Original Article

Construction of the prognostic model in non-metastatic renal cancer patients with venous tumor thrombus

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Background: Venous system invasion is a prominent characteristic of local progression in renal cancer and treatment-naïve renal cancer patients with venous tumor thrombus (VTT) gained short natural course and poor prognosis. This study aimed to investigate the efficacy of the surgery and prognostic factors in non-metastatic renal cancer patients with VTT and to construct a nomogram prognostic model.

Methods: Clinical data of 114 non-metastatic renal cancer patients with VTT who underwent surgical treatment from January 2011 to September 2022 were retrospectively analyzed. In order to find independent risk factors of prognosis, survival analysis was performed via univariate and multivariate Cox regression models and Kaplan-Meier method. Nomogram prognostic model was established to calculate patients' risk scores. Receiver operating characteristic curve and decision curve analysis were conducted to evaluate the efficacy of the prognostic model.

Results: A total of 114 patients were included in this study and there were 48, 12, 25, 23, and 6 cases of grade 0–IV VTT. No perioperative death occurred. The 3-year probabilities of overall survival (OS) and 5-year probabilities of OS were 67% and 43.8%, respectively. Multivariate Cox regression analysis revealed that kidney tumor diameter, preoperative lactate dehydrogenase (LDH), and preoperative neutrophils were independent risk factors. Nomogram was constructed to predict prognosis in renal cancer patients with VTT based on above indicators and Mayo VTT grading. The area under the ROC curve of 1-, 2-, 3-, and 5-year OS of the patients were 0.82, 0.67, 0.57, and 0.55 respectively.

Conclusions: Surgical treatment enables renal cancer patients with VTT to gain a better prognosis. Kidney tumor diameter, preoperative LDH, and preoperative neutrophils were independent risk factors. The nomogram perfects the Mayo grading, and provides a reliable reference for evaluation of prognosis of renal cancer patients with VTT.

Keywords: Venous tumor thrombus (VTT); renal cancer; prognosis; nomogram model; surgical treatment

Submitted Jun 13, 2023. Accepted for publication Oct 20, 2023. Published online Nov 14, 2023.
doi: 10.21037/tau-23-341
View this article at: https://dx.doi.org/10.21037/tau-23-341

Introduction

Renal cell carcinoma (RCC) is a malignant tumor originating from the kidney parenchyma, and its incidence accounts for 2–3% of adult malignancies (1), increasing by 1–2% annually (2). Venous system invasion is a prominent characteristic of local progression in renal cancer, affecting about 4% to 10% of all patients with RCC (3). Treatment-naïve renal cancer patients with venous tumor thrombus (VTT) gained short natural course and poor prognosis,

with median survival time of 5 months and 1-year cancer-specific survival (CSS) of 29% (4). A comprehensive review of a substantial patient series, which underwent systemic targeted therapy for *in situ* RCC tumor thrombi, indicated limited clinical efficacy in reducing the tumor thrombus level. Additionally, the study failed to uncover a noteworthy influence on the surgical approach among those who eventually required thrombectomy (5,6). Radical nephrectomy (RN) and VTT extraction have become the preferred treatment for non-metastatic renal carcinoma patients with VTT, of which the 5-year disease-free survival (DFS) is 39–60% (7-9). The surgery performed on these patients is characterized by its complexity, high-risk nature, and the potential for pulmonary arterial embolism due to detachment of cancer emboli. Such embolism poses a significant threat to patient survival. Furthermore, there exists a direct correlation between the grade of cancer emboli and the perioperative mortality rate, with higher-grade emboli associated with an incremental increase in mortality risk (10-12). The great difficulty and risk of surgery require researchers to predict the prognosis of patients according to the different clinical and pathological characteristics of each patient, so as to better formulate treatment strategies. The objectives of this study were to investigate the efficacy of the surgery in non-metastatic renal cancer patients with VTT and to analyze the clinicopathologic elements for the establishment of the prognostic model, and thus providing a theoretical basis for the development of individualized therapy. We present this article in accordance with the TRIPOD reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-23-341/rc).

Highlight box

Key findings

- We first found that preoperative lactate dehydrogenase (LDH) and preoperative neutrophils might influence the prognosis of renal cell carcinoma patients with venous tumor thrombus (VTT).

What is known and what is new?

- The Mayo grading has long been regarded as the standard for assessing the prognosis of patients with renal cancer accompanied by VTT.
- We constructed a new nomogram including tumor diameter, preoperative LDH, and preoperative neutrophils to perfect the Mayo grading.

What is the implication, and what should change now?

- Now Mayo grading with our nomogram provides a more accurate assessment of the prognosis for patients with renal cancer accompanied.

Methods

Study cohort

Clinicopathologic and prognostic data of 114 non-metastatic renal cancer patients with VTT who underwent surgical treatment in Shanghai Changhai Hospital from January 2011 to September 2022 were retrospectively analyzed. The study protocol was designed in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of Changhai Hospital (No. CHEC2021-191). Informed consent was waived by Ethics Committees due to the retrospective nature of the study.

Inclusion criteria: (I) non-metastatic renal carcinoma patients with VTT grading 0–IV; (II) patients who underwent RN and VTT extraction without VTT detachment and perioperative death; and (III) postoperative pathological confirmed RCC.

Exclusion criteria: (I) patients displaying evidence of metastasis based on preoperative imaging; (II) patients who underwent exploratory laparotomy but did not undergo complete surgical intervention; and (III) patients who were lost to follow-up during the study period.

Postoperative follow-up

The follow-up data of all the patients were obtained through telephone calls or outpatient visits. Last follow-up time was on 10th February, 2023. The primary endpoint was overall survival (OS), which was defined as the time from surgery to death or the last follow-up.

Statistical analyses

Continuous variables were presented as the mean ± standard deviation, and categorical variables were summarized by frequencies and percentages. The chi-squared test or Fisher's exact test was applied to compare categorical variables, and the *t*-test or nonparametric Wilcoxon's test was used to compare continuous variables between groups. Among all patients enrolled in this work, two-sided P value <0.05 indicated statistical significance. Univariate and multivariate Cox regression analyses were used to determine the effect of

selected variables on OS. Nomogram model was constructed with four clinical parameters based on multivariate Cox regression analysis. A novel risk score system was developed in this study, incorporating four clinical parameters. The integration of these parameters resulted in the creation of a new risk system, which was represented using a nomogram. The construction of the nomogram was facilitated by the utilization of the R package rms. Calibration curve was also depicted to compare the real and predicted incidence. Receiver operating characteristic (ROC) curve of 1-, 2-, 3-, and 5-year OS of all patients was utilized to access the sensitivity and specificity of risk system, and area under the ROC curve (AUC) larger than 0.6 was considered as suitable, while lager than 0.75 was considered as well performed. AUC was visualized by using R package 'pROC' packages. To compare the clinical benefit of applying novel risk score system in clinical practice when comparing with other parameters, including lactate dehydrogenase (LDH), neutrophil, thrombus grading and tumor diameter, we applied DCA curve to assess prognostic benefit of risk score system, which was illustrated by R package ggDCA. Decision curve analysis (DCA) is a statistical method used to assess and contrast the clinical utility of different prediction models or diagnostic tests. It provides a framework to assess the net benefit of using a particular model or test in clinical decision-making. In DCA, an assortment of threshold probabilities is defined, representing the clinician's willingness to treat or intervene based on the predicted probability of an outcome. The calculation of the net benefit involves an assessment of advantages and disadvantages associated with each threshold probability. By plotting the net benefit against the threshold probability, the performance of different models or tests can be compared. A model or test with higher net benefit over a wide range of threshold probabilities indicates superior clinical utility. Furthermore, calibration curve, known as a calibration plot or reliability diagram, is a graphical representation that evaluates the performance and calibration of a predictive model, was adopted to evaluate how well the predicted probabilities from our risk score system with the actual observed outcomes and determine whether our model is overconfident or underconfident in its predictions.

Results

Baseline characteristics of included patients

Of all the 114 patients, 85 were male and 29 were female, aging 58.5±12.3 years, body mass index (BMI) 23.5±3.2 kg/m^2. The tumors were located on the left side in 56 cases and right side in 58 cases. The average diameter of the tumors was 8.52±3.79 cm. Ninety cases are clear cell RCC (ccRCC) while 24 were non-ccRCC [8 papillary RCC (pRCC), 3 collecting duct kidney cancer, 3 renal cancer associated with *TFE3* gene fusions, 1 renal oncocytoma, 1 FH deficient RCC, 2 sarcomatoid RCC, 1 renal cell carcinoma unclassified, and 5 other types]. Grading 0–IV (the Mayo classification) VTT involved 48, 12, 25, 23, and 6 cases respectively. We can observe that compared to the group alive, patients in the group dead had higher values in proportion of open surgery, length of stay, preoperative neutrophil, and tumor diameter. More baseline data are provided in *Table 1*. More detailed clinical data of the patients are shown in Table S1.

Survival analysis and risk factors for prognosis

All the 114 patients were followed up and by the time of the last follow-up, 64 patients had died. Three- and five-year OS were 67% and 43.8% respectively.

Univariate Cox regression analysis was performed using gender, age, BMI, the presence of hypertension, the presence of diabetes, preoperative hemoglobin, preoperative creatinine, preoperative LDH, preoperative neutrophils, tumor side, pathological type, the presence of lymphatic metastasis, the presence of perirenal adipose tissue invasion, tumor thrombus grading, tumor diameter, Clavien grading, postoperative targeted therapy, five of which were included into multivariate Cox regression analysis ($P<0.05$). Multivariate Cox regression analysis indicated that tumor diameter, preoperative LDH and preoperative neutrophils were independent risk factors for survival (*Table 2*).

Construction and validation of nomogram model

Considering the generality of VTT Mayo grading, the new nomogram model for non-metastasis renal cancer patients with VTT was established using tumor diameter, preoperative LDH, preoperative neutrophils and Mayo grading (*Figure 1*). The prognosis of high-risk group (*Figure 2A*, risk score >136.34) is poorer than that of low-risk group (*Figure 2B*).

Under the nomogram model, the AUC of 1-, 2-, 3-, and 5-year OS of patients was 0.82, 0.67, 0.57, and 0.55, respectively (*Figure 3*). In the bootstrapped DCA analysis conducted on patients with thrombus, the risk score

Table 1 Baseline data of 114 included patients

Characteristics	Group alive (n=54)	Group dead (n=60)	P value
Gender			0.108
Female	10 (8.8)	19 (16.7)	
Male	44 (38.6)	41 (36.0)	
Hypertension			0.164
No	33 (28.9)	44 (38.6)	
Yes	21 (18.4)	16 (14.0)	
Diabetes			0.620
No	46 (40.4)	53 (46.5)	
Yes	8 (7.0)	7 (6.1)	
Tumor side			0.859
Left	27 (23.7)	29 (25.4)	
Right	27 (23.7)	31 (27.2)	
Surgical operative methods			0.009
Laparoscopic surgery	23 (20.2)	12 (10.5)	
Open surgery	31 (27.2)	48 (42.1)	
Tumor thrombus grading			0.941
Grade 0	24 (21.1)	24 (21.1)	
Grade I	5 (4.4)	7 (6.1)	
Grade II	12 (10.5)	13 (11.4)	
Grade III	11 (9.6)	12 (10.5)	
Grade IV	2 (1.8)	4 (3.5)	
Clavien-Dindo grading			0.593
Grade I	27 (23.7)	27 (23.7)	
Grade II/III	27 (23.7)	33 (28.9)	
ASA scoring			0.661
1	2 (1.8)	3 (2.6)	
2	44 (38.6)	44 (38.6)	
3	8 (7.0)	11 (9.6)	
4	0 (0.0)	2 (1.8)	
Lymphatic metastasis			0.394
Metastasis	6 (5.3)	10 (8.8)	
Non-metastasis	48 (42.1)	50 (43.9)	
Perirenal adipose tissue invasion			0.359
Invasion	18 (15.8)	25 (21.9)	
Non-invasion	36 (31.6)	35 (30.7)	
Pathological type			0.529
ccRCC	44 (38.6)	46 (40.4)	
Non-ccRCC	10 (8.8)	14 (12.3)	

Table 1 (*continued*)

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Characteristics	Group alive (n=54)	Group dead (n=60)	P value
Age (years)	58 [53, 65]	60 [51.75, 69]	0.388
BMI (kg/m^2)	24.21±3.09	22.9±3.24	0.030
Operation time (hours)	3 [2.3, 3.77]	3 [2.45, 4.05]	0.408
Length of stay (days)	10 [7, 13.75]	14.5 [10, 17]	<0.001
Intraoperative blood loss (mL)	850 [200, 1,575]	1,200 [500, 2,025]	0.208
Preoperative LDH (U/L)	173 [152.25, 191.5]	169.5 [148, 248.75]	0.658
Preoperative creatinine (μmol/L)	84.5 [75, 98.5]	86.5 [69.75, 101.5]	0.827
Preoperative neutrophils (×10^9/L)	3.7 [3, 4.97]	4.95 [3.58, 5.73]	0.019
Preoperative hemoglobin (g/L)	126 [107, 137]	114 [96.75, 130.25]	0.176
Tumor diameter (mm)	70 [50, 90]	80 [60, 110]	0.033
Postoperative targeted therapy			0.353
No	25 (21.9)	33 (28.9)	
Yes	29 (25.4)	27 (23.7)	

Data are presented as n (%), median [IQR], or mean ± SD. ASA, American Society of Anesthesiologists; ccRCC, clear cell renal cell carcinoma; BMI, body mass index; LDH, lactate dehydrogenase; IQR, interquartile range; SD, standard deviation.

Table 2 Univariate and multivariate Cox regression analysis

Variation	Univariate Cox regression analysis		Multivariate Cox regression analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender (male *vs.* female)	0.64 (0.37–1.11)	0.109		
Age	1.01 (0.99–1.04)	0.244		
BMI	0.93 (0.85–1.01)	0.077	0.94 (0.87–1.04)	0.117
Tumor side (left *vs.* right)	0.99 (0.60–1.65)	0.978		
Hypertension (yes *vs.* no)	0.97 (0.55–1.73)	0.928		
Diabetes (yes *vs.* no)	0.88 (0.39–1.95)	0.746		
Tumor thrombus grading	1.21 (1.01–1.46)	0.039	1.12 (0.90–1.40)	0.310
Pathological type (non-ccRCC *vs.* ccRCC)	1.50 (0.82–1.76)	0.189		
Preoperative hemoglobin	0.98 (0.97–1.00)	0.004		
Preoperative creatinine	1.00 (0.99–1.01)	0.715		
Preoperative neutrophil	1.28 (1.06–1.54)	0.010	1.29 (1.07–1.55)	0.007
Preoperative LDH	1.00 (1.00–1.01)	<0.001	1.00 (1.00–1.01)	0.008
Lymphatic metastasis	1.78 (0.90–3.54)	0.098		
Perirenal adipose tissue invasion	1.70 (0.99–2.92)	0.052		
Clavien-Dindo grading (grade I *vs.* grade II/III)	1.29 (0.77–2.14)	0.335		
Tumor diameter	1.02 (1.01–1.02)	<0.001	1.01 (1.00–1.03)	0.011
Postoperative targeted therapy	0.97 (0.58–1.62)	0.894		

HR, hazard ratio; CI, confidence interval; BMI, body mass index; ccRCC, clear cell renal cell carcinoma; LDH, lactate dehydrogenase.

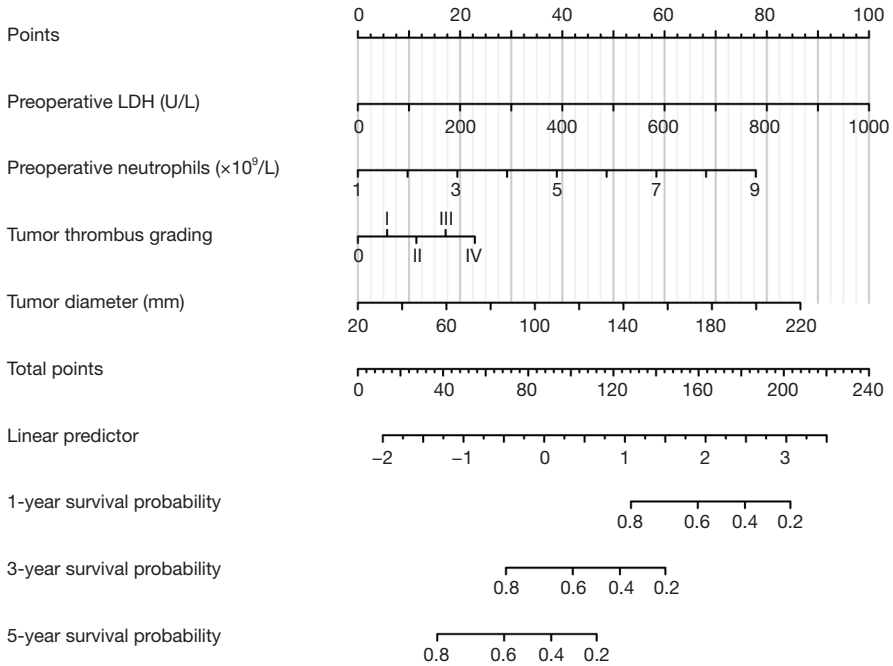

Figure 1 Establishment of a nomogram predicting 1-, 3-, and 5-year OS based on the independent prognostic factors in patients with tumor thrombus grading. Firstly, each individual subject's value was located on the corresponding axis of the nomogram. Secondly, a vertical line was drawn upward from this point to intersect with the "Points" axis, thereby generating a specific point. This process was repeated for all variables of interest. In the next step, the points obtained for each variable were summed up, and the total sum was located on the "Total points" line. Finally, by projecting this point onto the 1-, 3-, and 5-year OS lines, the corresponding probabilities of survival at each time point were determined. LDH, lactate dehydrogenase; OS, overall survival.

exhibited a significantly higher net benefit in accurately predicting OS, particularly in the 5-year period. This was in comparison to preoperative LDH, neutrophil count, tumor thrombus grading, and tumor diameter (*Figure 4A*). Moreover, when examining the bootstrapped calibration plots of the risk score, it can be observed that there were no adverse deviations between the predicted risk and observed risk for 1-, 2-, 3-, and 5-year OS across the entire range (*Figure 4B*).

Discussion

RCC with VTT is always a conundrum in urology. Treatment-naïve renal cancer patients with VTT gained short natural course with median survival time of 5 months and 1-year CSS of 29% (4). In recent years, with the advancements in surgical techniques and laparoscopic devices, the success rate of RN and VTT extraction has been greatly enhanced, and 5-year OS of patients after surgery was 39–60%, significantly better than those with no surgery, which shows that surgery is the most efficient method (13-15). This study showed that 3- and 5-year OS was 67% and 43.8% respectively, and in fact, similar studies were also reported before. In the realm of prognostic models for patients with RCC and VTT, a unified standard is currently lacking, as reported in the literature. Additionally, certain models within this domain incorporate non-conventional diagnostic variables as predictive factors, significantly diminishing their clinical applicability. Meanwhile, survival models for RCC patients with VTT, based on patient data and exhibiting practicality, do possess limitations such as suboptimal calibration and small sample sizes within specific subgroups of predictive variables (16-19). Therefore, this study sought to analyze the data of 114 patients with non-metastatic RCC accompanied by VTT who were treated at Changhai Hospital. The primary objective was to determine the independent prognostic factors for postoperative OS in this specific patient cohort and develop a more robust and effective personalized survival model for them.

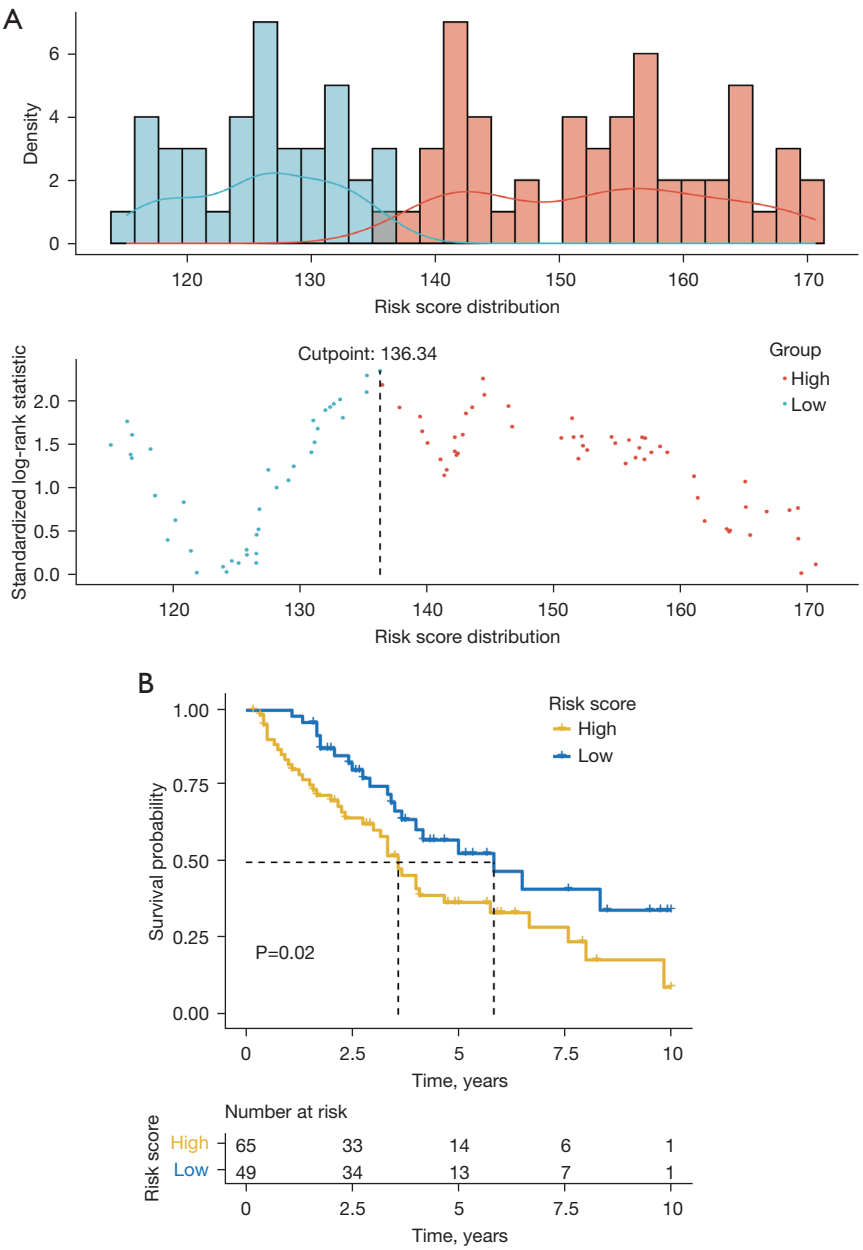

Figure 2 Prognostic value of risk score based on nomogram. (A) The optimal cutoff value of the risk score from nomogram. (B) KM curves between low and high-risk subgroups based on optimal cutoff value. KM, Kaplan-Meier.

Tumor diameter influences surgical difficulties and patients' OS, which are the focus of clinicians all the time. Previous studies demonstrated that the malignancy and invasion of renal cancer increased with the tumor size (20). Yang *et al.* proved that smaller ccRCC has less malignant and better prognosis than bigger one (21). Similar clinical research mentioned that large tumor diameter and renal vein invasion predicted worse DSS and progression-free survival (PFS) (22). Coincidentally, this study indicated that with the tumor diameter increasing, RCC patients with VTT had worse prognosis. In fact, larger primary tumor closely adhere to surrounding tissues so more tissues are stripped to expose the kidney, leading to longer operation time, more blood loss and higher probability

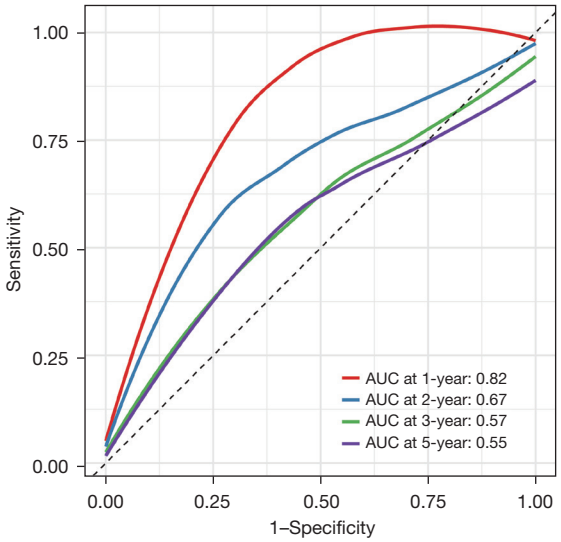

Figure 3 ROC curves of the nomogram at 1-, 2-, 3-, and 5-year OS in our cohort. AUC, area under the ROC curve; ROC, receiver operating characteristic; OS, overall survival.

of postoperative complications (17), which contributes to preoperative risk analysis and long-term prognosis evaluation. Abel *et al.* reported the prognostic data of 636 non-metastasis renal cancer with VTT, finding the correlation between tumor diameter and recurrence rate, and constructed a nomogram to predict tumor postoperative recurrence rate including six factors (23). The discovery that tumor diameter has an impact on patient prognosis highlights several important considerations: Firstly, preoperative imaging examinations play a critical role in accurately delineating tumor borders. Secondly, meticulous surgical techniques during the procedure are essential for discerning tumor boundaries. Lastly, postoperative follow-up should be given special attention for patients with larger tumor diameters, and when necessary, preventive medication should be considered.

The impact of VTT grading on prognosis still remains controversial. In our study, univariate Cox regression

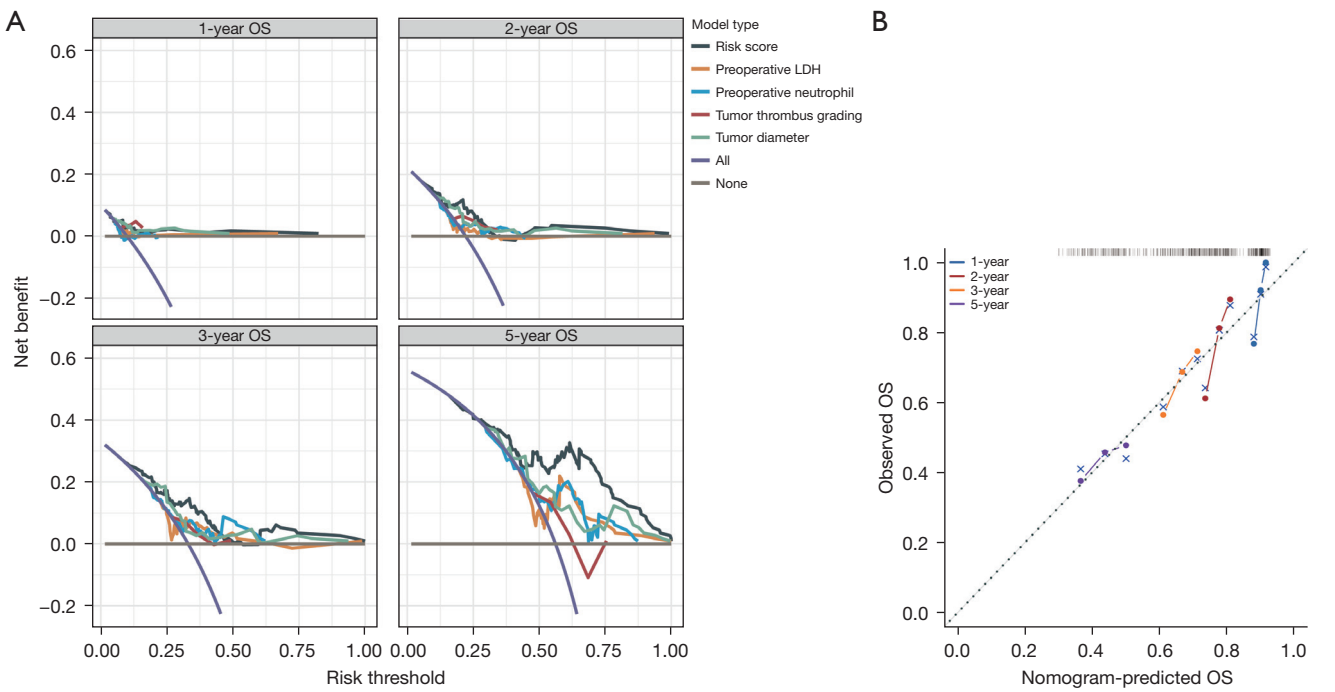

Figure 4 Performance of risk score in our cohort. (A) Comparison of the DCA of the nomogram and other parameters including preoperative LDH level, preoperative neutrophil count, tumor thrombus grading and tumor diameter for 1-, 2-, 3-, and 5-year OS in our cohort. (B) Calibration plots of the nomogram for 1-, 2-, 3-, and 5-year OS in our cohort. OS, overall survival; LDH, lactate dehydrogenase; DCA, decision curve analysis.

analysis suggested that VTT grading was related to the prognosis of patients, but multivariate Cox regression analysis indicated no correlation. This phenomenon may be because the sample numbers were relatively small and grade 0 VTT accounts for a relatively large proportion. This observation could potentially be attributed to several factors. Firstly, the relatively small sample size and the significant proportion of grade 0 VTT cases might have influenced the results. Additionally, advancements in surgical techniques, mean duration of follow-up, and the specific clinicopathologic factors investigated alongside tumor thrombus levels could have contributed to these discrepancies. It is worth noting that significant factors predicting OS may vary depending on the duration of follow-up, which can lead to conflicting conclusions regarding the impact of tumor thrombus extension on survival outcomes. A research from Shengjing Hospital of China Medical University revealed no differences in CSS between renal vein group and inferior vena cava (IVC) group (24). Another study subdivided 142 patients with VTT into high-Mayo group and low-Mayo group, indicating that VTT grading did not affect long-term survival (9). However, high Mayo grading was associated with postoperative 12-month death risk. By contrast, several studies showed that the prognosis of patients with renal VTT was better than patient with IVC tumor thrombus (25,26). Martínez-Salamanca *et al.* analyzed 1122 patients with different grade VTT, indicating that 5-year OS of VTT in renal vein, above the renal vein but below the diaphragm, above the diaphragm was respectively 43.2%, 37%, 22% (27). Unexpectedly, they reported that VTT grading was the risk factor for prognosis of patients with VTT. We are aware that Mayo grading is subdivided by tumor thrombus position in vein, and different grade tumor thrombus means different surgical strategies and difficulties. So, the correlation between VTT grading and prognosis still deserves further investigation.

Moreover, researchers raised some prognostic factors based on laboratory measures including preoperative hemoglobin, preoperative serum alkaline phosphatase (ALP), preoperative alanine transaminase (ALT), preoperative albumin, and so on (26,28). This study also indicated that preoperative LDH and preoperative neutrophils were independent risk factors for OS. LDH, one of the most important enzymes of glycolysis, is a glycolytic enzyme that catalyzes the conversion of pyruvate to lactic acid. In tumor cells, glycolysis is extremely elevated regardless of oxygen availability, which is known as the Warburg effect. Low LDH expression inhabits tumor invasion and metastasis by reducing the proliferative capacity and resistance of chemotherapy (29). Recent years, a multitude of studies demonstrated that serum LDH level was associated with prognosis (30,31). Our research found that high-level preoperative LDH was related to poor prognosis. The level of serum LDH is a convenient and economic prognostic indicator. However, the reason of serum LDH promotion in renal cancer patients with VTT is still not clear. Large multi-center studies are needed to confirm these findings. These years, some systemic inflammatory and immune response indicators such as C-reactive protein and neutrophil to lymphocyte ratio (NLR) were considered to predict prognosis (32). Our nomogram included preoperative neutrophils, which was one of independent risk factor of OS. Thus, with the preoperative neutrophils increasing, the prognosis of patients are poorer. This situation may be in contacted in the change of tumor immune microenvironment (TIME). Ghatalia *et al.* (33) reported that neutrophil augmented renal cancer postoperative recurrence by analyzing tumor-infiltrating immune cell and located ccRCC recurrence rate. The above simple preoperative blood biochemical indicators can be easily analyzed and may help select high-risk patients. Consistent with previous research, our study has yielded further evidence supporting the use of preoperative LDH and preoperative neutrophil as independent prognostic indicators in non-metastatic renal cancer patients with VTT. Moreover, incorporating these parameters into prognostic nomograms has demonstrated improved predictive accuracy and clinical utility. These findings highlight the potential of preoperative LDH and preoperative neutrophils as valuable tools for risk stratification and treatment decision-making in this patient population.

Lymph node dissection plays a pivotal role in the surgical management of malignant tumors in the genitourinary system. However, the value of lymph node dissection in RN has been a subject of ongoing debate. At our institution, lymph node dissection is performed selectively, based on evidence of lymph node enlargement on preoperative imaging studies. Only when tumor cells are identified in the resected lymph node specimens during surgery are patients classified as N1. According to our established criteria, our study findings did not demonstrate a significant association between lymph node metastasis and patient survival. While some studies have reported potential oncological benefits of lymph node dissection (34,35), others argue that it does not

confer any survival advantages for kidney cancer patients (36,37). Clinical practice involving regional lymph node dissection is often driven by the desire to determine the local extent of the tumor and potentially guide decisions regarding adjuvant therapy. However, it remains uncertain whether lymph node dissection itself provides inherent survival benefits. Karmali *et al.* (38) analyzed sentinel lymph nodes in renal cancer patients, and found that RCC is more inclined to hematogenous dissemination rather than lymphatic spread. Patients with regional lymph node metastasis typically already exhibit distant metastasis, with only a small percentage (2–5%) presenting solely with lymph node involvement and no distant spread. Consequently, lymph node metastasis may not necessarily function as an independent prognostic factor, and the inferior prognosis observed in lymph node-positive patients could potentially be attributed to the presence of pre-existing microscopic distant metastasis.

Several researchers have made analyses on the prognosis of renal cancer patients with VTT, and some studies have suggested that risk factors abound such as lymphatic invasion, perirenal adipose tissue invasion, tumor diameter, tumor necrosis, preoperative hemoglobin, pathological type, tumor thrombus grading (9,39-41). Meanwhile, these influential factors remain many controversies, needing to be further explored. This study analyzed clinical data of 114 non-metastasis renal cancer patients with VTT, and performed Cox regression analyses on potential factors. Results indicated that tumor diameter, preoperative LDH and preoperative neutrophils were independent risk factors for OS. A new nomogram model was constructed based on the above data and Mayo grading to quantified and analyzed prognosis, helping clinicians to guide treatment and discuss decisions with patients.

Compared with the traditional tumor-node-metastasis (TNM) staging system, nomograms based on results of multivariate analysis were proved to better predict prognosis in various cancer types (42,43). Multivariate Cox regression analysis indicated that tumor diameter, preoperative LDH and preoperative neutrophils were independent risk factors for OS in non-metastasis renal cancer with VTT and these three factors binding Mayo grading effectively predict prognosis. The nomogram is verified to be effective via Kaplan-Meier (KM) plots, ROC and DCA curve. The AUC of 1- and 2-year OS is 0.82 and 0.67, but long-term OS is only 0.57 and 0.55 considering the limited number of samples and different treatment method after surgery in this study. Most importantly, the indicator that our nomogram included are easy to gain, embodying the practicality, availability and economy of the nomogram.

The present study is subject to several limitations: Firstly, it should be noted that only cases with complete clinical and follow-up data were included in this study, which may introduce a certain degree of selection bias. Secondly, the survival model established in this study may not be generalizable to patients with RCC accompanied by VTT who exhibit extremely abnormal laboratory parameters. Additionally, due to the relatively low number of patients in our cohort who had tumor thrombus invading the vein wall, they were not included in the study. Lastly, it is important to acknowledge that the survival model established based on our dataset has yet to undergo validation using patient data from other institutions. Therefore, further validation of the model is warranted through large-scale, multi-center, and prospective studies. This will help to enhance the robustness and generalizability of the findings and ensure the reliability of the survival model in clinical practice.

When considering the collective impact of various factors on the OS of non-metastatic renal cancer patients with VTT, several independent risk factors stand out. These include renal tumor diameter, preoperative LDH, and preoperative neutrophil. By taking these factors into account, clinicians can gain valuable insights into the prognosis of patients and make informed decisions regarding their treatment. To enhance the accuracy of prognosis prediction, a nomogram model can be developed. This model combines the aforementioned risk factors with the traditional Mayo grading system, allowing for a comprehensive and quantitative analysis of prognosis. The nomogram serves as a visual tool that enables clinicians to estimate the likelihood of survival and identify patients at a higher risk of adverse outcomes. By utilizing this nomogram model, clinicians can more effectively identify high-risk patients who require early intervention and tailored treatment strategies. This proactive approach not only improves the individualized care provided to patients but also enhances overall treatment outcomes. Ultimately, the integration of the nomogram model with traditional Mayo grading empowers healthcare professionals to make more precise prognostic assessments and deliver optimal care to renal cancer patients with VTT.

Conclusions

In a word, surgical intervention improves the prognosis of renal cancer patients with VTT. Independent risk

factors include kidney tumor diameter, preoperative LDH levels, and preoperative neutrophil count. The nomogram enhances the Mayo grading system and serves as a dependable tool for prognostic evaluation in renal cancer patients with VTT.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-23-341/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-23-341/dss

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-23-341/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-23-341/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Changhai Hospital (No. CHEC2021-191). Informed consent was waived by Ethics Committees due to the retrospective nature of the study.

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Cite this article as: Zhu B, Yang Y, Huangfu Z, Zhang W, Jiang A, Wang L. Construction of the prognostic model in non-metastatic renal cancer patients with venous tumor thrombus. Transl Androl Urol 2023;12(11):1645-1657. doi: 10.21037/tau-23-341

