World J Urol (2012) 30:671–676
DOI 10.1007/s00345-012-0961-7

ORIGINAL ARTICLE

Laparoscopic and robotic partial nephrectomy without renal ischaemia for tumours larger than 4 cm: perioperative and functional outcomes

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Received: 25 June 2012 / Accepted: 20 September 2012 / Published online: 30 September 2012

Abstract
Purpose To evaluate the technical feasibility, safety and functional outcomes of zero ischaemia laparoscopic and robotic partial nephrectomy with controlled hypotension for renal tumours larger than 4 cm.
Methods We evaluated 121 consecutive patients with American Society of Anaesthesiologists (ASA) scores 1–2 who underwent laparoscopic ($n = 70$) or robotic ($n = 51$) partial nephrectomy with controlled hypotension with either tumour size $\leq$4 cm (group 1, $n = 78$) or tumour size >4 cm (group 2, $n = 43$) performed by a single surgeon from December 2010 to December 2011. Operative data, complications, serum creatinine, estimated glomerular filtration rates and effective renal plasma flow calculated from 99mTc-mercaptoacetyltriglycine renal scintigraphy were compared. Differences between groups were evaluated by the Chi-square test and the Student's t test.
Results A significant difference in mean intraoperative blood loss and postoperative complications was found between the two groups: 168 ml (range: 10–600 ml in group 1) and 205 ml (range: 90–700 ml in group 2); $p = 0.005$, and 6.4 % versus 18.6 %; $p = 0.004$, respectively. The mean percentage decrease of ERPF of the operated kidney was 1.8 % in group 1 and 4.1 % in group 2.
Conclusions Laparoscopic and robotic partial nephrectomy with controlled hypotension for tumours >4 cm in ASA 1–2 patients was feasible with significant higher intraoperative blood loss and postoperative complications compared to smaller renal masses. The benefits of avoiding hilar clamping to preserve kidney function seem excellent.

Keywords Renal ischaemia · Partial nephrectomy · Kidney tumour · Laparoscopy · Robotic · Unclamped

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Introduction

Currently, there is not a size threshold beyond which elective nephron-sparing surgery (NSS) should be excluded. For larger tumours, partial nephrectomy (PN) has demonstrated feasibility, safety and superior renal functional outcomes compared with laparoscopic radical nephrectomy [1].

Bigger tumours may require longer warm ischaemia time (WIT) to be resected. Renal artery occlusion plus a later reperfusion yields a decrease in glomerular filtration rate and urinary production undermining renal function [2].

Zero ischaemia minimally invasive partial nephrectomy (ZIMIPN) is emerging as a novel approach for NSS. Ng et al. [3] recently provided technical details to facilitate and better address the indications of the no-clamp PN procedure.

In a recent study, we evaluated the feasibility of ZIM-IPN (laparoscopic or robotic) with controlled hypotensive anaesthesia without hilar clamping, and the preliminary results were encouraging [4]. The present study focuses on evaluating the technical feasibility, safety, perioperative functional results, and expansion of indications for ZIM-IPN with transient controlled hypotension (CH) for clinical stage T1b–T2 tumours compared with T1 renal masses.

Materials and methods

From December 2010 to December 2011, 121 patients underwent zero ischaemia LPN ($n = 70$) and RAPN ($n = 51$) with CH. The surgical approach (robotic or laparoscopic) was based on robot's availability for urologists. Data were collected in an institutional prospectively maintained database. Informed consent was obtained from all patients, and the study underwent institutional review board approval. Inclusion criteria for hypotensive anaesthesia comprised all patients with American Society of Anaesthesiologists (ASA) 1–2 scores with renal tumours eligible for LPN or RAPN with CH. Nineteen patients of the group 1 and all patients of the group 2 with central tumours underwent ultraselective vascular microdissection (VMD) without CH.

All patients underwent 1-mm-slice computed tomography scan with a three-phase acquisition.

For all patients, the following information was prospectively recorded: age, body mass index (BMI), site, clinical size, PADUA, RENAL nephrometry scores, haemoglobin, creatinine value and estimated glomerular filtration rate (eGFR) using the MDRD formula, preoperatively at discharge and 3 mo thereafter, operative time, blood loss, intraoperative and postoperative transfusion, and complications. Intraoperative haemorrhage was defined as haemorrhage requiring transfusion. Postoperative haemorrhage was defined as an acute blood loss necessitating transfusion or angioembolisation. Urine leak was defined as drain output consistent with urine greater than 48 h after the procedure.

In all patients, technetium Tc 99m mercaptoacetyltriglycine (^{99m}TC-MAG-3) renal scintigraphy was performed preoperatively and 1 and 3 mo after surgery. The only exclusion criterion was an ASA score >2. All procedures were performed by a single experienced surgeon. The surgical technique with CH was described in a previous paper [4]. Informed consent was obtained from all patients, and the study received institutional review board approval. Patients were divided into two groups according to tumour size: control group 1 with tumours ≤4 cm and study group 2 with tumours >4 cm.

Differences between the groups were evaluated by the Chi-square test for categorical variables. The student's *t* test was used to verify differences in the mean values of continuous variables.

Results

Table 1 summarises the demographic data and tumour characteristics. ZIMIPN in a solitary kidney was performed only in two patients with tumours ≤4 cm. Eight patients (15 %) with ASA scores >2 were excluded from the study: six belonged to group 1 and two to group 2.

Conversion to open surgery was necessary in one patient in group 2 (2.3 %) due to excessive intraoperative bleeding impeding direct vision of the PN bed. Table 2 summarises the intraoperative data.

A significant difference in intraoperative blood loss was found between the two groups: 168 ml (range: 10–600 ml in group 1) and 205 ml (range: 90–700 ml in group 2); $p = 0.005$. A statistically significant difference concerning 90 days postoperative complications was observed for cT1b–T2 tumours compared with T1a renal masses (6.4 vs 18.6 %; $p = 0.04$).

Retroperitoneal haematoma (Clavien grade 2) treated conservatively occurred in two patients (2.5 %) in group 1 and in four patients (9.3 %) in group 2, respectively. One patient of each group experienced postoperative haemorrhage (Clavien grade 3A) treated with transarterial superselective embolisation. Urinary leakage (Clavien grade 3A) treated with ureteral stenting was observed in five patients (4.1 %), two (2.5 %) in group 1 and three (6.9 %) in group 2, respectively (Table 3).

Pathologic features are reported in Table 4. Positive surgical margins were detected in only one patient in group 2. Mean preoperative serum creatinine levels were 0.93 mg/dl in both groups; postoperative serum creatinine levels were 1.12 mg/dl in group 1 and 1.05 mg/dl in group 2.

Mean preoperative and postoperative eGFRs for groups 1 and 2 were 87.6 and 86.1 and 76.38 and 75.8 ml/min, respectively. No significant differences were found in the 3-mo eGFR values.

Seven patients did not complete the follow-up with ^{99m}TC-MAG-3 renal scintigraphy, and two patients with a solitary kidney did not receive renal scintigraphy.

Table 5 summarises the 1- and 3-month effective renal plasma flow (ERPF) of the operated and contralateral kidneys, respectively.

Discussion

MIPN with hilar clamping has usually been performed for stage T1a tumours, although its indications are continually

Table 1 Demographic data and tumour characteristics

Characteristics	Total	Tumour size		
		Group 1 (≤4 cm)	Group 2 (>4 cm)	
Patients, no. (%)	121	78 (64.5)	43 (35.5)	
Age, mean (SD), years	59.1 (14.2)	59.8 (14)	57.6 (14.5)	0.45
BMI, mean, (SD)	26 (3.27)	25.8 (3.6)	26.2 (2.5)	0.50
Sex				
Male no. (%)	82 (67.8)	51 (65)	31 (72)	0.51
Female no. (%)	39 (32.2)	27 (34.6)	12 (27.9)	
Site				
Right kidney, no. (%)	58 (48)	38 (48.7)	20 (46.5)	0.88
Left kidney, no. (%)	63 (52 %)	40 (51.2)	23 (53.4)	
Tumour size mean (SD),cm	3.9 (1.9)	2.8 (0.74)	5.9 (1.8)	<0.01
Central tumours, no. (%)	32 (26.4)	27 (34.6)	5 (11.6)	0.006
Solitary kidneys, no. (%)	2 (1.65)	2 (2.5)	0	
Mean PADUA score	–	7.6	8.5	0.01
Mean R.E.N.A.L. score	–	6.3	7.3	0.03

Table 2 Intraoperative data

Characteristics	Total	Tumour size		*p*
		Group 1 (≤4 cm)	Group 2 (>4 cm)	
Patients, no. (%)	121	78 (64.5)	43 (35.5)	
Conversion to OPN, no. (%)	1 (0.8)	0	1 (2.3)	n.e.
Pelvicaliceal repairs, no. (%)	9 (7.4)	4 (5.1)	5 (11.6)	0.35
Warm ischaemia time, mean, min	0	0	0	n.e.
Blood loss, mean (SD), ml	181.4 (116)	167.9 (101.4)	205.3 (136)	0.09
Operative time, mean (SD)	58 (11.6)	57.8 (12.3)	58.3 (10.6)	0.82
Hospital stay, mean (SD)	4.23 (1)	4.1 (0.8)	4.4 (1.3)	0.12

Table 3 Intraoperative and postoperative complications

Characteristics	Total	Tumour size		*p* value
		Group 1 (<4 cm)	Group 2 (>4 cm)	
Patients, no (%)	121	78 (64.5)	43 (35.5)	–
Intraoperative complications, no (%)	1 (0.8)	0	1 (2.3)	–
Postoperative complications, no (%)	13 (10.7)	5 (6.4 %)	8 (18.6)	0.04
Haematoma	6(4.9 %)	2 (2.5 %)	4 (9.3)	
Haemorrhage	2 (1.6 %)	1 (1.2 %)	1 (2.3)	
Urinary leakage	5 (4.1 %)	2 (2.5 %)	3 (6.9)	
Transfusions, no (%)	8 (6.6)	3 (3.8)	5 (11.6)	0.10
Superselective embolisation, no (%)	2 (1.6)	1 (1.2)	1 (2.3)	–

expanding to clinical stage T1b–T2 tumours [5, 6]. We started to perform LPN without hilar clamping by using a preoperative superselective embolisation of the arteries feeding the tumour, and this technique provided excellent oncologic and functional results [7, 8]. In a recent series, we evaluated the feasibility and safety of zero ischaemia LPN for renal masses with a low nephrometry score, highlighting how it was not indispensable to clamp the renal hilum and even a sutureless procedure was feasible in most cases [9]. Data reported by Ng et al. on the novel ZIMIPN technique with and without VMD provided encouraging outcomes. In this series, the incidence of major complications was 0 and 9 %, and the incidence of minor complications was 18 and 14 %, respectively. This

Table 4 Pathologic data

Characteristics	Total	Tumour size		*p* value
		Group 1 (≤4 cm)	Group 2 (>4 cm)	
Patients, no. (%)	121	78 (64.5)	43 (35.5)	
Carcinoma, no. (%)	89 (73.5)	53 (68)	36 (83.7)	0.36
Clear cell	70 (57.8)	41 (52.6)	29 (67.5)	
Papillary	12 (10)	9 (11.5)	3 (7)	
Chromophobe	7 (5.8)	3 (3.8)	4 (9.3)	
Benign lesions, no. (%)	32 (26.4)	25 (32.1)	7(16.2)	0.31
Grading, no. (%)	70 (57.8)	41 (52.5)	29 (67.5)	0.22
G1	7 (10)	4 (9.7)	3 (10.3)	
G2	46 (65.7)	32 (78)	14 (48.2)	
G3	19 (27.1)	10 (24.3)	9 (31)	
G4	2 (2.8)	0	2 (6.8)	
Stage, no. (%)	89 (73.5)	53 (68)	36 (84)	–
T1a	52 (58.4)	52 (98.1)	0	
T1b	30 (33.7)	4 (7.5)	26 (72.2)	
T2a	5 (5.6)	0	5 (13,8)	
T2a	1 (1.1)	0	1 (2,7)	
T3 a	3 (3.3)	0	3 (8.3)	
Positive margins, no (%)	1 (0.8)	0	1 (2.7)	–

Table 5

ERPF (mean (SD), ml/min per 1.73 m^2)	Group 1				Group 2			
	Operated kidney	*p*	Normal kidney	*p*	Operated kidney	*p*	Normal kidney	*p*
Preoperative vs 1 month	199.4(58.0) vs 174(57.1)	0.001	217.4(56.7) vs 225.4(50.6)	0.23	198.9(48.1) vs 186.3(50.8)	0.12	231.3(62.1) vs 239.7(72.4)	0.45
Preoperative vs 3 months	196.3(58.3) vs 192.7(58.4)	0.58	225.9(63.2) vs 253.6(66.4)	0.001	194.1(44.3) vs 186.2(45.1)	0.41	213.1(50.8) vs 239.1(61.2)	0.02

study concluded that even for tumours in challenging locations, the ultraselective control of tumour-specific renal arterial branches facilitates ZIMIPN. Hence, global surgical renal ischaemia was estimated to be unnecessary for most of the cases [4]. Larger renal masses are putatively more complex tumours requiring a prolonged WIT and at an increased risk of intraoperative and postoperative complications when treated in a minimally invasive fashion. To assess these hypotheses, we evaluated ZIMIPN in patients with tumours >4 cm and compared these data with outcomes of tumours ≤4 cm. The study population consisted of all consecutive ASA 1–2 patients who were candidates for MIPN. This study focussed particularly on the incidence of complications and the perioperative and short-term outcomes.

Eight patients (6.6 %) were excluded from the study due to ASA scores >2, indicating that most patients are suitable for zero ischaemia PN with transitory CH. This also shows that >90 % of patients presenting with a renal mass are relatively healthy and thus have good renal reserve. Although Huang et al. [10] reported stage 3 CKD in 27 % of patients with a small renal mass at the time of diagnosis, in our series only five patients (4.1 %) had pre-existing CKD. Factors predicting renal function outcomes after PN consist of tumour size, quality and quantity of the remnant kidney, and WIT [11]. Tumour size and the quality and quantity of the remnant kidney have to be considered an independent variable of outcomes, whereas eliminating WIT eliminates the possibility of developing ischaemic damage that has been proven to be detrimental for the renal parenchyma in any given condition [12]. This is particularly significant when treating larger renal masses where a lower percentage of kidney residues and a higher WIT might be required to complete the procedure laparoscopically or robotically. A total of 35.5 % of patients presenting a renal mass >4 cm were referred to our centre between December 2010 and December 2011. Establishing the safety of avoiding hilar clamping in those patients is mandatory.

Concerning the systemic effects of CH, no data support the hypothesis that it could be detrimental to vital organs. Induced hypotensive anaesthesia is a well-established blood-sparing technique in major surgery. Studies on the cerebral effects of hypotensive anaesthesia showed no significant differences in cognitive performance between the hypotensive and normotensive anaesthesia groups [13, 14]. The heart and the kidney are other organs believed to be commonly affected by hypotensive anaesthesia. Based on the best current evidence, deliberate hypotension seems to cause no additional adverse effects on the cardiovascular system and renal perfusion [15]. In our experience, CH was well tolerated in all patients, and there were no adverse effects. Superior intraoperative blood loss was observed in group 2 (205 ml vs 168 ml; $p = 0.005$); no statistically significant difference was detected for pelvicaliceal repair, operative time and hospital stay ($p > 0.05$). Positive surgical margins were found in one patient in group 2. Analysing the intraoperative and postoperative complications of the entire cohort (0.8 vs 10.7 %), they can be considered low, acceptable and favourably comparable with other clamped series [16].

The postoperative transfusion rate in group 2 was 11.6 %, whereas in group 1, it was 3.8 %. These data reflect the superior blood loss in group 2.

The short-term functional outcomes of this series appear encouraging. Even if a kidney is of excellent quality at baseline, renal microvessels are susceptible to noxious insults, especially to ischaemia that compromises the integrity of the endothelium and may cause early swelling and dysfunction of endothelial cells. Consequent dysfunction of endothelial cells impairs vascular reactivity, endothelial barrier function, angiogenic capability, proliferative capacity and migratory properties, and it blunts protection from inflammatory cell infiltration [17]. Hence, renal ischaemic injury secondary to pedicle clamping could appear irrelevant if we look at functional renal outcomes per se in the short term. The clinical consequences of renal ischaemia during clamped PN might be observed as long-term sequelae, which represents a strong rationale to endorse and encourage zero ischaemia PN.

Limitations of this study include the prospective cohort study, the nonrandomised study design and the acquisition of operative data from a single institution by a single experienced surgeon.

The clamping techniques remain the gold standard for MIPN in most centres, but available data on zero ischaemia PN performed in tertiary referred institutions encourage us to believe that clamping the renal pedicle could be dispensable in most cases. We await further studies to address this topic more thoroughly.

Conclusions

In high-volume centres with experienced surgeons performing the procedure, ZIMIPN for tumours larger than 4 cm is feasible. Significant higher intraoperative blood loss and postoperative complications were superior to those observed in tumours smaller then 4 cm.

Conflict of interest The authors have nothing to disclose.

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