

# Preoperative Lymphocyte-to-Monocyte Ratio as a Predictor of Prognosis in Patients who Underwent Resection of Renal Cell Carcinoma with Inferior Vena Cava Tumor Thrombus

**Zheng Lv**

Medical College of Nankai University: Nankai University School of Medicine

**Hua-Yi Feng**

Medical School of Chinese PLA: Chinese PLA General Hospital

**Tao Wang**

Medical School of Chinese PLA: Chinese PLA General Hospital

**HongZhao Li**

Chinese PLA General Hospital

**Xin Ma**

Chinese PLA General Hospital

**Xu Zhang** (✉ [xzhang301@163.com](mailto:xzhang301@163.com))

Chinese PLA General Hospital <https://orcid.org/0000-0003-4283-409X>

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## Research Article

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# Abstract

**Background:** The aim of the study was to evaluate the prognostic value of preoperative lymphocyte to monocyte ratio (LMR) in patients with renal cell carcinoma and inferior vena cava tumor thrombus (RCC-IVCTT) after surgery.

**Methods:** We retrospectively reviewed the medical data of 144 consecutive patients who underwent RCC-IVCTT after surgery. Time-dependent receiver operating characteristic curve analysis was performed to calculate the optimal cutoff value for preoperative LMR. The Kaplan-Meier method was used to assess and compare survival. Univariable and multivariable Cox proportional hazard models were constructed to identify independent prognostic factors for survival. The Harrell concordance index was used to assess the predictive accuracy.

**Results:** Decreased preoperative LMR was significantly correlated with clinicopathological features related to tumor progression. Patients in the high LMR group featured longer postoperative hospital stays and greater blood loss during surgery than those in the low LMR group. Decreased preoperative LMR was an independent risk factor for decreased overall survival (OS) ( $P < 0.05$ ) and progression free survival (PFS) ( $P < 0.05$ ). For PFS, integrating LMR into each model led to an increased predictive accuracy of 6.9% for the TNM staging model ( $P = 0.014$ ), 6.8% for the UISS model ( $P = 0.006$ ), and 3.4% for the SSIGN model ( $P = 0.017$ ). Incorporating LMR into the SSIGN model led to an increased predictive accuracy of 6.5% for OS ( $P < 0.001$ ).

**Conclusions:** Preoperative LMR is an independent prognostic factor for patients with RCC-IVCTT after surgery. Adding preoperative LMR to prognostic models enhances their predictive accuracy.

## 1. Introduction

Renal cell carcinoma (RCC) is the most frequent cancer in the kidney, representing 2-3% of all cancers<sup>1</sup>. Venous tumor thrombus formation is a unique feature of RCC, occurring in approximately 4-10% of all RCC cases<sup>2</sup>. Tumor thrombus can invade the renal vein and/or inferior vena cava (IVC). Radical nephrectomy with thrombectomy remains the standard curative therapy for localized advanced RCC<sup>3</sup>. However, the morbidity and mortality rates of this procedure is high in IVC tumor thrombus, with complication rates ranging from 12.4-46.9%<sup>4</sup>. In addition, the presence of IVCTT negatively affects tumor progression, with a high incidence of local recurrence and distant metastasis after surgery<sup>5</sup>.

Identifying novel prognostic biomarkers would facilitate diagnosis, risk stratification and treatment decision-making. Many prognostic features, including tumor size, Fuhrman grade, clinical symptoms and performance status, have been used to predict the prognosis of localized RCC. However, these prognostic features are not always accurate when used alone. To improve predictive accuracy, several prognostic models combining several prognostic features have been developed. Several models, including the eight TNM staging system<sup>6</sup>, UCLA Integrated Staging System (UISS) model<sup>7</sup> and Mayo Clinic's Stage, Size,

Grade, and Necrosis (SSIGN) score model<sup>8</sup>, have been used to predict the prognosis of localized RCC. Nevertheless, some patients with similar clinicopathological features or risk group can have different oncological and clinical outcomes. Therefore, novel biomarkers are needed to improve prediction of the prognosis of RCC-IVCTT.

Inflammation-based biomarkers, including lymphocytes, monocytes, platelets and neutrophils, are routinely tested in clinical settings and can be used to monitor or predict oncologic outcomes in many types of cancers<sup>9, 10</sup>. Systemic inflammatory/immune indices, such as the neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR), are calculated based on the peripheral neutrophil, lymphocyte, and monocyte counts. Several studies have confirmed that lower LMR is associated with poor prognosis in various cancer types<sup>11, 12</sup>. In particular, Hutterer et al. reported that preoperative LMR can be used independently to predict cancer-specific survival, metastasis-free survival and overall survival (OS) of patients with localized RCC<sup>13</sup>. However, the prognostic value of preoperative LMR in patients with RCC-IVCTT treated with radical nephrectomy and thrombectomy remains unclear. The purpose of this study was to assess the prognostic significance of preoperative LMR and investigate whether preoperative LMR could optimize prognosis prediction of well-established risk models in patients with RCC-IVCTT after surgery.

## 2. Patients And Methods

### 2.1 Patients and Clinical Data Collection

We enrolled 164 consecutive patients with RCC-IVCTT treated with radical nephrectomy and thrombectomy at our center between January 2008 and December 2018. The exclusion criteria for patients were: (1) level of venous tumor thrombus of 0 according to Mayo classification<sup>14</sup>, (2) incomplete clinical data, (3) surgery-related mortality, (4) presence of other malignant tumors, (5) prior use of targeted drug therapy before surgery or immune therapy, and (6) acute/chronic inflammatory diseases, including acute cystitis, pneumonia, and gastroenteritis. Following exclusions, 144 patients was included in this study. The medical records of patients with RCC-IVCTT in our institution database were retrospectively reviewed. Clinical data included age, sex, body mass index, symptoms at presentation, surgical records (operating time, postoperative hospital stays, hemorrhage during surgery and perioperative complications), Eastern Cooperative Oncology Group performance status, surgical approach, primary cancer characteristics (tumor size, histological subtype, tumor necrosis, tumor thrombus classification) and serum laboratory test results. All patients were staged according to the eighth TNM staging system<sup>6</sup> and graded according to the Fuhrman's nuclear grading system<sup>15</sup>. The histological subtype of RCC was defined according to the 2016 World Health Organization classification of urogenital tumors<sup>16</sup>. Perioperative complications were classified according to the Clavien-Dindo classification of surgical complications<sup>17</sup>. The level of IVCTT is determined according to the Mayo classification. LMR was calculated from the preoperative full blood count measured within 1 week before surgery. All patients underwent routine evaluation after surgery, including physical examination,

laboratory tests and either computed tomography or magnetic resonance imaging. Progression-free survival (PFS) was calculated as the duration (in months) from the date of surgery to the date of tumor progression, death, or last follow-up. OS was calculated as the time (in months) from the date of surgery to the date of death or last follow-up. This study was approved by the Medical Ethics Committee of PLA General Hospital. Written informed consent was obtained from each patient.

## 2.2 Statistical Analysis

The Kolmogorov-Smirnov test was used to check the normality of continuous data. Continuous variables were expressed as median (interquartile range, IQR). For comparisons between means among subgroups, nonparametric tests of Kruskal-Wallis tests or Wilcoxon rank-sum tests were used. To make LMR more convenient for clinical use, it was examined as a categorical variable. Cutoff points were obtained using time-dependent receiver operating characteristic (ROC) curve analysis. Optimal cutoffs were calculated using the Manhattan distance method. The relationship between categorized LMR and patient clinicopathologic features was analyzed using the Pearson's  $\chi^2$  test or Fisher's exact test. Survival of the different groups was estimated using the Kaplan-Meier method with log-rank test. Variables that were significant ( $P < 0.05$ ) in the univariate analysis were included in the multivariate Cox analysis. The Harrell concordance index (C-index) was calculated to assess the predictive accuracy. The C-index ranges from 0.5 to 1, where 1 indicates perfect prediction and 0.5 indicates no predictive power. The statistical analyses were performed using SPSS Statistics 20.0 software (IBM, Armonk, NY, USA) and R Statistical Software Package Version 3.2.1 (Core Team R. 2015). All comparisons were performed using two-tailed tests. Statistical significance was defined as a two-sided P-value  $< 0.05$ .

## 3. Results

### 3.1 Relationships Between Preoperative LMR and Clinicopathological Characteristics

The clinicopathological characteristics of the 144 patients in our cohort are summarized in Table 1. The median age of the patients at the time of surgery was 56 years (IQR 48–64). The median lymphocytes count was  $1.5 \times 10^9$  /L (IQR 1.1–1.8). The median monocytes count was  $0.44 \times 10^9$  /L (IQR 0.31–0.54). The median LMR was 3.73 (IQR 2.67–4.48). After a median follow-up period of 26.8 months (IQR 7.0–40.5), 70 (48.6%) patients experienced local and/or systemic tumor progression, and 44 (30.6%) patients died from all causes. When LMR was assessed as a continuous variable, rather than a dichotomous variable, elevated LMR was associated with lower N stage (N0) ( $P = 0.043$ ), lower Fuhrman grade (G1 + G2) ( $P = 0.029$ ) and more favorable SSIGN risk groups (intermediate) ( $P = 0.042$ ). To make it convenient for clinicians, ROC curve analysis was performed to determine the optimal cutoff value for LMR. To determine the optimal cutoff value for LMR, time-dependent ROC analyses (1-, 3-, and 5-year survival) were performed. The areas under the curve (AUC) of the 1-, 3-, and 5-year ROC curves were 0.583, 0.695, and 0.752, respectively (Figure 1). The cutoff value of 3.5 best distinguished patient' clinical outcome in the 5-year time-dependent ROC curve analysis. Consequently, the clinical features of the patients were

compared between the low and high LMR groups. Low LMR was associated with a larger tumor size (> 7 cm), higher Fuhrman grade (G3 + G4), higher N stage (N1), and unfavorable SSIGN risk groups (poor risk) (all P < 0.05).

## 3.2 Relationships Between Preoperative LMR and Surgical Outcome

We further analyzed whether preoperative LMR could predict the surgical outcomes of patients with RCC-IVCTT. As shown in Table 2, patients in the low LMR group had a longer postoperative hospital stay of 9 (7–11) days than those in the high LMR group with 7 (6–9) days (P = 0.009). The average hemorrhage during surgery was 700 (225–1175) ml, which was more severe than that in the high LMR group 400 (50–750) ml (P=0.025). However, there was no statistical differences in operating time (P=0.244) and the incidence of perioperative complications (p=0.524) between the two groups. The average hemorrhage volume during surgery in the low LMR group was 700 ml (IQR 225–1175), which was more severe than that in the high LMR group (400 ml, IQR 50–750 ml) (P = 0.025). However, there were no significant differences in operating time (P = 0.244) and the incidence of perioperative complications (P = 0.524) between the two groups.

Table 2  
The relationship between the LMR and surgical outcome

Characteristic	Total	High LMR (n=78)	Low LMR (n=66)	p-value
Operating time (min), median (IQR)	157.50(120-225)	150 (100-195)	170 (109-232)	0.244
Hemorrhage during surgery (ml), median (IQR)	500.00(100-1000)	400 (50-750)	700 (225-1175)	0.008
Postoperative hospital stays (day), median (IQR)	8(6-10)	7(6-9)	9(7-11)	0.009
Perioperative complications, n (%) <sup>a</sup>				0.524
Grade I	28 (19.44)	10(12.82)	18(27.27)	
Grade II	10 (6.94)	4(5.13)	6(9.09)	
Grade III	4 (2.78)	1(1.28)	3(4.55)	
Grade IV	2 (1.39)	1(1.28)	1(1.52)	
Abbreviations: LMR = lymphocyte to monocyte ratio; IQR = interquartile range.				
<sup>a</sup> According to Clavien-Dindo classification of surgical complications				

## 3.3 Relationships Between Preoperative LMR and Prognosis

We further investigated the relationship between preoperative LMR and prognosis. The results of univariate analysis revealed that continuous LMR ( $P = 0.004$ ), age ( $P = 0.009$ ), tumor size ( $P = 0.015$ ), and Fuhrman grade ( $P = 0.017$ ) were significantly correlated with OS (Table 3). The results of the univariate analysis are shown in Table 4. Continuous LMR ( $P < 0.001$ ), tumor size ( $P = 0.038$ ), M stage ( $P = 0.004$ ), and Fuhrman grade ( $P = 0.002$ ) were also correlated with PFS. The variables that were significant in the univariate analysis were included in the multivariable analysis. In this analysis, continuous LMR was an independent predictor of OS ( $P = 0.010$ ) and PFS ( $P = 0.001$ ) in patients with RCC-IVCTT after surgery. When used as a categorical variable, low LMR was correlated with decreased OS ( $P < 0.001$ ) and PFS ( $P = 0.002$ ) in patients with RCC-IVCTT after surgery (Figure 2a, b). The results of univariate and multivariate analyses are presented in Supplemental Tables 1 and 2. The analyses revealed that the dichotomized LMR was an independent prognostic factor for OS ( $P = 0.001$ ) and PFS ( $P = 0.015$ ).

Table 3  
Univariate and Multivariate Cox proportional hazards regression analyses for OS

Variable	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
Age, y			0.009			0.013
≤60	1 (Referent)			1 (Referent)		
≥60	2.213	1.218- 4.019		2.203	1.184- 4.097	
Gender			0.178			
Male	1 (Referent)					
Female	1.587	0.810- 3.106				
Tumor size, cm			0.015			0.052
≤7	1 (Referent)			1 (Referent)		
≥7	2.602	1.207- 5.608		2.239	0.993- 5.084	
BMI, kg/m <sup>2</sup>			0.270			
≤24	1 (Referent)					
≥24	1.396	0.772- 2.525				
Presentation			0.186			
Incidental	1 (Referent)					
Symptomatic	1.566	0.806- 3.043				
N stage			0.305			
N0	1 (Referent)					
N1	1.528	0.680- 3.430				

Abbreviations: LMR = lymphocyte to monocyte ratio; BMI = body mass index; IQR= interquartile range.

Variable	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
M stage			0.190			
M0	1 (Referent)					
M1	1.637	0.784- 3.418				
Fuhrman grade			0.017			0.238
G1+G2	1 (Referent)			1 (Referent)		
G3+G4	2.143	1.147- 4.002		1.499	0.765- 2.935	
T stage			0.394			
T3	1 (Referent)					
T4	1.576	0.553- 4.491				
Invasion of IVC wall			0.702			
Absence	1 (Referent)					
Presence	1.200	0.471- 3.061				
Necrosis			0.431			
Absence	1 (Referent)					
Presence	1.269	0.701- 2.229				
LMR (Continuous)	0.707	0.557- 0.896	0.004	0.438	0.234- 0.818	0.010
Abbreviations: LMR = lymphocyte to monocyte ratio; BMI = body mass index; IQR= interquartile range.						

Table 4  
Univariate and Multivariate Cox proportional hazards regression analyses for PFS

Variable	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
Age, y			0.112			
≤60	1 (Referent)					
≥60	1.467	0.914- 2.353				
Gender			0.555			
Male	1 (Referent)					
Female	1.184	0.676- 2.073				
Tumor size, cm			0.038			0.403
≤7	1 (Referent)			1 (Referent)		
≥7	1.747	1.031- 2.961		1.269	0.726- 2.218	
BMI, kg/m <sup>2</sup>			0.472			
≤24	1 (Referent)					
≥24	1.191	0.740- 1.914				
Presentation			0.077			
Incidental	1 (Referent)					
Symptomatic	1.599	0.951- 2.689				
N stage			0.297			
N0	1 (Referent)					
N1	1.429	0.730- 2.798				

Abbreviations: LMR = lymphocyte to monocyte ratio; BMI = body mass index; IQR= interquartile range.

Variable	Univariate			Multivariate		
	HR	95%CI	P	HR	95%CI	P
M stage			0.004			0.272
M0	1 (Referent)			1 (Referent)		
M1	2.232	1.290- 3.863		1.399	0.768- 2.546	
Fuhrman grade			0.002			0.021
G1+G2	1 (Referent)			1 (Referent)		
G3+G4	2.152	1.317- 3.517		1.848	1.095- 3.120	
T stage			0.906			
T3	1 (Referent)					
T4	1.063	0.387- 2.922				
Invasion of IVC wall			0.069			
Absence	1 (Referent)					
Presence	1.873	0.953- 3.679				
Necrosis			0.692			
Absence	1 (Referent)					
Presence	1.099	0.688- 1.757				
LMR (Continuous)	0.712	0.593- 0.856	0.000	0.733	0.607- 0.884	0.001

Abbreviations: LMR = lymphocyte to monocyte ratio; BMI = body mass index; IQR= interquartile range.

### 3.4 Improvement in Predictive Accuracy of Prognostic Models

Kaplan–Meier curves were used to verify the prognostic value of the TNM, UISS, and SSIGN models. Advanced TNM stage, poor UISS risk group, and poor SSIGN risk group exhibited poor PFS ( $P = 0.003$ ,  $0.024$ , and  $0.002$ , respectively). The poor SSIGN risk group exhibited poor OS ( $P = 0.001$ ). No association was observed between TNM stage and UISS risk group concerning the prognosis in terms of OS ( $P = 0.185$  and  $0.063$ , respectively) (Figure 3). Univariate and multivariate analyses demonstrated that the TNM, UISS, and SSIGN models were independent predictors of PFS ( $P < 0.05$ ) and that the SSIGN model was an independent predictor of OS ( $P < 0.05$ ). Because the TNM, UISS, and SSIGN models are well-established, it was important to assess whether the categorical LMR enhanced the predictive accuracy of these models. For PFS, integrating LMR into each model led to an increased predictive accuracy of 6.9% for the TNM staging model ( $P = 0.014$ ), 6.8% for the UISS model ( $P = 0.006$ ), and 3.4% for the SSIGN model ( $P = 0.017$ ). For OS, incorporating LMR into the SSIGN model led to an increased predictive accuracy of 6.5% ( $P < 0.001$ ) (Table 5).

Table 5  
Improvement of predictive accuracy of established models.

Model	Overall survival		$p$	Progression free survival		$p$
	C-index	95%CI		C-index	95%CI	
TNM	0.562	0.487-0.637	<0.001	0.560	0.507-0.612	0.014
TNM+LMR	0.664	0.583-0.746		0.629	0.563-0.694	
UISS	0.556	0.487-0.742	<0.001	0.547	0.495-0.597	0.006
UISS+LMR	0.663	0.584-3.608		0.615	0.549-0.681	
SSIGN	0.626	0.549-0.704	0.002	0.598	0.537-0.659	0.017
SSIGN+LMR	0.691	0.622-0.760		0.632	0.571-0.694	

Abbreviations: LMR = lymphocyte to monocyte ratio; TNM = the eighth TNM staging system; UISS = University of California at Los Angeles Integrated Staging System; SSIGN = Stage, Size, Grade, and Necrosis score system.

## 4 Discussion

Advances in molecular biology have improved our understanding of RCC carcinogenesis. As a result, various strategies including immunotherapies and molecular-targeted therapies have been developed to treat patients with localized or metastatic RCC<sup>18</sup>. Although many potential molecular biomarkers might influence the prognosis and therapeutic decisions of RCC, none are presently available for routine clinical testing owing to the complexity of molecular changes and the lack of validated evidence<sup>19</sup>. The routine clinical prognostic judgment of RCC is still primarily based on conventional pathological examination and clinicopathologic prognostic factors. Typically, peripheral blood is easy to obtain. Blood analyses, such as white blood cell, lymphocyte, platelet, neutrophil, and monocyte counts, are also frequently used in clinical practice, making them ideal biomarkers to predict the treatment outcomes in cancer patients<sup>20</sup>.

Thus, we assessed the prognostic significance of preoperative LMR in patients with RCC-IVCTT after surgery.

Systemic inflammation is a hallmark of cancer and participates in tumor occurrence and progression<sup>21</sup>. Many classic markers of systemic inflammation are based on the ratios of circulating white cells, such as LMR, NLR and lymphocyte-to-platelet ratio. LMR has been recently evaluated for its ability to predict the prognosis of various cancers. Xia et al. reported that pretreatment LMR is an independent prognostic factor for OS and metastasis-free survival in RCC patients treated with nephrectomy. Gu et al.<sup>22</sup> also demonstrated that decreased pretreatment LMR is associated with poor OS and PFS in patients with metastatic clear cell RCC. However, there are no published data describing the prognostic role of preoperative LMR in patients with RCC-IVCTT who underwent radical nephrectomy and thrombectomy. The present findings revealed the significant correlation of decreased preoperative LMR with clinicopathological features associated with tumor progression. Furthermore, the low preoperative LMR group tended to have decreased PFS and OS. These results remained significant after adjusting for other variables that may have affected our results. Therefore, LMR was an independent prognostic factor in patients with RCC-IVCTT after surgery.

Although radical nephrectomy with IVCTT thrombectomy is the current standard mortality treatment for RCC-IVCTT, this procedure has been associated with high surgical morbidity, ranging from 12.4–46.9%<sup>23</sup>. Therefore, factors that could predict poor perioperative outcomes should be considered during the presurgical treatment period. The present findings showed that high preoperative LMR is associated with prolonged postoperative hospital stays and increased hemorrhage during surgery, demonstrating that the procedure is more difficult in the high preoperative LMR group than in the low preoperative LMR group. Thus, preoperative LMR may have the potential to predict surgical difficulty and help surgeons make individual perioperative care decisions.

Lymphocytes in the peripheral blood display anti-tumor activity by supporting host defense<sup>24</sup>. High lymphocyte numbers are significantly associated with favorable clinical outcomes in several types of cancer<sup>25–27</sup>. High levels of lymphocytic attractant chemokines, such as gamma-interferon inducible protein-10 and monokine induced by gamma-interferon, can predict a favorable prognosis in RCC patients<sup>28</sup>. A low lymphocyte count might be associated with a immunosuppressive state, indicating a deficient immunologic reaction to tumors<sup>29</sup>. Monocytes, which comprise 5% of the circulating white blood cells that circulate in the bloodstream, are innate immune cells of mononuclear phagocytes<sup>30</sup>. Monocytes could differentiate into macrophages or dendritic cells, which are essential in establishing innate and adaptive immune processes. Recently, monocytes have emerged as important mediators in the modulation of tumor progression in various human cancers. The role of macrophages/monocytes in the progression of malignant tumors remains contentious, as different subsets have diverse functions in malignant tumor growth<sup>31</sup>. Nevertheless, ample evidence indicates that tumor-associated macrophages (TAMs) can inhibit anti-tumor immunity and facilitate tumor progression<sup>32</sup>. Pushalkar et al<sup>33</sup> and Yin et al<sup>34</sup> revealed that TAMs promote cancer cell invasiveness and metastasis by inducing epithelial-

mesenchymal transition, tumor angiogenesis, and immunosuppression. Other studies have shown that once recruited by tumor-secreted attractants to the tumor microenvironment, macrophages can shift to a pro-tumor state (M2-like TAMs) in response to various stimuli, such as IL-10 and tumor necrosis factor  $\beta$ <sup>35</sup>. Moreover, M2-like TAMs was shown to counteract the efficacy of chemotherapy and radiotherapy through suppression of CD8+ T cell function, contributing to cancer progression and poor prognostic outcomes. Moreover, M2-like TAMs can counteract the efficacy of chemotherapy and radiotherapy by suppressing CD8+ T cell function, contributing to cancer progression and poor prognostic outcomes<sup>36</sup>. In addition, the clinical prognosis of RCC is poor, as macrophage infiltration facilitates the growth of RCC via angiogenesis<sup>37</sup>. This collective evidence suggests that monocytes exert pro-tumorous influences and contribute to tumor growth by altering macrophage phenotypes. To enhance the predictive value, LMR, as an alliance of peripheral lymphocytes and monocytes, was found to be an independent prognostic predictor of various cancers.

To predict the prognosis of RCC-IVCTT more accurately, there is an urgent need to find a simple, inexpensive, and reliable clinical tool. The TNM, UISS, and SSIGN prognostic models are well-established prognostic models for localized RCC. Nevertheless, it remains unclear whether preoperative LMR could improve the prediction accuracy in patients with RCC-IVCTT after surgery. Based on a previous study by Gu et al.<sup>22</sup>, we incorporated preoperative LMR into the TNM, UISS, and SSIGN prognostic models. The adjusted model had better discriminatory ability than the TNM, UISS, and SSIGN models, with an increased predictive accuracy for PFS of 6.9%, 6.8%, and 3.4%, respectively. Moreover, incorporating LMR into the SSIGN model led to an increased predictive accuracy of 6.5%. Therefore, the combination of preoperative LMR and current prognostic models may be used to refine the outcome prediction for patients with RCC-IVCTT after surgery. Intense and stringent postoperative surveillance and consideration of participation in clinical trials may help to improve the survival outcomes of high-risk RCC patients. In the present study, the UISS and SSIGN models were not independent predictors of OS ( $P > 0.05$ ). This may be because previous studies enrolled patients with all TNM stages of RCC for prognosis prediction<sup>13</sup>, while our study mainly focused on patients with RCC-IVCTT.

There are some limitations in the present retrospective study. First, the sample size was relatively small. The prognostic value of preoperative LMR in patients with RCC-IVCTT remains to be further confirmed in larger multicenter studies and prospective trials. Second, no established cutoff point for preoperative LMR has been determined in patients with RCC-IVCTT. Although ROC curve analysis was performed to determine the optimal cutoff point in this study, this unaccepted statistical analysis may have affected our results to a certain extent.

## 5 Conclusion

Despite the limitations, the present study demonstrates that decreased preoperative LMR is an independent risk factor for survival in patients with RCC-IVCTT after surgery. By incorporating preoperative LMR, the existing prognostic models improved their predictive accuracy.

# Declarations

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**Ethical approval:** This study received approval of the ethics committee of the Chinese People's Liberation Army (PLA) General Hospital and conformed to the Declaration of Helsinki.

**Conflict of interest:** The authors declared no conflict interests.

**Consent for publication:** All the patients and /or their guardians signed for consent after being informed about the use of their clinical specimens for scientific research.

**Data availability:** All data can be requested from the corresponding author.

**Author contributions:** the study design, Z. Xu and L. Zheng.; The experiment and performed data analysis, HY. Feng.; The clinical data analysis, L. Zheng and HY. Feng.; Manuscript writing, reviewing, and revision: L. Zheng.; Study supervision: X. Ma and Z. Xu.

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## Figures

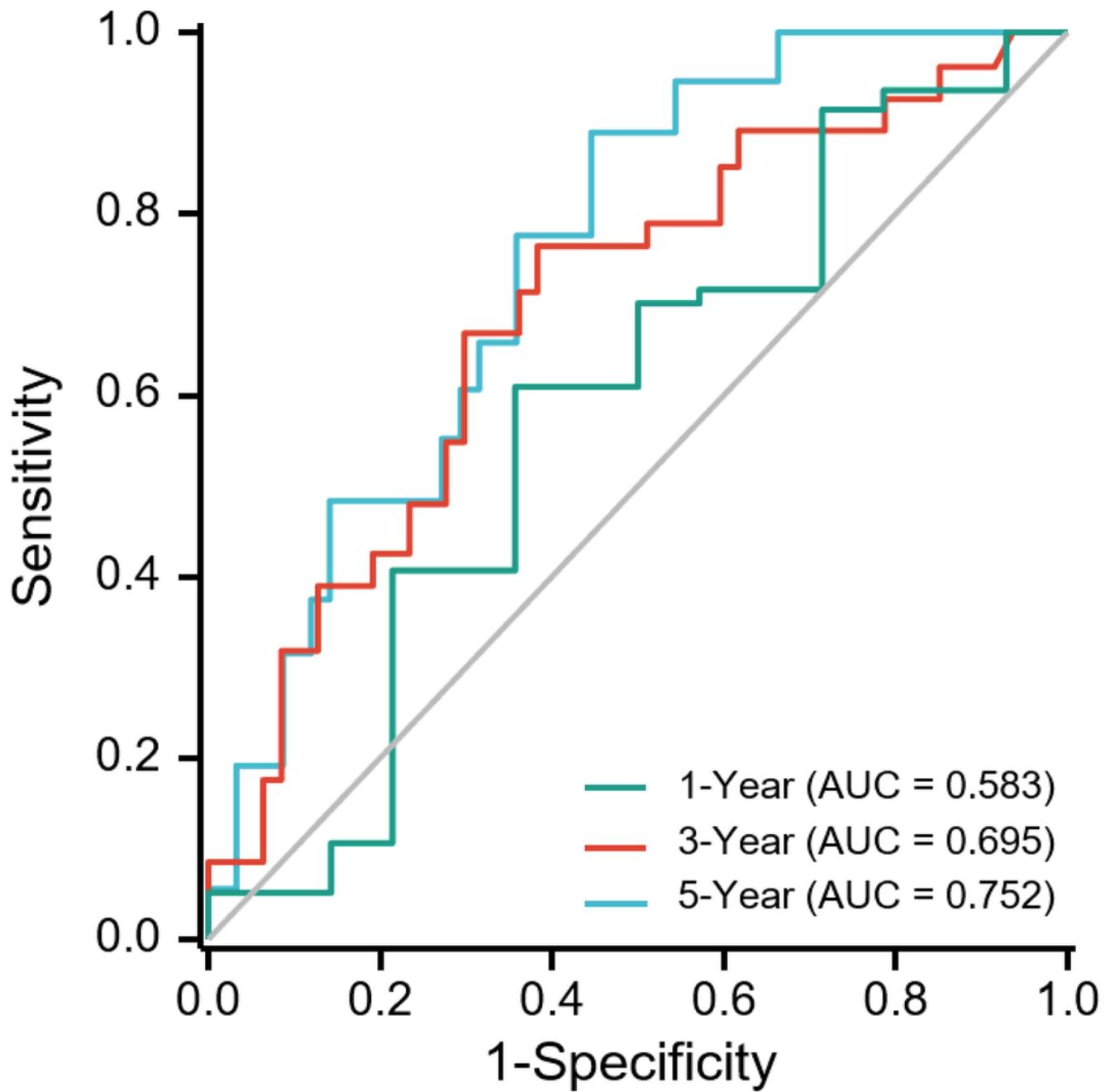
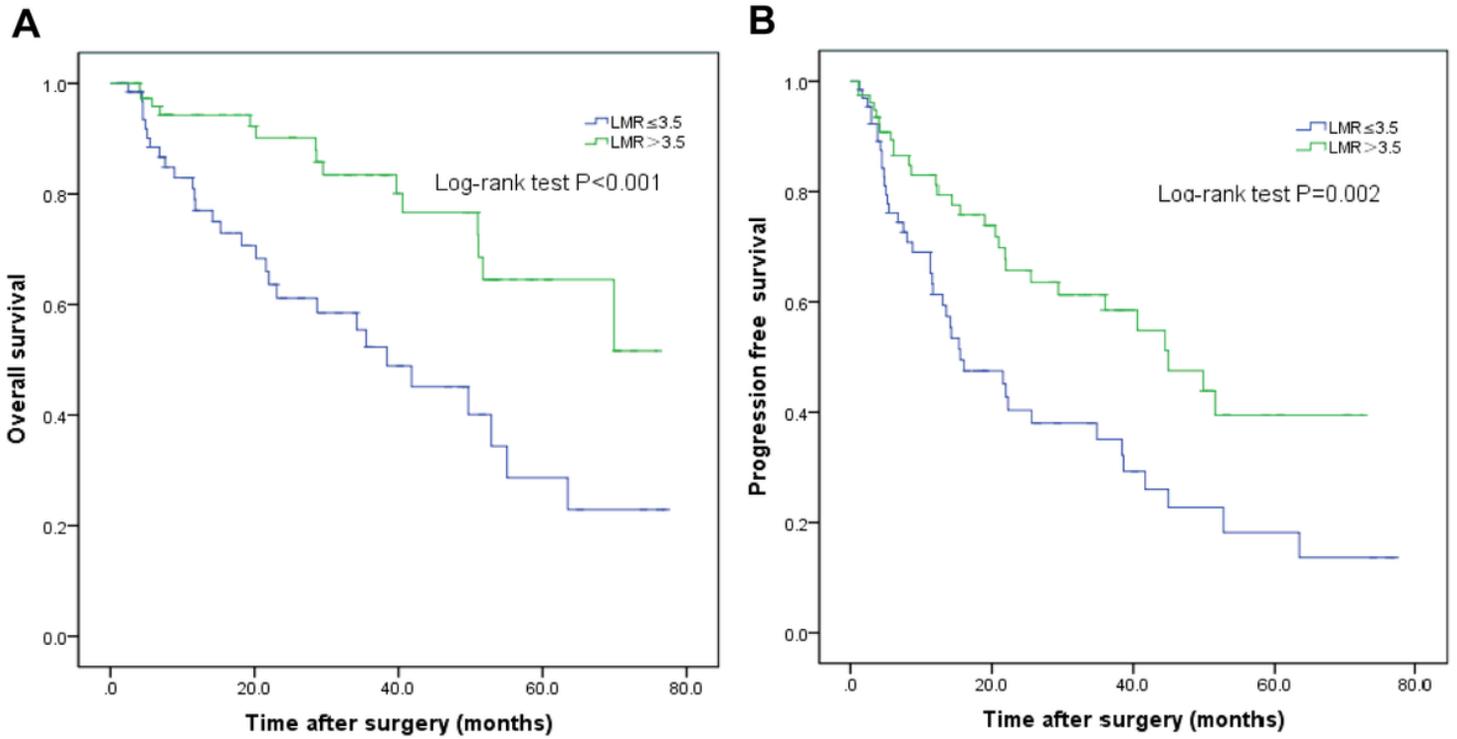


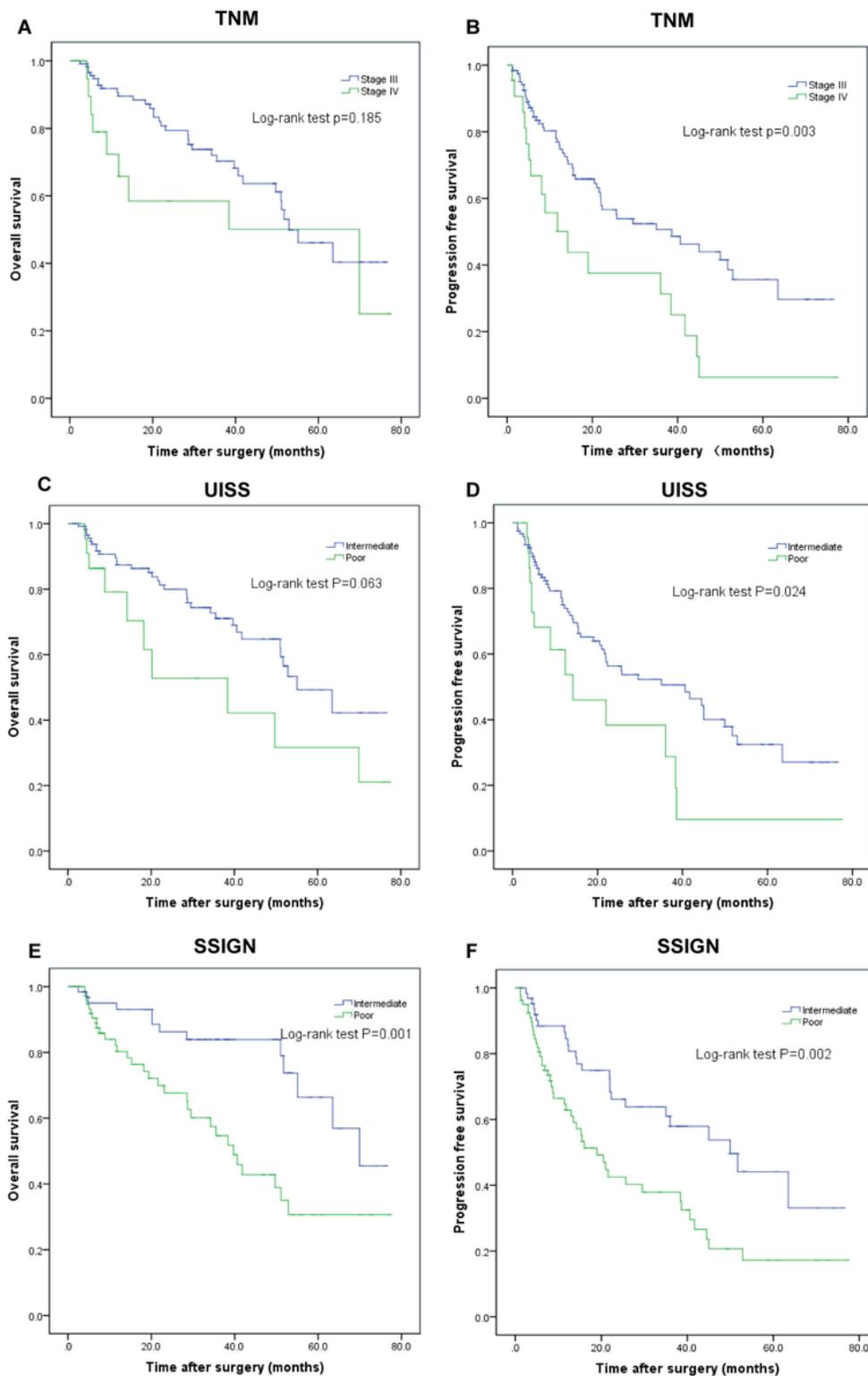
Figure 1

Time-dependent ROC analysis of SIRI for 1-, 3-, and 5-year survival. AUC, area under the curve; ROC, receiver operating characteristic; SIRI, systemic inflammation response index



**Figure 2**

Kaplan–Meier curves according to preoperative LMR for OS (a) and PFS (b) in RCC-IVCTT patients. LMR, lymphocyte-to-monocyte ratio; OS, overall survival; PFS, progression-free survival; RCC-IVCTT, renal cell carcinoma and inferior vena cava tumor thrombus



**Figure 3**

Kaplan–Meier curves according to the TNM, UISS and SSIGN models for OS (a, c, and e) and PFS (b, d, and f) in RCC-IVCTT patients after surgery. OS, overall survival; PFS, progression-free survival; RCC-IVCTT, renal cell carcinoma and inferior vena cava tumor thrombus; UISS, UCLA Integrated Staging System; SSIGN, Stage, Size, Grade, and Necrosis

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