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ORIGINAL ARTICLE

Laparoscopic partial nephrectomy for large renal masses: results of a European survey

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Abstract
Objective To evaluate the perioperative effectiveness of laparoscopic partial nephrectomy (LPN) for large (4–7 cm) renal masses, with a review of the experience of six European advanced laparoscopic centres.
Patients and methods A survey was planned; data were extracted from each institutional data base to obtain information about patients who had undergone LPN for renal masses larger than 4 cm. Demographic, radiological growth patterns of the tumours and intraoperative data were collected. Post-operative complications and pathological data were also recorded. All data were processed through statistical software.
Results Data on 63 patients were collected. Radiological tumour size was 4.7 cm (4.1–7), growth pattern was cortical in 33 cases and cortico-medullar in 30 cases. Warm ischemia time (WIT) was 25.7 min in 7.3% cases bleeding occurred intra-operatively, post-operative surgical complications occurred in 14.6% cases. Pathological analyses revealed malignant lesion in 73% and positive margins in 6.5%. Complications and positive margins are more frequent for cortico-medullar lesions.
Conclusions This survey confirms that LPN for tumours 4–7 cm in size is feasible in experienced hands. WIT and overall complication rate remain questionable points.

Keywords Laparoscopy · Renal tumours · Partial nephrectomy · RCC · Warm ischemia

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Introduction

Partial nephrectomy (PN) is an established curative approach for the treatment of patients with small renal masses (SRMs) (≤4 cm) [1–4]. It can be performed for selected tumours with a maximum diameter of 7 cm in centres with experience [5–10]. Moreover, the benefits of PN are well established and include, above all, a decreased risk of long-term renal insufficiency and consequently a positive impact on the quality of life [11–13].

In the last few years, laparoscopic partial nephrectomy (LPN) has gained more importance in the treatment of SRMs, and in some centres it has become the "first-choice treatment" as it is able to duplicate the principles of open partial nephrectomy (OPN) adding the advantages of mini-invasiveness [14–16].

While the role of LPN for SRMs is well documented, literature is poor for LPN for large masses (more than 4 cm). To give a contribution on this topic, we designed this survey, and we reviewed the experience of six European laparoscopic centres for LPN for renal masses from 4 to 7 cm in

order to evaluate the role of this procedure in the treatment of this kind of mass.

Patients and methods

Data collection

Our database was sent to 15 highly experienced laparoscopic urological centres, and data concerning their LPN for renal masses up to 7 cm of diameter were requested. Patients' data were extracted from each institutional database to obtain information only for those LPN performed for 4–7 cm masses, according to computed tomography (CT) scans. Inclusion criteria were the same in all centres: a single, organ-confined, contrast-enhancing renal mass. Exclusion criteria included renal vein involvement, lymphadenopathy, or extrarenal tumour extension.

Demographic and radiological features of the lesions were recorded. Based on a previously reported classification [17], tumour growth pattern was defined as central when tumour involved the central sinus fat or the collecting system on pre-operative computed tomography (CT) scan; as cortical when the lesions seemed to involve only the renal cortical at CT scan, and cortico-medullar when the lesions involved the medulla too.

The following variables were also reported.

Intraoperative data: surgical access, type of tumour resection (pure enucleation, enucleo-resection, wedge resection), estimated blood loss, type of vascular clamping (artery or artery and vein), WIT (starting from the clamping to the declamping of vessels), operative time, type of suture (running or interrupted), collecting system repair, use of biological glue, intraoperative complications. Intraoperative haemorrhage was defined as bleeding necessitating transfusion during the procedure, as required by the anaesthesiologists.

Post-operative data: complications which have been classified according to Clavien System [18] and subsequent treatment, post-operative hospital stay.

Pathological data: the pathologist of each Centre evaluated the surgical specimen. Tumour histology was reported; malignant tumour were classified according to World Health Organization (WHO) 2004, graded according to Fuhrman grade and staged according to 2002 Union International Contre le Cancer (UICC) revised TNM classification [19]. Data from surgical margins (positive or negative) were also collected. No frozen section analyses were reported.

In case of missing data, analyses were performed considering the available information and specifying the number of patients involved.

Statistical analyses

All data were processed through statistical software. Descriptive analysis was used to evaluate all considered variables, qualitative analyses were compared by using X^2 (Fisher exact tests), and quantitative analyses were compared by using Student's *t*-test. Multiple regression analysis was used to evaluate risk factors for complications and for positive surgical margins, blood losses, Spearman *R* test was used to investigate correlation between WIT and lesion size.

In all analyses, the differences were considered statistically significant when $P < 0.05$.

Results

This study includes all patients who underwent LPN from January 2002 to September 2008 in the six Urological Centres which answered our request. The overall number of LPN was 450 performed in six centres. In 63 patients (14%), the procedure was performed for large tumour (>4–7 cm).

The number of procedures from each institution was 24 (38.2%) from Orbassano—Torino (Italy); 22 (35%) from Bordeaux (France); 5 (7.9%) from Milano (Italy); 5 (7.9%) from Roma—Italy; 4 (6.3%) from Basel (Switzerland); and 3 (4.7%) from Linz (Austria). In each centre, a single surgeon performed all the procedures.

Demographic data and tumour characteristics are reported in Table 1.

Table 1 Demographic data and tumour characteristics

Characteristic	Total
Number of cases	63
Age, mean (SD), years	59.8
Age (range), years	27–80
Male	39 (62%)
Left kidney	25 (40%)
Tumour size, mean (SD), cm	4.7 (1.2)
Tumour size, range, cm	4.1–7
Location	
Upper pole (%)	21 (33%)
Middle (%)	15 (24%)
Lower pole (%)	27 (43%)
Growth pattern	
Central	0
Cortical	30 (47%)
Cortico-medullar	33 (53%)
Solitary kidney or non-functioning contralateral kidney	3 (4.7%)

SD standard deviation

Procedures and morbidity

Operative data are summarized in Table 2. In all patients, an intraoperative ultrasonography with laparo-endoscopic probe was performed, and enucleo-resection (tumour excision with removal of peri-tumoural healthy tissue) was also performed, and the renal artery was clamped from the beginning of tumour resection to the end of the parenchymal suture. No frozen sections were performed during the procedure.

In 8 patients (12.7%) WIT was longer than 30 min. At statistical analyses, no correlation was recorded between WIT and lesion size ($P > 0.05$) nor between WIT, side, location, growth pattern, type of suture or urinary tract repair. Hypothermia was not used in any patient.

Complete data on complications were available for 41 patients; Table 3 shows details of complications and their management. Intraoperative complications were recorded in 3 (7.3%) patients; in all patients bleeding occurred requiring conversion to open surgery but without the need of nephrectomy. Post-operative complications were recorded in 11 (26%) patients. Comparing this subgroup (14/41) with patients without complications (27/41), a significant difference was recorded in terms of pathological lesion size (4.9 vs. 4.4 cm, $P = 0.048$); moreover, a higher number of patients with cortico-medullar lesion was recorded in the first subgroup ($P = 0.02$). Multiple regression analyses confirmed the correlation between overall complications and tumour size ($P = 0.04$).

Table 2 Operative data

Characteristic	Total
Transperitoneal cases no (%)	39 (62%)
Conversion to open surgery	3/41 (7.3%)
Heminephrectomy[a]	11/63 (17%)
Estimated blood losses, mean (SD), cc	230 (143)
Operative times, mean (SD), min	154 (62)
Renal artery clamping	63 (100%)
WIT, mean (SD), min	25.7 (8.3)
WIT range, min	15–46
Running suture of renal parenchyma	36 (57%)
Interrupted suture of renal parenchyma	27 (43%)
Use of biological glue	15 (24%)
Use of bolster	3 (4.7%)
Biological glue + bolster	18 (27%)
Urinary tract repair	27 (43%)
Hospital stay, mean (SD), days	7 (3.5)

[a] Defined as >30% of kidney resection [27]

Pathological data

Pathological data are summarized in Table 4. Focal positive margins were found in 3/46 patients with malignant tumours (6.5%), and in all patients this occurred in cortico-medullar tumours. No tumour violation was recorded. In three patients (6.5%), tumour size was slightly greater than that evaluated by CT scans.

Multiple regression analyses did not reveal correlations between surgical margin status and tumour side, size, and location or growth pattern ($P > 0.05$).

Discussion

Laparoscopy has been widely used in the last decade for many urological diseases, and LPN is performed for peripheral SRMs in some centres [14–17]. On the other hand, whilst some surgeons expanded from 4 to 7 cm the size limit for OPN with excellent results, few large masses have been removed by LPN [20–27].

In order to further clarify the role of LPN for large tumours, we designed a survey involving European centres in which LPN is currently used for the treatment of renal masses.

To our knowledge, this is one of the largest series of LPN for tumour 4–7 cm in size. We have chosen cut-off size of 7 cm based on CT scans in order to include (in case of RCC) only clinical T1b stage.

Table 3 Post-operative complications

Number of cases ($n = 11$)	Type of complication	Management of complications	Grade
2	Fever	Antipyretics, antibiotics	I
1	Chiluria	Total parenteral nutrition	II
2	Retroperitoneal haematoma	Blood transfusion	II
4	Acute bleeding	Embolization [2]	IIIa
		Reoperation	IIIb
		Reoperation (nephrectomy)	IIIb
2	Urinary fistula	Endoscopic JJ placement	IIIa
		Reoperation and JJ placement	IIIb

Grade of complications are indicated according to Clavien System

Table 4 Pathological data

Histological subtypes in Benign tumours (n = 17, mean pathological size: 4.8 cm)	Number of cases (%)
Angiomyolipoma	6 (35.3%)
Oncocitoma	8 (47%)
Other	3 (17.7%)
Histological subtypes in malignant tumours (n = 46, mean pathological size: 4.6 cm)	
Clear cell carcinomas	32 (69.5%)
Papillary carcinomas	5 (10.8%)
Chromophobe carcinomas	6 (13.2%)
Other	3 (6.5)
Fuhrman grade in malignant tumours (n = 46)	
Grade 1	8 (17.2%)
Grade 2	22 (48%)
Grade 3	16 (34.8%)
Grade 4	0
T stage according to UICC classification in malignant tumour (n = 46)	
T1b	42 (91%)
T2	3 (6.5%)[a]
T3a	1 (2.5%)
Surgical margin status (n = 46)	
Positive	3 (6.5%)
Negative	43 (93.5%)

No differences in terms of lesion size was observed between the groups

[a] In these cT1b stage tumours, pathological size was greater than CT size (slightly greater than 7 cm)

Intra-operative data were comparable to those reported in literature for LPN for SRMs and for OPN and LPN for large masses [3, 8, 16, 27].

As far as renal vessels clamping and WIT are concerned in all cases, the sole renal artery was clamped from the beginning of tumour resection to the end of parenchymal suture. Nguyen et al. [26] has suggested removing the clamp before the end of renal suture in order to reduce the WIT; nevertheless, in our opinion, this technique makes suturing more difficult and can contribute to significant bleeding. We recorded a mean WIT of 25.7 min, and our data confirm that WIT during LPN is longer than during OPN. These aspects could be considered a potential advantage for OPN [3, 8]. In spite of this, one should note that WIT in the present series is comparable to that reported by many others during LPN for SRMs [14, 16, 17]. This aspect could be related to patient selection: we have not treated central lesions and all patients had elective indications. With the aim to reduce the kidney damage related to WIT, some proposed hypothermia during LPN [28, 29]. Few cases (<30) have been reported, and operative techniques are tricky and time-consuming; perhaps for these reasons, none of the surgeons involved in this survey used this approach. Nevertheless, when a large mass has to be treated and long ischemia times are supposed, this approach should be considered.

Unfortunately, we were unable to retrieve data on perioperative complications in one of the centres limiting our evaluations of this aspect to 41 cases. This could make our data less reliable. We recorded significant complications (Clavien system grade $\geq$ III) in 14% cases, and we believe that our complication rate is acceptable for this kind of surgery, and this is comparable to those reported for LPN for SRMs, LPN and OPN for large masses, even though one should note that complication rate of OPN in recent series is relatively low [8, 10, 14–17, 21, 27].

Our data confirm that bleeding is the most frequent complication during LPN, while urinary fistula is a rarer event. We point out that statistical analyses identified lesion size as a risk factor for overall complications ($P = 0.04$), and this suggests that other studies are required in order to identify a "safety cut-off" size.

Our data show that cortico-medullar lesions increased significantly the chance of complications. This suggests that the surgeon should be cautious in treating this kind of lesion laparoscopically and should offer this approach especially when a cortical lesion has to be treated.

As far as pathology is concerned, surgical margins were positive in 3 (6.5%) patients. In all cases, a focal (microscopic) interruption of normal renal parenchyma was recorded, but in no case violation of tumour was recorded. Due to these pathological characteristics, no further therapies were required, and a close follow-up was scheduled for these patients. This rate is greater than that reported after OPN, but it is comparable to those reported in the already cited recent series of LPN [16, 27]. All positive margins were recorded for cortico-medullar lesions, while no positive surgical margins were found for cortical tumours. These data, even if not statistically significant, suggest that cortical lesions were removed more effectively.

As far as RCC is concerned, when considering data about surgical margins and data about complications, we advise that cortical rather than cortico-medullar lesion should be treated with laparoscopic approach.

We did not report data concerning the follow-up of the patients, basically because of our follow-up is too short to give helpful information. Intermediate-term oncological outcomes will be reported in a further analysis for this cohort.

This survey has some limitations. First, due to its retrospective character, some information was missing. Six different surgeons and difference in centre "volume", which are crucial points in this kind of surgery, could affect the results. Even if the lack of central pathology review could be an adjunctive limitation, one should note that each

centre has an uro-pathologist experienced in kidney cancer, and this has warranted a homogeneous evaluation of specimen.

Although these limitations could affect the results, we believe that this study can give a useful message to the urological community. Our data suggest LPN could be an emerging for the treatment of the large tumours, particularly for cortical tumours. We observed a slight increase in both morbidity and WIT, in comparison with OPN, while no difference was noted in comparison with LPN data available in literature for small and large masses. Since complication rate is not negligible also in skilled hands, a significant laparoscopic experience is mandatory before embarking on LPN for large mass. Nevertheless, one should note that this is an initial experience, and further improvements will be observed for LPN for large lesions too, as usually happens with new techniques or extended indications.

Finally, we would like highlight as when a large renal mass has to be treated and the surgeon is not skilled in LPN, a well-performed OPN is better than a poor LPN or a well-performed laparoscopic radical nephrectomy.

In conclusion, this survey confirms that LPN for tumours 4–7 cm in size is feasible in experienced hand. WIT and complication rate are still questionable points, and further studies are required in order to better clarify the role of LPN in the management of this size tumour.

Conflict of interest statement There is no conflict of interest.

References

1. Hafez KS, Fergany AF, Novick AC (1999) Nephron sparing surgery for localized renal cell carcinoma: impact of tumour size on patient survival, tumour recurrence, and TNM staging. J Urol 162:1930–1933
2. Pasticier G, Timsit M-O, Badet L et al (2006) Nephron-sparing surgery for renal cell carcinoma: detailed analysis of complications over a 15-year period. Eur Urol 49:485–490
3. Patard J-J, Pantuck AJ, Crepel M et al (2007) Morbidity and clinical outcome of nephron-sparing surgery in relation to tumour size and indication. Eur Urol 52:148–154
4. Ljungberg B, Hanbury DC, Kuczyk MA et al (2007) Renal cell carcinoma guidelines. Eur Urol 51:1502–1510
5. Patard JJ, Shvarts O, Lam JS et al (2004) Safety and efficacy of partial nephrectomy for all T1 tumours based on an international multicenter experience. J Urol 171:2181–2185
6. Pahernik S, Roos F, Rohrig B, Wiesner C, Thuroff JWE (2008) lective nephron-sparing surgery for renal cell carcinoma larger than 4 cm. J Urol 179:71–74
7. Leibovich BC, BluteML ChevilleJC, Lohse CM, Weaver AL, Zincke H (2004) Nephron-sparing surgery for appropriately selected renal cell carcinoma between 4 cm and 7 cm results in outcome similar to radical nephrectomy. J Urol 171:1066–1070
8. Becker F, Siemer S, Hack M, Humke U, Ziegler M, Stockle M (2006) Excellent long-term cancer control with elective nephron-sparing surgery for selected renal cell carcinomas measuring more than 4 cm. Eur Urol 49:1058–1064
9. Dash A, Vickers AJ, Schachter LR, Bach AM, Snyder ME, Russo P (2006) Comparison of outcomes in elective partial versus radical nephrectomy for clear cell renal cell carcinoma of 4–7 cm. BJU Int 97:939–945
10. Antonelli A, Cozzoli A, Nicolai M, Simeone C et al (2008) Nephron-sparing surgery versus radical nephrectomy in the treatment of intracapsular renal cell carcinoma up to 7 cm. Eur Urol 53(4):803–809
11. Lin J, Knight EL, Hogan ML, Singh AK (2003) A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. J Am Soc Nephrol 14:2573–2580
12. Levey AS, Coresh J, Balk E et al (2003) National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 139: 137–147
13. Huang WC, Levey AS, Serio AM et al (2006) Chronic kidney disease after nephrectomy in patients with renal cortical tumours: a retrospective cohort study. Lancet Oncol 7:735–740
14. Haber G-P, Gill IS (2006) Laparoscopic partial nephrectomy: contemporary technique and outcomes. Eur Urol 49:660–665
15. Rassweiler J, Tsivian A, Kumar AV et al (2003) Oncological safety of laparoscopic surgery for urological malignancy: experience with more than 1, 000 operations. J Urol 169(6):2072–2075
16. Porpiglia F, Volpe A, Billia M, Scarpa RM (2008) Laparoscopic versus open partial nephrectomy: analysis of the current literature. Eur Urol 53(4):732–742
17. Porpiglia F, Volpe A, Billia M, Renard J, Scarpa RM (2008) Assessment of risk factors for complications of laparoscopic partial nephrectomy. Eur Urol 53:590–593
18. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–210
19. Sobin LH, Wittekind C (2003) TNM Classification of Malignant Tumours UICC International Union Against Cancer, 6th edn. Wiley-Liss, New York, pp 193–195
20. Lerner SE, Hawkins CA, Blute ML et al (1996) Disease outcome in patients with low stage renal cell carcinoma treated with nephron sparing or radical surgery. J Urol 155:1868–1873
21. Carini M, Minervini A, Lapini A, Masieri L, Serni S (2006) Simple enucleation for the treatment of renal cell carcinoma between 4 and 7 cm in greatest dimension: progression and long-term survival. J Urol 175(6):2022–2026
22. Campbell SC, Novick AC, Streem SB, Klein E, Licht M (1994) Complications of nephron-sparing surgery for renal tumours. J Urol 151:1177–1180
23. Stephenson AJ, Hakimi AA, Snyder ME, Russo P (2004) Complications of radical and partial nephrectomy in a large contemporary cohort. J Urol 171:130–134
24. Thompson RH, Leibovich BC, Lohse CM, Zincke H, Blute ML (2005) Complications of contemporary open nephron sparing surgery: a single institution experience. J Urol 174:855–858
25. Gill IS, Kavoussi LR, Lane BR et al (2007) Comparison of 1, 800 laparoscopic and open partial nephrectomies for single renal tumours. J Urol 178:41–46
26. Nguyen MM, Gill IS (2008) Halving ischemia time during laparoscopic partial nephrectomy. J Urol 179:627–632
27. Simmons MN, Chung BI, Gill IS (2009) Perioperative efficacy of laparoscopic partial nephrectomy for tumors larger than 4 cm. Eur Urol 55(1):199–207
28. Gill IS, Abreu SC, Desai MM et al (2003) Laparoscopic ice slush renal hypothermia for partial nephrectomy: the initial experience. J Urol 170:52–56
29. Janetschek G, Abdelmaksoud A, Bagheri F, Al-Zahrani H, Leeb K, Gschwendtner M (2004) Laparoscopic partial nephrectomy in cold ischemia: renal artery perfusion. J Urol 171:68–71