Preoperative Anemia and Thrombocytosis Predict Adverse Prognosis in Non-Metastatic Renal Cell Carcinoma With Tumor Thrombus

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Abstract

Objection: The aim of the study was to determine the prognostic value of preoperative blood parameters in patients with renal cell carcinoma (RCC) and tumor thrombus (TT) treated surgically.

Method: we retrospectively analyzed 152 patients diagnosis with RCC and TT and treated surgically. Clinicopathologic data and blood parameter were obtained. Univariable and multivariable analysis using the Cox regression model were performed to determine risk factors that were associated with progression-free survival (PFS) and overall survival (OS). Kaplan-Meier curve and logistic regression were performed to analyze the risk factors.

Results: Preoperative Hgb≥120g/L (HR=2.48, P=0.024) and lymph node metastasis (HR=3.98, P=0.032) were an independent prognostic factors associated with OS. Preoperative PLT≥300×10^9/L (HR=2.10, P=0.014) and lymph node metastasis (HR=3.42, P=0.021) were an independent prognostic factors associated with PFS. In Kaplan–Meier survival analysis, preoperative anemia had worse OS than without anemia (P=0.003) and thrombocytosis had worse PFS than without thrombocytosis (P=0.001). Preoperative anemia were associated with more symptomatic (P=0.009), surgical time≥6h (P=0.016), Blood loss≥1000ml (P=0.014), transfusion(P=0.012), higher thrombus level (III-IV) (P=0.004) and higher nuclear grade (III-IV) (P=0.002) while thrombocytosis were associated with more symptomatic (P=0.008) and higher nuclear grade (III-IV) (P=0.042)

Conclusions: Preoperative anemia and thrombocytosis was associated with adverse prognosis in patients with non-metastatic RCC with TT. Both preoperative hemoglobin level and platelet count may be clinical useful for risk stratifying patients receiving operation for non-metastatic RCC with TT.

Introduction

Renal cell carcinoma (RCC) accounts for 3% of all malignant tumors worldwide[1]. With improvement of surgical procedures and adjuvant therapy, the long-term prognosis of RCC has favorable outcome with 5-year survival rate of 80%-90% in most of histologic type[2]. Several prognostic factors based on pathologic data have been reported, such as RCC subtype, tumor grade, sarcomatoid and rhabdoid features and TNM classification[3]. Thus some studies have established nomogram or prognostic model systems to predict survival combining these factors, and the usefulness of them have been confirmed in external validated populations[3, 4].

Preoperative blood parameters can reflect patients' inflammatory status and healthy conditions in a cheap and convenient way. As we all known, inflammation is strongly associated with tumor genesis, progression and metastasis[5]. Preoperative Inflammation indicators such as neutrophils, lymphocytes, platelets, neutrophil-lymphocyte ratio (NLR) and the platelet lymphocyte ratio (PLR) have been demonstrated to be prognostic value in some urologic malignancies like prostate cancer and bladder cancer[6, 7]. In RCC, elevated neutrophils, platelets, NLR, PLR and decreased lymphocytes was associated with worse survival in previous study[8–11]. Besides, other preoperative blood parameters like
hemoglobin, AST/ALT, albumin have been reported as prognostic factors in predicting RCC survival[12]. Recently, new prognostic system incorporating preoperative blood parameters have been designed with improved accuracy[13, 14].

However, 4–10% of RCC patients have thrombus in the renal vein or inferior vena cava[15]. Because of the complexity of inflammatory status and the rarity of these populations, the prognostic significance of preoperative blood parameters has not been reported in the previous study. The aim of present study was to determine the prognostic value of preoperative blood parameters in patients with tumor thrombus treated surgically.

Methods

Patient population

After receiving approval from the Peking University Third Hospital Medical Science Research Ethics Committee, we retrospectively analyzed clinicopathologic data of 278 patients’ diagnosis with renal neoplasms and tumor thrombus treated with nephrectomy and thrombectomy at our institute from Jan 2014 to Dec 2019. Exclude criteria include: (1) non renal cell carcinoma; (2) suspicious distant metastasis preoperatively; (3) bilateral tumor or recurrent tumor. The flow chart of patients’ inclusion was shown in Fig.1. Finally we included 152 patients to conduct further research. Clinicopathologic data and blood parameter were collected through medical records and pathologic reports.

Clinical and pathologic evaluation

The clinicopathologic variables recorded included age, gender, body mass index (BMI), symptoms at presentation, American Society of Anesthesiologists (ASA) score, surgical approach, tumor thrombus level (TT), tumor size, nuclear grade and histologic type. Tumor thrombus level were defined according to the Mayo classification by preoperative imaging. Nuclear grade were defined according to Fuhrman grade before 2016 and WHO/IUSP classification after 2016. Laboratory examination were routinely analyzed within a week before surgery in each patient. blood parameter were obtained include neutrophil count (Neu), platelet count (PLT), lymphocyte count (Lym), hemoglobin level (Hgb), albumin level (Alb), serum creatine (SCr), plasma AST and ALT, serum calcium (SCa) and alkaline phosphatase (ALP). NLR and PLR were calculated by dividing the neutrophil count and platelet count by the lymphocyte count respectively. Platelet count ≥300×10⁹/L were defined as thrombocytosis (normal range of platelet counts at our institution were 100~ 300×10⁹/L). Hemoglobin level ≤120g/L were defined as anemia (normal range of Hemoglobin level at our institution were 120~160g/L).

Follow up

After surgery, patients were followed up. Prognostic data were obtained through clinic or telephone by our research secretary until July 2020. We recommend patients to follow up every 3 months for the first years, every 6 months for the next 2 years and yearly thereafter. Laboratory examinations and X-ray, ultrasonic
scan or abdominal CT were performed at each visit. Overall survival (OS) was calculated from the date of surgery to death. Progression free survival (PFS) was calculated from the date of surgery to tumor recurrence or metastasis.

**Statistical analysis**

We assessed the prognostic value (OS and PFS) of preoperative blood parameters and clinicopathologic data based on univariate and multivariate analysis by Cox's proportional hazards regression model. All blood parameters and clinicopathologic data were transformed to category variable. The cut-off value we determined mainly according the previous published study. OS and PFS were estimated from Kaplan–Meier curves and the log-rank test was used to compare survival differences. Logistic regression model were used to analyze the association of anemia and thrombocytosis with clinicopathologic characteristics. All statistical analyses were conducted with SPSS Statistics 22.0 (IBM Corp, Armonk, NY, USA) and GraphPad prism 8. Two-tailed tests were used for all comparisons, and p < 0.05 was considered statistically significant.

**Result**

The baseline clinical and pathologic variables of 152 patients treated surgically for RCC with TT were shown in the Table.1. Among these patients, the majority (n = 118, 77.6%) were male. The median age of these patients was 56.6 year (IQR:54 ~ 66.7). Most of these patients were treated in laparoscopic than opened approach (58.6% vs 41.4%). The median surgical time was 320 min (IQR:228 ~ 409.7) and median blood loss was 600 ml (IQR:200 ~ 1950). Of these patients, the majority of TT level were classified to mayo 0-II (n = 122, 80.3%) than mayo III-IV (n = 30, 19.7%). The median tumor size was 8.3 cm (IQR:6.5 ~ 10). Regarding histological subtypes, 129 of patients (84.9%) had clear cell RCC and 16 (10.5%) had papillary RCC. More than half of these patients (n = 90, 59.2%) had III-IV nuclear grade. Lymph node metastasis had pathologically confirmed in 9 (5.9%) cases. At the last follow up, 146 (96.1%) patients received follow up with mean 21 months (IQR:8 ~ 31). The Kaplan-Meier curve of OS and PFS were shown in Fig. 2. Estimated 3-year-OS were 71.6% while estimated 3-year-PFS were 49.2%.

The baseline preoperative blood parameter of study cohort were shown in Table.2. In the univariate analysis, Hgb≥120 g/L (HR = 3.12, P = 0.005), ALT ≥ 30u/L (HR = 2.19, P = 0.045), AST ≥ 25u/L (HR = 2.63, P = 0.010) and lymph node metastasis (HR = 3.98, P = 0.026) were a significant predictor of OS. In the multivariate analysis, Hgb≥120 g/L (HR = 2.48, P = 0.024) and lymph node metastasis (HR = 3.98, P = 0.032) were an independent prognostic factors associated with OS (shown in Table.3). Besides. Univariable analysis demonstrated that PLT ≥ 300 × 10⁹/L(HR = 2.45, P = 0.002), nuclear grade (III-IV)(HR = 2.01, P = 0.018), lymph node metastasis(HR = 2.87, P = 0.018) were significant predictors of PFS. Stepwise multivariable analysis showed that PLT ≥ 300 × 10⁹/L (HR = 2.10, P = 0.014) was an independent predictor of PFS, along with lymph node metastasis (HR = 3.42, P = 0.021) (shown in Table.4). In Kaplan–Meier survival analysis, patients with preoperative anemia had an increased risk of mortality compared to those who without. (shown in Fig. 3, P = 0.003). Besides, preoperative
thrombocytosis was associated with an increased the risk of earlier recurrence or metastasis than that without thrombocytosis. (shown in Fig. 4, p = 0.001).

To determine the association of anemia and thrombocytosis with clinicopathologic characteristics., we found that preoperative anemia were associated with more symptomatic (OR = 3.14, P = 0.009), surgical time ≥ 6 h (OR = 2.28, P = 0.016), Blood loss ≥ 1000 ml (OR = 2.32, P = 0.014), transfusion(OR = 2.34, P = 0.012), higher TT level (III-IV) (OR = 3.41, P = 0.004) and higher nuclear grade (III-IV) (OR = 3.13, P = 0.002). Besides, Patients with thrombocytosis were associated with more symptomatic (OR = 7.33, P = 0.008) and higher nuclear grade (III-IV) (OR = 2.39, P = 0.042) (shown in Table 5).

Discussion

This study examined the 152 patients with RCC and TT treated surgically from a high volume center and found patients with preoperative anemia had significantly adverse OS than that without anemia. Besides, patients with thrombocytosis was associated with worse PFS than those without thrombocytosis. In multivariable analysis, we found preoperative anemia and thrombocytosis was an independent worse prognostic factor even adjusting for other known pathologic prognostic factors. To our knowledge, this is the first study of the preoperative blood parameters specically focused on the population of RCC and TT.

In the previous study, anemia could be used as a prognostic factors in RCC. Kim SH et al retrospectively analyzed 4,260 patients with non-metastatic RCC and found factors include anemia were associated with worse recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS)[16]. Jiwei Huang et al analyzed 352 patients with papillary RCC and found patients with preoperative anemia had significantly worse RFS, CSS, and OS than patients without anemia (P < 0.001). Multivariable analysis revealed that anemia was an independent prognostic factor in terms of RFS, CSS, and OS (P < 0.001)[17]. Xia L et al conducted a meta-analysis and found preoperative anemia was associated with increased all-cause mortality, cancer-specific mortality, and disease recurrence[18]. Combine with previous study, our study found preoperative anemia was an independent predictor of worse OS compared to those without anemia in RCC with TT populations. We suspected reason may as follows: Anemia was strongly related to more aggressive cancer biology and worse pathologic characteristics. Combined with our study, patients with preoperative anemia had higher TT level and higher nuclear grade, which may cause a worse prognosis. As is shown in our study, preoperative anemia had higher rate of blood transfusion during operation. Some research have already confirmed transfusion had a worse impact on RCC patients after surgery[19]. Patients with anemia preoperatively may suffered from chronic blood loss, which can cause a worse nutrition status. Despite we need further study to verify our hypothesis, anemia was not a negligible prognostic factor associated with worse survival.

Thrombocytosis had been found as a worse prognostic predictor in different kind of cancer, include nasopharyngeal carcinoma[20], gynecologic malignancies[21], melanoma[22] and colorectal cancer[23]. In RCC, thrombocytosis also could be regard as a prognostic indicator. Several study had already shown patients with preoperative thrombocytosis had a worse survival than those who
Although none of these study had confirmed the thrombocytosis had worse prognosis in population of RCC with TT, previous study had found that bland thrombus in RCC with TT was associated with adverse survival\cite{27}. Combine with our study, patients with thrombocytosis had an increased recurrence or metastasis risk than those who without. Besides, our study had confirmed that thrombocytosis is an independent prognostic factor predicting PFS. Interestingly, previously we thought the function of platelets were mainly in limiting blood loss and promoting wound healing. Recently, preclinical and clinical studies showed that platelets can promote tumorigenesis and metastasis through a wide variety of crosstalk between platelets and cancer cells\cite{28}. This may explain why preoperative thrombocytosis had high risk of recurrence or metastasis after surgery. Therefore, follow up plan should be given more closely in populations with RCC and TT when we found thrombocytosis preoperatively.

Although some researcher found NLR, PLR and AST/ALT and Alb level could be used as prognostic factors in RCC \cite{8–12}, in population of RCC with TT we could not found any statistically significant difference. Firstly, we supposed in patients of RCC with TT, the inflammatory status could be more complex, thus these kinds of blood marker may not suitable for specific kind of populations. Secondly, the number of patients included in the study may not sufficient to obtain statistical differences. Owing to the rarity of these population, multi-institutional study should be conducted to further investigate the prognostic value of blood parameter in this certain kind of population.

This retrospective study has several limitations. Firstly, our research is single-institutional retrospective review, which inherently include missing data and confounding bias that we could not control. Secondly, we did not collect the information about concomitant drugs, which may have an influencing on blood counts (e.g., steroids). Despite these limitations, our study is significant because we are the only research focus on the impact of preoperative blood parameter on the patients with RCC and TT.

**Conclusion**

Both preoperative anemia and thrombocytosis are an important independent prognostic factor for patients with RCC and TT. Anemia is associated with an increased risk of mortality while thrombocytosis is associated with an increased risk of earlier recurrence or metastasis. Both preoperative hemoglobin level and platelet count may be clinical useful for risk stratifying patients receiving operation for non-metastatic RCC with TT.

**Abbreviations**

RCC: renal cell carcinoma; TT: tumor thrombus; SCr: serum creatinine; Alb: albumin; Hgb: hemoglobin; NLR: neutrophil-lymphocyte ratio; PLR: platelet lymphocyte ratio; Neu: neutrophil count; PLT: platelet count; Lym: lymphocyte count; Alb: albumin level; SCa: serum calcium; ALP: alkaline phosphatase; BMI: body mass index; ASA: American Society of Anesthesiologists score; OS: overall survival; PFS: Progression free survival.
Declarations

Ethics approval and consent to participate
The study was approved by the Peking University Third Hospital Medical Science Research Ethics Committee. All of the procedures were performed in accordance with the Declaration of Helsinki and relevant policies in China. Because of the retrospective nature of the study, patient consent for inclusion was waived.

Consent to publish
Not applicable.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

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Not applicable.

Authors’ Contributions
RX collected and analyzed the data and wrote the manuscript. CX, WH, LL, HZ made substantial contributions to the design of this work. LM and CL substantially revised the work and manuscript. All authors have read and approved the manuscript.

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Tables

Table 1: Clinical and pathologic features of patients with RCC and TT treated surgically.
| Characteristics                                           | All cohort (n=152)              |
|----------------------------------------------------------|---------------------------------|
| **Age, y, median. (IQR)**                                | 59.6 (54~66.7)                  |
| **Gender, no. (%)**                                      |                                 |
| Male                                                     | 118 (77.6)                      |
| Female                                                   | 34 (22.3)                       |
| **BMI, no. (%)**                                         |                                 |
| ≥28                                                      | 26 (17.2)                       |
| <28                                                      | 126 (82.9)                      |
| **Symptoms, no. (%)**                                    |                                 |
| Incidental                                               | 38 (25)                         |
| Symptomatic                                              | 114 (75)                        |
| **ASA, no. (%)**                                         |                                 |
| I-II                                                     | 134 (88.1)                      |
| III-IV                                                   | 18 (11.9)                       |
| **Approach, no. (%)**                                    |                                 |
| Open                                                     | 63 (41.4)                       |
| Laparoscopic                                              | 89 (58.6)                       |
| **Surgical time, min, median. (IQR)**                    | 320 (228~409.7)                 |
| **Blood loss, ml, median. (IQR)**                        | 600 (200~1950)                  |
| **Transfusion, no. (%)**                                 | 75 (49.3)                       |
| **segmental resection of vena cava, no. (%)**             | 28 (18.4)                       |
| **Side, no. (%)**                                        |                                 |
| Left                                                     | 54 (35.5)                       |
| Right                                                    | 98 (64.5)                       |
| **Size, cm, median. (IQR)**                              | 8.3 (6.5~10)                    |
| **Tumor thrombus level, no. (%)**                        |                                 |
| 0-II                                                     | 122 (80.3)                      |
| III-IV                                                   | 30 (19.7)                       |
| *Adhesion, no. (%)                                       | 56 (36.8)                       |
Histology type, no. (%)

| Type      | No. (%) |
|-----------|---------|
| Clear cell| 129(84.9)|
| Papillary | 16(10.5) |
| Other type| 7(4.6)   |

Nuclear grade, no. (%)

| Grade | No. (%) |
|-------|---------|
| I-II  | 62(40.8) |
| III-IV| 90(59.2) |

Lymph node metastasis, no. (%)

| Metastasis | No. (%) |
|------------|---------|
|            | 9(5.9)  |

*tumor thrombus adhesion to the vena cava wall

Table 2: Preoperative blood parameters of patients with RCC and TT treated surgically.

| Blood parameters (unit) | Mean (IQR)       |
|-------------------------|------------------|
| Neu (×10⁹/L)            | 4.6(3.6~5.1)     |
| Lym (×10⁹/L)            | 1.3(1~1.6)       |
| PLT (×10⁹/L)            | 248.9(186~297)   |
| Hgb (g/L)               | 123.3(111~138)   |
| Alb (g/L)               | 38.8(35.8~43)    |
| SCr (umol/L)            | 99(80~107)       |
| ALT (u/L)               | 25.1(11.2~27)    |
| AST(u/L)                | 23.9(14.7~24.2)  |
| SCa (mmol/L)            | 2.3(2.2~2.4)     |
| ALP (u/L)               | 92.4(66~103)     |
| NLR                     | 3.5(2.4~4.5)     |
| PLR                     | 187.9(124~272)   |
| AST/ALT                 | 1.1(0.8~1.5)     |

Table 3: Univariate and multivariate analysis of prognostic factors of overall survival by Cox regression model.
| Variable                                | Univariate analysis |          |          |          | Multivariate analysis |          |          |
|----------------------------------------|----------------------|----------|----------|----------|-----------------------|----------|----------|
|                                        |                      | HR       | 95%CL    | P-value  | HR                    | 95%CL    | P-value  |
| Neu ≥ 5.5×10⁹/L                        | 1.68                 | 0.71~3.95| 0.232    | 1.68     | 0.71~3.95             | 0.232    |          |
| Lym ≥ 1×10⁹/L                         | 1.23                 | 0.54~2.79| 0.622    | 1.23     | 0.54~2.79             | 0.622    |          |
| PLT ≥ 300×10⁹/L                       | 1.62                 | 0.69~3.82| 0.266    | 1.62     | 0.69~3.82             | 0.266    |          |
| NLR ≥ 4                                | 1.68                 | 0.81~3.50| 0.168    | 1.68     | 0.81~3.50             | 0.168    |          |
| PLR ≥ 250                              | 1.77                 | 0.83~3.75| 0.137    | 1.77     | 0.83~3.75             | 0.137    |          |
| Hgb ≥ 120g/L                           | 3.12                 | 1.39~6.15| 0.005    | 2.48     | 1.12~5.48             | 0.024    |          |
| Alb ≥ 35g/L                            | 1.39                 | 0.61~3.15| 0.432    |          | 1.39                  | 0.61~3.15| 0.432    |
| SCr ≥ 110umol/L                       | 0.92                 | 0.39~2.15| 0.848    |          | 0.92                  | 0.39~2.15| 0.848    |
| ALT ≥ 30u/L                            | 2.19                 | 1.01~4.73| 0.045    | 1.07     | 0.44~2.61             | 0.870    |          |
| AST ≥ 25u/L                            | 2.63                 | 1.26~5.49| 0.010    | 1.95     | 0.83~4.54             | 0.123    |          |
| AST/ALT ≥ 1.3                         | 1.27                 | 0.59~2.70| 0.530    |          | 1.27                  | 0.59~2.70| 0.530    |
| SCa ≥ 2.4mmol/L                       | 0.91                 | 0.31~2.63| 0.864    |          | 0.91                  | 0.31~2.63| 0.864    |
| ALP ≥ 90u/L                            | 1.68                 | 0.81~3.52| 0.166    |          | 1.68                  | 0.81~3.52| 0.166    |
| Tumor thrombosis level (III-IV)       | 1.97                 | 0.91~4.26| 0.084    |          | 1.97                  | 0.91~4.26| 0.084    |
| Tumor size ≥ 10cm                     | 1.35                 | 0.61~3.01| 0.457    |          | 1.35                  | 0.61~3.01| 0.457    |
| With adhesion                         | 1.61                 | 0.77~3.34| 0.205    |          | 1.61                  | 0.77~3.34| 0.205    |
| Nuclear grade (III-IV)                | 2.14                 | 0.94~4.85| 0.067    |          | 2.14                  | 0.94~4.85| 0.067    |
| lymph node metastasis                 | 3.98                 | 1.18~13.48| 0.026    | 3.98     | 1.12~14.10            | 0.032    |          |

Table 4: Univariate and multivariate analysis of prognostic factors of progression free survival by Cox regression model.
| Variable                        | Univariate analysis | Multivariate analysis |
|--------------------------------|---------------------|-----------------------|
|                                | HR  | 95%CL   | P-value | HR   | 95%CL   | P-value |
| Neu≥5.5×10^9/L                 | 1.37| 0.71~2.65| 0.345   |      |        |        |
| Lym≥1×10^9/L                   | 0.88| 0.47~1.64| 0.696   |      |        |        |
| PLT≥300×10^9/L                 | **2.45**| **1.40~4.31**| **0.002** | **2.10**| **1.16~3.78**| **0.014** |
| NLR≥4                          | 1.09| 0.59~1.78| 0.916   |      |        |        |
| PLR≥250                        | 1.57| 0.91~2.69| 0.100   |      |        |        |
| Hgb≥120g/L                     | 1.64| 0.97~2.76| 0.062   |      |        |        |
| Alb≥35g/L                      | 1.42| 0.81~2.52| 0.222   |      |        |        |
| SCr≥110umol/L                  | 0.92| 0.51~1.69| 0.798   |      |        |        |
| ALT≥30u/L                      | 1.51| 0.85~2.65| 0.157   |      |        |        |
| AST≥25u/L                      | 1.33| 0.75~2.36| 0.316   |      |        |        |
| AST/ALT≥1.3                    | 0.86| 0.49~1.49| 0.597   |      |        |        |
| SCA≥2.4mmol/L                  | 1.72| 0.91~3.29| 0.096   |      |        |        |
| ALP≥90u/L                      | 1.04| 0.61~1.78| 0.880   |      |        |        |
| Tumor thrombosis level (III-IV)| 1.21| 0.67~2.18| 0.532   |      |        |        |
| Tumor size≥10cm                | 1.11| 0.61~2.01| 0.743   |      |        |        |
| With adhesion                  | 1.43| 0.84~2.42| 0.180   |      |        |        |
| Nuclear grade (III-IV)         | **2.01**| **1.13~3.58**| **0.018** | 1.75| 0.95~3.23| 0.070   |
| lymph node metastasis          | **2.87**| **1.02~8.05**| **0.018** | **3.42**| **1.20~9.77**| **0.021** |

Table 5 Odds ratios and 95 % confidence interval for the association of anemia and thrombocytosis with clinicopathologic characteristics.
|                                | Anemia (Hgb≤120g/L) | Thrombocytosis (PLT≥300×10⁹/L) |
|--------------------------------|---------------------|-------------------------------|
|                                | OR      | 95%CL     | P-value | OR      | 95%CL     | P-value |
| Age≥70yr                       | 1.02    | 0.42~2.46 | 0.953   | 1.74    | 0.68~4.47 | 0.248   |
| Symptomatic                    | 3.14    | 1.32~7.45 | 0.009   | 7.33    | 1.66~32.22 | 0.008   |
| Surgical time≥6h               | 2.28    | 1.16~4.48 | 0.016   | 0.68    | 0.30~1.52 | 0.352   |
| Blood loss≥1000ml              | 2.32    | 1.18~4.54 | 0.014   | 0.63    | 0.28~1.41 | 0.269   |
| Transfusion                    | 2.34    | 1.20~4.54 | 0.012   | 1.26    | 0.59~2.69 | 0.542   |
| segmental resection of vena cava | 0.49   | 0.21~1.13 | 0.095   | 0.87    | 0.33~2.27 | 0.784   |
| Tumor thrombosis level (III-IV)| 3.41    | 1.48~7.84 | 0.004   | 1.27    | 0.51~3.19 | 0.598   |
| Larger than 10cm               | 0.76    | 0.36~1.58 | 0.468   | 1.71    | 0.76~3.81 | 0.188   |
| With adhesion                  | 1.58    | 0.81~3.09 | 0.182   | 0.73    | 0.32~1.64 | 0.450   |
| Nuclear grade (III-IV)         | 3.13    | 1.53~6.39 | 0.002   | 2.39    | 1.03~5.54 | 0.042   |
| lymph node metastasis          | 1.24    | 0.32~4.82 | 0.754   | 0.95    | 0.18~4.81 | 0.953   |

**Figures**
Figure 1

Flow chart of patients who met study inclusion/exclusion criteria.
Figure 2

Kaplan-Meier curves for patients with RCC and TT. (A) overall survival; (B) Progression-free survival.
Figure 3

Kaplan-Meier curves of overall survival for patients with RCC and TT categorized by anemia.

log-rank P=0.003

[Graph showing overall survival over time for non-anemia and anemia categories]

log-rank P=0.001

[Graph showing progression-free survival over time for non-thrombocytosis and thrombocytosis categories]
Figure 4

Kaplan-Meier curves of progression-free survival for patients with RCC and TT categorized by thrombocytosis.