# Peking University Third Hospital score: a comprehensive system to predict intra-operative blood loss in radical nephrectomy and thrombectomy

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## Abstract

**Background:** Radical nephrectomy and thrombectomy is the standard surgical procedure for the treatment of renal cell carcinoma (RCC) with tumor thrombus (TT). But the estimation of intra-operative blood loss is only based on the surgeon's experience. Therefore, our study aimed to develop Peking University Third Hospital score (PKUTH score) for the prediction of intra-operative blood loss volume in radical nephrectomy and thrombectomy.

**Methods:** The clinical data of 153 cases of renal mass with renal vein (RV) or inferior vena cava tumor thrombus admitted to Department of Urology, Peking University Third Hospital from January 2015 to May 2018 were retrospectively analyzed. The total amount of blood loss during operation is equal to the amount of blood sucked out by the aspirator plus the amount of blood in the blood-soaked gauze. Univariate linear analysis was used to analyze risk factors for intra-operative blood loss, then significant factors were included in subsequent multivariable linear regression analysis.

**Results:** The final multivariable model included the following three factors: open operative approach (P < 0.001), Neves classification IV (P < 0.001), inferior vena cava resection (P = 0.001). The PKUTH score (0–3) was calculated according to the number of aforementioned risk factors. A significant increase of blood loss was noticed along with higher risk score. The estimated median blood loss from PKUTH score 0 to 3 was 280 mL (interquartile range [IQR] 100–600 mL), 1250 mL (IQR 575–2700 mL), 2000 mL (IQR 1250–2900 mL), and 5000 mL (IQR 4250–8000 mL), respectively. Meanwhile, the higher PKUTH score was, the more chance of post-operative complications (P = 0.004) occurred. A tendency but not significant overall survival difference was found between PKUTH risk score 0 *vs.* 1 to 3 (P = 0.098).

**Conclusion:** We present a structured and quantitative scoring system, PKUTH score, to predict intra-operative blood loss volume in radical nephrectomy and thrombectomy.

Keywords: Renal cell carcinoma; Venous thrombosis; Blood loss; Inferior vena cava

## Introduction

In locally advanced renal cell carcinoma (RCC), 4% to 10% patients have tumor thrombus (TT) involving the renal vein (RV) or inferior vena cava (IVC).<sup>[1]</sup> Radical nephrectomy and thrombectomy is the standard surgical procedure for the treatment of RCC with IVC TT and it can effectively improve the prognosis. The 5-year tumor-specific survival rate is 40% to 65%.<sup>[2]</sup> However, radical nephrectomy and thrombectomy is one of the most difficult and complicated urology operation because of its high injury rate and intraoperative blood loss.<sup>[3]</sup> If the TT extends to the IVC, the classical surgical procedure requires that the IVC vessel wall should be cut after temporary occlusion to remove the TT,

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and then the vascular incision is closed with non-absorbable sutures. Even in experienced hands, the large blood loss still is the main problem that cannot be ignored.

Full and effective preparation is needed before the operation, including blood preparation. For a confine operation like RCC, sufficient blood is essential, so that it can be carried out step by step. In most cases, the blood bank will have sufficient blood resources. However, fewer blood donors, excessive consumption of blood in other emergency, special blood types, and other exceptional circumstances may lead to insufficient pre-operative blood preparation and the surgery will be suspended and delayed. Therefore, a predictive model is needed to estimate intra-operative blood

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loss by collecting pre-operative clinical data. This will be helpful for clinical blood preparation before operation.

To our knowledge, there are few pre-operative prediction models to predict intra-operative blood loss volume in radical nephrectomy and thrombectomy. Therefore, the estimation of intra-operative blood loss is only based on the surgeon's experience. This may lead to massive bleeding or even hemorrhagic shock due to insufficient blood preparation or overestimation of intra-operative bleeding and excessive blood preparation, resulting in unsatisfactory of blood bank. The clinical data of RCC with RV or IVC TT admitted to Department of Urology, Peking University Third Hospital from January 2015 to May 2018 are retrospectively analyzed. We present a structured, reproducible, quantitative scoring system which is named Peking University Third Hospital score (PKUTH score) to predict intra-operative blood loss volume in radical nephrectomy and RV or IVC thrombectomy.

## Methods

## Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Peking

University Third Hospital Medical Science Research Ethics Committee (No. IRB00006761-M2018178). Informed consent was obtained from all patients prior to their enrollment in this study.

#### Patient selection

The clinical data of 153 cases of renal mass with RV or IVC TT admitted to Department of Urology, Peking University Third Hospital from January 2015 to May 2018 were retrospectively analyzed. Patients without surgical treatment, with recurrence of tumor thrombectomy, nephroblastoma, urothelial carcinoma, or other pathological types were excluded. Finally, 123 cases with follow-up were included in the study. Patient selection is shown in Figure 1.

The total amount of blood loss during operation was equal to the amount of blood sucked out by the aspirator plus the amount of blood in the blood-soaked gauze. The method of weighing was usually used to calculate the amount of bleeding in the blood-soaked gauze. We divided the study population into ten groups according to the total intra-operative blood loss volume taking 400 mL as a classification increment. Frequency distribution of blood loss is shown in Figure 2.

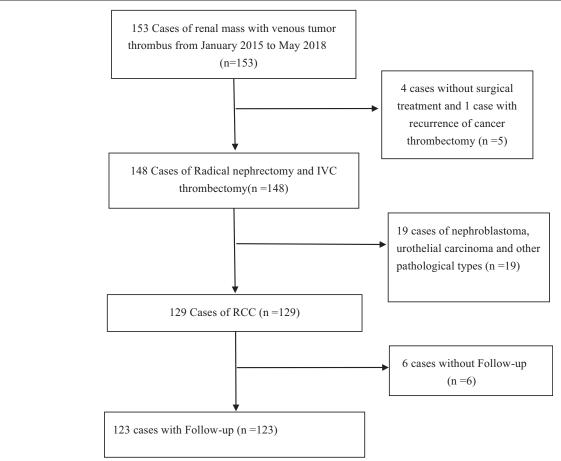
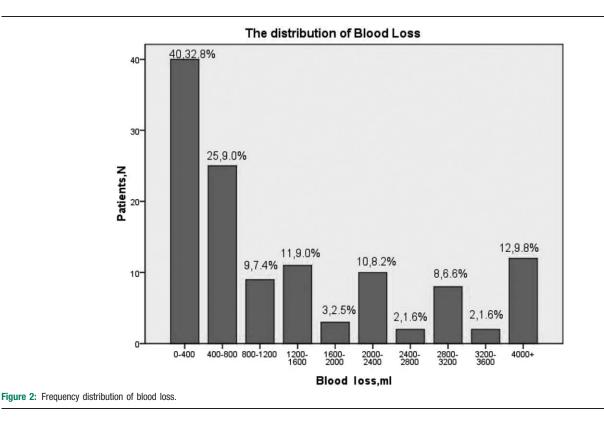


Figure 1: Summary of our study cohort and flow chart of exclusion criteria. IVC: Inferior vena cava; RCC: Renal cell carcinoma.



# Clinical and pathology information

All patients underwent B-mode ultrasonography, abdominal computed tomography (CT) and/or magnetic resonance imaging (MRI) scan before operation to assess the renal mass, including the tumor side, location, diameter, and relationship with renal vessels and collecting system. Chest CT scan and abdominal CT scan were performed for TNM staging of renal tumors (2010 International Union Against Cancer, UICC). Patients underwent abdominal MRI scan to measure the length of TT, whether the TT invaded vessel wall. Echocardiography was performed to determine cardiac function and whether atrial TT was present. Karnofsky performance score (KPS) was used to classify patients according to their physical condition and surgical risk. Those with a score greater than 80 had a better post-operatively condition and a longer survival period.

Serum hemoglobin, white blood cell count, neutrophil count, lymphocyte count, platelet count, total protein, albumin, blood urea nitrogen, serum creatinine, and alkaline phosphatase were collected pre-operatively. Serum creatinine was retested 1 week after surgery. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and systemic immune-inflammation index (SII) were calculated and included in the analysis because some studies had shown that they were associated with the prognosis.<sup>[4]</sup> The SII was equal to the neutrophil count multiplied by the platelet count and divided by the lymphocyte count.<sup>[5]</sup> Pre-operative distant metastasis status was routinely confirmed by positron emission CT or chest CT, abdominal CT, cranial MRI, and bone scans. Post-operative immunotherapy or targeted molecular therapies were suggested if distant metastasis existed before surgery.

# Surgery and complications

In laparoscopic radical nephrectomy and thrombectomy, establishment of retroperitoneal space was made by balloon method. A 13-mm trocar was inserted to establish a carbon dioxide pneumoperitoneum. An 11-mm trocar was placed on the iliac crest of the midaxillary line and 5-mm trocar was placed under the costal margin of the anterior axillary line. If necessary, another 5-mm assistant trocar was inserted. In the procedure of open radical nephrectomy and thrombectomy. Right RCC was treated with a chevron incision from xiphoid process to axillary midline at 2 cm below the right rib margin, extending about 5 cm below the left rib margin. For left renal tumors, the open incision was symmetrical to the right renal tumors. In level IV TT, the central tendon of the diaphragm could be cut around the IVC, and the TT could be squeezed into the IVC by gently pushing and squeezing, so that the thrombus could be changed into level III. Conventional right atrial thrombectomy needed to open the chest to establish cardiopulmonary bypass (CPB) and under beating or non-beating conditions.

Modified Clavien grading system was used to evaluate the post-operative complications.<sup>[6]</sup> Complications of grade >III were defined as severe complications.<sup>[7]</sup>

# Monitoring and follow-up

The first follow-up was carried out at 1 month after operation, and then every 3 months in the first 2 years, and

every 6 months after 2 years. Appropriate treatments were provided in cases of local recurrence or distant metastasis. Follow-up information was obtained from phone interviews and outpatient records. The last follow-up was completed in December 2018. During follow-up, the cause of patient's death was confirmed by the death certificate offered by the hospital.

## Statistical analysis

Continuous parametric variables were reported as the mean  $\pm$  standard deviation, or median (interquartile range [IQR]). Categorical variables were summarized with frequency counts and percentages. The survival time was calculated from the date of operation to death or the date of last follow-up (when the patient was confirmed to be alive). The Kaplan-Meier method was used to analyze the survival curve, and differences between groups were tested using the log-rank test. Univariate linear analysis was used to analyze risk factors for intra-operative blood loss, then significant factors were included in subsequent multivariable linear regression analysis. The results were summarized with odds ratios and 95% confidence intervals. Then we used Mann-Whitney U test and Pearson Chi-squared test to analyze blood loss and post-operative complications between different PKUTH scores. The statistical tests were performed with SPSS 24.0 (IBM Inc., Chicago, IL, USA). All tests were two-sided, and P values < 0.05 were considered to be statistical significance.

#### Results

Clinical and radiographic features of our cohort are shown in Table 1. Surgical average blood loss volume was  $1372.2 \pm 1679.3$  mL (10–10,000 mL). Univariate and multivariate associations of pre-operative clinical and radiographic features predicting intra-operative blood loss volume are shown in Tables 2 and 3. Univariate analysis confirmed that clinical N (cN) stage, absolute value of monocytes, pre-operative serum creatinine, alkaline phosphatase, serum urea nitrogen, KPS, operative approach, Neves classification, and IVC resection were significantly associated with intra-operative blood loss.

Although there were many prediction features on univariable analysis, the final multivariable model includes three features that combined to discern intra-operative blood loss volume with the greatest discriminatory ability: open operative approach (P < 0.001), Neves classification IV (P < 0.001), and IVC resection (P = 0.001) were the only factors associated with intra-operative blood loss.

According to the odds ratio value, the prediction formula of the bleeding volume is:  $y = 1205.853 \times (\text{open approach}) + 2097.358 \times (\text{Mayo grade IV}) + 1134.090 \times (\text{IVC wall} resection}) + 372.202$ . To ensure the convenience of the model, we assigned the weights of three independent variables (open pathway, Mayo grade IV, IVC wall resection) to 1, 2, and 1. Because all patients of Mayo IV grade in this group adopt the open approach, there are only six possibilities divided by the three variables. Because of 2 points and 3 points have similar bleeding volume in this classification, we merged them and simplified to the

# Table 1: Clinical characteristics of the patients with renal mass with renal vein or inferior vena cava tumor thrombus (N = 123).

Characteristics	Values		
Age (years)	$58.6 \pm 11.2 \ (15-83)$		
BMI $(kg/m^2)$	$23.6 \pm 3.9 (15.2 - 39.0)$		
Tumor diameter (cm)	$8.7 \pm 3.4 (0.6 - 21.1)$		
Hemoglobin (g/L)	$121.1 \pm 23.4 (50.0 - 185.0)$		
Platelet count $(\times 10^{9}/L)$	$242.7 \pm 96.7 (70.0-689.0)$		
Leukocyte count ( $\times 10^{9}$ /L)	$7.0 \pm 3.8 \ (2.4-35.8)$		
Absolute value of neutrophils	$4.9 \pm 2.6 (1.4 - 20.7)$		
$(\times 10^{9}/L)$ Absolute value of lymphocyte	$1.3 \pm 0.5 \ (0.1 - 3.4)$		
(×10 <sup>9</sup> /L)			
Absolute value of monocytes $(\times 10^{9}/L)$	0.45 ± 0.21 (0.01–1.19)		
PLR	$206.9 \pm 109.2 (34.2 - 708.8)$		
NLR	$4.3 \pm 3.3 (1.2 - 21.1)$		
SII	$1024.8 \pm 773.9$ (160.3–5448.6		
Serum calcium (mg/dL)	$8.6 \pm 1.1 \ (4.1 - 11.9)$		
Albumin (g/L), $n = 122$	$38.3 \pm 5.8 \ (21.0 - 51.0)$		
Pre-operative serum creatinine $(\mu \text{mol/L}), n = 122$	98.9±53.0 (32.0-616.0)		
Serum creatinine one week after operation (μmol/L)	122.4 ± 126.5 (47.0-813.0)		
Alkaline phosphatase (IU/L)	95.2 ± 49.7 (29.0-338.0)		
Total protein (g/L), $n = 116$	$68.5 \pm 7.4 \ (43.0 - 85.0)$		
Serum urea nitrogen (mmol/L)	$6.0 \pm 1.9 (3.0 - 13.0)$		
Operative time (min)	$332.3 \pm 125.6 (108.0-694.0)$		
Surgical blood loss volume (mL)	$1372.2 \pm 1679.3 (10 - 10000)$		
Surgical blood transfusion volume (mL)	$848.0 \pm 1279.0 \ (0-9000)$		
Plasma transfusion volume (mL) Sex	248.0 ± 517.6 (0-2400)		
Male	92 (74.8)		
Female	31 (25.2)		
Side			
Left	47 (38.2)		
Right	75 (61.0)		
Both	1 (0.8)		
ASA score	- (0.0)		
1	10 (8.1)		
2	95 (77.2)		
3	18 (14.6)		
Clinical symptoms			
No	33 (26.8)		
Yes	90 (73.2)		
cN stage			
cN0	55 (44.7)		
cN1	68 (55.3)		
cM stage			
cM0	87 (70.7)		
cM1	36 (29.3)		
Neves classification			
0	28 (22.8)		
I	36 (29.3)		
I	35 (28.5)		
III	13 (10.6)		
IV	11 (8.9)		
Operative approach	11 (0.2)		
Laparoscopy	58 (47.2)		
Open	65 (52.8)		
Open	03 (32.0)		

(continued)

Table 1	

(continued).		
Characteristics	Values	
IVC resection		
No	104 (84.6)	
Yes	19 (15.4)	
Adrenalectomy		
No	59 (48.0)	
Yes	64 (52.0)	
Pathology type		
Clear cell carcinoma	103 (83.7)	
Non-clear cell carcinoma	20 (16.3)	
Fuhrmans grade		
1–2	45 (36.6)	
3–4	78 (63.4)	
Sarcomatoid differentiation		
No	102 (82.9)	
Yes	21 (17.1)	
Post-operative complications		
0	83 (67.5)	
Ι	6 (4.9)	
II	26 (21.1)	
III	1 (0.8)	
IV	5 (4.1)	
V	2 (1.6)	
Post-operative adjuvant targeted		
therapy		
No	50 (40.7)	
Yes	73 (59.3)	

Values are shown as mean  $\pm$  standard deviation (range), or n (%). BMI: Body mass index; PLR: Platelet-to-lymphocyte ratio; NLR: Neutrophil-tolymphocyte ratio; SII: Systemic immune-inflammation index; ASA: American Society of Anesthesiologists; IVC: Inferior vena cava.

current score. The weights of three independent variables (open pathway, Mayo grade IV, IVC wall resection) were assigned as 1 point, 1 point, and 1 point, respectively.

The blood loss of different PKUTH risk score cohorts is shown in Figure 3. A significant increase of blood loss was noticed along with higher risk score. Median blood loss and its IQR were presented with each score. For a patient with Neves classification 0 to III IVC TT, the surgeon assessed that laparoscopic surgery will be performed without conversion into open surgery. Moreover, there was no adhesion or invasion between the TT and the IVC wall, segmental resection of the IVC wall was not necessarily required. Such patients would fit the characteristic description of PKUTH risk score 0. The estimated median blood loss was 280 mL (IQR 100-600 mL). Because all patients of Mayo IV grade in this group adopted the open approach, there are only two possibilities of "PKUTH score 1" and two possibilities of "PKUTH score 2." Patient would fit the characteristic description of PKUTH risk score 1 if he had only one risk factor such as open approach only or IVC resection only. The estimated median blood loss was 1250 mL (IOR 575-2700 mL). Patient would fit the characteristic description of PKUTH risk score 2 if he had two risk factors such as open approach and IVC vascular wall resection only or Mayo IV

grade TT and open approach only. The estimated median blood loss was 2000 mL (IQR 1250-2900 mL). Simultaneous existence of three risk factors would fit the characteristic description of PKUTH risk score 3. The estimated median blood loss was 5000 mL (IQR 4250-8000 mL). There is no significant difference in bleeding volume in different cases of the same PKUTH risk score.

Modified Clavien grading system was used to evaluate the post-operative complications.<sup>[8]</sup> Complications of grade ≥III were defined as severe complications.<sup>[9]</sup> The higher the PKUTH risk score was the higher the incidence of postoperative complications was, as is showed in Table 4 (P = 0.004). Although there was no statistical difference in the incidence of serious complications, we could still see an upward trend that the higher the PKUTH risk score was the higher the incidence of serious complications after operation was (P = 0.279).

The median follow-up time was 14.0 months (0-44.0 months). The survival information of all patients was available. At the last follow-up, 32 patients deceased, and all of them were cancer-related deaths. Overall survival of RCC with venous tumor thrombus (VTT) stratified by PKUTH risk score (0 vs. 1–3) is showed in Figure 4. Nonsignificant but a tendency of difference was noticed between these two groups (P = 0.098).

## Discussion

We try to present a structured, reproducible, quantitative scoring system PKUTH score to predict intra-operative blood loss volume in radical nephrectomy and thrombectomy. The final multivariable model included the three features: open operative approach, Neves classification IV, and IVC resection were the only factors associated with intra-operative blood loss. A significant increase of blood loss was noticed along with higher risk score.

Open radical nephrectomy and thrombectomy are traditional and effective treatment for RCC with RV or IVC TT.<sup>[8]</sup> With the popularization of laparoscopic and robotic techniques in urology, laparoscopic or robotic-assisted thrombectomy have been carried out in some centers.<sup>[9]</sup> Complete laparoscopic surgery can be used for Neves classification II or less.<sup>[10]</sup> Laparoscopic surgery is minimally invasive and has the same therapeutic effect as open surgery.<sup>[10]</sup> Laparoscopic surgery has the following advantages: (1) small trauma reduces the bleeding caused by open incision; (2) good visual field exposure can help directly separate and cut off the renal artery, reducing the blood supply of tumors; (3) intra-operative pneumoperitoneum can reduce collateral blood vessels bleeding. However, laparoscopic thrombectomy requires high professional skills, especially vascular suture skills. In contrast, for high-level TT, open approaches are often used with greater complexity. And the open approach itself is traumatic, which may result in increased intra-operative bleeding.<sup>[11]</sup>

Neves classification IV is another factor contributing to increased intra-operative bleeding.<sup>[12]</sup> Neves classification IV refers to the TT extension to the IVC above the

Table 2: Univariate associations of clinical and radiographic features predicting intra-operative bleeding loss volume in radical nephrectomy	
and IVC thrombectomy.	

Items	Р	<b>Regression coefficients</b>	95% CI
Sex	0.311	-354.425	-1044.778 to -335.928
Age	0.714	-4.996	-31.961 to -21.969
BMI	0.096	64.254	-11.567 to 140.076
Tumor side	0.491	-209.731	-810.117 to -390.655
Tumor diameter	0.593	23.994	-64.735 to 112.723
cN stage	0.048	601.869	6.219 to 1197.519
cM stage	0.176	451.667	-204.898 to 1108.232
Hemoglobin	0.058	-12.341	-25.092 to -0.411
Absolute value of neutrophils	0.308	20.227	-18.920 to 59.375
platelet count	0.153	-2.254	-5.354 to -0.847
Absolute value of lymphocyte	0.504	195.744	-382.025 to 773.514
Leukocyte count	0.586	21.790	-57.213 to 100.794
Absolute value of monocytes	0.030	1551.184	156.526 to 2945.841
PLR	0.778	-0.396	-3.163 to -2.371
NLR	0.274	18.210	-14.614 to 51.034
SII	0.720	0.057	-0.259 to 0.374
Pre-operative serum creatinine	0.003	5.545	1.967 to 9.124
Albumin	0.143	-38.504	-90.230 to -13.222
Alkaline phosphatase	0.012	7.617	1.687 to 13.548
Serum urea nitrogen	< 0.001	184.715	83.059 to 286.372
Clinical symptoms	0.264	382.768	-293.112 to 1058.648
KPS KPS	< 0.001	1474.730	665.496 to 2283.965
Ipsilateral adrenalectomy	0.180	407.487	-190.560 to 1005.533
Operative approach	< 0.001	1781.292	1270.571 to 2292.012
Neves classification	< 0.001	731.724	519.442 to 944.005
IVC resection	< 0.001	2012.338	1262.292 to 2762.384

IVC: Inferior vena cava; CI: Confidence interval; BMI: Body mass index; PLR: Platelet-to-lymphocyte ratio; NLR: Neutrophil-to-lymphocyte ratio; SII: Systemic immune-inflammation index; KPS: Karnofsky performance score.

Table 3: Multivariate associations predicting intra-operative bleeding loss volume in radical nephrectomy and IVC thrombectomy.				
Model	Р	Regression coefficients	95% CI	
Constant	0.022	372.202	53.818-690.586	
Operative approach	< 0.001	1205.853	739.627–1672.080	
Neves classification IV	< 0.001	2097.358	1283.718-2910.998	
IVC resection	0.001	1134.090	497.026-1771.154	
Neves classification I	0.770			
Neves classification II	0.409			
Neves classification III	0.646			
cN stage	0.784			
KPS	0.339			
Absolute value of monocytes	0.183			
Alkaline phosphatase	0.074			
Serum urea nitrogen	0.204			
Pre-operative serum creatinine	0.631			

IVC: Inferior vena cava; CI: Confidence interval; KPS: Karnofsky performance score.

diaphragm or to the atrium. Surgery requires a larger scope of vascular control, extracorporeal circulation assistance, and multi-disciplinary collaboration to complete. Generally, open radical nephrectomy and IVC thrombectomy are the standard surgical methods for treatment of Neves IV TT.<sup>[13]</sup> In this center, we usually use the following two methods to deal with Neves classification IV thrombus. When the TT grows above the diaphragm but does not reach the right atrium, the technique of excision of the diaphragm without thoracotomy can be used to remove the thrombus above the diaphragm. The diaphragm is opened longitudinally, and the atrial TT is squeezed into the IVC by finger compression, and the upward-shifting access is blocked. The IVC is blocked by blocking-tape at the proximal end of the TT, or the thrombus can also be removed by balloon urethral catheter. This method can

3- 2- 1- 0- 0	2000 400	0.0001 0 6000 8000 10 0 000 8000 10	0000 12000
PKUTH Scor	e Number	BL median (ml)	BL IQR (ml)
3 5 5000 4250 - 8000		4250 - 8000	
2	17	2000	1250 – 2900
1	46	1250	575 – 2700
0	55	280	100 – 600

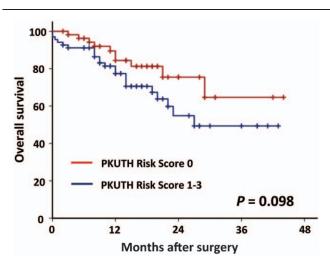


Figure 4: Overall survival of RCC with VTT stratified by PKUTH risk score (0 vs. 1–3). PKUTH: Peking University Third Hospital; RCC: Renal cell carcinoma; VTT: Venous tumor thrombus.

Figure 3: The blood loss of different PKUTH risk score cohorts. PKUTH: Peking University Third Hospital; BL: Blood loss; IQR: Interquartile range.

Table 4: The relationship between PKUTH risk score and the incidence of post-operative complications.

Complications	PKUTH risk score					
	0	1	2	3	χ <b>2</b>	Р
Post-operative complications					12.646	0.004
No	45 (82%)	29 (63%)	7 (41%)	2 (40%)		
Yes	10 (18%)	17 (37%)	10 (59%)	3 (60%)		
Severe post-operative complications					2.723	0.279
No	52 (94%)	44 (96%)	15 (88%)	4 (80%)		
Yes	3 (6%)	2 (4%)	2 (12%)	1 (20%)		

PKUTH: Peking University Third Hospital.

effectively simplify the procedure, reduce the amount of bleeding and reduce the complications caused by CPB. However, if the TT grows into the right atrium and exceeds 2 cm or longer, CPB is needed. We open the chest through a median thoracic incision and open the pericardium to expose the heart and great vessels. After heparinization, ascending aorta, femoral vein, and superior vena cava are intubated, and then CPB is started. We open the atrium and remove the cancer thrombus in the atrium without blood.

IVC resection is also a factor contributing to increased intra-operative bleeding.<sup>[14]</sup> The objective of surgical treatment for RCC with TT is to completely remove all tumor loads. If the TT invades the IVC wall, the involved vena cava wall should be removed thoroughly, so that the surgical margin can be negative, so as to improve the survival rate of the patients after operation.<sup>[15]</sup> In contrastenhanced CT, the invasion of the IVC wall can be characterized by the irregular contour of the IVC. Preoperative color Doppler ultrasonography and contrastenhanced magnetic resonance angiography can be further improved to assess the involvement of IVC.<sup>[16]</sup> Contrastenhanced magnetic resonance angiography showed that the wall of IVC was invaded<sup>[17]</sup>: (1) the wall of IVC was rough and not smooth, which could be characterized as "burr sign"; (2) the diameter of IVC was enlarged; and (3) the "Edema zone" wall of IVC was visible. In this study, the so-called IVC vessel wall resection includes: resection of the invaded part of the IVC vessel wall and segmental resection of the IVC. Whether the resection of the blood vessel wall is necessary or not can be preliminarily judged by some imaging examination before operation. However, its limitation is that pre-operative imaging cannot absolutely predict the need for vascular wall resection.

In this study, tumor size is not a factor affecting the amount of bleeding. In previous studies, we found that compared with the diameter of primary renal cancer tumor, the height of TT had a greater impact on the amount of bleeding.<sup>[18]</sup>

To reduce intra-operative blood loss effectively, our experience is as follows: (1) Before the treatment of TT, cutting off the renal artery can effectively reduce the blood supply of renal tumors, and reduce bleeding when the kidney is free along the perirenal fascia. In addition, renal artery occlusion can also reduce the size of the kidney and

tumors to a certain extent, reducing the difficulty of surgery. (2) Full exposure of IVC is necessary. Only after cutting off the lumbar vein and other branches of IVC can the related vessels be blocked. Otherwise, incision of the IVC wall will cause massive bleeding and blurred vision. (3) Hemorrhage during IVC wall incision is mostly caused by incomplete vascular occlusion. The most common is incomplete IVC occlusion below the RV. We used the vascular occlusion band to complete the occlusion. If incomplete occlusion is found, the vascular occlusion band can be pulled up and Hem-o-lok can be clamped after tightening. (4) To shorten the incision of IVC as far as possible on the premise of ensuring the complete removal of thrombus. The needle spacing should be uniform (about 2 mm). The blood loss of different PKUTH risk score cohorts show a significant increase of blood loss was noticed along with higher risk score. Overall survival of RCC with TT stratified by PKUTH risk score (0 vs. 1-3) shows non-significant but a tendency of difference is noticed between these two groups (P = 0.098). Though a tendency of survival difference was noticed between high/ low risk score groups, the limited sample size and relatively short follow-up resulted in a non-significant P value. As blood loss was reported as an independent prognostic factor in RCC with TT, the exact role of our risk score in prognostic stratification needs further confirming.

Our study has some limitations. This study is a retrospective analysis. Intra-operative blood loss is determined by many complex factors. For example, the clinical experience of the surgeon, the application of hemostatic devices, the factors of the tumor itself, etc.<sup>[19]</sup> The experience of the surgeon has a great influence on the amount of intraoperative blood loss. In addition, with the rich experience of the surgeon, the learning curve may reduce the amount of intra-operative bleeding. To reduce the bias caused by these aspects, we selected three doctors with similar seniority in our center. These surgeons have similar surgical experience. In the study population, we chose patients with shorter time span to minimize the impact of learning curve on intra-operative blood loss volume. The choice of hemostatic devices is also an important factor affecting intra-operative bleeding. In this group, we choose bipolar electrocoagulation for hemostasis through laparoscopy, and ligasure for hemostasis in open surgery. The use of these hemostatic devices can reduce the amount of bleeding during operation to a certain extent.

In conclusion, we found that open operative approach, Neves classification IV, and IVC resection were independently associated with intra-operative blood loss of nephrectomy and thrombectomy. The PKUTH score containing these factors correlated with blood loss significantly. It may help urologists prepare such a challenging surgery in a more quantitative way, though external validation is warranted before generalization of this score system.

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### **Conflicts of interest**

None.

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