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ORIGINAL ARTICLE

Evaluating the perioperative safety of laparoscopic radical nephrectomy for large, non-metastatic renal tumours: a comparative analysis of T1-T2 with T3a tumours

E. M. Bolton[1] · D. Hennessy[1] · P. E. Lonergan[1] · F. T. Darcy[1] · R. P. Manecksha[1] · T. H. Lynch[1]

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Abstract
Objective With increasing surgeon experience, the use of laparoscopic radical nephrectomy (LRN) in large and locally advanced renal tumours (T3a) is gaining favour in urological practice. There are limited studies reporting surgical outcomes in such groups. The aim of this study was to review our experience with LRN in these patients.
Methods Data was retrospectively collected on 201 consecutive patients who underwent LRN for renal cancer by a single surgeon. Perioperative parameters assessed were age, gender, American Society of Anaesthesiologists score (ASA), waist circumference, tumour size, specimen size, histological subtypes, anaesthetic duration, operative approach and technique, surgery duration, blood loss, pre and postoperative renal function, complication rate and duration of hospital stay.
Results Of 201 patients undergoing LRN, 43 (21%) patients had T3a tumours (group 2). The remaining 158 (79%) patients had T1 tumours (group1). Mean tumour size in group 2 was 12.2 cm. Renal cell carcinoma (RCC) was more common in males than females (131/201; 65%). Patients with T3a disease were more likely to have an ASA score of 2 (37/201; 18%). In the majority of patients across both groups, LRN was completed using a 3-port approach (173/201; 86%). There were no significant differences between groups in terms of mean anaesthetic duration, average surgical time, average estimated blood loss, complication rate and mean hospital stay.
Conclusion Our study shows that LRN has equivalent perioperative outcomes and safety in larger and locally advanced renal tumours.

Keywords Laparoscopic nephrectomy · Renal cancer · Surgical outcomes · T3a tumours

✉ E. M. Bolton
evabolton@rcsi.ie

[1] St. James's Hospital, James's St., Dublin 8, Ireland

Introduction

The overall incidence of renal cell carcinoma (RCC) is rising and now accounts for 2–3% of all adult human malignancies [1]. This is largely attributed to increased use of abdominal imaging and the accompanying detection of small kidney "incidentalomas". This is the presenting feature in up to 50% of RCC cases [2]. Despite this, we still encounter a substantial number of large and advanced tumours owing to the asymptomatic growth and silent progression of RCC. Since Clayman et al. pioneered the use of laparoscopic radical nephrectomy (LRN) in 1991, it has been considered the standard of care for localized RCCs (typically T1 tumours, <7 cm) in patients not considered eligible for nephron sparing surgery [3–5]. More recently, this indication has been extended to T2 and T3 tumours [6].

The benefits of LRN over open radical nephrectomy (ORN) with respect to perioperative pain and morbidity, recovery time and duration of hospital stay have been validated by numerous studies [7]. For larger tumours and in larger patients, the conventional approach with open surgery has generally been favoured as most of the studies on LRN were performed in cohorts of patients with tumour size <7 cm (T1 tumours) [4, 5]. The intermediate term oncological outcomes for LRN compared to open in this group are well established

and now longer term outcomes (>10–15 years) are also described [8–10]. The literature in recent years has suggested that LRN can be performed safely in patients with large renal tumours (T2 RCC, >7 cm) and T3a tumours (invasion of perirenal fat and/or gross extension into renal vein/segmental branches of renal vein), although the procedure is technically more challenging [6, 10, 11].

We report a single-surgeon experience of LRN in T3a renal tumours and compare perioperative outcomes to a contemporary cohort of patients undergoing LRN for T1-T2 disease.

Material and methods

Patient data was retrospectively collected on 201 patients who underwent LRN in our institution for RCC between July 2010 and July 2014. Data was obtained from patient charts, electronic patient records, histopathology reports, radiological imaging, operative notes and theatre records.

Preoperative RCC staging was based on standard imaging criteria using contrast enhanced renal CT images and or MRI. RCCs with invasion into the perinephric fat were routinely performed via laparoscopic approach. For the most part, patients with renal vein tumour thrombus were also completed laparoscopically. All cases with inferior vena cava (IVC) extension were performed openly.

LRN was performed using the transperitoneal approach [12]. Pneumoperitoneum was created under direct vision using Hassan technique and typically a triangulated 3-port technique was used. The laterocolic tissue was firstly dissected, followed by medial mobilization of the colon. Dissection was performed to the renal hilum and the vessels isolated. As is standard technique, the renal artery was ligated preceding the renal vein with three Hem-O-Lock clips. In a minority of patients, dissection near the renal hilum was challenging as the renal mass prevented direct access to the renal vessels. In such situations, a posterior dissection technique was used, allowing the lower renal pole to be elevated and control of the renal vessels gained. In cases with renal vein tumour thrombus, the artery was ligated first and the pneumoperitoneum increased temporarily to 20 cmH_2O. The margins of the tumour thrombus were identified as a prominence in the renal vein. The renal vein was controlled with a vascular loop which was then positioned to compress the renal vein distally and induce retraction of the tumour thrombus back towards the kidney. Once the distal margin of the tumour thrombus was identified, safe ligation of the renal vein was possible by applying Hem-O-Lock clips. Specimens were removed intact through an extended port site incision in an Endo-Catch bag.

Lymphadenectomy was not routinely performed in clinically node negative patients in either group as the survival benefit is unclear. Data on lymph node dissection in clinically node positive patients is not included due to small number size [13].

The American Joint Committee on Cancer (AJCC) guidelines were used for staging. Patients with tumours limited to the kidney, irrespective of size (T1-T2) comprised group 1 and those with tumours extending into the renal vein or segmental branches, or perinephric tissues but not beyond Gerota fascia (T3a) comprised group 2 [1, 14]. Statistical analysis was performed using standard parametric analysis on Prism 5; chi-square test for categorical variables and paired *t* test for variable data, with statistical significance set at $p < 0.05$.

Results

A total of 201 patients undergoing LRN for RCC were studied. The T1–2 group contained 158/201 (79%) of patients whilst the remaining 43/201 (21%) patients formed the T3a group as outlined above, of which 15/201 (8%) had tumour thrombus extending into renal vein. Patient demographics are given in Table 1. One hundred thirty-one (65%) patients were male and 70 (35%) patients were female. The median age was 60 years in the T1–2 group and 67 years in the T3a group ($p < 0.05$*; paired *t* test). The spread of ASA grades amongst the groups are presented in Table 1 with no significant difference found between the groups.

Tumour characteristics are shown in Table 2. The mean tumour size in the T1–2 group was 4.2 cm (range; 1.5–3.5 cm) and mean specimen size 10.5 cm (range; 8.5–15.5 cm). The most common histological variant was clear cell renal cell carcinoma (77%). In the T3a group, the mean tumour size was 12.2 cm (range; 8.5–21 cm) and mean specimen size was 19.6 cm (range; 11.8–25 cm). Again, the most common histological variant was clear cell renal cell carcinoma (74%). Figure 1 demonstrates axial and coronal views of a

Table 1 Patient demographics

Characteristic		Total	T1–2	T3a	*p**
Total		201	158 (79%)	43 (21%)	
Median age (years)		57	60	67	<0.05*
Range		25–85	25–75	42–85	
Gender					
Male		131 (65%)	98 (62%)	33(77%)	
Female		70 (35%)	60 (38%)	10 (23%)	
Male versus female					<0.05*
ASA Grade					
	1	123 (61%)	119 (75%)	4 (9%)	<0.05*
	2	65 (32%)	28 (18%)	37 (86%)	<0.05*
	3	13 (7%)	11 (7%)	2 (5%)	0.7893
	4	–	–	–	–

The asterisk implies a significant *p*-value of <0.05

Table 2 Tumour characteristics

Characteristics	Total $N = 201$	T1–2 $N = 158$	T3a $N = 43$	p*
Mean tumour size (cm)	10.3	4.2	12.2	<0.05*
Range (cm)	1.5–21	1.5–13.5	8.5–21	
Specimen size (cm)	12.5	10.5	19.6	0.00145*
Range (cm)	8.5–25	8.5–15.5	11.8–25	
Histological subtype				
Clear cell RCC	153 (76%)	121 (77%)	32 (74%)	<0.05*
Papillary RCC	23 (12%)	16 (10%)	7 (17%)	0.0022*
Chromophobe RCC	11 (5%)	7 (4%)	4 (9%)	0.079
Collecting duct RCC	4 (2%)	4 (3%)	0	0.3173
Multilocular cystic RCC	0	0	0	NA
Mixed subtypes	10 (5%)	5 (6%)	0	NA
Furhman grade				
1	0	0	0	0.1572
2	54 (27%)	52 (33%)	2 (5%)	<0.05*
3	106 (53%)	77 (49%)	29 (67%)	<0.05*
4	41 (20%)	29 (18%)	12(28%)	<0.05*

The asterisk implies a significant p-value of <0.05

computed tomography (CT) showing a 16.5-cm tumour removed laparoscopically.

In terms of operative approach, 195 (97%) patients had their surgery completed laparoscopically. Conversion to an open procedure was necessary in six (3%) patients (Table 3). Overall, 173 (86%) completed surgery using a 3-port technique. Twenty (13%) patients in the T1–2 group and eight (19%) patients in the T3a group required insertion of an additional port. There were no significant differences in mean anaesthetic duration, surgical duration or blood loss between the groups as demonstrated in Table 3.

For patients in the T1–2 group, mean preoperative and postoperative creatinine was 86 and 113 respectively and average estimated glomerular filtration rate (eGFR) was 85 and 63, respectively. The mean preoperative and postoperative creatinine for patients in the T3a group was 112 and 154, with an average pre and postoperative eGFR of 62 and 51, respectively (Table 4). Complications occurred in 65 (41%) patients in the T1–2 group and 26 (60%) patients in the T3a group **(**Table 4**)**. The median duration of hospital stay was 4.5 days (range; 3–11 days) in the T1–2 group patients and 6.1 days (range; 4–15 days) in the T3a group patients.

Discussion

The therapeutic applications of minimally invasive surgery continue to expand with increasing surgeon experience, case volume and technological advancements. Despite having an established role in the treatment of T2 renal malignancies, there are relatively few studies reporting on safety of LRN

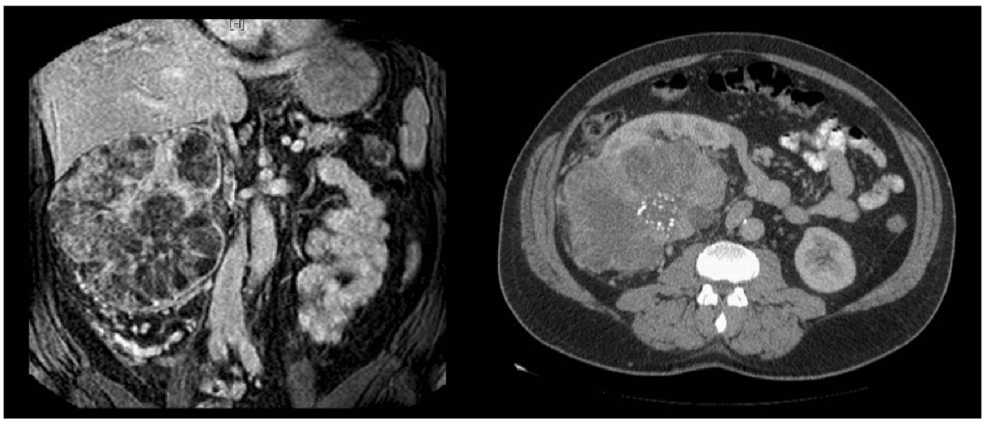

Fig. 1 Axial and coronal slices of computed tomography demonstrating a large T3 tumour excised laparoscopically

Table 3 Operative approach

Characteristic	Total $N = 201$	T1–2 $N = 158$	T3a $N = 43$	p*
Approach and completion				
Laparoscopic	195 (97%)	156 (99%)	39 (91%)	NA
Laparoscopic converted to open	6 (3%)	2 (1%)	4(9%)	NA
No. ports				
3	173 (86%)	138 (87%)	35 (81%)	0.1543
4	28 (12%)	20 (13%)	8 (19%)	0.1654
Ligation of hilum				
Hem-O-Lock	197	158	39	NS
Endo GIA	2	0	2	NS
Suture	2	0	2	NS
Mean anaesthetic duration (min)	197.4	165.5	289.2	0.0426
Mean surgery duration (min)	143.48	136.8	198.4	0.0532
Mean blood loss (ml)	403.67	427.5	612.4	0.4231

The asterisk implies a significant p-value of <0.05

for T3a disease. A summary of the evidence to this effect is presented in Table 5. To date, comparative studies on this matter have evaluated open versus laparoscopic cohorts, whereas this study was designed to compare two laparoscopic groups. In keeping with other groups, we have demonstrated the suitability and feasibility of LRD in locally advanced disease. Our results reveal comparable rates of blood loss, ASA grades, anaesthetic time, operative time, complication rates and hospital stay in concurrence with the literature presented in Table 5. The pre and postoperative renal function was less favourable in the group 2 patients but this finding was not significant. This observation was also reported by Guzzo et al. in a series of 37 patients with T3b disease [8, 15, 16].

We observed a low overall conversion to open rate, even within the T3a group. This may be reflected in the single institution design of the study which incurs greater technical experience with increasing case volume. Surgical outcomes for LRN in T3a disease have previously been shown to be worse than outcomes for LRN in T1 and T2 disease, stressing the complexity of the procedure in larger and more advanced tumours. Surgery for larger tumours is more difficult due to limited working space and bleeding as a result of neovascularization of larger tumours. For this reason, we stress the importance of surgeon expertise in case selection [9]. In our institution, all cases of T3a RCCs, confined to the renal vein, are considered for laparoscopic surgery whilst tumours with IVC extension are managed using the open technique thus adhering to a safer operative environment for advanced disease.

With the advent of LRN in more advanced tumours, a number of series in the literature describe LRN in patients with preoperative diagnosis of venous system involvement. Future long-term survival outcome studies will be capable of comparing LRN with ORN for this patient group and should produce outcomes comparable to open. One group has published outcomes on a series of 37 such cases, highlighting the complexity of the surgery and the necessity of expert laparoscopic skills [17].

There are a number of limitations with this study. Firstly, this is a single-surgeon and single-institutional analysis with standardization of LRN technique. This may infer an element of bias and limit generalization of results to other cohorts. Secondly, overall survival and cancer specific survival were not assessed here due to the short follow-up period from

Table 4 Perioperative outcomes

Characteristic	Total $N = 201$	T1–2 $N = 158$	T3a $N = 43$	p*
Renal function				
Pre-op creatinine	88.6	86	112	0.1017
Pre-op eGFR	76	85	62	0.4889
Post-op creatinine	120.8	113	154	0.0495*
Post-op eGFR	55.9	63	51	0.0521
Complications (Clavien-Dindo)				
None	110 (55%)	93 (59%)	17 (40%)	0.1654
Complications	91 (45%)	65 (41%)	26 (60%)	0.1432
Grade I	47 (23%)	31 (20%)	16 (37%)	–
Grade II	21 (10%)	14 (9%)	7 (16%)	–
Grade III	16 (8%)	14 (9%)	2 (5%)	–
Grade IV	7 (3%)	6 (3%)	1 (2%)	–
Grade V	0	0	0	–
Median hospital stay (days)	4.6	4.5	6.1	0.4329
Range (days)	3–15	3–11	4–15	–

The asterisk implies a significant p-value of <0.05

Table 5 Summary of literature on laparoscopic surgery for T3a renal tumours

Studies	Primary aim	Population studied	Major findings
Laird World J Urol (2015)	ORN versus LRN for T3 RCC	*n* = 252 (total) 25 Matched pairs with T3 RCC	LRN has superior perioperative profile [6]
Laird J Endourol (2013)	Determine stage specific operative, postoperative, and oncological outcome in patients undergoing LRN	*n* = 397 cT1-T4 *n* = 120 cT3-T4 patients	EBL greater for T3; LRN in T3 technically more demanding but feasible [19]
Montisci Urologica (2012)	Compared LRN in T1 versus T2–3	*n* = 132 *n* = 78 T1 *n* = 54 T2–3	No difference between groups in transfusion rate and postoperative renal function [20]
Stewart BJUI (2012)	Determine operative, postoperative, and oncological outcomes of LRN for T3–4 tumours	*n* = 94 (total) *n* = with curative intent *n* = 17 with CRN	LRN in T3–4 is safe but patients must be carefully selected in the context of suitable personnel [21]
Bensalah BJUI (2009)	Comparion of oncological outcomes in ORN versus LRN in T3	*n* = 44 LRN *n* = 135 ORN	No difference in overall survival between groups [11]
Bragayrac J Endourol (2016)	Comparion of oncological outcomes in ORN versus LRN in T3–4	*n* = 172	No difference in overall survival between groups [22]
Nayak Can Urol Assoc J (2015)	Clinical and oncological outcomes of patients with LRN in T3 tumours	*n* = 176	For properly selected cases, LRN yields acceptable short-term oncological outcomes [23]
Bird J Endourol (2009)	To evaluate LRN as a minimally invasive technique in locally advanced tumours	*n* = 252 *n* = 197 T1 *n* = 55 T2–3	No difference between groups in transfusion rate and postoperative renal function [24]

ORN open radical nephrectomy, *LRN* laparoscopic radical nephrectomy, *CRN* cytoreductive nephrectomy, *EBL* estimated blood loss

surgery and the low number of deaths within the follow-up period. For this reason, the primary focus of this study is on perioperative parameters. In this regard, LRN appears technically safe and feasible in this population. Finally, a comparative of patients with T3a disease receiving open surgery is not provided here and this.

There are also potential cost benefits for LRN compared to open surgery. This is reflected in terms of hospital stay and reduced incidence of complications in patients undergoing LRN [18].

Conclusion

The introduction of minimally invasive surgery has resulted in a surgical revolution and with this greater technology and more informed patients. We advocate the use of LRN for selected T3 RCCs. The advantages of LRN persist despite tumour size and stage and offer patients a procedure with minimal morbidity, shorter hospital stay and a rapid recovery. Nevertheless, adequate laparoscopic experience is necessary before performing radical nephrectomy for large T2-T3 tumours.

Compliance with ethical standards

Funding There was no funding obtained for this study.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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