the non-tumour group. Mean haemoglobin drop was lower in the non-tumour group at 0.74±0.69 g/dl, while the mean drop in the tumour group was 1.20±1.03g/dl. However, statistically it was not significant (p=0.240). There was no statistical significance in the requirements for blood transfusion (p=0.116) between both groups. Two patients in the tumour group had blood transfusion, whereas there was one patient in the non-tumour group. The mean increase in creatinine between the two groups was statistically significant (p=0.012). The mean increase was 23.40±17.21µmol/l in the tumour group. In contrast, it was 5.35±0.012µmol/l in the non-tumour group (Table V).

Post-operatively, three patients in the non-tumour group developed sepsis, one had renal bed abscess who was readmitted, and the other two patients developed pneumonia. There was no incidence of fever or septic complication, or readmission in the tumour group. However, this finding was not statistically significant (P=0.262). There were no statistically significant differences in the mean time to return to normal full diet (p=0.173) and mean duration of post-operative hospital stay (p=0.536). The respective mean time to normal diet in the tumour and the non-tumour groups were 1.10±0.30 days and 1.35±0.73 days. Whereas the mean time of post-operative hospital stay were 2.10±1.45 days and 2.46±1.55 days respectively. There was no statistical difference in the requirement for postoperative high dependency unit stay (p=0.529). One patient from the non-tumour group was admitted to our High Dependency Unit for monitoring post-operatively, while there were no cases requiring such support in the tumour group.

DISCUSSION

The rapid and widespread adoption of laparoscopic nephrectomy following its introduction over 20 years ago was due in large part to the many physiological advantages afforded by the laparoscopic approach in com-parison to open nephrectomy, which include reduced postoperative pain, earlier return to normal function, shortened postoperative hospital stay, and improved cosmetic results.[9] When performed for cancer cases, it has been repeatedly demonstrated that oncological efficacy was not compromised by the laparoscopic ap-proach.[9,10] From a technical perspective there are two approaches to LN, namely transperitoneal and ex-tra/retroperitoneal approaches. Neither has been conclusively demonstrated to be superior over the other; while the latter provides early access to renal vasculature and avoids contact with intraperitoneal viscera, it is ergonomically more cumbersome due to limitations in working space. Also, more surgeons previously trained in laparoscopic surgery are familiar with the transperitoneal approach, which results in a less steep learning curve and more desirable surgical outcomes. One study suggests that in the setting of benign renal disease, the retroperitoneal approach may be associated with shorter operating time and more rapid return of normal bowel function.[11] In our centre transperitoneal LN is the rule of thumb, with the exception of cases in which severe intraabdominal adhesions are anticipated; in such cases extraperitoneal LN or open nephrecto-my will be considered.

A search of the available reports showed several studies which provided head-to-head comparisons between surgery for benign disease and for malignancies; the results of these studies were, however, mostly conflict-ing. An early study by Gill et al in 1995 demonstrated a higher complication rate in LN performed for renal malignancies than those performed for benign conditions (34% vs 12%; overall 16%).[12] On the other hand, a much more recent study by Zelhof et al in 2015 suggested that simple nephrectomy for benign conditions actually resulted in poorer outcomes (significantly higher conversion and blood transfusion rates; also longer operating times, more blood loss, and more intra- and post-operative complications, of which are not statisti-cally significant) than radical nephrectomy for malignant disease.[4] As demonstrated by the results of our study, there was no statistically significant differences in nearly all analysed parameters between the two study populations in terms of perioperative outcomes and this is in conflict with the findings presented by Zelhof et al, that suggested worse outcomes in LN for non-tumour disease. A possible explanation for this may be that all 'radical' LNs performed in their study were for T1 tumours, whereas in our study the most prevalent tumour stage was T3 (50%), and there was even one case involving a T4 tumour. Such locally ad-vanced cancers invariably lead to hypervascularity of the surrounding tissues along with disruption of normal anatomical planes, both of which make for more difficult dissection during surgery and results in prolonged operating time, as well as increased blood loss. Indeed, two intraoperative parameters, namely drop in hae-moglobin (reflection of blood loss) and need for transfusion were indeed higher in the tumour surgery group, though neither achieved statistical significance.

Among the studies performed solely on non-malignant disease, Katz et al demonstrated that LN was feasible in cases of obstructed, infected, non-functioning kidneys with severe perirenal fibrosis, *albeit* with an aver-age operating time approaching 4 hours per case.[13] Gulpinar et al., found that surgery on hydronephrotic kid-neys had longer operating times and higher conversion rates than those performed on atrophic kidneys, prob-ably due to peritoneal adhesions resulting from recurrent infections in obstructed systems.[14] When a retroper-itoneoscopic approach was taken, non-functioning kidneys resulting from renal calculi required longer oper-ating times and had higher complication rates than those without calculi.[15] Two other similar studies, however, did not report concurring results. In the study by Kurt et al., no significant differences in perioperative outcomes were demonstrated between inflammatory and non-inflammatory kidneys apart from post-operative fever which was commoner in the inflammatory group.[16] A similar result was obtained by Kurt et al., in which LN for kidneys with and without stones were compared.[17]

In our study, the longer mean operating time needed for non-tumour LN (165.6 minutes versus 139.7 minutes in tumour LN), though not statistically significant, appears to be in agreement with the studies by Gulpinar et al., and Tepeler et al.[14,15] Apart from adhesions arising from chronic infection, this may also be related to the fact that a much greater percentage of non-tumour cases have had some previous abdominal surgery or ipsilateral percutaneous renal surgery; both of which may have induced and exacerbate perirenal adhesions (38.5% of non-tumour cases, versus 10% of tumour cases). Unfortunately, a search through the literature did not yield any studies that specifically investigated the effects of previous abdominal or renal surgery on LN outcomes, and as such no comparisons could be made.

In our study when post-operative complications are taken into consideration, it is notable that all cases of septic complications occurred within the non-tumour surgery group (but none were statistically significant). This can be explained by the fact that the majority of our non-functioning kidney patients had harboured ob-structed, infected systems (88.5% hydronephrotic, 92.3% with renal stones, all showing pyelonephritis on post-operative histology) and as such may all be considered 'inflammatory' lesions. During LN some spill-age of infected intrarenal contents in the peritoneal cavity is inevitable, resulting in post-operative fever, de-lay in return of normal bowel function, and in one case formation of a renal bed abscess. These findings are in agreement with those of Kurt et al, as mentioned earlier.

It is pertinent to note that in our study, the only type of postoperative complication that was analysed were those of septic nature. As such, our complication rate was 11.5% in the non-tumour surgery group (three cas-es in 26), whilst no complications occurred in the tumour surgery group. This is somewhat lower than the complication rates reported by contemporary studies. However, most of these studies include all types of complications, and utilise the Clavien-Dindo classification for segregation of complications. As such, even though these studies may appear to report higher complication rates than our study, a greater proportion of their complications may actually be minor in nature (Clavien grade 1 and 2). The only parameter in our study that achieved statistical significance was the post-operative rise in serum creatinine, which was greater in the tumour surgery group (23.4 versus 5.35, $p = 0.012$). The explanation for this finding is straightforward as in tumour cases, prior to extirpation the filtration load was shared by the diseased kidney, and upon removal of the kidney a sizeable number of functional nephrons are lost, with a resultant spurious increase in serum cre-atinine levels. In non-tumour cases, the diseased kidney had already not been participating in the filtration process, so its removal does not produce any significant alteration in serum creatinine levels.

Based on the findings in our study, it may be concluded that 'simple' LN for benign renal disease and 'radi-cal' LN for renal malignancies represent two distinct procedures, each with their own set of technical chal-lenges and potential risks for complications, and that neither is 'simpler' to perform than the other. The fact that there were almost no statistically significant differences between the two surgery groups in terms of perioperative outcomes merely suggests that the perceived technical advantage each group over the other has been cancelled out by some other aspect of the procedure, or the nature of the underlying condition. It is also to be borne in mind that both tumour and non-tumour surgery groups are heterogenous on their own (e.g. stone versus non-stone disease in benign cases, localised versus locally advanced tumours in malignant dis-ease) so that equal comparisons between the two groups may not be possible, unless analysis is performed upon very focused populations with closely matched disease characteristics.

A number of limitations are present in our study. Firstly, the retrospective nature of the study does not allow for randomised comparison between the two study populations. Secondly, both groups are relatively small and not evenly distributed, so the results may not be representative of the larger study population. With re-spect to postoperative complications, the severity of these complications was not qualified with a validated grading system, unlike a number of similar studies. Finally, the study only included cases in which LN was completed successfully without conversion to open surgery. While the number of excluded cases was small, there is a possibility of selection bias in which cases that may have been destined for conversion (and thus produce poorer perioperative outcomes, particularly prolonged operating time) have already been excluded from analysis. Such limitations may be circumvented in the future by conducting larger, multi centre trials utilising prospective methods of data collection.

CONCLUSION

Laparoscopic transperitoneal nephrectomy is a safe and effective treatment modality for both renal tumours and non-functioning kidneys. The only study parameter that demonstrated a statistically significance be-tween the two treatment populations was the mean postoperative rise in serum creatinine, which was greater in the tumour surgery group. With the continuous advancements in surgical technology, specifically in the area of nephron-sparing surgery, it may be expected that such postoperative declines in renal function will be further minimised, or even eliminated altogether.

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