Original Article

Laparoscopic partial nephrectomy in obese patients: how can the body mass index influence the surgical and functional outcomes?

Francesco Greco[1,2], Francesco Lembo[1,2]

Department of Urology, Policlinico S Pietro, Gruppo San Donato, Bergamo
Urology Unit, Centro Salute Uomo, Bergamo

Corresponding author: Prof Francesco Greco
Department of Urology, Policlinico S Pietro, Gruppo San Donato and
Centro Salute Uomo, Bergamo
E-Mail: francesco_greco@ymail.com

Abstract

Objective: To evaluate the impact of body mass index (BMI) on surgical and functional outcomes of laparoscopic partial nephrectomy (LPN) for T1 renal tumors.

Patients and methods: In this retrospective single-centre study, 240 consecutive patients underwent LPN for localized incidentally discovered renal masses of < 7 cm (cT1). Patients were categorized into four groups according to their BMI, as follows: group 1, normal weight (BMI < 25 kg/m2); group 2, overweight (BMI 25 - 29.9 kg/m2); group 3, obese (BMI 30 - 39.9 kg/m2); and group 4, morbidly obese (BMI ≥ 40 kg/m2).

Results: The median operative time presented no statistically significant differences between BMI, whereas estimated blood loss was higher in morbidly obese patients than in all other groups. Warm ischemia time (WIT) and changes in eGFR were not influenced by the BMI groups but a decrease in the WIT was reported for obese and morbidly obese patients when an early unclamping technique (EUT) was used. An increase in BMI was not significantly associated with the occurrence of postoperative complications. In fact, the median complication rate was 3.3% for normal BMI, 4.5 % for overweight patients, 4.8% for obese, and 3.6% for morbidly obese patients.

Conclusion: LPN could be considered a viable treatment option for renal masses amenable to nephron-sparing surgery in patients with higher BMI. An EUT should be always used in obese and morbidly obese individuals, considering the statistically significant decrease of the WIT and the higher risk for chronic renal insufficiency in those patients.

Keywords: kidney cancer, partial nephrectomy, laparoscopy, obesity, surgical outcomes

1. Introduction

The widespread use of modern imaging methods has led to the earlier diagnosis and improved staging of renal cell carcinoma (RCC), resulting in a marked increase in the number of renal tumors detected incidentally in patients with no urological symptoms [1].

These tumors are often of lower grade and stage and the need for RN for such asymptomatic locally confined lesions has therefore been questioned. Nephron-sparing surgery (NSS) could offer a good alternative for small renal lesions (<4 cm) [1-3]. Whereas open NSS represents the gold standard in the surgical therapy of T1 renal tumors [1], with the advances in laparoscopic surgery, the refinement of intracorporeal suturing, and the availability of haemosealant substances, the laparoscopic approach has recently gained popularity for NSS. However, laparoscopic partial nephrectomy (LPN) is currently performed in a few high-volume reference centers, and its diffusion has been limited by the steep learning curve [1].

Because laparoscopy is generally less invasive than an open surgical technique, laparoscopy may be preferable if it can be shown to achieve the same results, with the same safety for the patient.

Obesity represents a major health problem in industrialized countries, where its prevalence has dramatically increased over the last two decades. In the United States, 25.6% to 29% of adults aged 40 years or older were considered obese in 2005[4]. A higher risk of developing renal cell carcinoma (RCC) has been found in obese patients than in non-obese patients [5-7], and currently, most patients undergoing surgical treatment for RCC are overweight or obese.

On the other hand, improved survival after partial nephrectomy has been reported in obese patients with organ-confined disease [8-10]

The objective of the present study was to investigate if LPN could be safely performed in obese and morbidly obese patients when compared with non-obese ones.

2. Patients and methods

This was a retrospective single-center study including 240 patients who underwent LPN between May 2001 and April 2013.

Patients were categorized into four groups according to their BMI, as follows: group 1, normal weight (BMI < 25 kg/m^2); group 2, overweight (BMI 25 – 29.9 kg/m^2); group 3, obese (BMI 30 – 39.9 kg/m^2) and group 4, morbidly obese (BMI $\geqslant$ 40 kg/m^2) [8,11].

The study was approved by the institutional review board. Written informed consent was obtained from all patients. All operations were performed for localized incidentally discovered renal masses of < 7 cm (cT1); all indications were elective.

Before surgery, all patients underwent renal ultrasonography and CT to give detailed information about tumor size, location, extent of parenchymal infiltration, proximity to the pelvi-calyceal system.

Patients with severe heart failure (The New York Heart Association Functional Classification III–IV), chronic renal insufficiency, and/or with an American Society of Anesthesiology (ASA) score of ≥ 3 were excluded from this study.

Demographic data, peri- and postoperative variables, including operative duration, estimated blood loss, warm ischemia time (WIT), complications, hospital stay, renal function, histological tumor staging, and surgical margins were collected and analyzed. The function of the kidney was evaluated by measuring estimated GFR (eGFR) preoperatively and at 1-year follow-up. eGFR was calculated using the modification of diet renal disease (MDRD)-equation.

All complications were recorded with a grade (I, II, IIIa, IIIb, IVa, IVb, or V) assigned according to the modified Dindo-Clavien classification [12].

The R.E.N.A.L (tumor size-[R]adius, location and depth-[E]xophytic or endophytic; nearness to the renal sinus fat or collecting system [N]; anterior or posterior position [A], and polar vs non-polar location [L]) nephrometry score was used to assess the characteristics of the tumors in all groups [13].

All operations were performed by two surgeons (F.G., P.F.), who had completed at least 100 LPNs each before the beginning of the study, thus reducing the learning-curve effect.

Our surgical techniques were previously reported [14]. Shortly, a transperitoneal approach was used in all patients. The renal artery was clamped with one laparoscopic bulldog clamp. The tumour was excised with cold scissor in a near-bloodless field. Targeted excisional biopsies of the tumour bed were sent for frozen section in case of suspicion regarding margin status.

Collecting system was suture repaired with a running 2-0 Vicryl on CT-1 needle. Renal parenchymal repair was performed with three to five interrupted sutures. A Hem-o-Lok clip was secured on the suture to prevent it from pulling through. Another Hem-o-Lok clip was applied to the suture flush with the opposite renal surface, compressing the kidney. The bulldog clamp was then removed and fibrin glue was applied to the cut renal parenchymal surface. The en bloc specimen is extracted in an Endocath (Covidien formerly Tyco Healthcare GmbH, Neustadt/Donau, Germany) and a flat suction drain was placed in the renal loge. Since 2008, we adopted an early unclamping technique in order to minimize the warm ischemia time. In patients undergoing LPN with an early unclamping, only the initial collecting system suturing was performed under ischemia, with the renal parenchymal repair of the bolstered renorrhaphy being performed in the re-vascularized kidney.

The median follow-up period was 45.7 ±18.4 months**.** Follow-up was calculated from the date of surgery to the date of the most recent documented examination. In all

patients a physical examination and ultrasonography were performed every 3 months in the first year, every 6 months in the second and third years and yearly thereafter. CT or MRI was performed every 6 months in the first and second years, and yearly in the third, fourth and fifth years after surgery.

Statistical analysis was performed using SigmaPlot® software version 11.0 (SPSS Inc., Chicago, IL, USA). Patients' baseline characteristics and surgical outcomes were reported as frequencies (percentages) for categorical variables, median and interquartile range (IQR) for continuous ones and statistical significance was accepted at $p < 0.05$. Fisher's exact test was applied to evaluate statistical between-group differences in pathological stages.

3. Results

The baseline characteristics of the patients are summarized in **Table 1.**

Table 1 Preoperative patient data

Variables	**Normal weight (n=60)**	**Overweight (n=110)**	**Obese (n=42)**	**Morbidly obese (n=28)**	***p-value***
Median (IQR) age, years	56 (40-67)	58 (44-77)	58 (49-74)	56.5 (50-73)	*0.3*
Median (IQR) ASA-score	2 (2 – 3)	2 (2 – 3)	3 (2 – 3)	3 (2 – 3)	*0.03*
Men/women, n	42/18	70/40	23/19	16/12	*0.18*
Left/right kidney, n	39/21	53/57	24/18	17/11	*0.16*
Median (IQR) tumor size, cm	3.2 (2-6)	2.8 (1.5-6)	3.3 (2-5)	3.1 (2-5)	*0.4*
Median (IQR) R.E.N.A.L. nephrometry score	7 (5 – 9)	7 (5 – 9)	7 (6 – 9)	7 (6-8)	*0.5*
Median (IQR) preoperative glomerular filtration rate, mL/min/1.72m^2	92 (82-98)	89 (73-97)	88.5 (72-95)	88 (70-93)	*0.07*

Of 240 patients, 60 (25% of the entire cohort) were non-obese, 110 (45.8%) were overweight, 42 (17.5%) were obese, and 28
(11.7%) were morbidly obese. There was a higher ASA score in obese and morbidly obese patients than in others (*P* = 0.03). The median (IQR) R.E.N.A.L nephrometry score per group was 7(5 – 9) for normal BMI, 7 (5 – 9) for overweight patients, 7 (6 – 9) for obese and 7 (6-8) for morbidly obese patients (*P* = 0.5)

The median operative time presented no statistically significant differences between BMI groups (*P = 0.4),* whereas estimated blood loss was higher in morbidly obese patients than in all other groups (median 200 ml vs 150, 155 and 160 ml for normal weight, overweight and obese patients, respectively, *P = 0.03* **Table 2**).

Warm ischemia time and changes in eGFR were not influenced by the BMI groups and no kidney was postoperatively lost because of warm ischaemic injury. Concerning the WIT, we noted statistically significant differences only in the 3 and 4 groups in presence of delayed (DUT) vs early unclamping technique (EUT) [group 3: median DUT/WIT: 16.2 min; median EUT/WIT: 11.5min (p=0.03); group 4: median DUT/WIT: 17 min; median EUT/WIT: 12.2min (p=0.02)] **(Table 2).**

Mean (IQR) hospital stay did not present any statistically significant difference between the 4 groups (*P = 0.2*).

Furthermore, an increase in BMI was not significantly associated with the occurrence of postoperative complications. In fact, the median complication rate was 3.3% for normal BMI, 4.5 % for overweight patients, 4.8% for obese, and 3.6% for morbidly obese patients (*P = 0.2*). There were no grade 4 or 5 complications and no conversion to radical nephrectomy was necessary.

Table 2 Intra- and postoperative patient data

Variables	Normal weight (n=60)	Overweight (n=110)	Obese (n=42)	Morbidly obese (n=28)	*p-value*
Median operating time, min	145 (90-180)	150 (110-210)	155 (130-210)	160 (145-230)	*0.4*
Median (IQR) EBL ml	150 (100-210)	155 (100-250)	160 (150-280)	200 (180-450)	*0.03*
Median (IQR) WIT, min	11 (7-18)	11 (7-18)	13 (11-20)	15 (12-20)	*0.06*
EUT (min)	9.7 (7-14)	10.7 (7-14)	11.5 (9-15)	12.2 (10-15)	*0.06*
DUT (min)	11.1 (9-14)	12.1 (10-15)	16.2 (14-20)	17 (15-20)	*0.03*
Postoperative transfusion, n [%]	1 (1.67)	1 (0.9)	1 (2.4)	1 (3.6)	*0.5*
Complication rates, n (%)	2 (3.3)	5 (4.5)	2 (4.8)	1 (3.6)	*0.2*
Median (IQR) hospital stay, days	4 (3-6)	4 (3-7)	4.5 (4-6)	5 (4-7)	*0. 2*
Median (IQR) postoperative glomerular filtration rate, mL/min/1.72m^2 (at 1-year-follow-up)	88 (79-95)	85 (69-95)	84.5 (69-90)	84 (65-90)	*0.07*

The definitive pathological results showed a high incidence of clear-cell tumors in all groups. Surgical margins were positive only in 2 (1.8%) overweight patients and in 1 obese patient (2.3 %) (*p=0.3* ; **Table 3**). In one overweight patient, a tumor seeding to the port site developed 24 months after surgery.

Table 3: Oncologic outcomes

Tumour stage (n):					
pT1a	44	99	32	19	*0.3*
pT1b	16	11	10	9	
Median tumor size, cm:	3.7 (2.5-6)	3.3 (2-6)	3.6 (2-6)	3.4 (2-6)	*0.4*
Cell type, %:					
clear-cell	78	82	84	83	*0.2*
chromophobe	12	10	9	12	
oncocytoma	6	5	5	3	
angiomyolipom	4	3	2	2	
Positive margins, n (%):	0	2 (1.8%)	1 (2.3 %)	0	*0.3*

4. Discussion

Obesity is a medical condition in which excess body fat (BMI of 30 or greater) has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and/or increased health problems [15]. Obese or older patients frequently have associated medical conditions (e.g. diabetes, heart failure, hypertension, and renal failure), which are not prone to further improvement.

Furthermore, obesity has been associated with increased incidence of several cancers, including of the esophagus, pancreas, colon, breast and kidney [8,16]. There is no direct explanation as to the role of obesity in the development of cancer but it has been related to chronic tissue hypoxia, insulin resistance, compensatory hyperinsulinemia, obesity-induced inflammatory response, and lipid peroxidation [8,17], an increased concentration of adipokines that support tumor growth and a lower concentration of the tumor suppressor adiponectin [8,18].

Such patients have diminished reserves and tolerance to complications, and they are usually assigned a higher ASA score. The above-mentioned comorbidities increase the risk of postoperative complications and make anesthesia riskier [15].

Laparoscopic surgery in obese patients is likely to be more technically demanding, with the possible need for longer trocars, decreased range of motion, and an increase in the volume of retroperitoneal adipose tissue surrounding the kidney [19]. Nevertheless, it is well known that these patients can extremely benefit from a minimally invasive surgical approach, which, through a minor surgical trauma, decreases postoperative morbidity [20-23].

NSS has been initially reserved for patients at high risk of developing renal failure after kidney surgery to treat renal cancer and open partial nephrectomy (OPN) to be equivalent to open radical nephrectomy in terms of long-term cancer-free survival with unilateral renal involvement, unifocal disease and a tumor size of < 4 cm [24].
In the last years, LPN has been proposed to be a valid alternative to OPN for the therapy of T1 RCC [14, 25,26].
The anatomical characterization of renal tumors before LPN is fundamental for a correct evaluation of the outcomes [27]. The first anatomical characterization to evaluate the predictable difficulty of NSS was reported by Kutikov et al. [13].
After categorizing the patient population into four groups based on BMI according to the WHO classification of obesity, the BMI groups did not present any statistically significant difference for tumor size and R.E.N.A.L. nephrometry score and they were also equivalent in relation to age and gender distribution.
In 2007, Gong et al. [21]. reported on their experience of laparoscopic kidney surgery in the obese population. They also separated their cohort based on BMI, and they also found laparoscopy in obese patient to be feasible. Nevertheless, the authors could not provide any correlation between BMI, R.E.N.A.L scores, surgical techniques (EUT vs DUT),WIT and renal function.
The more widespread use of grading schemes in reporting complications has facilitated standardization to some degree. Dindo et al. [12] proposed a modification of the Clavien system of surgical complications. When we applied this system to the present data, an increase in BMI was not significantly associated with the occurrence of postoperative complications, with a median complication rate of 3.3% for normal BMI, 4.5 % for overweight patients, 4.8% for obese, and 3.6% for morbidly obese patients. Moreover, any grade 4 or 5 complications could be registered.
In all patients it could be achieved a WIT ≤ 20 minutes, whereas a WIT ≤ 15 min was reached when using an EUT. This is an advantage of the laparoscopic technique, where the presence of the pneumoperitoneum, with an intra-abdominal pressure set at 15–20 mmHg, avoids possible bleeding from small vessels allowing resection of the tumor even with unclamped renal vessels [14]. Interestingly, an important advantage in terms of WIT was noted when an EUT was used in obese and morbidly obese patients. The best cut-off to consider for a safe NSS procedure has been debated over the last few years, and it has been recently suggested to be 20 minutes. In general, the concept that every minute of ischemia may count is recognized considering that WIT can affect the postoperative renal function [28].
This represents an important aspect to be considered when performing LPN, as obesity increases the risk of developing chronic renal insufficiency, above all in elderly patients [29].

Nevertheless, at 1-year follow-up, there was no statistically significant difference in the eGFRs between the groups and this can be explained by the young age of the recruited patients.

Our data are comparable with the outcomes described in obese patients after LPN reported in the literature [4-9]

Colombo et al. [7] compared the perioperative outcome of laparoscopic partial nephrectomy in obese and non-obese patients, using a cohort of patients undergoing retroperitoneal or transperitoneal approach. There was no significant difference between groups regarding EBL, operation duration, WIT, conversion rate, or hospital stay for the transperitoneal approach group.

In another study performed by Feder *et al.* [30], analyzing patients who underwent laparoscopic partial or radical nephrectomy, there was also no significant difference between obese and non-obese groups with regard to EBL, operation duration, hospital stay, and number of open conversions or complications.

Concerning the oncological data, we noted a higher incidence of clear-cell tumors in all 4 groups. Surgical margins were positive only in 2 (1.8%) overweight patients and in 1 obese patient (2.3 %)**.** Moreover, in one overweight patient, a tumor seeding to the port site developed 24 months after surgery, due to a rupture of the specimen during the procedure and not to positive margins.

There are several limitations to the present study that must be acknowledged, however. Firstly, this was a retrospective study hence imparting an inherent selection bias that cannot be overcome.

It is also limited by the small number of patients in the obese BMI and morbidly obese groups, thus limiting the ability to determine a precise correlation between obesity and the complexity of the operation. Lastly, this experience is from a tertiary referral center with a high volume of LPN procedures and therefore the current findings might not apply to other populations in different hospital settings.

5. Conclusion

Although it may require higher surgical skills, LPN in obese and morbidly obese individuals presents similar surgical outcomes to those in normal and overweight individuals. An EUT should be always used in obese and morbidly obese individuals, considering the statistically significant decrease of the WIT and the higher risk for chronic renal insufficiency in those patients.

Author Disclosure Statement.

All authors disclose any commercial associations that might create a conflict of interest in connection with the submitted manuscript.

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