



# Retroperitoneal Laparoscopic Radical Nephrectomy for Renal Cell Carcinoma: Indications and Long-term Outcome of a Cohort Study in Vietnam

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## Abstract

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**OBJECTIVE:** Laparoscopic radical nephrectomy (LRN) has been suggested as the standard care for cancer patients in the T<sub>1-2</sub> stage. However, whether this advanced technique is most indicated suitable for renal tumors higher than T<sub>3a</sub> and N<sub>1</sub> is unclear, especially in different regions and countries, such as the difference between European and Asia.

**METHODS:** From 2013 to 2021, the data of pathologically diagnosed renal cell carcinoma (RCC) patients who received laparoscopic retroperitoneal radical nephrectomy was subjected to the present study.

**RESULTS:** Overall, all the registered Vietnamese patients were eligible for the study. The average operative time was 86.8 ± 21.2 min and the percentage number of patients in stages 1, 2, and 3 were 134 (70.2%), 30 (15.7%), and 27 (14.1%), respectively. Patients in the 3rd stage had a significantly longer operative time than stages 1–2 (p = 0.0001). No Lymph-node dissection (LND) was recorded in 10 patients (5.2%), limited LND in 163 patients (85.3%), regional LND in 13 patients (6.8%), extended LND (eLND) in 5 patients (2.6%). eLND showed only prolongation of operative time (p = 0.000), however, did not increase intraoperative complications as well as prolonged the duration of analgesia and hospital stay when compared with the other 2 groups (p = 0.82, 0.85, 0.91). Mean follow-up time: 42.3 ± 24.7 months. The 5-year recurrent free survival and 5-year overall survival of the stage 1, 2, 3 were: 98.3%, 100%, 87.8%, and 98.9%, 100%, and 91.3%, respectively. (p = 0.0011, p = 0.0082).

**CONCLUSION:** Retroperitoneal LRN could be an important technique in improving long-term oncological outcomes for Vietnamese patients, especially in the stage of T1-3N0-1M0 tumors. Radical retroperitoneal nephrectomy is safe and technically feasible as well as providing favorable long-term oncological outcomes for stage T1-2-3aN1M0 RCC.

## Introduction

Based on GLOBOCAN data in 2018, there are approximately 2.2% of all cancer diagnosed with neoplasms of the kidney. North America is one of the most incidents (Age-standardized rates (ASR) ASR = 10.9/100,000), including Western Europe (9.7) and New Zealand/Australia (9.6) [1]. Renal cell carcinoma (RCC) is the 7<sup>th</sup> most common form of neoplasm in developed countries. In the US, there is around 4.2% of all cancer diagnoses with 74,000 new cases of kidney diagnosed cancer in 2019. The incidence was firstly reported in 1975 as 7.1/100,000, while in 2016, this resulted in an incidence rate of 14.9/100,000, subsequently eliciting that kidney cancer is becoming one of the fastest-growing cancer diagnoses in the US. However, since culminating at 16.0/100,000 in 2008, kidney cancer incidence has plateaued [2].

In lower-middle countries, especially in Vietnam, although there are no completed statistics yet, RCC is still ranked 3<sup>rd</sup> in cancer disease of the urinary

system. Nowadays, surgical treatment is still considered the backbone standard for kidney cancer treatment, while other treatments have not been effective [3], [4]. Laparoscopic nephrectomy was initially performed by Clayman *et al* in 1990 [5], thereby opening a revolution in the minimally invasive treatment of renal tumors. Currently, laparoscopic radical nephrectomy (LRN) is considered the standard method for treating local renal tumors that is not feasible with pN [6]. The advantage of laparoscopic surgery (LS) compared to open surgery is extremely clear and has been demonstrated in numerous recent studies [6]. The main controversy among the authors is about the safety and feasibility of LS for advanced tumors [6]. In Vietnam, LS for RCC has been performed over the last decade, then there have been many reports on the effectiveness of this method, but there are no studies evaluating the long-term outcome of LS for RCC and its feasibility in advanced stages. This article aims to report the long-term outcomes of 191 patients with local and advanced RCC who underwent retroperitoneal LRN (RLRN) in Vietnam, a lower-middle country.

## Methods

### **Study population**

Our study was carried out on 191 RCC patients who underwent RLRN at Viet Duc University Hospital (Hanoi) - one of the largest surgical centers in Vietnam, from February 2013 to March 2021.

### **Ethics approval and consent to participate**

Written informed consent was obtained from all patients and their family members before participation. The study was approved by our research committee, Viet Duc University Hospital, Hanoi, Vietnam, and this was approved by Hanoi Medical University Institutional Ethical Review Board (No NCS07/BB-HĐĐĐ) date February 14, 2019.

### **Human and animal rights**

No animals were used for studies that are the basis of this research. This research was conducted on humans in accordance with the Helsinki Declaration of 1975, as revised in 2013 (<http://ethics.iit.edu/ecodes/node/3931>).

Prospective and retrospective descriptive studies based on prebuilt case samples. Retrospective patient group: Collecting necessary data through medical records at the record-keeping room of Viet Duc University Hospital from February 2013 to January 2018. Prospective patient group: Includes patients diagnosed and treated between January 2018 and March 2021.

### **Case-ascertainment**

Define: Indications of Surgery. Long-term outcome:  $\geq 5$  years. Criteria for patient selection: Patients with complete medical records, ultrasound, X-ray, multislice computer tomography [MSCT], were diagnosed with renal cell cancer; preoperative diagnosis at stage T1-3aN0-1M0 (based on computed tomography [CT]); opposite kidney with normal function: normal kidney function test, normal kidney morphology, no pathology in the contralateral kidney on ultrasound, MSCT; the pathology results showed that it was renal cell cancer; do not have other types of cancer.

### **Follow-up**

The recorded data include preoperative characteristics of the patient and disease: history, clinical, liver, and kidney function tests, chest X-ray, ultrasound, CT; intraoperative and postoperative development: operative time, bleeding, vascular injury, organ damage, conversion to open surgery, lymphatic

leakage, incision infection, re-operation; data on postoperative developments: length of hospital stay, time of defecation, duration of pain medication.

Patients were scheduled for reexamination for the first time, 1 month after surgery, then every 3 months in the first year, and every 6 months in the following years. Patients reexamined had chest X-ray, abdominal ultrasound, and blood test to evaluate kidney function. In the first year, take a CT scan every 6 months, in the following years take a CT scan once a year or when an ultrasound shows signs of recurrence.

At the end of the study in December 2021, determine the time and cause of death, the time and location of recurrence or distant metastasis.

Any recurrent mass in the ipsilateral fossa is considered local recurrence and metastasis anywhere outside this region is considered distant metastasis. Port site metastases were defined as tumor recurrence at the site of laparoscopic ports or specimen collection incision.

### **Availability of data and materials**

The data supporting the findings of the article is available within the article.

### **Supplementary material**

Supplementary material is available on the publisher's website along with the published article.

### **Statistical analysis**

All data are extracted from medical records and data analysis was performed by using IBM SPSS Statistics program, version 16, Statacorp LLC, TX, USA. Descriptive statistical analysis was used to describe patient characteristics (frequency and percentage for qualitative variables; mean and standard deviation for quantitative variables). Data of the groups were compared statistically using the Chi-square test and Fisher's exact test for categorical variables, and one-way analysis of variance test for continuous variables. The primary endpoint of the study was cancer-specific survival (CSS), which was defined as the time from the date of surgery to cancer-specific death or last available follow-up. Patients were censored in case of non-RCC-related death or at the time of the last follow-up. Survival times were estimated with the Kaplan–Meier method and compared using the log-rank test. Kaplan–Meir survival analysis was used to estimate 5-year overall survival (OS), 5-year CSS, and 5-year recurrence-free survival (RFS). The log-rank test was used to compare survival rates among groups. Cox proportional hazard regression model was used to identify prognostic factors for patient mortality. All p values were two-sided and  $p < 0.05$  was considered statistically significant.

## Results

The clinical, intraoperative, and postoperative characteristics are shown in Table 1.

The average age and men/women ratio was 52.6 ± 13.2 and 1.48, respectively, while the average operative time was 86.8 ± 21.2 min. Herein, we observed that the operative time was significantly longer in the 3<sup>rd</sup> stage compared with stages 1 and 2 (p = 0.0001). Intraoperative bleeding is the main dangerous complication in 14 patients (7.3%) including vascular injury (6), ipsilateral adrenal gland injury, accompanying adrenalectomy (2), from dissection area and lymph node dissection (LND) (6), one patient had to be converted to open surgery due to massive bleeding. The average blood loss in these 14 patients was 137.5 ± 56.9 ml. Two patients had to reoperate on the 1<sup>st</sup> day due to postoperative bleeding: slip off hem-o-lok from the renal artery (1) and the lumbar artery (1). There was no difference in the rate

of intraoperative and postoperative complications at 3 stages with p = 0.24 and p = 0.67. The length of hospitalization and duration of pain medication of the 3 groups were not statistically significant with p = 0.2164 and 0.6389.

Results by lymph node dissection (LND) group are shown in Table 2.

There were observed in 10 patients (5.2%) with no LND, 163 patients (85.3%) with limited LND, 13 patients (6.8%) with regional LND, and 5 patients (2.6%) with extended LND (eLND). Among these 5 patients with eLND, there was 1 patient who had pathologically lymph node (LN) metastasis. The average number of removed LNs was 3.9 ± 2.3 nodes with a minimum of 1 node and a maximum of 15 nodes. The average number of the eLND group was 7.6 nodes. eLND elicited only prolongation of operative time (p = 0.000), however, did not increase intraoperative complications as similar as prolonged the duration of analgesia and hospital stay compared to the remaining groups (p = 0.82, 0.85, 0.91).

**Table 1: Histopathological results, follow-up record of the patients**

Characteristics	Stage I	Stage II	Stage III	p-value	Total (%) (n = 191)
	pT <sub>1</sub> N <sub>0</sub> M <sub>0</sub> (n = 134)	pT <sub>2</sub> N <sub>0</sub> M <sub>0</sub> (n = 30)	pT <sub>3a</sub> N <sub>0</sub> M <sub>0</sub> (26) + pT <sub>1b</sub> N <sub>0</sub> M <sub>0</sub> (1) (n = 27)		
Age	53.0 ± 13.1	47.1 ± 13.3	57.0 ± 11.6	0.01	52.6 ± 13.2
Male/female	80/54	15/15	19/8	0.294	114/77
Tumor size (mean ± SD)	46.6 ± 10.4	80.0 ± 13.1	58.6 ± 17.0	0.001	5.35 ± 1.7
Incidental finding/symptomatic	78/56	7/23	11/16	0.001	96/95
RCC tumor subtypes (%)	134	30	27 (26+1)		191 (100)
ccRCC	90	17	17	p <sub>123</sub> = 0.098	124 (64.9)
chRCC	31	13	5	p = 0.087	49 (25.7)
pRCC	8	0	3		11 (5.8)
sRCC	2	0	2		4 (2.1)
Rare subtypes	3	0	0		3 (1.6)
Fuhrman grade	100	17	21		138 (100)
1	11	0	2	0.235	13 (9.4)
2	66	10	10		86 (62.3)
3	20	5	8		33 (23.9)
4	3	2	1		6 (4.3)
Microvascular invasion (%)	7 (5.2)	5 (16.7)	6/27 (22.2)	0.006	18 (9.4)
Mean follow-up time (months)	43.8 ± 25.5	40.6 ± 22.9	36.7 ± 22.4	0.48	42.3 ± 24.7
PSM	2	0	0		2 (1.0)
Number of local recurrence	1	0	2		3 (1.5)
Number of distant metastasis (%)	0	2	1		3 (1.5)
Total mortality (%)	2	1	1		4 (2.1)
Cancer-specific	2	1	1		4
Unrelated	0	0	0		0
OS/CSS <sub>5 years</sub> (%)	98.9	100	91.3	0.0082	94.04
RFS <sub>5 years</sub> (%)	98.3	100	87.8	0.0011	92.7

SD: Standard deviation, RCC: Renal cell carcinoma, ccRCC: Clear cell RCC, chRCC: Chromophobe RCC, pRCC: Papillary RCC, sRCC: Sarcomatoid RCC, PSM: Port site metastases, OS: Overall survival, RFS: Recurrence free survival, CSS: Cancer specific survival.

**Table 2: Survival analysis after laparoscopic radical nephrectomy**

Research	Stage	n	Tumor size (cm)	Follow-up (months)	PSM	Local recurrence	RFS <sub>5 years</sub> (%)	OS <sub>5 years</sub> (%)
Ono <i>et al.</i> , 2001 [9]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	103	< 5.0	29	0	1	95	95
Portis <i>et al.</i> , 2002 [10]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	54	4.3 (overall)	54 (overall)	0	1 (overall)	92	97*
	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	10					87	100*
Saika <i>et al.</i> , 2003 [11]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	195	3.7	40	0	0	91	94
Permpongkosol <i>et al.</i> , 2005 [12]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	46	5.1 (overall)	73 (overall)	0	0	98	98*
	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	8			0	0	84	95*
Cheung <i>et al.</i> , 2005 [13]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	80	4.6 (overall)	30 (overall)	0	2 (overall)	98	-
	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	9					88.9	-
	T <sub>3a</sub> N <sub>0</sub> M <sub>0</sub>	6					80	-
Hemal <i>et al.</i> , 2007 [14]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	87	4.21	56	0	0	84.3–97.2	86.3–97.2*
	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	45	9.9	57.9	0	0	82	82.2*
Süer <i>et al.</i> , 2013 [15]	T <sub>1-2</sub> N <sub>0</sub> M <sub>0</sub>	275	7.3	36.07 (overall)	-	-	88.6	-
	T <sub>3a</sub> N <sub>0</sub> M <sub>0</sub>	63	5.9		-	-	56.7	-
Brookman-May <i>et al.</i> , 2015 [16]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	5342	4.0 (overall)	56.7 (overall)	-	-	-	95–98*
	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	795			-	-	-	83–89*
	T <sub>3a</sub> N <sub>0</sub> M <sub>0</sub>	1247	6.58	62.7	-	-	-	85*
Zhang <i>et al.</i> , 2016 [17]	T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	1049	-	43.6 (overall)	-	-	-	97.24*
	T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	139	-		-	-	-	92.01*
	T <sub>3a</sub> N <sub>0</sub> M <sub>0</sub>	125	-		-	-	-	77.99*

\*CSS: PSM: Port site metastases, OS: Overall survival, RFS: Recurrence free survival, CSS: Cancer specific survival.



**Pathological features and distant follow-up**

Third stage had 27 patients, including pT<sub>3a</sub>N<sub>0</sub>M<sub>0</sub> (26) and pT<sub>1b</sub>N<sub>1</sub>M<sub>0</sub> (1). There was no difference in the male/female ratio between the 3 periods (p = 0.294). Stages 2 and 3 tumors were significantly larger than Stage 1 (p = 0.001), and had a higher proportion of patients with symptoms/accidental discovery (p = 0.001). Patients in Stage 3 had a higher mean age (p = 0.001). There was no difference in the distribution of histological type and Fuhrman grade in the 3 Stage groups, however, the highest rate of Sarcomatoid RCC (sRCC) was 7.4% in pT3a compared to 1.49% for pT1 and 0% for pT2. The median follow-up time was 42.3 ± 24.7 months (from 10 to 105 months). 5-years OS and 5-years RFS at Stage 3 were significantly lower than pT1-2 (p = 0.0011 and p = 0.0082, respectively) as shown in Table 1.

At the end of the study, 187 (97.9%) patients were still alive, 8 patients had a recurrence and/or distant metastasis, of which 4 (2.1%) patients died of RCC, and no patient died of other causes. Two patients proceeded with other cancers unrelated to RCC, including adenocarcinoma of the rectum (1) and lung adenocarcinoma, non-small-cell lung cancer (1). Two patients showed port site recurrence: one patient with sRCC pT1bN0M0, intact specimen, and one patient with Clear cell (ccRCC) pT1bN0M0 F4, microvascular invasion, specimen obtained by morcellation with the substandard bag. Local recurrence in 3 patients: ccRCC-pT1bN1M0-F2 (1); ccRCC-pT3aN0M0-F2 (1); ccRCC-pT1bN0M0-F3 (1). Distant metastasis in

3 patients: sRCC-pT3aN0M0 (1): brain and lung metastasis; ccRCC-pT2aN0M0-F3 (1): brain and lung metastasis; ccRCC-pT2aN0M0-F2 (1): liver metastasis.

Kaplan–Meier curves for patients in pT<sub>1</sub>, pT<sub>2</sub>, and pT<sub>3a</sub> of RFS and OS are presented in Figure 1a and b, respectively. The 5-year RFS, 5-year OS (CSS) were significantly lower in pT<sub>3a</sub> + N<sub>1</sub> compared to pT<sub>1-2</sub>N<sub>0</sub>M<sub>0</sub> (p = 0.0011 and 0.0082, respectively).

**Discussion**

**Patient characteristics**

RCC accounts for 90% of renal malignancies and ranks in 3<sup>rd</sup> among urological malignancies. The disease occurs in both sexes, the cause is not really clear, but some factors have been shown to increase the risk of RCC, such as smoking, being overweight or obese, or hereditary diseases such as Von Hippel-Lindau syndrome, Hereditary Papillary Renal Carcinoma, Birt- Hogg- Dubé syndrome [7]. In the present study, the mean age of the disease was 52.6 ± 13.3, the lowest age was 18 year old, and the highest age was 88-year-old, while the most common age was approximately 40–60 years old, the male/female ratio was 1.41. Research by A.K. Hemal (2007) also reported similar results, the mean age of the laparoscopic nephrectomy group was 52.5 ± 11.3 and the male/female ratio was 1.73 [8].

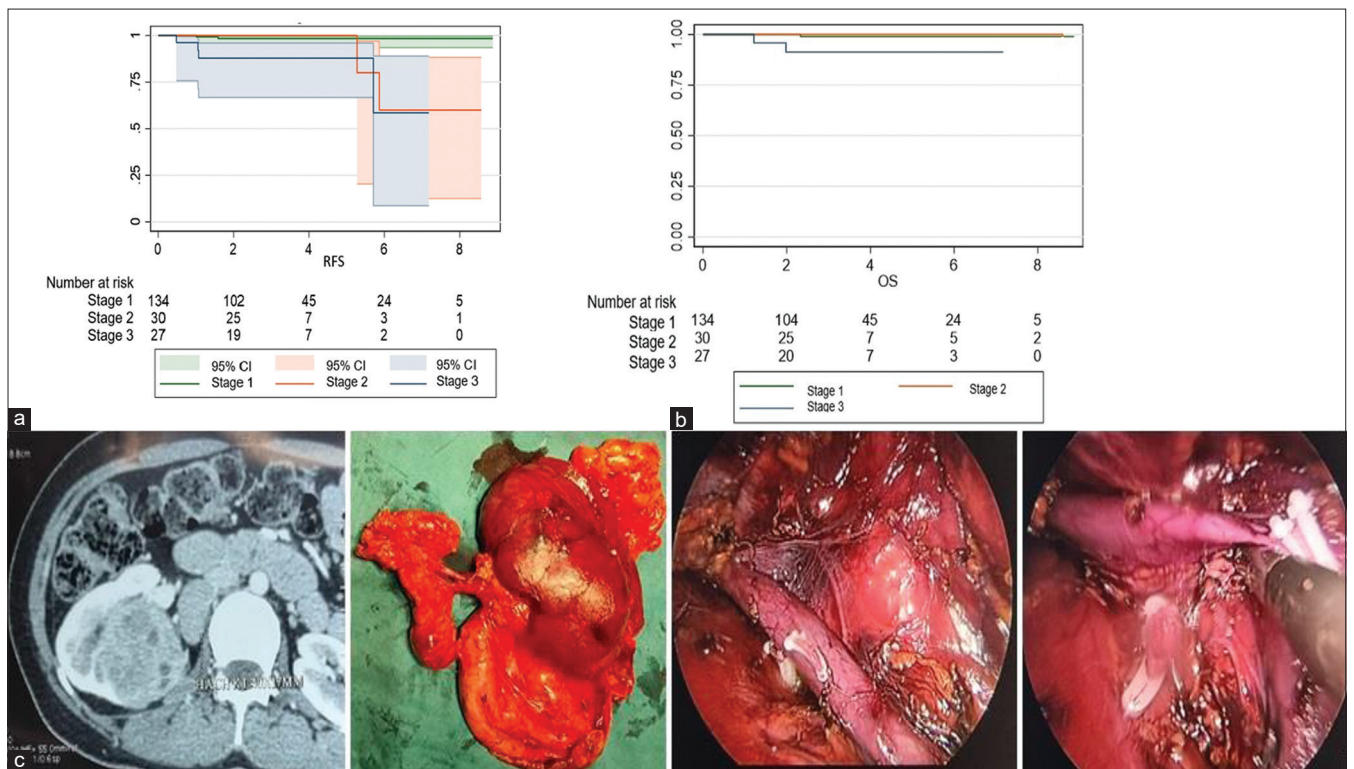


Figure 1: (a) Kaplan-Meier curve for recurrence-free survival. (b) Kaplan-Meier survival curve for overall survival. (c) RLRN and eLND for ccRCC T1bN0M0. RLRN: Retroperitoneal laparoscopic radical nephrectomy, eLND: Extended lymph-node dissection.

### Long-term follow-up surgery

All 191 patients were reexamined, or information was obtained through phone and email interviews. The mean follow-up time was  $42.3 \pm 24.7$  months, the shortest was 10 months, and the longest was 105 months. At the end of the study, 187/191 patients were alive, 8 patients had a recurrence or distant metastasis, 4 of which (2.1%) had died, including pT<sub>1</sub> (2), pT<sub>2</sub> (1), and pT<sub>3a</sub> (1). The earliest death is 14 months; the latest is 102 months after nephrectomy.

RFS5-years in period 1–2–3 were 98.3%, 100%, 87.8% and OS5-years in period 1–2–3 were 98.9%, 100%, 91.3%, respectively. Our results are similar when compared to other authors (Table 2).

### Indication of laparoscopic radical nephrectomy for advanced renal cell carcinoma

Indications for LS at this stage are still controversial about its safety and effectiveness compared to traditional open surgery.

### Lymph node dissection

Although the presence of LN metastases suggests a poor prognosis, the role of LND in treatment remains unclear. According to Giuliani, 6% of patients had regional LN metastases for local tumors, 46% for locally advanced tumors, and 62% for tumors with distant metastases [18]. However, many reports do not show the role of LND in improving survival [19], Minervini (2001) identified the 5-year survival between 2 groups of LND and no LND was 79% and 78% and found that there was no difference [20]. European Association of Urology (EAU) and American Urological Association (AUA) Guideline indicated that LND is not recommended for local tumors and there was no evidence of LN metastasis. However, LND may be valuable in high-risk groups, such as tumors over 10cm, T<sub>3-4</sub>; Furman 3–4, sRCC, tumor necrosis and when LN metastasis is suspected intraoperative or on preoperative imaging [6], [21]. Phillip (1993) showed that regional LND reduced the local recurrence rate from 11% to 2.5%–8% [22]. The number of LN metastases ( $\leq 4$ ) was similar to the intracapsular and extracapsular extension of intra-nodal metastasis correlated with the patients' clinical prognosis in several studies. Better survival outcomes were observed in patients with a low number of positive LNs ( $<4$ ) and no extranodal extension [23], [24]. Whitson et al. (2011) retrospective surveillance with more than 9000 patients indicated that eLND had no effect on Disease-specific survival (DSS) in patients with negative lymph node findings on pathology. However, in patients with pathologically proven lymphogenic spread (pN+), an increase of 10 in the number of nodes dissected resulted in a 10% absolute increase in DSS [25]. In

addition, in a larger cohort of 1983 patients, Capitanio *et al.* demonstrated that eLND results in a significant prolongation of CSS in patients with unfavorable prognostic features (sarcomatoid differentiation, large tumor size) [26]. Gershman B (2018) from a large single-center database showed that eLND is not associated with an increased risk of Clavien grade  $\geq 3$  complications. Furthermore, LND was not associated with the length of hospital stay or estimated blood loss [27]. Many authors agree that laparoscopic LND is safe and feasible and necessary in suspected cases, and the overall risk of complications was similar between the 2 groups (with lymphadenectomy and without lymphadenectomy) [28], [29].

In our study, LND was performed in 181 patients (95.3%), mainly limited LND 85.3% (163/191), region LND 13/191 (6.8%), and 5 patients (2.6%) suspected LN metastasis based on CT scan with eLND. Pathological results have 1 patient with positive LN (in the group of eLND). This patient had a local recurrence 13 months after LRN. We did not perform routine LND during nephrectomy. However, LNs along the renal vessels are often removed as part of a radical nephrectomy (limited LND). Our results (Table 3 and Figure 1c) elicited that laparoscopic eLND is potentially safe, but it only requires increasing the operating time but does not enhance the rate of intraoperative complications as similar as the postoperative outcome.

**Table 3: Intra- and post-operative characteristics according to lymph node dissection**

Characteristics	Total	LND			p
		Limited and no	Region	Extend	
Bleeding complications					
No	177 (92.7)	162 (93.6)	11 (84.6)	4 (80)	0.264
Yes	14 (7.3)	11 (6.4)	2 (15.4)	1 (20)	
Operating time (min), mean $\pm$ SD	86.8 $\pm$ 21.2	86.5 $\pm$ 21.5	84.6 $\pm$ 15.6	102 $\pm$ 20.5	0.000
Painkiller time (days), mean $\pm$ SD	3.5 $\pm$ 0.8	3.5 $\pm$ 0.7	3.6 $\pm$ 0.6	3.4 $\pm$ 0.5	0.85
Hospital stays (days), mean $\pm$ SD	5.04 $\pm$ 1.1	5.05 $\pm$ 1.2	4.8 $\pm$ 0.4	5.0 $\pm$ 0.0	0.91

LND: Lymph node dissection, SD: Standard deviation.

### Indication of laparoscopic radical nephrectomy in T<sub>3a</sub> tumors

T3a (AJCC) locally advanced tumor: the tumor proceeds into the renal vein or its segmental branches, or invades the pelvicalyceal system or invades the perirenal and/or renal sinus fat, but not beyond gerota fascia. 4–10% of RCCs have venous thrombosis, of which 50–75% are found in the right renal tumor. Venous thrombosis is one of the poor prognostic factors [30]. However, in RCC without metastases, thrombectomy surgery significantly improves survival, 5-year survival rate according to several reports from 18% to 68% [31], [32]. Thrombectomy is a difficult technique and is often performed under traditional open surgery, however, LS is increasingly being used in some centers to allow removal of level 0, I or II thrombus. Preliminary results have demonstrated LS to be safe and feasible in selected patients [30]. The outcome of LRN at T<sub>3a</sub> compared with

**Table 4: Patient and disease characteristics, intra-operative and post-operative data**

Characteristics	Stage I	Stage II	Stage III	p-value	Total (%)
	pT <sub>1-2</sub> N <sub>0</sub> M <sub>0</sub>	pT <sub>2-3a</sub> N <sub>0</sub> M <sub>0</sub>	pT <sub>3a</sub> N0M <sub>0</sub> (26) + pT <sub>1-2-3a</sub> N <sub>1</sub> M <sub>0</sub> (1)		
Number of patients	134	30	27		191
Mean age (years)	53.0 ± 13.1	47.1 ± 13.3	57.0 ± 11.6	0.01	52.6 ± 13.2
BMI	22.4 ± 2.4	22.2 ± 1.7	22.4 ± 2.2	0.94	22.4 ± 2.2
Men/women	80/54	15/15	19/8	0.294	114/77
Incidental finding/symptomatic	78/56	7/23	11/16	0.001	96/95
Mean tumor size (cm)	46.6 ± 10.4	80.0 ± 13.1	58.6 ± 17.0	0.001	5.35 ± 1.7
Mean operating time (min)	82.5 ± 20.3	89.0 ± 18.7	105.2 ± 18.5	0.0001	86.8 ± 21.2
Remove specimen					191
Intact/morcellation	105/29	19/11	21/6	0.214	145/46
Intraoperative complications					
Vascular injury	4	1	1		6 (3.1)
Bleeding	8	2	4		14 (7.3)
Adrenal gland injury	2	0	0		2 (1.0)
Conversions to open (%)	0	0	1		1 (0.5)
Total (%)	8	2	4	0.24	14 (7.3)
Post-operative complications					
Wound infection	1	1	0		2
Re-operation due to bleeding	1	0	1		2
Lymphatic leak	0	0	0		0
Total (%)	2	1	1	0.67	4 (2.1)
Mean painkiller time (days)	3.5 ± 0.76	3.5 ± 0.68	3.7 ± 0.88	0.6389	3.52 ± 0.77
Mean hospital stay (days)	5.03 ± 1.03	4.8 ± 1.3	5.3 ± 1.5	0.2164	5.0 ± 1.1

BMI: Body mass index.

T<sub>1-2</sub> has previously been shown to be worse, which both emphasize the technical complexity. Surgery for large tumors is more difficult due to limited working space and easier to bleed due to increased angiogenesis. For this reason, some authors emphasize the importance of a surgeon with good surgical skills and appropriate case selection. EM Bolton (2018): all T<sub>3a</sub> patients, confined to the renal vein, were considered for LS while tumors extending into the IVC were managed by open technique, the author also observed a low conversion rate to open surgery in T<sub>3a</sub> [35]. Recent studies have suggested that LRN can be performed safely in patients with large renal tumors and T<sub>3a</sub> tumors, although the procedure is technically more challenging [28], [34]. The only acceptable contraindication is significant LN metastasis, invasion of the IVC wall, and adjacent organs. Operative time, blood loss, and risk of major complications were not significantly different compared to LRN at T<sub>1-2</sub>. The approach (transperitoneal or retroperitoneal) depends on surgeon preference, rather than the superiority of any technique [35].

Barbas-Bernardos G (2020) also showed that LRN is safe for pT<sub>3a</sub> stage and LRN at this stage not only increases operative time, but reduces hospital stay and postoperative complications and especially does not affect RFS and OS [36]. Xiaojun Tian MD (2020) performed RLRN with thrombectomy for 78 patients with Grade 0, I, II RCC from March 2015 to September 2018 with promising initial results [37].

In our study group, there were 26/191 patients diagnosed at stage T<sub>3a</sub>, in which: renal vein thrombosis (1), invades perirenal fat (20), invades renal sinus fat, and renal calyx system (5). RFS<sub>5-years</sub> and OS<sub>5-years</sub> of stage 3 were: 87.8% and 91.3%, respectively, like other authors (Table 2). The safety and feasibility of LS at this stage are shown in Table 4 and Supplemental Figure 1, indicating that LS at Stage 3 only increases operative time, other parameters such as intra- and postoperative complications, duration of pain medication, hospital stay was not different from T<sub>1-2</sub>.

## Conclusion

Retroperitoneal LRN for RCC stage T<sub>1-2</sub> gives results comparable to open surgery and presents outstanding advantages. For the advanced stage, LS has been shown to be safe and feasible for eLND as well as in the management of T<sub>3a</sub> tumors, positive long-term results of LS at this stage have also been reported. We believe that LRN should be the first choice for the management of stage T<sub>1-2-3a</sub>N<sub>1</sub> renal tumors that are not feasible with partial nephrectomy.

### Limitation of the study

In Vietnam, we have just implemented RLRN for patients with stage T<sub>3a</sub> and enlarged LND, so the number of patients in these 2 groups is small and the follow-up time is not enough. Therefore, we can only draw preliminary conclusions in their research. However, we will continue to perform RLRN with a larger number of patients and longer follow-up in the T<sub>3a</sub>N1M0 group and continuously do report the results in the near future.

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## Author Contribution

Study concept and design: H.H.N, T.T.Do.  
Operated patients: H.H.N, T.T.D, L.H, M.D.N, S.N.D.



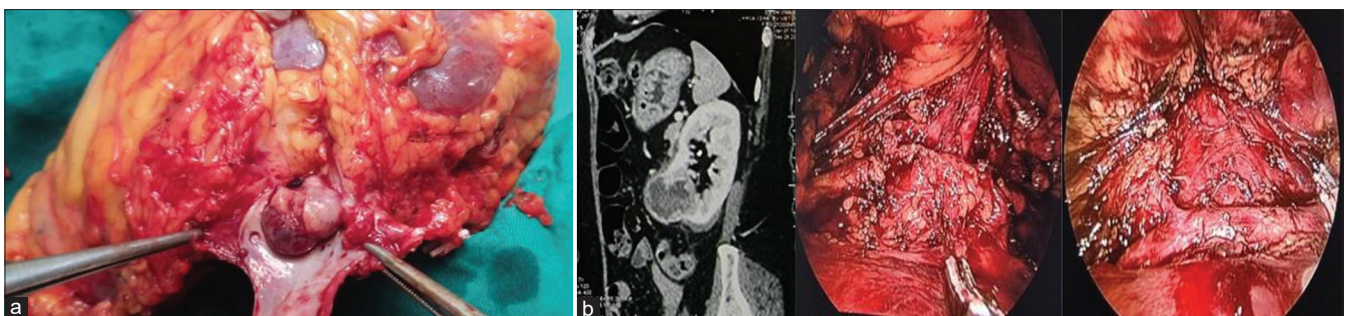
Data acquisition: H.H.N, M.D.N. Data analysis: H.H.N, S.N.D. Drafting of manuscripts: H.H.N, L.H, T.C.V. Critical revision of the manuscript: T.T.D, L.H.

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## Supplementary Figure



Supplemental Figure 1: (a) T3a - renal vein thrombosis. (b) Preoperative T3aN1 → Postoperative T3aN0.