Treatment outcomes of laparoscopic partial nephrectomy for cT1bN0M0 renal cell carcinoma at Binh Dan Hospital

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Abstract

Introduction: This study aims to evaluate perioperative, oncological, and functional outcomes of laparoscopic partial nephrectomy performed for cT1bN0M0 renal cell carcinoma at Binh Dan Hospital.

Materials - Methods: Data were collected on 37 patients who had undergone laparoscopic partial nephrectomy for cT1bN0M0 renal cell carcinoma from January 2021 to September 2023. Demographic, radiological growth patterns of the tumors and intraoperative data were collected. Post-operative complications and pathological data were also recorded. Patients were followed for an average of 13.6 months to review oncological and functional outcomes.

Results: Radiological tumor size was 48.1 ± 8.2 mm. The average operative time was 157.4 ± 55.3 minutes. The mean estimated blood loss was 213.4 ± 239.8 ml. Warm ischemia time (WIT) was 20.3 ± 7.7 min. Pathological analyses revealed renal cell carcinoma in 37/37 patients and positive margins in 2.7% of cases. 37/37 cases (100%) had no local recurrence with a minimum follow-up time of 6 months. Warm ischemia time (WIT) was associated with acute kidney injury (AKI) with a rate of 4.5% if WIT was shorter than 20 minutes. This rate was 26.7% in the WIT longer than 20 minutes group.

Conclusion: This survey confirms that laparoscopic partial nephrectomy for cT1bN0M0 renal cell carcinoma is feasible in experienced hands with reasonable oncological and functional outcomes.

Keywords: Laparoscopic partial nephrectomy (LPN), renal cell carcinoma (RCC), warm ischemia time (WIT), acute kidney injury (AKI), glomerular filtration rate (GFR)

1. INTRODUCTION

Since 2010, laparoscopic partial nephrectomy (LPN) has been widely accepted for kidney tumors smaller than 4 cm [1]. In addition, indications can be considered for tumors larger than 4 cm with experienced surgeons. In 2018, according to the American Urological Association (AUA) and the European Association of Urology (EAU) Guidelines, partial nephrectomy became the standard treatment for all localized renal cell cancer with size less than 7cm, including stage T1a and T1b [2], [3].

In Vietnam, in 2018, authors at Binh Dan Hospital reported the results of laparoscopic partial nephrectomy for T1a kidney tumors with favorable results in oncology and preserving renal function [5], [6]. On that basis, since 2016, the surgeons at Binh Dan Hospital have also performed laparoscopic partial nephrectomy for some tumors measuring 4 - 7 cm. Initial perioperative results show feasibility and safety. However, in Vietnam, for stage T1b renal cell cancer (RCC), the number of studies on laparoscopic partial nephrectomy is limited. Most studies only evaluate the early results

of surgery and lack of follow-up outcomes in oncology and kidney function preservation.

2. MATERIALS - METHODS

2.1. Data collection

Patients' data were reviewed, from January 2021 to September 2023, for patients undergone LPN for renal tumors measuring 4 - 7 cm in size, according to computed tomography (CT) scan. The inclusion criteria were a single organ-confined, contrast-enhancing renal mass. Exclusion criteria included renal vein involvement, lymphadenopathy, or extrarenal tumor extension, and post-operative pathological analysis revealed benign lesions or any malignant tumors other than renal cell carcinoma (RCC).

We collected demographic data and radiological features of the lesions in a CT scan. The following variables were recorded. Intraoperative data: surgical access, type of tumor resection (pure enucleation, enucleo-resection, wedge resection), estimated blood loss, type of vascular clamping (artery or artery and vein), warm ischemia time (WIT) (starting from the clamping to the declamping of vessels), operative time, type of suture (running whip stitch or interrupted), collecting system repair, use of biological glue or hemostatic material, intraoperative complications. Intraoperative hemorrhage complication is defined as bleeding necessitating transfusion during the procedure.

2.2. Pathological data

The pathologists evaluated the surgical specimen. Tumor histology was reported; malignant tumors were classified according to the World Health Organization (WHO) 2004, graded according to Fuhrman grade and staged according to the 2002 Union International Cancer Control (UICC) revised TNM classification. Surgical margin outcomes (positive or negative) were also collected.

2.3. Post-operative data

Complications were classified according to Clavien - Dindo System and subsequent treatment, post-operative hospital stay, and creatinin test to assess renal function after 48 - 72 hours. Patients were then followed for a minimum of 6 months after surgery. Patients were indicated CT scan at least once to monitor local recurrence. Renal function outcomes were evaluated by renal scan one month after surgery.

2.4. Statistical analyses

All data were processed through statistical software. Descriptive analysis was used to evaluate all considered variables, qualitative analyses were compared by using X2 (Fisher exact tests), and quantitative analyses were compared by using Student's t-test. In all analyses, the differences were considered statistically significant when $p < 0.05$.

3. RESULTS

This study includes all patients who underwent LPN from January 2021 to September 2023 at Binh Dan Hospital. The laparoscopic partial nephrectomy (LPN) procedure was performed for cT1bN0M0 RCC in 37 patients.

3.1. Demographic data and tumor characteristics are reported in Table 1

Table 1. Demographic data and tumor characteristics

Characteristics	Total
Number of cases	37
Age, mean, years	58.3
Age, range, years	22 - 76
Male	22/37 (59.5%)
Left kidney tumor	18/37 (48.6%)
Tumor size, mean (SD)	48.7 ± 9.0 mm
Tumor size, range	40 - 70 mm
Location	
● Upper pole (%)	29.7 %
● Middle (%)	32.4 %
● Lower pole (%)	37.8 %
Endophytic pattern	
● < 50%	21.6 %
● > 50%	78.4%

3.2. Procedures and morbidity

Operative data is summarized in Table 2.

We used transperitoneal or retroperitoneal approaches according to tumor features (location, size) and patient characteristics (Body mass index (BMI), prior abdominal/flank surgery). We found no differences in 'Trifecta' outcomes between retro- and trans-peritoneal approaches, but in selected patients,

the operative time of retroperitoneal approach may be shorter (157 mins vs. 176 mins; p = 0.046) and equally safe compared with the transperitoneal approach.

In 36/37 cases, vessel clamping was performed and warm ischemia time (WIT) was recorded. In the remaining case, a 4.5 cm exophytic tumor was resected without renal artery clamping (off-clamp), with minimal bleeding. The enucleation technique was performed in most cases (34/37) to reduce the risk of major bleeding and collecting system perforating. In other 3/37 cases, we applied the pure resection technique due to the completely endophytic upper/lower pole tumors.

In only 1/37 patient, WIT was longer than 30 min. In statistical analyses, no correlation was recorded between WIT and lesion size (p>0.05) nor between WIT and location. However, the endophytic pattern (endophytic < 50% group vs. endophytic > 50% group) may prolong WIT (p = 0,002).

Table 2. Operative data

Characteristics	Total
Transperitoneal cases no. (%)	13/37 (35%)
Conversion to open surgery	1/37
Enucleation	34/37 (92%)
Estimated blood loss, mean, cc	213.4 ± 239.8 cc
Operative time, mean, min	157.4 ± 55.3 min
Renal artery clamping	36/37
WIT, mean, min	20.3 ± 7.7 min
WIT, range, min	0 - 45
Urinary tract repair	35/37
Running suture for parenchyma	30/37
Interrupted suture for parenchyma	7/37
Hospital stay, mean, days	5.2 ± 1.5 days

3.3. Pathological data

Pathological data are summarized in Table 3. Focal positive margins were found in 1/37 patients with malignant lesions. Postoperative upstage (invasion to perinephric fat - pT3a) was identified in one patient. In both cases, no local recurrence was recorded after more than 12 months of follow-up.

Table 3. Pathological data

Pathological data	No. (%)
- Clear cell	21
- Papillary	9
- Chromophobe	7
RCC	**37**
Positive margin	**1/37 (2.7%)**

3.4. Complications

Table 4 shows details of complications and their management. Intraoperative complications were recorded in 3/37 (8.1%) patients. All were bleeding with one case requiring conversion to open surgery (900 cc) but without the need for nephrectomy. The other two cases required blood transfusion, but no more than two red blood cell units. Urinary leakage occurred in 3/37 patients. All of them responded with minimally invasive intervention (double J or mono J placement). None of the complications was classified into Clavien grade 4 or 5.

Table 4. Operative complications

Complication (management)	No.	Rate	Clavien - Dindo
Fever	2		II
Hematoma	4	5.4	I
Acute bleeding	**3**	10.8	
● Conversion to open surgery	**1**	**8.1**	**IIIb**
● Blood transfusion	**2**		**II**
Urinary leakage	3		IIIa
● JJ placement	2	**8.1**	IIIa
● Mono J placement	1		
Complication	**12**	**32.4**	
No complication	25	67.6	
Total	**37**	**100**	

3.5. Oncological outcomes

All 37/37 patients had at least one CT scan imaging 1 - 3 months after surgery. Normal findings were recorded in 30/37 cases (81.1%). Abnormal findings included: enhancing mass, soft tissue heterogeneity, and indeterminate fluid collection. 7/37 patients with abnormal imaging were for the indication of a ''follow-up'' study. On subsequent imaging, 100% of abnormal studies were downgraded to normal.

Table 5. Imaging findings post-operative 1 - 3 months

Findings	No.	Rate (%)
Normal findings	**30**	**81.1**
- Fluid collection	**5**	**13.5**
- Enhancing mass/Soft tissue heterogeneity	**2**	**5.4**
Total	**37**	**100**

3.6. Functional outcomes

Table 6 shows the changes in renal function (Glomerular Filtration Rate - GFR) at the time of post-operative 48-72 hours, 1-3 months, six months, and 12 months.

Renal scans using 99m-Tc DTPA were performed in 37/37 patients one month after surgery. No differences in the split renal function were found post-op 30 days when compared to pre-op renal function (39.7 ml/min vs. 36.5 ml/min; $p = 0.21$).

Table 6. Changes in renal function

Renal function	Pre-operative	Post-op 48-72 h	Post-op 1-3 months	Post-op 6 months	Post-op 12 months
eGFR (creatinine)	86.3	77.9 ($p = 0.032$)	84.4 ($p = 0.35$)	87.4 ($p = 0.29$)	82.5 ($p = 0.17$)
Split GFR (renal scan)	39.7		36.5 ($p = 0.21$)		

Acute kidney injury (AKI) occurred in 5/37 patients (13.5%) based on RIFLE criteria at the moment of 48 - 72 hours post-op. However, all of these cases did not have oliguria, no clinical manifestations, and no indication for dialysis. These patients were re-tested for serum creatinine one week post-operative, and in all 5/5 cases, creatinine level decreased to smaller

than 1.5 times pre-operative level.

Warm ischemia time associated with AKI occurrence (p = 0.032). With the "cut-off" value of 20 minutes, 4/15 patients in the WIT > 20 minutes group (26.7%) had acute kidney injury after surgery. In contrast, only 1/22 patients had acute kidney injury after surgery (4.5%) if WIT was < 20 minutes.

4. DISCUSSION

4.1. Surgical techniques

4.1.1. Trans- or retro-peritoneal approach?

We found no differences in 'Trifecta' outcomes between retro- and trans-peritoneal approaches, but in selected patients, the retroperitoneal approach may be faster and equally safe compared with the transperitoneal approach. This is also similar to the results of Fan et al. when comparing surgical outcomes of LPN between trans- and retro-peritoneal approaches [6].

We found that for the upper pole, posterior surface tumors, or tumors smaller than 5cm in size, the retroperitoneal approach predominated. On the contrary, for anterior lesions, or tumors larger than 5cm in size, the transperitoneal approach may be more favorable than the retro-approach. Other factors, including the surgeon's experience, the patient's BMI, or history of abdominal/flank surgery, also affect the choice of approach. However, being familiar and proficient with both approaches will help surgeons feel confident and have the optimal approach to perform the LPN procedure.

4.1.2. Vessel clamping technique

Effective vascular control needs to ensure the surgical field is clear and reduce blood loss. However, prolongation of the ischemia time will lead to a reduction of renal function after surgery [7], [8]. Warm ischemia time and post-operative renal function are associated. Therefore, surgeons must always try to balance these two factors during surgery. In our opinion, surgeons should attempt to shorten the duration of warm ischemia while limiting the amount of blood loss at a level that does not require a blood transfusion. We found that an effective vascular control does not require the surgical field to be completely 'dry', but only to be clear enough

for effective tumor resection and hemostasis. With the retroperitoneal approach, we found that an intraoperative inflation pressure of 10 - 15 mmHg was enough to effectively control renal vein bleeding. Therefore, the surgeons only needed to clamp the renal artery without clamping the vein in 24/24 patients (100%) with the retroperitoneal approach.

For the transperitoneal approach, when exposing the renal hilum, the renal vein will be dissected in front (superficial plane) and the renal artery in the back (deep plane), then we marked both the renal artery and vein with vessel loops. We will clamp the renal artery first and then proceed to resect the tumor. If surgeons recognize that bleeding has not been effectively controlled when removing the tumor, the renal vein will be clamped. We found that, for the transperitoneal approach on the left side, most cases only needed to control the renal artery. It is necessary to clamp the renal vein for some right-sided partial nephrectomy cases due to the high pressure of the right renal vein, which is a close branch of the inferior vena cava (IVC).

4.1.3. Tumor resection technique

Van Poppel et al. (2010) concluded that a negative surgical margin is safe in oncological outcomes. The thickness of the surgical margin does not affect the likelihood of local recurrence or progression [9]. Based on studies on surgical margins, Minervini et al. (2021), through a study on 507 patients evaluating the oncological results of the tumor resection technique, showed no difference in the positive margin rate between tumor enucleation and resection techniques (4.9% vs. 2 - 10%) [10].

Based on this study, we found that T1b RCCs are more likely to involve the renal blood vessels and the collecting system due to their increased size. Therefore, the enucleation technique for large renal masses will help reduce the risk of major bleeding and urine leakage and preserve more normal kidney parenchyma while ensuring oncological safety. At the same time, the tumor bed after tumor removal will often be "flatter", making the renorrhaphy process easy and more favorable. In comparison to preserving renal function, enucleation reduces kidney function less (20.7%) than the resection technique (32%) [10].

4.1.4. Renorrhaphy and hemostatic technique

Most cases (35/37) required a two-layer kidney repair suture. In particular, the first layer suture (deep layer) is essential to help control urine leakage and bleeding. We prioritized the early unclamp technique, which not only reduced the warm ischemia time but also helped detect bleeding points from the bottom of the tumor bed after releasing the clamp. From there, the second layer suture closed the parenchyma and improved hemostasis at the points where bleeding was observed. Bertolo et al. (2018) researched the effects of renorrhaphy technique on post-operative renal function and noted that a single-layer stitch can help preserve kidney function better than a double-layer stitch (GFR - 3.19 ml/min versus - 6.07 ml/min; p = 0.001) [11]. However, authors Porpiglia and Bertolo (2019) also found that double-layer suturing helps reduce complications of pseudoaneurysm and urine leakage [12].

Johnston et al. (2005) compared the hemostatic effect between biological glue and Surgicel bolster in partial nephrectomy. They found that surgicel bolster had good hemostatic results in closing the renal parenchyma, especially in cases of largely tissue defects after tumor removal [13].

However, during the course of our study, we discontinued the use of the surgicel bolster even in the situations of a largely parenchymal defect. There are two reasons. First, it is possible to completely suture renal parenchyma in all cases if we mobilize the kidney widely enough. Second, according to Connor et al., the dissolution of surgicel bolster after surgery will increase the risk of secondary bleeding and pseudoaneurysm formation [14], [15]. The situation of secondary bleeding after 5-7 days due to pseudoaneurysm in patients using surgicel bolster was recorded at Binh Dan Hospital from 2016 - 2019 (not in the study cases).

4.2. Oncological outcomes

Tubre et al. (2017) surveyed the postoperative CT imaging findings of 180 patients who had undergone partial nephrectomy. Abnormal findings were soft tissue heterogenity, enhancing masses, and indeterminate fluid collection. Theses authors recorded that 60% of cases with abnormal characteristics suspected of local recurrence on imaging at the time of post-op three months will become normal after 6 - 12 months. The cause may be due to inflammation and wound healing at the resection site [16].

In our study, there are two patients of suspected local recurrence on CT scan imaging at 1 - 3 months post-op (one with a mixed attenuation lesion and one with enhancing masses). However, followed up after 6 - 9 months, they all disappeared.

The American Urological Association (AUA) recommends monitoring for local recurrence with a CT scan or MRI after 3 – 12 months after surgery [3]. However, if there are no risk factors (such as positive surgical margin, or upstage pT3a), it can be delayed for up to 6 - 12 months due to wound healing and re-organization.

4.3. Functional outcomes

Bravi (2019) studied 1,893 patients and recorded that the rate of AKI after partial nephrectomy was 20% (388 patients). AKI doubles the risk of progression to chronic kidney disease after 12 months [17], [18]. In the group post-op AKI, Bravi noted that if kidney function recovers within a week to a level above 75% of baseline eGFR, it is a good prognostic factor for recovery. In comparison, we recorded similar results when 5/37 patients (13.5%) had AKI post-op 48 - 72 hours. However, the positive point is that all 5/5 patients had no clinical manifestations and recovered after at most 72 hours.

Regarding the relationship between warm ischemia time and postoperative acute kidney injury, similarly, Zhang et al. (2016) found that the risk of AKI in the WIT < 20 minutes and WIT > 35 minutes groups were 6.4% and 24.4%, respectively [19]. We also suggest that the cut-off value of WIT < 20 minutes is considered optimal for minimizing the risk of postoperative AKI when the decrease in eGFR between the two groups WIT < 20 minutes and WIT > 20 minutes is significant (p = 0.032). The risk of acute kidney injury in the WIT group < 20 minutes was 4.5%; while in the WIT > 20 minutes group, it was 26.7%.

A question that arises is: 'Does post-op AKI increase the risk of progressing chronic kidney disease? Following up on our 05/37 patients with AKI after surgery, no case was recorded with a decrease in eGFR of more than 25% of preoperative eGFR after 6 - 12 months. According to Bravi et al., studying 1893 patients undergoing partial nephrectomy, renal function 6 - 12 months post-op if lower than 90% of baseline GFR will be a risk factor for new onset or worsening disease progression of chronic kidney disease [17]. Compared to our study, we noted that 1/5 patient, who had AKI post-op, had an eGFR < 90% of the preoperative level (102 ml/min compared to 121 ml/min) at time 12. month of follow-up was recorded.

All current studies agree that AKI within 48 - 72 hours after partial nephrectomy is a prognostic factor for the future progression of chronic kidney disease [20], [21]. However, in our study, the positive feature is that all 5/5 patients recovered their eGFR after 72 hours of monitoring, without oliguria or anuria, which helped reduce 3–4 times the risk of chronic kidney disease progression according to Zhang et al [19].

In this study, renal scintigraphy was used to evaluate kidney function of pathological kidneys (kidneys with tumors) 1 - 3 months after surgery. Research results evaluating split glomerular filtration rate (GFR) did not show a statistically significant decrease in GFR. Even in the group of patients with WIT > 20 minutes, we did not find a decrease in GFR of tumor-bearing kidneys 1 - 3 months after surgery compared to preoperative. However, the follow-up time was short, a longer follow-up time is needed to have more conclusions about the impact of warm ischemia time or post-operative AKI on long-term kidney function.

5. CONCLUSIONS

Laparoscopic partial nephrectomy (LPN) for cT1bN0M0 renal cell carcinoma (RCC) is feasible in experienced hands with reasonable oncological and functional outcomes. Enucleation seems to be a safe and effective strategy, especially in highly complex renal tumors. Follow-up CT scan imaging can be delayed for up to 6 - 12 months if there are no risk factors (positive surgical margin, upstage pT3a). The warm ischemia time (WIT) is associated with the risk of postoperative acute kidney injury (AKI). However, renal function from 30 days after surgery does not have a statistically significant difference.

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