Surgical and Oncologic Outcomes of Laparoscopic Versus Open Radical Nephrectomy with Venous Thrombectomy: A Propensity-Matched Retrospective Cohort Study

COHORT STUDY

YU ZHANG
HAI BI
YE YAN
ZHUO LIU
GUOLIANG WANG
YIMENG SONG
JINGHAN DONG
SHUDONG ZHANG
CHENG LIU
LULIN MA

*Author affiliations can be found in the back matter of this article

IJS Press
Part of the IJS Publishing Group

ABSTRACT

Background: To compare the surgical and oncologic outcomes between laparoscopic and open radical nephrectomy with venous thrombectomy (LRN-VT, ORN-VT) in patients with renal tumor and venous thrombus.

Materials and Methods: We conducted a propensity-matched retrospective cohort study of 302 patients with renal tumor and venous thrombus from January 2014 to January 2021. We compared surgical outcomes and we used the Kalan-Meier method to assess the overall survival (OS), tumor-specific survival (TSS), metastasis-free survival (MFS) and local recurrence-free survival (LRFS). The Pearson chi-square test and Fisher exact test, Wilcoxon rank sum test, Cox proportional hazards regression model and log-rank test were used.

Results: After 1:1 matching, 94 patients were identified in each group and baseline characteristics were comparable. The LRN-VT group had less operative time (median 292min vs 326min, $P < 0.001$), less blood loss (median 500 ml vs 1000 ml, $P < 0.001$), fewer packed red blood cells transfusion (median 800 ml vs 1200 ml, $P < 0.001$) and less fresh frozen plasma transfusion (median 400 ml vs 600 ml, $P < 0.001$). The ORN-VT group had higher complication rate (39.4% vs 21.3%, $P = 0.007$), higher Clavien grade ($P = 0.005$) and longer postoperative hospital stay (median 10d vs 8d, $P < 0.001$). The median time to local recurrence were 36mon after a median follow-up of 31mon in the LRN-VT group and 8mon (IQR 6-15 mon) after a median follow-up of 32mon in the ORN-VT group ($P = 0.007$). The hazard ratio of LRFS for the LRN-VT group was 0.18 (95% CI 0.05–0.62, $P = 0.007$).

Conclusions: LRN-VT can result in favorable surgical outcomes and a better LRFS compared with ORN-VT.

CORRESPONDING AUTHORS:
Cheng Liu and LuLin Ma
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, China
chengliu@bjmu.edu.cn; malulinpku@163.com

KEYWORDS:
venous thrombectomy; laparoscopic procedure; open procedure; propensity-matched; renal tumor

TO CITE THIS ARTICLE:
Zhang Y, Bi H, Yan Y, Liu Z, Wang G, Song Y, Dong J, Zhang S, Liu C, Ma L. Surgical and Oncologic Outcomes of Laparoscopic Versus Open Radical Nephrectomy with Venous Thrombectomy: A Propensity-Matched Retrospective Cohort Study. *International Journal of Surgery: Oncology*. 2021; 6(1), 59–70. DOI: *https://doi.org/10.29337/ijsonco.127*

Highlights:

- This single-center retrospective cohort study compared the surgical and oncologic outcomes between laparoscopic and open radical nephrectomy with venous thrombectomy.
- LRN-VT is a reliable and effective procedure in the treatment of renal tumor with venous thrombus and LRN-VT has advantages in operative time, blood loss, complications and postoperative hospital stay compared with ORN-VT.
- LRN-VT is not inferior to ORN-VT with regard to OS, TSS and MFS.
- LRN-VT can result in a better LRFS than ORN-VT.

1. INTRODUCTION

Renal tumors, especially the renal cell carcinoma (RCC), can enlarge from the kidney and involve the venous system. Venous thrombus occurs up to 10% in patients with RCC [1]. Radical nephrectomy and venous thrombectomy (RN-VT) can offer reasonable long-term survival in such patients and the 5-yr disease-specific survival rate can be 53% to 64% [2, 3]. Open surgery remains the preferred treatment option [4]. Nevertheless, several reports have introduced the application and confirmed the feasibility of pure laparoscopy or hand-assisted laparoscopy in RN-VT [5–10]. Until now, less literature reported the comparative analysis between laparoscopic radical nephrectomy with venous thrombectomy (LRN-VT) and open radical nephrectomy with venous thrombectomy (ORN-VT) in patients with renal tumor and venous thrombus.

In this study, we performed a propensity-matched retrospective cohort study to compare the surgical and oncologic outcomes following LRN-VT and ORN-VT in patients with renal tumor and venous thrombus. We hypothesized that LRN-VT could achieve comparable outcomes compared with ORN-VT.

2. MATERIALS AND METHODS

2.1 DATA SOURCE AND STUDY COHORT

We followed the STROBE statement and this study is fully compliant with the STROCSS criteria [11]. Our registration unique identifying number is researchregistry7016.

Following institutional review board approval, we retrospectively reviewed our database (Peking University Third Hospital Thrombus Database, PUTH-TD) containing medical records of all patients with renal vein thrombus or inferior vena cava (IVC) thrombus from January 2014 to January 2021 (n = 350). The database has been constructed prospectively since January 2014. Two full-time clinical data managers had all access to the data through electric case report forms (eCRF) and were responsible for data entry, verification and quality control. The demographic, perioperative, postoperative and follow-up data were accurately recorded. The inclusive criteria were as follows: (1) pathologically confirmed tumor of renal origin; (2) detailed information on surgical procedures; (3) no comorbidity of hemorrhagic disease; (4) minimum follow-up of 6 mon. The patients who were treated by robot-assisted LRN-VT (RALRN-VT) or who didn't receive surgical treatment were excluded.

2.2 SURGICAL PROCEDURES

The techniques of LRN-VT and ORN-VT at our institution have been described previously [8, 12–14]. For LRN-VT, both transperitoneal approach and retroperitoneal approach were used in our center depending on the thrombus level, tumor side, surgery history and invading the IVC wall or not. For level 0 thrombus, we didn't block the IVC and we cut off the renal vein from the segment without tumor thrombus. For level I thrombus, the IVC was partially clamped using a Satinsky clamp. We incised the IVC and removed the thrombus and then irrigated the IVC with heparinized saline before suturing. For level II thrombus, we clamped the IVC below the thrombus, the contralateral renal vein and the IVC above the thrombus sequentially after we cut off the renal artery on the tumor side. The contralateral renal artery was blocked for the left tumor, while the left renal artery was not blocked for the right tumor. Segmental resection of the IVC would be considered if the thrombus invaded the IVC wall extensively. If minor involvement of the IVC wall occurred, we performed resection of the invaded vessel wall rather than segmental resection. For level III or IV thrombus, the first porta hepatis should be blocked and the Foley catheter-assisted six-step thrombectomy technique [12] was used in our center. If the right atrium was involved, ORN-VT is usually needed. We usually incised the thoracoabdominal midline and the "milking" technique is performed to squeeze the intra-atrial thrombus back into the IVC.

2.3 FOLLOW-UP

We provided the same follow-up plan to all patients and follow-up data were regularly collected (symptoms and signs, laboratory tests, imaging examination of the chest,

abdomen and pelvis). The laboratory tests included routine blood test and blood biochemical test. The imaging examination included computed tomography (CT), magnetic resonance imaging (MRI) and X ray. Patients were followed up every 3 mon after surgery in the first year, then 6 mon to the third year, then annually thereafter. We determined the death reason according to the death certificate issued by the local medical institution if a patient died during the interval of follow-up visit or we determined that by the treating physicians.

2.4 OUTCOMES AND DEFINITIONS

Primary outcomes contained surgical outcomes and oncologic outcomes. The surgical outcomes were represented by perioperative and postoperative outcomes (operative time, blood loss and complication rate, et al) between the two groups and the oncologic outcomes were represented by the overall survival (OS), tumor-specific survival (TSS), metastasis-free survival (MFS) and local recurrence-free survival (LRFS). Complications were evaluated within 30 days after surgery. OS meant the length of time from surgery to death from any cause. TSS was defined as the time from surgery to death due to tumor. LRFS was defined as the time from surgery to local recurrence (tumor recurrence in or abutting the previous surgical bed) based on CT or MRI. MFS was defined as the time from surgery to the development of metastatic disease (new lesions in other organs, brain, lung, liver, bone, et al) based on CT or MRI. MFS was only assessed in patients with M0 diseases.

The presence of local symptoms was defined as a palpable mass, pain, gross hematuria. Patients with edema, fever, swelling, fatigue and weight loss, et al were thought to have systemic symptoms. The American Society of Anesthesiologists Physical Status classification system (ASA level) [15] was introduced to estimate the operative risk of patients. Thrombus level was classified using the Mayo Clinic classification of tumor thrombus level [1]. Postoperative complications were graded according to the Clavien-Dindo grading system [16].

The histological diagnosis of renal tumors was based on the World Health Organization (WHO) classification (2004 and 2016 version) [17, 18]. The Fuhrman system was applied to RCC nuclear grading [19]. A sarcomatoid differentiation was defined as RCC accompanied by histological appearance of spindle-cell sarcoma. The 2017 version of the tumor-node-metastasis (TNM) classification was used for clinical staging based on postoperative pathological specimen.

2.5 DATA QUALITY AND BIAS CONTROL

We designed a precise eCRF containing all the necessary medical information and standardized the definition, naming method and data type of each variable. We set up mandatory fields to reduce data missing and two trained data managers performed data entry to reduce logic errors. The data managers were blinded to the study design. A third party checked the database regularly to keep the authenticity and accuracy.

We set strict criteria for inclusion and exclusion to reduce the selection bias. We performed a propensity-matched comparative analysis to minimize the influence of confounding bias and to identify a cohort of patients with comparable baseline characteristics. The propensity score was estimated by a multivariable logistic regression model and the 1:1 matching without replacement was performed with a caliper width equal to 0.02. Patients were matched regarding age, body mass index (BMI), ASA level, comorbidity, tumor diameter, thrombus level and metastasis at diagnosis. Matching was performed by a researcher who didn't know the outcomes.

An independent researcher who was blinded to the matched-cohort analyzed the outcomes to control the information bias. Except for the routine review after surgery, the data managers conducted telephone interviews every 3–6 mon and collected the follow-up information to reduce the withdraw bias.

2.6 STATISTICAL ANALYSIS

Baseline characteristics were shown for categorical variables and continuous variables. We reported the medians and interquartile ranges for non-normally distributed continuous variables and the means and standard deviations for normally distributed continuous variables. Categorical variables were reported as frequencies and proportions. The chained multiple imputation was used to resolve the missing data. We compared differences between non-normally distributed continuous data and ordered categorical data with the Wilcoxon sum rank test and compared differences between unordered categorical data with the Chi-square test and Fisher exact test. In the matched cohort, the paired t-test, the Wilcoxon signed rank or the McNemar test was applied to compare differences. We used the Kaplan-Meier method to perform survival analysis and assessed the differences between the propensity-matched groups with log-rank test. Cox proportional hazards regression model was used to estimate the relative oncologic outcomes after adjusting the variables that satisfied the proportional hazards assumptions (thrombus level, lymph node metastasis and distant metastasis, perinephric fat invasion, adjuvant therapy, et al). A hazard ratio (HR) less than 1.0 favored LRN-VT. All statistical tests were performed by SPSS version 25.0 (IBM, Armonk, NY, USA) and the R statistics package version 3.6.1 (R Project for Statistical Computing, *www.r-project.org*). All tests were two-sided, and the significance level was set at $p < 0.05$.

3. RESULTS

3.1 PATIENT CHARACTERISTICS

Of consecutive 350 patients identified, 32 patients were excluded for pathologically confirmed tumors that were not renal origin, 6 patients were excluded for RALRN-VT, 6 patients were excluded because of conservative treatment and 4 patients were excluded for shorter than 6 mon of follow-up. 302 patients were matched, including 148 patients treated with LRN-VT and 154 patients treated with ORN-VT. Before propensity matching, significant differences existed in several baseline variables (***Table 1***). After matching, 94 patients were matched in each group and no significant differences were found in baseline characteristics.

	BEFORE PROPENSITY-MATCHING			AFTER PROPENSITY MATCHING		
	LRN-VT (N = 148)	ORN-VT (N = 154)	P VALUE	LRN-VT (N = 94)	ORN-VT (N = 94)	P VALUE
Age (yr), median (IQR)	58 (51–65)	60 (53–67)	<0.001	60 (53–68)	59 (52–66)	0.80
Gender (n/%)			0.83			0.28
Male	106 (71.6)	112 (72.7)		60 (63.8)	67 (71.3)	–
Female	42 (28.4)	42 (27.3)		34(36.2)	27 (28.7)	–
BMI (kg/m2), median (IQR)	23.4 (21.3–26.1)	24.0 (20.5–26.0)	<0.001	23.1(21.2–25.8)	23.8(20.7–26.4)	0.29
Laterality (n/%)			0.22			0.29
Left	61 (41.2)	53 (34.4)		31 (33.0)	38 (40.4)	–
Right	87 (58.8)	101 (65.8)		63 (67.0)	56 (59.6)	–
ASA level (n/%)			<0.001			0.88
1	10 (6.8)	8 (5.2)		7 (7.5)	5 (5.3)	–
2	107 (72.3)	56 (36.4)		79 (84.0)	82 (87.2)	–
3	42 (28.4)	89 (57.8)		8 (8.5)	7 (7.5)	–
4	0 (0)	16 (10.4)		–	–	–
Symptoms (n/%)			0.26			0.32
Local	88 (59.5)	102 (66.2)		56 (56.6)	66 (66.7)	–
Systemic	9 (6.1)	17 (11.0)		10 (10.1)	7 (7.1)	–
Comorbidity (n/%)	88 (59.5)	95 (61.7)	0.69	54 (57.4)	62 (66.0)	0.23
Hypertension	60 (40.5)	63 (40.9)		36 (38.3)	41 (43.6)	
Coronary heart disease	7 (4.7)	7 (4.5)		3 (3.2)	6 (6.4)	–
Diabetes mellitus	16 (10.8)	20 (13.0)		11 (11.7)	13 (13.8)	–
Cerebrovascular disease	2 (1.4)	3 (1.9)		1 (1.1)	2 (2.1)	–
Chronic lung disease	0 (0)	2 (1.3)		0 (0)	2 (2.1)	–
Surgery history	36 (24.8)	44 (28.6)		21 (22.3)	29 (30.9)	–
Preoperative targeted therapy (n/%)	5 (3.4)	9 (5.8)	0.30	3 (3.2)	5 (5.3)	0.72
Tumor diameter (cm), median (IQR)	8.2 (6.8–9.9)	9.2 (6.6–12.0)	0.004	8.4 (6.8–10.2)	8.6 (5.9–11.6)	0.72
Preoperative SCR (μmoL/L), median (IQR)	89 (78–107.5)	91 (79–111)	0.13	91 (75–108.5)	92 (81–111.3)	0.60
Thrombus level (n/%)			<0.001			0.27
0	50 (33.8)	18 (11.7)		21 (22.3)	18 (19.1)	–
I	37 (25.0)	17 (11.0)		16 (17.0)	16 (17.0)	–
II	52 (35.1)	67 (43.5)		49 (52.1)	50 (53.2)	–
III	7 (4.7)	26 (16.9)		7 (7.5)	7 (7.5)	–

(Contd.)

	BEFORE PROPENSITY-MATCHING			AFTER PROPENSITY MATCHING		
	LRN-VT (N = 148)	ORN-VT (N = 154)	P VALUE	LRN-VT (N = 94)	ORN-VT (N = 94)	P VALUE
IV	1 (0.7)	26 (17.9)		1 (1.1)	3 (3.2)	–
Pulmonary embolism (n/%)	1 (0.7)	7 (4.5)	0.07	1 (1.1)	3 (3.2)	0.62
Hepatic vein invasion (n/%)	1 (0.7)	1 (0.6)	1.0	1 (1.1)	1 (1.1)	1.0
Metastasis at diagnosis (n/%)	95 (64.2)	115 (74.7)	0.05	61 (64.9)	67 (71.3)	0.35
Suspected Lymph node metastasis	82 (55.4)	105 (68.2)	0.02	54 (57.5)	61 (64.9)	0.30
Suspected Adrenal metastasis	11 (7.4)	23 (14.9)	0.04	7 (7.5)	11 (11.7)	0.32
Distant metastasis	36 (24.3)	52 (33.8)	0.07	21 (22.3)	29 (30.9)	0.19
Lung	28 (18.9)	31 (20.1)		17 (18.1)	18 (19.1)	
Liver	9 (6.1)	11 (7.1)		6 (6.4)	7 (7.5)	
Bone	1 (7.4)	11 (7.1)		5 (5.3)	6 (6.4)	

Table 1 Baseline characteristics of patients undergoing LRN-VT and ORN-VT before and after propensity matching.

LRN-VT, laparoscopic radical nephrectomy with venous thrombectomy; ORN-VT, open radical nephrectomy with venous thrombectomy; BMI, body mass index; ASA, American Society of Anesthesiologists; IQR, interquartile range; SCR, serum creatine.

3.2 SURGICAL OUTCOMES

Surgical outcomes were showed in ***Table 2***. Twenty-four patients (25.5%) in the LRN-VT group converted to open surgery. Forty-one patients (43.6%) received adrenalectomy in the LRN-VT group and 44 patients (46.8%) received adrenalectomy in the ORN-VT group (P = 0.66). Nine patients (9.6%) in the LRN-VT group and 23 patients (24.5%) in the ORN-VT group underwent segmental resection of IVC (P = 0.01). The median operative time of ORN-VT was longer than that of LRN-VT (326min vs 292min, P = 0.002). The median blood loss of ORN-VT was significantly greater than that of LRN-VT (1000 ml vs 500 ml, P < 0.001). Sixty-three patients (67%) in the ORN-VT group received intraoperative or postoperative blood transfusion, while only 38 patients (40.4%) in the LRN-VT group needed blood transfusion (P < 0.001). The median packed red blood cells transfusion and fresh frozen plasma transfusion in the ORN-VT group were significantly greater than those in the LRN-VT group (1200 ml vs 800 ml, 600 ml vs 400 ml, all P < 0.001). The complication rate of ORN-VT was higher than that of LRN-VT (39.4% vs 21.3%, P = 0.007) and the Clavien grade was higher in the ORN-VT group than that in the LRN-VT group (P = 0.005). The median postoperative hospital stay of LRN-VT group was shorter than that of ORN-VT group (8d vs 10d, P < 0.001).

3.3 ONCOLOGIC OUTCOMES

After a median follow-up of 31mon (IQR 19–44 mon) in the LRN-VT group and 32 mon (IQR 17–40 mon) in the ORN-VT group, 28 deaths occurred in each group (29.8% vs 29.8%, P = 1.0). Twenty-four deaths (25.5%) in the LRN-VT group contributed to tumor and all deaths in the ORN-VT group contributed to tumor. The median time to death in the LRN-VT group and ORN-VT group were 17 mon (IQR 9–26 mon) and 12 mon (IQR 9–20.5 mon), respectively (P = 0.29). Among patients with M0 disease (LRN-VT group, n = 73 vs ORN-VT group, n = 65), 33 patients (45.2%) in the LRN-VT group and 36 patients (55.4%) in the ORN-VT group developed distant metastases (P = 0.23). The most common new metastatic sites were lung (n = 44), bone (n = 24) and liver (n = 18). Local recurrence occurred in 1 patient in the LRN-VT group and 5 patients in the ORN-VT group (P = 0.28). The median time to local recurrence in the LRN-VT group and ORN-VT group were 36 mon and 8 mon (IQR 6–15 mon), respectively (P = 0.007). ***Table 3*** summarized the data on follow-up in each group.

Figure 1 depicted the Kaplan-Meier curves of oncologic outcomes. We couldn't observe a statistically significant difference in either OS (Adjusted HR 0.96, 95%CI 0.67–1.40; P = 0.85), TSS (Adjusted HR 1.03, 95%CI 0.69–1.52; P = 0.90) or MFS (Adjusted HR 0.89, 95%CI 0.58–1.38; P = 0.61) between the two matched groups (***Figure 1A, B*** and ***C***). Patients who underwent LRN-VT had a lower risk of local recurrence compared to patients who underwent ORN-VT (Adjusted HR 0.18, 95% CI 0.05–0.62, P = 0.007) (***Figure 1D***).

3.4 PATHOLOGICAL OUTCOMES

Table 4 showed the pathological results of the renal tumors between the two groups. We couldn't observe a statistically significant difference in either T stage (P = 0.16), lymph node metastasis (0.09), perinephric fat invasion (0.39), histological type (P = 0.37), adrenal

	LRN-VT(N = 94)	ORN-VT(N = 94)	P VALUE
Surgical approach (n/%)			–
Transperitoneal	63 (67.0)	–	–
Retroperitoneal	25 (26.6)	–	–
Combined	6 (6.4)	–	–
Open conversion (n/%)	24 (25.5)	–	–
Adrenalectomy (n/%)	41 (43.6)	44 (46.8)	0.66
Segmental resection of IVC (n/%)	9 (9.6)	23 (24.5)	0.01
Resection of metastatic tumor (n/%)	2 (2.1)	0 (0)	0.50
Operative time (min), median (IQR)	292 (242–385)	326 (253–404)	0.002
Blood loss (ml), median (IQR)	500 (200–838)	1000 (400–2050)	<0.001
Blood transfusion(n/%)	38 (40.4)	63 (67.0)	<0.001
Packed RBC transfusion (ml), median (IQR)	800 (400–1600)	1200 (800–1600)	<0.001
FFP transfusion (ml), median (IQR)	400 (400–575)	600 (400–800)	<0.001
Postoperative SCR	97 (77.5–114.5)	98 (73.5–116)	0.87
Complications (n/%)	20 (21.3)	37 (39.4)	0.007
Cardiovascular or cerebrovascular events	1 (1.1)	0 (0)	–
Pneumonia or pleural effusion	3 (3.2)	2 (2.1)	–
Kidney insufficiency	3 (3.2)	4 (4.3)	–
Abdominal cavity infection	1 (1.1)	2 (1.9)	–
Incision infection	1 (1.1)	0 (1.3)	–
Deep venous thrombus	2 (2.1)	3 (3.2)	–
Anemia	3 (3.2)	14 (14.9)	–
Bowel obstruction	3 (3.2)	8 (8.5)	–
Lymphatic fistula	0 (0)	6 (6.4)	
Clavien grade of complications (n/%)			0.005
I	6 (6.4)	13 (13.8)	–
II	10 (10.6)	20 (21.3)	–
III	1 (1.1)	0 (0)	–
IV	3 (3.2)	4 (4.3)	
Postoperative hospital stay (d), median (IQR)	8 (6–10)	10 (8–13)	<0.001

Table 2 Comparison of surgical outcomes of LRN-VT group and ORN-VT group in the matched cohort.

LRN-VT, laparoscopic radical nephrectomy with venous thrombectomy; ORN-VT, open radical nephrectomy with venous thrombectomy; IVT, inferior vena cava; RBC, red blood cells; FFP, fresh frozen plasma; ASA, American Society of Anesthesiologists; IQR, interquartile range; SCR, serum creatinine.

metastasis (0.25), venous wall involvement (0.61), sarcomatoid differentiation (P = 0.49) or Fuhrman grade (P = 0.12) between the two matched groups.

4. DISCUSSION

LRN-VT has been proved to be an effective surgical approach [6, 10, 20–22] despite insufficient high-level medical-evidence support its overwhelming superiority over ORN-VT. Our propensity-matched cohort study favored that LRN-VT had advantages in operative time, blood loss, postoperative hospital stay as well as complications. However, the survival analysis showed that LRN-VT could not result in a better oncologic outcome when comparing OS, TSS and MFS. Our finding indicated that patients in the LRN-VT group had a better LRFS than those in the ORN-VT group.

The first laparoscopic procedure for renal vein thrombus was reported in 1996 [23] and after that,

	LRN-VT(N = 94)	ORN-VT(N = 94)	P VALUE
Adjuvant therapy (n/%)	38 (40.4)	45 (47.9)	0.3
Targeted therapy	36 (38.3)	41 (43.6)	–
Radiotherapy	2 (2.1)	2 (2.1)	–
Chemotherapy	0 (0)	2 (2.1)	–
Follow-up (mon), median (IQR)	31 (19–44)	32 (17–40)	0.78
Death (n/%)	28 (29.8)	28 (29.8)	1.0
Death of tumor	24 (25.5)	28 (29.8)	0.42
Other reasons	4 (4.3)	0 (0)	
Time to death (mon), median (IQR)	17 (9–26)	12 (9–20.5)	0.29
Local recurrence (n/%)	1 (1.1)	5 (5.3)	0.28
Time to local recurrence (mon), median (IQR)	36	8 (6–15)	0.007
New distant metastatic cases (n/%)	33 (45.2) n = 73	36 (55.4) n = 65	0.23
Lung	25 (34.2)	19 (29.2)	
Liver	8 (11.0)	10 (15.4)	
Bone	11 (15.1)	13 (20.0)	
Brain	5 (6.9)	2 (3.1)	
Time to new distant metastasis (mon), median (IQR)	20 (8.5–27.5)	23.5 (15.8–29)	0.85

Table 3 Comparison of oncologic outcomes between LRN-VT group and ORN-VT group in the matched cohort.

LRN-VT, laparoscopic radical nephrectomy with venous thrombectomy; ORN-VT, open radical nephrectomy with venous thrombectomy; RCC, renal cell carcinoma; IQR, interquartile range.

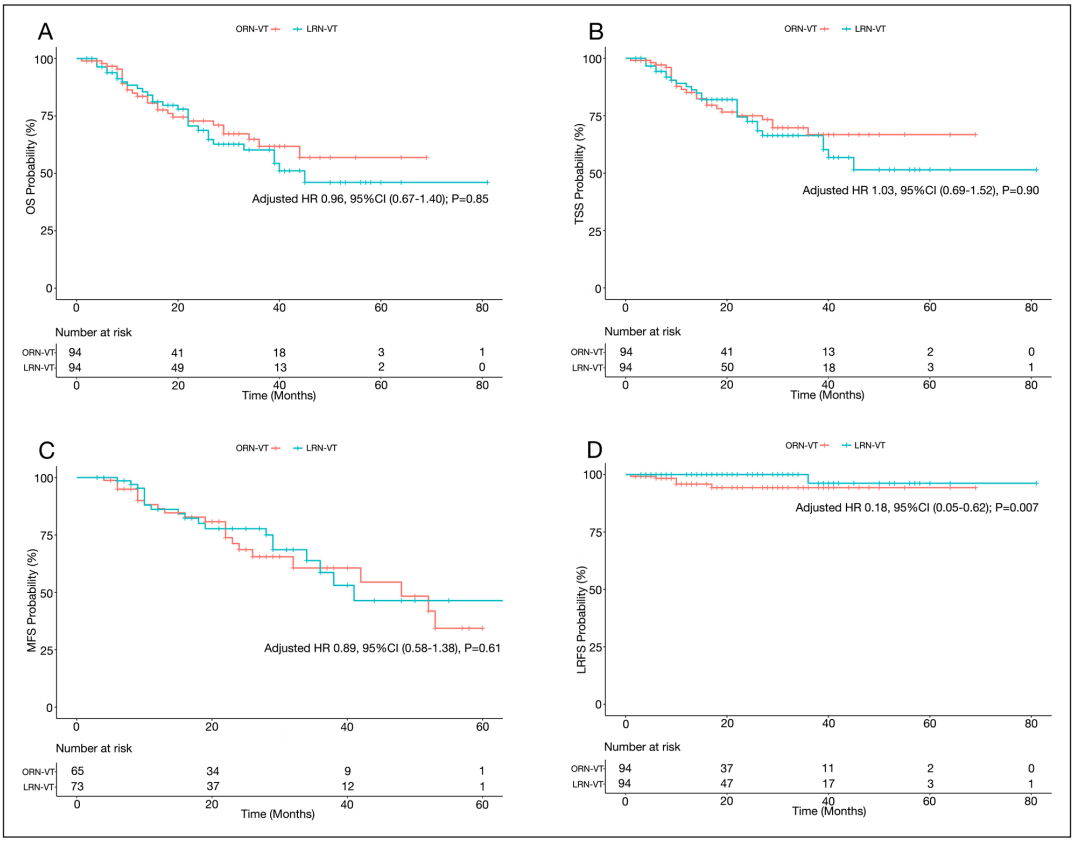

Figure 1 Survival analysis in the matched cohort. **A.** Adjusted OS of patients undergoing LRN-VT and ORN-VT; **B.** Adjusted TSS of patients undergoing LRN-VT and ORN-VT; **C.** Adjusted MFS of patients undergoing LRN-VT and ORN-VT; **D.** Adjusted LRFS of patients undergoing LRN-VT and ORN-VT.

	LRN-VT (N = 94)	ORN-VT (N = 94)	P VALUE
T stage (n/%)			0.16
pT3a	15 (16.0)	11 (11.7)	
pT3b	39 (41.5)	36 (38.3)	
pT3c	36 (38.3)	42 (44.7)	
pT4	4 (4.3)	5 (5.3)	
Lymph node metastasis (n/%)	54 (51.9)	60 (63.8)	0.09
Perinephric fat invasion (n/%)	20 (21.3)	25 (26.6)	0.39
Adrenal metastasis (n/%)	2 (2.1)	5 (5.3)	0.25
Involving the venous wall (n/%)	21 (22.3)	24 (25.5)	0.61
Histology (n/%)			0.37
Clear cell RCC	78 (83.9)	75 (79.8)	
Papillary type RCC	9 (9.6)	15 (16.0)	
Chromophobe RCC	1 (1.1)	0 (0)	
Unclassified RCC	1 (1.1)	2 (2.1)	
Ewing's sarcoma	3 (3.2)	1(1.1)	
Nephroblastoma	0 (0)	1(1.1)	
Angiomyolipoma	1 (1.1)	0 (0)	
Squamous cell carcinoma	1 (1.1)	0 (0)	
Sarcomatoid differentiation (n/%)	9 (9.6)	12 (12.8)	0.49
Fuhrman grade (n/%)			0.12
1	1 (1.1)	3 (3.2)	–
2	36 (38.3)	29 (30.9)	–
3	32 (34.0)	38 (40.4)	–
4	20 (21.3)	22 (23.4)	–

Table 4 Pathological outcomes of LRN-VT group and ORN-VT group.

LRN-VT, laparoscopic radical nephrectomy with venous thrombectomy; ORN-VT, open radical nephrectomy with venous thrombectomy; RCC, renal cell carcinoma.

many centers applied laparoscopic technique into IVC thrombectomy. Ioannis et al. [9] evaluated the feasibility of laparoscopic procedure in 4 patients with level I thrombus and found that no intra- or postoperative complications occurred. For level II thrombus, Wang et al. [22] reported the surgical outcomes of laparoscopic procedure in 5 patients and found that 1 patient required intraoperative transfusion and encountered bilateral lower limb deep vein thrombus. Tian et al. [8] once presented our laparoscopic experience in 78 patients with level 0–II thrombus and found that 24 patients (30.8%) needed transfusion and 13 patients (16.7%) had complications. Of the 94 patients in our matched LRN-VT cohort, 38 (40.4%) patients needed transfusion and 20 patients (21.3%) had Clavien I–IV complications. A higher transfusion rate and a higher complication rate were met in our LRN-VT cohort and the following reasons could explain the discrepancy. Firstly, we reported the surgical outcomes of level 0–IV thrombus, including 1 patient with level III thrombus and 3 patients with level IV thrombus. For level IV thrombus, Shao et al. [6] reported the transfusion rate was 80% (4/5) and the Clavien I–II grade complication rate was 80% (4/5). Secondly, 21 patients (22.3%) had pathologically confirmed thrombus involving the venous wall and 9 patients (9.6%) received segmental resection of IVC in our LRN-VT cohort. Lastly, 41 patients (43.6%) underwent adrenalectomy. All the factors made our LRN-VT more extensive and more traumatic and led to a relatively higher transfusion rate and a higher complication rate.

Randomized trials focusing on the comparative outcomes of LRN-VT and ORN-VT have not been reported. Some observational studies analyzed the outcomes of the two procedures. Xu et al. [24] compared the surgical outcomes of laparoscopic versus open procedure directly and found that LRN-VT had shorter operative time, less blood loss, shorter hospital stay and less transfusion than ORN-VT. Our surgical outcomes were consistent with

their findings. However, some differences still existed. First of all, their study only contained renal tumor with level I and II thrombus, while our study included patients with level 0–IV thrombus. Next, they used complete retroperitoneal approach while we performed both transperitoneal and retroperitoneal approaches. Finally, they reported no complication in the LRN-VT group and only 2 patients (6.3%) in the ORN-VT had perioperative complications. They didn't observe statistically significant difference in complication rate between the two groups. Ebbing et al. [25] reported that ORN-VT led to a two-fold higher complication rate than LRN-VT in patients with renal vein thrombus. In our study, we found a significant lower complication rate and a lower Clavien grade in the LRN-VT group than that in the ORN-VT group. We thought that was largely due to the wider and clearer vision of the laparoscope. Thanks to the improvement of surgical vision and high-definition picture, the surgeons could perform precise operation and avoid unnecessary injuries effectively, especially for the vessels. It was also noteworthy that open conversion due to anatomical difficulty, intraoperative bleeding or tumor control consideration occurred in 24 patients. That could reduce the postoperative complications and even the perioperative mortality which could have occurred in the LRN-VT group. The two most common complications in the ORN-VT group were anemia and bowel obstruction, while we didn't find any complication particularly associated to LRN-VT. These findings supported that LRN-VT had greater advantages in surgical outcomes over ORN-VT.

RALRN-VT has been clinically applied in several centers since its first report in 2011 [4, 26–28]. Kyle et al. [29] compared the perioperative and oncologic outcomes of level I–II thrombus between RALRN-VT and ORN-VT and found that RALRN-VT produced shorter hospital stay, less transfusion and a lower complication rate with no statistically significant difference in OS. Gu et al. [30] concluded that RALRN-VT can achieve more favorable perioperative outcomes and similar oncologic outcomes compared with ORN-VT. In our study, we excluded the patients treated with RALRN-VT to control the bias and we didn't compare RALRN-VT with either LRN-VT or ORN-VT. However, based on the results mentioned, we thought that the minimally invasive procedures, including RALRN-VT and LRN-VT, might be superior surgical options over open surgery. We encouraged attempts to apply the minimally invasive procedures to patients with renal tumor and venous thrombus. Besides, we advised high-level randomized controlled trials comparing the surgical outcomes of the three procedures to be conducted to confirm the superiority.

The precise operation of LRN-VT can minimize the surgical trauma and maximize the resection of tumor. However, when it comes to the oncologic outcomes, we didn't observe that LRN-VT could result in a better OS, TSS or MFS than ORN-VT after a median follow-up of 31 mon and 32 mon respectively. Xu et al. [24] found that laparoscopic approach had a similar TSS in level I–II thrombus compared with open surgery after a median follow-up of 18.2 mon. Gu et al. [30] also observed that robotic cohort had a comparable OS and TSS with open cohort in a propensity-matched cohort study after a median follow-up of 27 mon and 48 mon respectively. Rose et al. [29] reported that there was no statistically significant difference in OS and recurrence-free survival between robotic procedure and open procedure. However, in our study we found that LRN-VT was associated with a lower risk of local recurrence and the median LRFS was much longer in the LRN-VT group than that in the ORN-VT group. The patient with local recurrence in the LRN-VT group (postoperative 36 mon) had postoperative adjuvant targeted therapy with Sunitinib and Axinitib and only 1 patient with local recurrence (postoperative 17 mon) in the ORN-VT group (median local recurrence time 8 mon) had postoperative adjuvant targeted therapy with Pazopanib. We understand this from two perspectives. On the one hand, postoperative adjuvant targeted agents may help prolong the time from surgery to local recurrence. On the other hand, patients without adjuvant therapy in the LRN-VT group (n = 56) had no local recurrence and patients without adjuvant therapy in the ORN-VT group (n = 49) had 4 cases of local recurrence. This could better reflect the weight of surgery in local recurrence control and LRN-VT had superiority in LRFS over ORN-VT. However, owing to the relatively small number of recurrence events in the two groups, our results should not be taken as suggesting that surgical option determines LRFS. More local recurrence events and longer follow-up are necessary to better compare the LRFS between the two groups.

Our study has strengths that enhance the clinical applicability of the findings. To the best of our knowledge, this study represents the largest propensity-matched comparative analysis of LRN-VT versus ORN-VT. This study provided support to the application of laparoscopic procedure in the treatment of renal tumor with venous thrombus. In addition, we reported for the first time that LRN-VT could result in a better LRFS in such patients. However, this study has some limitations. The first one is its retrospective and non-randomized nature. Despite we matched, unknown confounders might exist and affect the results and then limit the internal validity. A large prospective cohort study or a randomized controlled study is needed to better compare the outcomes between the two surgical approaches. Furthermore, a relatively shorter follow-up time limited the observation of oncologic outcome events, especially for the local recurrence event. This study would definitely benefit from a longer follow-up.

5. CONCLUSIONS

LRN-VT is a reliable and effective procedure in the treatment of renal tumor with venous thrombus, despite open procedure remains the preferred surgical option. LRN-VT has advantages in operative time, blood loss, complications and postoperative hospital stay compared with ORN-VT. As for the oncologic outcomes, LRN-VT is not inferior to ORN-VT with regard to OS, TSS and MFS. LRN-VT can result in a better LRFS than ORN-VT and longer follow-up is needed to further validate the finding.

ADDITIONAL FILE

The additional file for this article can be found as follows:

- **Rawdata.** Rawdata of the study cohort. DOI: *https://doi.org/10.29337/ijsonco.127.s1*

ETHICS AND CONSENT

This article does not contain any studies with human participants or animals performed by any of the authors; and it receives ethics approval from Peking University Third Hospital Ethics Committee.

ACKNOWLEDGEMENTS

We thank all the stuff of department of urology in the Peking University Third Hospital. We also thank Mr. JiaJu Huang, who was the founder of BEYOND band. His music has inspired us to pursue the truth, freedom and essential nature of science in the past twenty years.

FUNDING INFORMATION

National Nature Science Foundation of China (81972381).

COMPETING INTERESTS

We confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property.

AUTHOR CONTRIBUTIONS

Yu Zhang: Study design/Project development/Data analysis/Manuscript writing-original draft
Hai Bi: Manuscript writing-reviewing/Project development/Critical revision
Ye Yan: Manuscript writing-reviewing/Project development/Critical revision
Zhuo Liu: Data collection/Supervision
GuoLiang Wang: Supervision
YiMeng Song: Material support
JingHan Dong: Data collection/Data analysis
ShuDong Zhang: Supervision/Critical revision
Cheng Liu: Supervision/Critical revision
LuLin Ma: Study design/Supervision/Critical revision/Material support/Funding acquision
Yu Zhang, Hai Bi, Ye Yan contributed equally to this article.

AUTHOR AFFILIATIONS

Yu Zhang *orcid.org/0000-0003-3223-5595*
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
Hai Bi
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
Ye Yan
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
Zhuo Liu
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
GuoLiang Wang
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
YiMeng Song
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
JingHan Dong
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN

ShuDong Zhang
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
Cheng Liu
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN
LuLin Ma *orcid.org/0000-0003-2646-405X*
Department of Urology, Peking University Third Hospital, Beijing, People's Republic of China, 49 North Garden Rd, Haidian District, Beijing 100191, CN

REFERENCES

1. **Blute ML, Leibovich BC, Lohse CM, Cheville JC, Zincke H.** The Mayo Clinic experience with surgical management, complications and outcome for patients with renal cell carcinoma and venous tumour thrombus. *BJU Int.* 2004; 94(1): 33–41. DOI: *https://doi.org/10.1111/j.1464-410X.2004.04897.x*
2. **Ciancio G, Manoharan M, Katkoori D, De Los Santos R, Soloway MS.** Long-term survival in patients undergoing radical nephrectomy and inferior vena cava thrombectomy: single-center experience. *Eur Urol.* 2010; 57(4): 667–672. DOI: *https://doi.org/10.1016/j.eururo.2009.06.009*
3. **Tilki D, Nguyen HG, Dall'Era MA,** et al. Impact of histologic subtype on cancer-specific survival in patients with renal cell carcinoma and tumor thrombus. *Eur Urol.* 2014; 66(3): 577–583. DOI: *https://doi.org/10.1016/j.eururo.2013.06.048*
4. **Abaza R.** Initial series of robotic radical nephrectomy with vena caval tumor thrombectomy. *Eur Urol.* 2011; 59(4): 652–656. DOI: *https://doi.org/10.1016/j.eururo.2010.08.038*
5. **Disanto V, Pansadoro V, Portoghese F, Scalese GA, Romano M.** Retroperitoneal laparoscopic radical nephrectomy for renal cell carcinoma with infrahepatic vena caval thrombus. *Eur Urol.* 2005; 47(3): 352–356. DOI: *https://doi.org/10.1016/j.eururo.2004.11.010*
6. **Shao P, Li J, Qin C,** et al. Laparoscopic Radical Nephrectomy and Inferior Vena Cava Thrombectomy in the Treatment of Renal Cell Carcinoma. *Eur Urol.* 2015; 68(1): 115–122. DOI: *https://doi.org/10.1016/j.eururo.2014.12.011*
7. **Sundaram CP, Jr., Landman J, Joseph OH.** Hand assisted laparoscopy radical nephrectomy for renal cell carcinoma with inderior vena cava thrombus. *Journal of Urology.* 2002; 168: 176–179. DOI: *https://doi.org/10.1016/S0022-5347(05)64855-0*
8. **Tian X, Hong P, Liu Z,** et al. En bloc retroperitoneal laparoscopic radical nephrectomy with inferior vena cava thrombectomy for renal cell carcinoma with level 0 to II venous tumor thrombus: A single-center experience. *Cancer.* 2020; 126(Suppl 9): 2073–2078. DOI: *https://doi.org/10.1002/cncr.32747*
9. **Varkarakis IM, Bhayani SB, Allaf ME, Inagaki T, Gonzalgo ML, Jarrett TW.** Laparoscopic-assisted nephrectomy with inferior vena cava tumor thrombectomy: preliminary results. *Urology.* 2004; 64(5): 925–929. DOI: *https://doi.org/10.1016/j.urology.2004.05.044*
10. **Bansal RK, Tu HY, Drachenberg D,** et al. Laparoscopic management of advanced renal cell carcinoma with renal vein and inferior vena cava thrombus. *Urology.* 2014; 83(4): 812–816. DOI: *https://doi.org/10.1016/j.urology.2013.09.060*
11. **Agha R, Abdall-Razak A, Crossley E,** et al. STROCSS 2019 Guideline: Strengthening the reporting of cohort studies in surgery. *Int J Surg.* 2019; 72: 156–165. DOI: *https://doi.org/10.1016/j.ijsu.2019.11.002*
12. **Liu Z, Tang S, Tian X,** et al. Foley catheter-assisted six-step thrombectomy technique in the surgical management of renal cell carcinoma with Mayo level II to IV tumor thrombus. *J Int Med Res.* 2019; 47(5): 2104–2115. DOI: *https://doi.org/10.1177/0300060519836912*
13. **Liu Z, Zhao X, Ge L,** et al. Completely laparoscopic versus open radical nephrectomy and infrahepatic tumor thrombectomy: Comparison of surgical complexity and prognosis. *Asian J Surg;* 2020. DOI: *https://doi.org/10.1016/j.asjsur.2020.12.003*
14. **Liu Z, Zhang L, Hong P,** et al. The influence of venous tumor thrombus combined with bland thrombus on the surgical treatment and prognosis of renal cell carcinoma patients. *Cancer Med.* 2020; 9(16): 5860–5868. DOI: *https://doi.org/10.1002/cam4.3264*
15. **Hackett NJ, De Oliveira GS, Jain UK, Kim JY.** ASA class is a reliable independent predictor of medical complications and mortality following surgery. *Int J Surg.* 2015; 18: 184–190. DOI: *https://doi.org/10.1016/j.ijsu.2015.04.079*
16. **Mitropoulos D, Artibani W, Graefen M,** et al. Reporting and grading of complications after urologic surgical procedures: an ad hoc EAU guidelines panel assessment and recommendations. *Eur Urol.* 2012; 61(2): 341–349. DOI: *https://doi.org/10.1016/j.eururo.2011.10.033*
17. **Ljungberg B, Bensalah K, Canfield S,** et al. EAU guidelines on renal cell carcinoma: 2014 update. *Eur Urol.* 2015; 67(5): 913–924. DOI: *https://doi.org/10.1016/j.eururo.2015.01.005*
18. **Ljungberg B, Albiges L, Abu-Ghanem Y,** et al. European Association of Urology Guidelines on Renal Cell Carcinoma: The 2019 Update. *Eur Urol.* 2019; 75(5): 799–810. DOI: *https://doi.org/10.1016/j.eururo.2019.02.011*
19. **Ficarra V, Novara G, Martignoni G.** The use of simplified versions of the Fuhrman nuclear grading system in clinical practice requires the agreement of a multidisciplinary panel of experts. *Eur Urol.* 2009; 56(5): 782–784; discussion 784–785. DOI: *https://doi.org/10.1016/j.eururo.2009.07.024*
20. **Romero FR, Muntener M, Bagga HS, Brito FA, Sulman A, Jarrett TW.** Pure laparoscopic radical nephrectomy with level II vena caval thrombectomy. *Urology.* 2006; 68(5): 1112–1114. DOI: *https://doi.org/10.1016/j.urology.2006.08.1084*

21. **Martin GL, Castle EP, Martin AD,** et al. Outcomes of laparoscopic radical nephrectomy in the setting of vena caval and renal vein thrombus: seven-year experience. *J Endourol*. 2008; 22(8): 1681–1685. DOI: *https://doi.org/10.1089/end.2008.0035*
22. **Wang M, Zhang J, Niu Y, Xing N.** Feasibility of Pure Conventional Retroperitoneal Laparoscopic Radical Nephrectomy With Level II Vena Caval Tumor Thrombectomy. *Urology*. 2016; 90: 101–104. DOI: *https://doi.org/10.1016/j.urology.2015.10.037*
23. **McDougall ECR, Elashry OM.** Laparoscopicradical nephrectomy for renal tumors: The Washington University experience. *J Urol*. 1996; 155: 1180–1185. DOI: *https://doi.org/10.1016/S0022-5347(01)66207-4*
24. **Xu B, Zhao Q, Jin J, He ZS, Zhou LQ, Zhang Q.** Laparoscopic versus open surgery for renal masses with infrahepatic tumor thrombus: the largest series of retroperitoneal experience from China. *J Endourol*. 2014; 28(2): 201–207. DOI: *https://doi.org/10.1089/end.2013.0519*
25. **Ebbing J, Wiebach T, Kempkensteffen C,** et al. Evaluation of perioperative complications in open and laparoscopic surgery for renal cell cancer with tumor thrombus involvement using the Clavien-Dindo classification. *Eur J Surg Oncol*. 2015; 41(7): 941–952. DOI: *https://doi.org/10.1016/j.ejso.2015.02.009*
26. **Chopra S, Simone G, Metcalfe C,** et al. Robot-assisted Level II-III Inferior Vena Cava Tumor Thrombectomy: Step-by-Step Technique and 1-Year Outcomes. *Eur Urol*. 2017; 72(2): 267–274. DOI: *https://doi.org/10.1016/j.eururo.2016.08.066*
27. **Gill IS, Metcalfe C, Abreu A,** et al. Robotic Level III Inferior Vena Cava Tumor Thrombectomy: Initial Series. *J Urol*. 2015; 194(4): 929–938. DOI: *https://doi.org/10.1016/j.juro.2015.03.119*
28. **Abaza R, Shabsigh A, Castle E,** et al. Multi-Institutional Experience with Robotic Nephrectomy with Inferior Vena Cava Tumor Thrombectomy. *J Urol*. 2016; 195(4 Pt 1): 865–871. DOI: *https://doi.org/10.1016/j.juro.2015.09.094*
29. **Rose KM, Navaratnam AK, Faraj KS,** et al. Comparison of Open and Robot Assisted Radical Nephrectomy With Level I and II Inferior Vena Cava Tumor Thrombus: The Mayo Clinic Experience. *Urology*. 2020; 136: 152–157. DOI: *https://doi.org/10.1016/j.urology.2019.11.002*
30. **Gu L, Ma X, Gao Y,** et al. Robotic versus Open Level I–II Inferior Vena Cava Thrombectomy: A Matched Group Comparative Analysis. *J Urol*. 2017; 198(6): 1241–1246. DOI: *https://doi.org/10.1016/j.juro.2017.06.094*

TO CITE THIS ARTICLE:
Zhang Y, Bi H, Yan Y, Liu Z, Wang G, Song Y, Dong J, Zhang S, Liu C, Ma L. Surgical and Oncologic Outcomes of Laparoscopic Versus Open Radical Nephrectomy with Venous Thrombectomy: A Propensity-Matched Retrospective Cohort Study. *International Journal of Surgery: Oncology*. 2021; 6(1), 59–70. DOI: *https://doi.org/10.29337/ijsonco.127*

Submitted: 06 July 2021 Accepted: 01 August 2021 Published: 30 August 2021