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

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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 single-center retrospective 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/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 ≥ 40 kg/m^2).
Results: Median operative time presented no statistically significant differences between BMI groups, 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 in 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 patients, 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 always be used in obese and morbidly obese individuals, considering the statistically significant decrease in WIT and the higher risk of chronic renal insufficiency in these patients.
Keywords: Kidney cancer, partial nephrectomy, laparoscopy, obesity, surgical outcomes

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 mini-invasive surgery, the refinement of intracorporeal suturing, and the availability of hemosealant substances, the robotic and laparoscopic approaches have gained popularity for NSS. If robotic surgery represents the most preferred approach in the treatment of uro-oncologic disease, the high cost associated with this technique remains an important issue for many urologic centers. Laparoscopic partial nephrectomy (LPN) is surely less expensive than robotic surgery but it is currently performed in a few high-volume referral centers, as its diffusion has been limited by the steep learning curve [1]. Since 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 increased dra-

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matically over the past two decades. In the United States, 25.6% to 29% of adults aged 40 years and 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 whether LPN could be safely performed in obese and morbidly obese patients compared with non-obese ones.

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 ≥ 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 on tumor size, location, extent of parenchymal infiltration, and proximity to the pelvicocalyceal system. Patients with severe heart failure (New York Heart Association functional class 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. Kidney function was evaluated by measuring estimated glomerular filtration rate (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.), each of whom had completed at least 100 LPNs each before the beginning of the study, thus reducing the learning curve effect.

Our surgical techniques have been reported previously [14]. Shortly, a transperitoneal approach was used in all patients. The renal artery was clamped with one laparoscopic bulldog clamp. The tumor was excised with cold scissors in a near-bloodless field. Targeted excisional biopsies of the tumor bed were sent for frozen section in case of suspicion regarding margin status. Collecting system was repaired with a running 2-0 Vicryl on a 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 pull-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 lobe. Since 2008, we have adopted an early unclamping technique to minimize warm ischemia time. In patients who underwent LPN with early unclamping, only the initial collecting system suturing was performed under ischemia and the renal parenchymal repair of the bolstered renorrhaphy was performed in the revascularized kidney. The median follow-up was 45.7 ± 18.4 months. Follow-up was calculated from the date of surgery to the date of the last documented examination. All patients underwent physical examination and ultrasonography every 3 months during the first year, every 6 months during the second and third years, and annually thereafter. CT or MRI was performed every 6 months during the first and second years, and annually during the third, fourth, and fifth years after surgery.

Statistical analysis was performed with SigmaPlot® software version 11.0 (SPSS Inc., Chicago, IL, USA). Patient 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 differences between groups in pathological stages.

Results

The baseline characteristics of the patients are summarized in Table 1. Of the 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. The ASA score was higher 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 patients and 7 (6–8) for morbidly obese patients ($P = 0.5$).

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 BMI groups, and no kidney was lost postoperatively due to warm ischemic injury. Regarding WIT, we noted

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Table 1. IHC of NE differentiation in prostate tumors.

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 GFR, mL/min/1.72m^2	92 (82–98)	89 (73–97)	88.5 (72–95)	88 (70–93)	0.07

statistically significant differences only in groups 3 and 4 in the presence of delayed (DUT) *vs*. early unclamping technique (EUT) [group 3: median DUT/WIT: 16.2 min; median EUT/WIT: 11.5 min (*P* = 0.03); group 4: median DUT/WIT: 17 min; median EUT/WIT: 12.2 min (*P* = 0.02)] (Table 2). The mean (IQR) length of hospital stay did not present a 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 patients, 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.

Definitive pathological results showed a high incidence of clear cell tumors in all groups. Surgical margins were positive in only 2 (1.8%) overweight patients and 1 obese patient (2.3%) (*P* = 0.3, Table 3). One overweight patient developed tumor seeding at the port site 24 months after surgery.

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 elderly patients often have associated medical conditions (*e.g.*, diabetes, heart failure, hypertension, and renal failure) that tend not to improve. Furthermore, obesity has been associated with an increased incidence of several cancers, including esophageal, pancreatic, colorectal, breast, and kidney cancer [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 are usually assigned a higher ASA score. These abovementioned comorbidities increase the risk of postoperative complications and make anesthesia more risky [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 was 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-

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 GFR, 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

Table 3. Oncologic outcomes.

Variables	Normal weight (*n* = 60)	Overweight (*n* = 110)	Obese (*n* = 42)	Morbidly obese (*n* = 28)	*P*-value
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	
chromophobe	12	10	9	12	0.2
oncocytoma	6	5	5	3	
angiomyolipoma	4	3	2	2	
Positive margins, *n* (%)	0	2 (1.8%)	1 (2.3%)	0	0.3

free survival with unilateral renal involvement, unifocal disease, and tumor size < 4 cm [2]. In recent years, LPN has been proposed as a valid alternative to OPN for the therapy of T1 RCC [14, 24, 25]. The anatomical characterization of renal tumors before LPN is fundamental for a correct evaluation of the outcomes [26]. 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 statistically significant differences in tumor size and R.E.N.A.L. nephrometry score, and they were equivalent in relation to age and gender distribution. In 2007, Gong *et al*. [21] reported their experience with laparoscopic kidney surgery in the obese population. They also separated their cohort based on BMI and found that laparoscopy was feasible in obese patients. Nevertheless, the authors did not find 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 extent. 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 patients, and 3.6% for morbidly obese patients. Moreover, all grade 4 or 5 complications could be registered. Moreover, although the median operative time presented no statistically significant differences between the BMI groups ($P = 0.4$), the median estimated blood loss was higher in morbidly obese patients than in all other groups. WIT ≤ 20 min was achieved in all patients, whereas WIT ≤ 15 min was achieved using an EUT. This is an advantage of the laparoscopic technique, where the presence of pneumoperitoneum, with 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 time to consider for a safe NSS procedure has been debated over the past few years and has recently been suggested to be 20 min. In general, the concept that every minute of ischemia may count is recognized, considering that WIT may affect postoperative renal function [27]. This is an important aspect to consider when performing LPN, as obesity increases the risk of developing chronic renal insufficiency, especially in elderly patients [28]. Nevertheless, there was no statistically significant difference in eGFR between groups at 1-year follow-up, which can be explained by the young age of the recruited patients. Our data are comparable to the outcomes described in the literature in obese patients after LPN [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 who underwent retroperitoneal or transperitoneal approach. There was no significant difference between groups regarding EBL, operative time, WIT, conversion rate, or hospital stay for the transperitoneal approach group.

In another study by Feder *et al*. [29], which analyzed 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 oncologic data, we noted a higher incidence of clear cell tumors in all 4 groups. Surgical margins were positive in only 2 (1.8%) overweight patients and 1 obese patient (2.3%). Moreover, one overweight patient developed tumor seeding at the port site 24 months after surgery, which was due to a rupture of the specimen during the procedure and not to positive margins. However, there are several limitations to the present study that must be acknowledged. First, this is a retrospective study, which introduces 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, which limits the ability to determine a precise correlation between obesity and complexity of the operation. Finally, this experience is from a tertiary referral center with a high volume of LPN procedures and therefore the current findings may not apply to other populations in different hospital settings.

Conclusions

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

Declarations

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