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ORIGINAL PAPER

Safety and efficacy of retroperitoneal sutureless zero ischemia laparoscopic partial nephrectomy for low nephrometry score masses

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Summary

***Objectives:** To evaluate oncological feasibility and oncological and functional results of retroperitoneal sutureless zero ischemia laparoscopic partial nephrectomy (LPN).*
***Patients and methods:** Patients with posterior renal masses with low nephrometry score (RENAL ≤ 7) treated who underwent retroperitoneal sutureless zero ischemia.in a single center from January 2016 to November 2017. Clinical, surgical and pathological data were prospectively collected. Complications were reported according to the modified Clavien classification.*
***Results:** Retroperitoneal sutureless zero ischemia laparoscopic partial nephrectomy was performed on 15 patients. The indication for nephron-sparing surgery was elective in 11 (73%) patients and imperative in 4 (27%). Median RENAL score was 5 (IQR: 5-7), median tumor diameter 25 mm (IQR: 20-35). In 11 cases, the tumor was located polar (85%), and in 2 cases hilar (15%). There were no intraoperative complications. No cases were converted to radical nephrectomy, and in no case parenchyma suture was necessary. Median operative time was 90 min (IQR:40-150), in no case clamping of the renal artery was necessary, median hospital stay was 4 days, median estimated blood loss (EBL) was 310 (180-500) ml. Pathological analysis showed renal cell carcinoma in 11 patients (85%), 9 (60%) staged T1a and 2 (13%) T1b. In 4 (27%) an oncocytoma was found. There were no positive surgical margins. One patient developed a major postoperative complication (postoperative renal bleeding requiring super-selective embolization). Trifecta rate was 93%.*
***Conclusions:** Sutureless retroperitoneal zero ischemia LPN for the treatment of low-complexity posterior renal masses showed to be safe and feasible. Longer follow-up and higher numbers of patients are, however, warranted to draw definitive conclusions on functional outcomes.*

KEY WORDS: *Laparoscopy; Kidney cancer; Oncological surgery; Partial nephrectomy; Nephron sparing surgery.*

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INTRODUCTION

Renal cell carcinoma represents 2-3% of all cancers, with the highest incidence in Western countries. Despite this, its mortality is slightly decreasing due to earlier detection and improved surgical and non-surgical treatments made available in the last decades (1). *Radical nephrectomy* (RN) has represented the gold standard approach for years, lately different *nephron sparing* (NS) approaches (enucleo-resection, wedge resection, pure enucleation etc.) have been proposed to minimize impact on renal function granting optimal oncologic control. Multiple retrospective series have demonstrated a *comparable cancer specific survival* (CSS) for NS *vs.* RN for patients with organ-confined RCC of limited size (pT1) (2 4) making this approach the new gold standard for T1 masses. Both EAU and AUA guidelines recognize PN as a valuable option to be performed whenever feasible irrespective of the surgical approach (open or minimally invasive) (1, 5). Both transperitoneal and retroperitoneal approaches have shown to provide similar results in terms of oncologic and surgical safety, with the retroperitoneal one being fitter for posterior located masses (6-8).
Nevertheless, improvements need to be performed to implement post-operative renal function preservation. Both ischemia time and parenchyma loss have been demonstrated to contribute to post-operative renal damage (9, 10). Along with complete tumor extirpation without complications, the primary goal for an ideal PN is the maximal preservation of *renal function* (RF) (11). Indeed, as suggested by extensive evidence, an impaired postoperative RF increases the risk of cardiovascular disease, use of specialized health care and death (12). With this regard, quantity and quality of preserved renal parenchyma are the most important determinants of functional recovery after surgery, with type and duration of ischemia possibly playing a secondary role (10).
Considering this, efforts should be done in both reducing (or eliminating, whenever feasible) ischemia time and reducing the amount of healthy parenchyma removed during tumor resection or destroyed with the haemostatic suture.
Objective of this study is to describe retroperitoneoscopic sutureless zero ischemia partial nephrectomy technique assessing its feasibility and safety, as well as short-term oncologic and functional outcomes.

No conflict of interest declared.

Patients and methods

Study population

From January 2016 to November 2017, 40 consecutive patients with localized renal masses were treated by a single experienced surgeon (FF) in a single institution, with zero ischemia tumor enucleation PN. Every patient gave written informed consent to be included in our prospectively maintained institutional database, where clinicopathological data as well as follow-up and complication data of every patient were recorded. Approval for the study was granted by the hospital ethics committee and the study conformed to the provisions of the *Declaration of Helsinki*. Comorbidity status was assessed using *Charson Comorbidity Index* (CCI) (13) and the *American Association of Anesthesiologists* (ASA) scores (14).

Figure 1.
Flank position, angled at IX-X coastal level for the left side and angled at X-XI coastal level for the right side to better expose the triangle of Petit.

Clinical procedure and patient monitoring

Fifteen patients with low nephrometry score (RENAL ≤ 7) renal masses, located on the posterior surface, were treated using retroperitoneal sutureless zero ischemia approach. Pre-operative exclusion criteria for sutureless technique was tumor close contact with collecting system at preoperative CT scan. The remaining patients treated at the hospital during the study timeframe underwent both transperitoneal PN according to mass location and, for those, sutures were used only for the more complex neoplasms, or to repair damaged collecting systems. Hemoglobin was dosed preoperatively, then 24 hours after intervention to detect potential postoperative bleeding. Renal function was assessed using the *estimated glomerular filtration rate* (eGFR), calculated with the *modification of diet in renal disease* (MDRD) equation (15) preoperatively, at discharge and at 3-mo post-operative visit.

Study endpoint

Primary endpoint was to assess feasibility and safety of retroperitoneal zero ischemia sutureless partial nephrectomy, secondary endpoint was renal function preservation and short-term oncologic outcomes.

Surgical technique

Patient's position and access to the retroperitoneum

The patient was placed on flank position, angled at IX-X coastal level for the left side and angled at X-XI coastal level for the right side to better expose the triangle of Petit (Figure 1).

The first incision was performed 3 cm above the iliac ridge, on the mid-auxiliary line. A blunt dissection of the anterior component of the lumbar-dorsal fascia with Mayo scissors and subsequently digital dissection is performed until the identification of the postero-lateral surface of the psoas muscle and the distal portion of Gerota's fascia. An inflatable space maker balloon is used to develop the retroperitoneal space. The remaining 2 trocars are placed under digital guide: the anterior one (10 mm) 2 cm above the optical trocar, keeping as much distance as possible from the peritoneal reflection. The posterior trocar, 2 cm higher than the optical trocar, on the posterior axillary or in some cases (depending on the body shape) between the angular line of the scapula and the posterior axillary line. As this trocar is placed through the mass of the large dorsal muscle limiting movements in laterality we prefer to use a 5-mm trocar. A 4^{th} trocar, usually placed at the apex of the 12^{th} coast is inserted during the intervention.

An intra-abdominal pressure between 12 and 15 mmHg was used during the entire intervention.

Identification of the mass and resection

The peritoneal reflection until the vena cava (right side) or ureter (left side) is identified. Subsequently, the surface of the psoas muscle is released, under the Gerota capsule, up to its proximal insertion on the diaphragm (Figure 2a). Laterally, the lateral-conal fascia is freed until the diaphragmatic insertion, to achieve posterior and lateral mobilization of the pre-renal fat. Gerota's fascia is bluntly dissected cranially, along the renal convexity, starting from its lower apex. The dissection of the perinephric fat is continued until the mass is identified (Figure 2b).

Figure 2.
A) *surface of the psoas muscle is released;* ***B)*** *dissection of the perinephric fat until the mass is identified;* ***C)*** *identifying the vascular pole of the neoplasm;* ***D)*** *coagulation with bipolar forceps along the enucleation margin.*

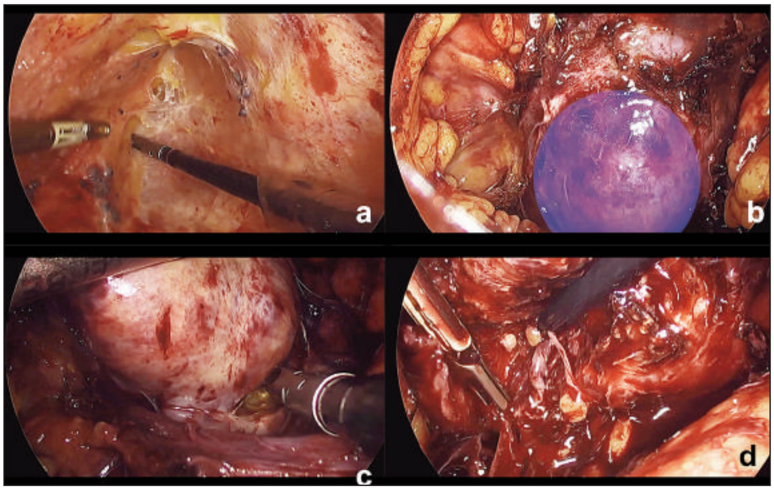
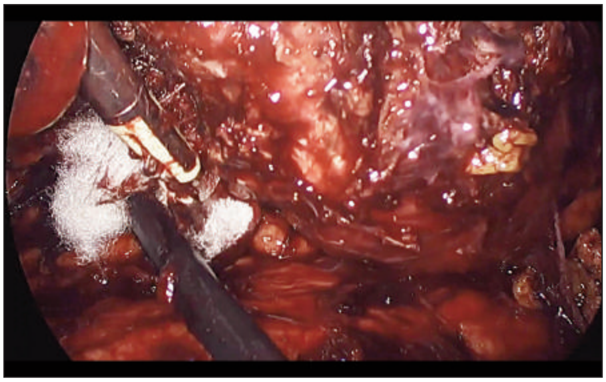


Figure 3.
Fibrin-based glue is applied on the resection area.



Identification of the vascular supply and hemostasis
The resection of the mass is performed with the aim of tumor enucleation whenever possible, using monopolar scissors and suction. This step is performed totally clampless, for this reason, identifying as soon as possible the vascular pole of the neoplasm, who's generally represented by an arterial branch lying on the resection burden, is crucial. Useful for this purpose is the blunt dissection performed with the tip of the suction device or with the bipolar forceps (Figure 2c), rising the lesion bottom to top, while the scissor proceeds with mechanical detachment, pandering to the convexity of the lesion. The vascular pole of the renal tumor is usually coagulated with bipolar forceps, except for some cases where the use of a titanium clip is mandatory due to the presence of larger vessels. The margins of the enucleation are not particularly bloody when the neoplasm is located at the lower pole, on the convexity (along the Brodel line, at whose level the interlobar vessels are thinner and fold medially towards the renal sinus), or at the upper pole. In these cases, coagulation with bipolar forceps is sufficient along the enucleation margin (Figure 2d). Conversely, when lesions are located on the posterior surface of the kidney, the risk to have more than one vascular pole is higher. In those cases, clipping of larger arterial branches could be necessary.

Final remarks
At the end of the procedure the pneumoretroperitoneum is lowered until 5 mm Hg to check for any residual bleeding.
Thereafter, fibrin-based glue (*Floseal - Baxter, USA*) or gauze (*Tabotamp - Ethicon, Inc., Somerville, NJ*) is applied on the resection area (Figure 3). In our experience this practice resulted more useful for lesions on the posterior surface of the kidney, where intra-renal vascular branches are more extensive.
Surgical specimen is removed using an endo-bag through the anterior trocar: this to avoid further stress, at the margins of the lumbar-dorsal fascia, which would lead to greater risk of hernial failure. No drain is left in place.

Postoperative measures
Pathological examination was performed by a dedicated uro-pathologist according to the 2016 *World Health Organization criteria* (16) and to the Fuhrman classification (17). Positive surgical margin was defined as cancer cells at the level of the inked parenchymal excision surface. The severity of complications was reported according to the modified Clavien Classification (18).
The Trifecta rate was calculated as the combination of warm ischemia time < 25 min, negative surgical margins and no complications (up to 90-day follow-up)(11). Patients were followed in outpatient setting 3 months after surgery and every 6 months for the first two years, then yearly. The follow-up protocol included: clinical visit, physical examination and a metabolic panel at 1, 3 and 6 month, annually thereafter; *computed tomography* (CT) at 6 and 12 month, annually thereafter. Patients were planned to be discharged at 4th post-operative day as per hospital protocol, eGFR was assessed at discharge and at 3 months post-operative visit.

RESULTS
The indication for nephron-sparing surgery was elective

Table 1.
Preoperative characteristics.

	Sutureless retroperitoneal (n = 15)	Transperitoneal (n = 25)	Overall (n = 40)	P value
Age, years, mean (SD)	64.0 (13.70)	61.4 (11.71)	62.0 (10.94)	> 0.05
BMI, Kg/m^2, mean (SD)	25.03 (2.11)	25.9 (2.14)	26.00 (2.12)	> 0.05
Sex m/f	8/7	17/8	25/15	> 0.05
ASA score, n (%)				> 0.05
1	3 (20)	7 (28)	10 (25)	
2	11 (73)	16 (64)	27 (67.5)	
3	1 (7)	2 (8)	3 (7.5)	
CCI, median (IQR)	4 (3-4)	4 (3-4)	4 (3-4)	> 0.05
Affected kidney				> 0.05
Right	5 (33)	14 (56)	19 (47.5)	
Left	10 (67)	11 (44)	21 (52.5)	
Tumor size, mm, median (IQR)	25 (20-35)	28 (2.5-4)	30 (25-35)	> 0.05
RENAL Score				> 0.05
< 5	3 (20)	2 (8)	5 (12.5)	
5-6	8 (53)	11 (44)	19 (47.5)	
7	4 (27)	6 (24)	10 (25)	
> 7	-	6 (24)	6 (15)	
Tumor location				> 0.05
Polar	13 (87)	18 (72)	31 (77.5)	
Hilar	2 (13)	7 (28)	9 (22.5)	
Exophitic rate				> 0.05
< 50%	5 (33)	7 (28)	12 (30)	
≥ 50%	10 (67)	18 (72)	28 (70)	
PN indication				> 0.05
Imperative	4 (27)	2 (8)	6 (15)	
Elective	11 (73)	23 (92)	34 (85)	

Table 2.
Post-operative outcomes.

	Sutureless retroperitoneal (n = 15)	Transperitoneal (n = 25)	Overall (n = 40)	P value
Operative time, min, mean (SD)	100 (31.5)	130 (31.4)	115 (33.2)	> 0.05
Length of stay, d, mean (SD)	4.13 (0.37)	4.7 (0.88)	4.55 (1.45)	> 0.05
Estimated blood loss, ml, mean (SD)	370 (299)	425 (285)	410 (275)	> 0.05
Histology, n (%)				> 0.05
Oncocytoma	4 (26.6)	2 (8)	6 (15)	
Renal Cell carcinoma	11 (73.4)	23 (92)	34 (85)	
Positive surgical margin, n (%)	0 (0)	0	0 (0)	
Maximal tumour-kidney margin, mm, mean (SD)	4.1 (0.7)	4.6 (1.2)	4.4 (0.8)	> 0.05
pT Stage				> 0.05
T1a	9 (60)	18 (72)	27 (67.5)	
T1b	2 (13.3)	3 (12)	5 (12.5)	
≥T2	0 (0)	2 (8)	2 (5)	
Fuhrman grade (for RCC), n (%)				> 0.05
I	2 (13.3)	3 (12)	5 (12.5)	
II	7 (46.7)	18 (72)	25 (62.5)	
≥III	2 (13.3)	2 (8)	4 (10)	
Complications*				> 0.05
I	3 (20)	2 (8)	5 (12.5)	
II	-	1 (4)	1 (2.5)	
≥III	1 (6.7)	1 (4)	2 (5)	
Mean (SD) eGFR				> 0.05
Preoperative	85.23 (29.95)	81.34 (24.22)	80.59 (24.28)	
Discharge	74.77 (23.22)	72.34 (21.24)	71.89 (21.31)	
3-Mo post-OP	81.78 (16.77)	79.12 (17.10)	69.25 (16.52)	

**According to Clavien-Dindo classification.*

	Present study	*Simone et al.*	*Minervini et al.*
Overall study population, n	15	380	100
Overall sutureless procedures, n (%)	15 (100)	101(26.6)	32 (32)
Transeritoneal	-	101 (26.6)	N.A.
Retroperitoneal	15 (100)	-	N.A.
Clampless Procedures, n (%)	15 (100)	101 (100)	18 (56.3)
RENAL score			
<5	3 (20)	94 (93.1)	N.A.
5-6	8 (53)	7 (6.9)	N.A.
7	4 (27)	-	N.A.
Tumour size, mm, median (IQR)	25 (20-35)	24 (15-40)	19 (15-21)
Exophytic rate, n (%)			
<50%	5 (33)	N.A.	5 (17)
≥50%	10(67)	N.A.	27 (83)
Sex m/f	8/7	63/38	N.A.
ASA score			
1	3 (20)	45 (44.6)	N.A.
2	11 (73)	30 (29.7)	N.A.
3	1 (7)	26 (25.7)	N.A.
Age, years, median (range)	68 (28-70)	59 (45-73)	62 (46-80)
BMI, Kg/m^2, meadian (IQR)	25.0 (24.2-27.6)	N.A.	26 (19.5-35)
Tumour location			
Polar	13 (87)	96 (95.1)	32 (100)
Hilar	2 (13)	5 (4.9)	-
Operative time, min, median (range)	90 (40-150)	60 (45-160)	115 (80-180)
sCr, mg/dL, median (range)			
Preoperative	0.8 (0.6-1.7)	0.9 (0.6-1.3)	N.A.
At discharge	0.9 (0.6-1.8)	-	N.A.
3-mo post-op	0.9 (0.6-1.9)	1 (0.6-1.4)	N.A.
eGFR, ml/min, median (range)			
Preoperative	88 (40-135)	96 (60-120)	N.A.
At discharge	79 (37-124)	-	N.A.
3-mo post-op	90 (36-121)	93 (58-125)	N.A.
Completed sutureless	15 (100)	97 (96)	32 (100) §

§ Supposed, as no clear statement for the authors is available in the manuscript.

in 11 (73%) patients and imperative in 4 (27%), of those 3 presented a solitary kidney and one had impaired renal function. Preoperative median (IQR) eGFR was 88 (40-135) ml/min/1.73 m^2. Median RENAL score was 5 (IQR: 5-7), median tumor diameter 25 mm (IQR: 20-35); 4 (27%) patients presented a mass with a RENAL score of 7. The tumor was located polar in 13 (87%) cases and hilar in 2 (13%) cases. Further patients' characteristics for the study population compared to the entire cohort of treated patients are listed in Table 1.

All interventions were successfully completed, with no report of intraoperative complication. No vascular lesions occurred during the procedure; no cases were converted to radical nephrectomy, in no case the use of parenchymal suture was necessary.

Median (IQR) operative time was 90 (40-150) min. All procedures were completed with zero ischemia technique as in no case clamping of the renal artery was necessary. Mean (SD) hospital stay was 4.1 (0.4) days. Median (IQR) GFR was 79 (37-124) at discharge and 90 (36-121) at 3-month post-operative visit. Median IQR GRF median (IQR) EBL was 310 (180-500) ml. Pathological analysis showed renal cell carcinoma in 11 patients (73%), 9 (60%) staged T1a and 2 (13%) T1b. In 4 (27%) an oncocytoma was found. There were no positive surgical margins. One patient (7%) developed a major postoperative complication, post-operative renal bleeding requiring super-selective embolization, while 3 (20%) developed minor complications (Clavien I). Trifecta was achieved in 93% of the patients treated with sutureless retroperitoneal approach. Furthermore, oncologic and functional results were similar when compared to the transperitoneal cohort (Table 2).

Comment

The reports on lower incidence of post-operative acute kidney injury and *chronic kidney disease* (CKD) after off-clamp PN in the solitary kidney model led to an increased use of this approach for all patients, possibly to avoid the detrimental effect of ischemia on RF (19).

Whereas the functional benefit of the off-clamp technique has been suggested by several authors both for patients with solitary and normal contralateral kidney (20-23), most of the studies do not include data on resection and reconstruction technique thus potentially either underestimate or overrate the actual effect of arterial clamping.

Pure tumor enucleation, for those reasons, could help in preserving the maximal amount of healthy parenchyma granting comparable oncologic and surgical outcomes of conventional partial nephrectomy in T1 renal cancer, as previously reported (24), facilitating a better recovery of post-operative renal function (25), although no general consensus exists yet.

Clampless approach, avoids on one side ischemia-related renal damage (26, 27) and on the other side, it permits to avoid any possible vascular damage related to hilum dissection reducing the time of the intervention. Additionally, in experienced hands, clampless approach could facilitate the surgeon to identify major arterial branches and seal it during enucleation.

Renal function was assessed at discharge and at 3-months post-op visit as per-hospital protocol, after this period, as previously described, no intervention related variations in RF should occur (28).

Renal function was not particularly affected as reported in Table 2, no de novo CKD grade ≥ 3a occurred. Additionally, the only two patients with a GFR in the range of CKD stage 3 did not experience any notable decrease in RF. The transitory decrease in RF evidenced at discharge, and the complete restoration of the original GFR values for most of the patients in our series could be considered a consequence of the off-clamp approach, as well as the enucleative technique.

Previous experiences with sutureless PN were reported, showing that under certain conditions it is a safe and effective procedure (29, 30) (Table 3). This study confirms previous experiences, demonstrating that this technique may also be applicable for masses with a RENAL score up to 7, without compromising oncologic and functional outcomes.

Main limitations of this study include small sample size and retrospective nature of the analysis, although data collection was prospective. Nonetheless, present study is unique as it represents the first, to our knowledge, description of this technique. Furthermore, our series investigates feasibility and safety retroperitoneoscopic clampless sutureless partial nephrectomy, reporting functional outcomes and trifecta rate with a minimum follow-up length of 6 mo.

Further studies, employing renal scintigraphy may help determine the real impact of the technique on the operated kidney parenchyma especially in case of imperative indication.

Although not comparable with larger series of PN, due to the very selective nature of the cohort and the short follow up period, our preliminary experience showed feasibility and safety of sutureless retroperitoneal zero ischemia LPN for the treatment of low-complexity (up to RENAL 7 score) posterior renal masses.

Longer follow-up and higher numbers of patients are, however, warranted to draw definitive conclusions.

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