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The Value of Neutrophil to Lymphocyte Ratio in Patients Undergoing Cytoreductive Nephrectomy with Thrombectomy

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Abstract

Background: The neutrophil-lymphocyte ratio (NLR) is an established signature of inflammation used for evaluating renal cell carcinoma (RCC).

Objective: To determine the utility of NLR and its relationship with known risk factors associated with poor survival in patients with metastatic RCC and tumor thrombus undergoing cytoreductive nephrectomy (CN).

Design, setting, and participants: Prognostic variables were reviewed for patients undergoing CN with thrombectomy between 2000 and 2014 from six different institutions. Patients were stratified for NLR >4.0 based on cut point analysis.

Outcome measurements and statistical analysis: Kaplan-Meier curves compared overall survival of the total cohort and established risk models (Memorial Sloan Kettering Cancer Center

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.euf.2018.08.023>.

[MSKCC], International Metastatic Renal-Cell Carcinoma Database Consortium [IMDC], and M.D. Anderson Cancer Center [MDACC]) stratified by NLR. Multivariable Cox regression determined predictors of overall survival. Receiver operator characteristic curves tested the predictive accuracy of survival at 12 mo, and area under the curve (AUC) was compared between models.

Results and limitations: In total, 332 patients were identified. Patients with NLR ≤ 4.0 had longer median survival (24.7 vs 15.2 mo, $p = 0.004$). NLR >4.0 distinguished patients with significantly shorter survival for non-poor-risk groups defined by MSKCC, IMDC, and MDACC criteria. Systemic symptoms, low hemoglobin, elevated lactate dehydrogenase, retroperitoneal adenopathy, level IV thrombus, elevated absolute neutrophil count, and NLR >4 were independent predictors of decreased survival ($p < 0.05$). These factors had higher predictive accuracy for survival at 12 mo (AUC = 0.755) than MSKCC, IMDC, and MSKCC models.

Conclusions: NLR >4.0 independently predicts poor survival and further distinguishes established risk model survival curves. We identified seven preoperative risk factors related to poor survival for patients with metastatic RCC with tumor thrombus undergoing CN.

Patient summary: The neutrophil-lymphocyte ratio and six additional preoperative variables can be used to better counsel patients regarding survival after surgery for metastatic renal cell carcinoma with tumor thrombus.

Keywords

Carcinoma; Mortality; Neoplasm metastasis; Renal cell; Survival; Thrombosis

1. Introduction

The neutrophil-lymphocyte ratio (NLR) is a well-established signature of inflammation and independent predictor of adverse oncologic outcomes for several malignancies [1]. Its utility in renal cell carcinoma (RCC) is well documented as an inexpensive prognostic test for patients with localized and advanced disease [2]. In metastatic RCC (mRCC) patients who may undergo cytoreductive nephrectomy (CN), an elevated NLR is associated with reduced survival in patients receiving vascular endothelial growth factor- or mammalian target of rapamycin-targeted therapy and has outcome implications for immune check point blockade therapy [3–5]. However, there are currently no mRCC predictive nomograms incorporating NLR.

Traditional estimates of survival and recurrence for CN patients are largely based on preoperative Karnofsky performance status (KPS), lactate dehydrogenase (LDH), and corrected calcium and hemoglobin (Hgb) of systemic therapy clinical trial patients [6,7]. Culp et al [8] identified albumin, T3 or T4 tumors, liver metastasis, metastatic symptoms, and retroperitoneal and/or supradiaphragmatic lymphadenopathy as additional predictive variables specific to mRCC patients undergoing CN. Several studies have examined the prognostic utility of NLR for mRCC prior to CN; however, no studies have examined preoperative NLR in mRCC with venous tumor thrombus (mRCCtt) undergoing CN [9–11].

Predicting mRCC patients who will benefit from CN is challenging [12]. This is particularly true and important when venous tumor thrombus is present due to the significant complexity of the surgery and increased risk of perioperative complications and mortality [13,14]. Recently, patients with mRCCt above the diaphragm were identified as having the highest risk of early mortality and no better survival than nonsurgical targeted therapy [15]. Herein we sought to evaluate the utility of NLR and established survival prognosticators to risk stratify mRCCt patients undergoing CN in a multiinstitutional series of tertiary care centers.

2. Materials and methods

2.1. Patient cohort

Institutional review board approval was obtained. We reviewed institutional comprehensive databases to identify patients with mRCCt treated with CN from 2000 to 2015. The cohort included patients from Moffitt and M.D. Anderson Cancer Centers, University of Wisconsin, University of Texas Southwestern, Emory University, and Penn State Health Medical Centers. Patients who had synchronous lymph node or distant metastatic disease along with venous tumor thrombus at the time of surgery were included. To avoid the confounding effects of preoperative systemic therapy, patients who received these therapies were excluded. Clinical and pathologic information for each patient was extracted and compiled into a single database.

Preoperative evaluation included serum laboratory data and abdominal and chest imaging. Laboratory data included absolute neutrophil, lymphocyte, and platelet counts, serum albumin, corrected calcium, LDH, and Hgb. NLR was calculated by dividing absolute neutrophil count over absolute lymphocyte count. Laboratory data was reported using standard units. Continuous lab values were converted to categorical values based on exceeding the upper (ULN) or lower limit of normal (LLN) specific to the test.

Clinical prognostic data was reported for each patient including age, sex, body mass index, KPS, smoking status, local symptoms (pain, hematuria), systemic symptoms (fatigue, fever, anorexia, and weight loss), symptoms from metastatic lesions, number and location of metastasis, and presence or absences of retroperitoneal and/or supradiaphragmatic lymphadenopathy ≥ 1 cm. Thrombus level was recorded based on the Neves classification [16]. Patients were assigned risk groups according to previously described systems by Heng et al. (International Metastatic Renal-Cell Carcinoma Database Consortium [IMDC] model) [6], Motzer et al (Memorial Sloan Kettering Cancer Center [MSKCC] model) [7], and Culp et al (M.D. Anderson Cancer Center [MDACC] model) [8].

Pathologic variables evaluated included RCC subtype, T stage, N stage, Furhman nuclear grading, perinephric fat invasion, sarcomatoid features, rhabdoid features, and necrosis. Genitourinary pathologists examined specimens and assigned histology according to the 2004 World Health Organization classification. Patients were generally followed every 3–6 mo following surgery with abdominal and chest imaging. Date of death or last follow-up visit was reported for survival data.

2.2. Statistical analysis

We performed cut point analysis of NLR using methods previously described by Contral and O'Quigley [17]. A value of 3.95 was the optimum cut point (Q -statistic = 1.63, $p = 0.009$). Our value was within range of previous reports, and we rounded to the nearest integer for simplicity [2,9]. Patients were grouped to NLR ≤ 4.0 or NLR >4.0 . A chi-square test or Fischer's exact test, as appropriate, was used to evaluate the association of NLR >4 with established preoperative variables.

Kaplan-Meier analysis with log-rank testing was used to estimate overall survival (OS) from the day of surgery until the day of death based on NLR group for the entire cohort and stratified within each risk group category (favorable-, intermediate-, or poor-risk) designated by MSKCC, IMDC, and MDACC models [6–8]. This allowed for sub-stratification of risk groups based on NLR across multiple models. Univariate Cox proportional hazard ratios for NLR and traditional preoperative risk variables were performed. Significant variables were evaluated with multivariable Cox proportional hazard logistic regression to determine independent associations of preoperative variables. Patients were grouped based on the number of independent risk factors identified. Cox proportional hazard regressions and Kaplan-Meier analysis were performed based on number of risk factors using the no-risk factor group as a referent.

We performed a receiver operator characteristic (ROC) analysis using time-dependent Cox proportional hazard regression comparing our multivariable analysis model to the MSKCC, IMDC, and MDACC models for survival at 6, 9, and 12 mo postoperatively. Follow-up time points were chosen based on the distribution of follow-up times and prior studies, suggesting that OS in patients treated with systemic therapy alone is approximately 9 months [8,18–20]. AUC and Harrell's concordance statistic were calculated by comparing models [21]. All analyses were performed using SAS version 9.4 or SPSS (IBM) software, and a p value < 0.05 was considered statically significant.

3. Results

We identified 447 mRCCt patients who underwent CN. Of these patients, 332 had available differential blood count data to calculate preoperative NLR; the study focused on these patients. Supplementary Tables 1 and 2 provide patient characteristics and preoperative variables. In total, 157 (47%) patients had an NLR >4 . Median follow-up time was 14.4 mo (interquartile range [IQR] = 5.0–32.8) and median OS was 21.1 mo (IQR = 7.1–42.8).

Patient characteristics, preoperative variables, and risk groups stratified by NLR ≤ 4 versus NLR >4 are illustrated in Supplementary Table 3. An NLR >4 was associated with male sex, increasing thrombus level, Furhman nuclear grade, absolute neutrophil count, and supradiaphragmatic adenopathy ($p < 0.05$ for all). Local symptoms, Hgb $< \text{LLN}$, sarcomatoid features, and retroperitoneal adenopathy were not significant ($p = 0.06$ for all). Median OS was shorter for patients with NLR >4 than for patients with NLR ≤ 4 (15.2 vs 24.7 mo, $p = 0.004$, Supplementary Fig. 1). There was no difference in the percentage of NLR >4 patients who received any postoperative systemic therapy (75.8% vs 71%, $p = 0.23$) or targeted therapy (47% vs 44.3%, $p = 0.36$).

Using available perioperative data, patients were risk stratified according to three previously described classification schemes (MSKCC, IMDC, and MDACC) [6–8]. For the MSKCC classification system, four (1.2%) were favorable, 164 (49.4%) were intermediate-risk, and 112 (33.7%) were poor-risk patients. Sub-stratification by NLR within the intermediate-risk group revealed prolonged OS for $\text{NLR} \leq 4$ versus $\text{NLR} > 4$ (30.4 vs 19.5 mo, $p = 0.046$, Fig. 1A). MSKCC poor-risk sub-stratification by $\text{NLR} \leq 4$ was not significant (14.7 vs 8.0 mo, $p = 0.09$). According to IMDC risk classification, nine (2.7%) were favorable, 176 (53.0%) were intermediate-risk, and 138 (41.6%) were poor-risk patients. IMDC sub-stratification by NLR within intermediate-risk group showed nearly identical median survival to the MSKCC classification with prolonged OS for $\text{NLR} \leq 4$ versus $\text{NLR} > 4$ (30.4 vs 19.5 mo, $p = 0.001$, Fig. 1B). There was no OS difference for the IMDC poor-risk group (15.5 vs 12.5 mo, $p = 0.71$). The MDACC risk classification system yielded 246 (74.1%) favorable and 58 (17.5%) unfavorable risk patients. NLR sub-stratification again revealed better OS for $\text{NLR} \leq 4$ versus $\text{NLR} > 4$ (30 vs 18.8 mo, $p = 0.021$) in the MDACC favorable group (Fig. 1C) and no difference in the unfavorable group (9.9 vs 8.8 mo, $p = 0.21$).

Table 1 shows Cox regression for OS of demographic information and established risk variables used within each risk model, including NLR and thrombus level. Multivariable analysis demonstrated that systemic symptoms, $\text{Hgb} < \text{LLN}$, $\text{LDH} > \text{ULN}$, absolute neutrophil count $> \text{ULN}$, retroperitoneal adenopathy, level IV thrombus, and $\text{NLR} > 4$ remained significant independent predictors of decreased OS ($p < 0.05$). Redistributing patients according to their number of risk factors revealed increasing risk of death with each additional risk factor and an inverse relationship with median survival (Table 2, Fig. 2). Patients with more than four risk factors had a three-fold hazard ratio increase compared with those with 0–1 risk factors and a median survival of 8.0 mo ($p < 0.001$).

To understand the predictive ability of $\text{NLR} > 4$ and other independent predictors in the context of previously published prognostic variables, we performed a comparative ROC curve analysis for OS at 6, 9, and 12 mo postoperatively. Fig. 3 illustrates ROC curves predicting OS at 12-months OS for our study model versus MSKCC (KPS < 80 , low Hgb, corrected calcium > 10 , and $\text{LDH} > \text{ULN}$), IMDC (KPS < 80 , low Hgb, corrected calcium > 10 , absolute neutrophil count $> \text{ULN}$, platelet count $> \text{ULN}$, and < 1 yr diagnosis to treatment), and MDACC ($\text{LDH} > \text{ULN}$, metastatic symptoms, systemic symptoms, liver metastasis, retroperitoneal, and supradiaphragmatic adenopathy). For 12-month OS, AUCs were 0.755 for the current study model, 0.688 for MDACC model, 0.586 for IMDC model, and 0.643 for MSKCC model. Harrell's C-statistic was 0.683, 0.650, 0.591, and 0.633, respectively. Our study model also had improved AUCs at 6 and 9 mo, Supplementary Fig. 2.

4. Discussion

Understanding risk factors associated with early postoperative mortality is critical in selecting CN patients. This is particularly true with the added surgical complexity of tumor thrombus [13,22]. In this contemporary multicenter consortium analysis, we found that $\text{NLR} > 4$, a simple signature of inflammation, is an independent predictor of poor OS. For MSKCC, IMDC, and MDACC non-poor-risk classified patients, an $\text{NLR} \leq 4$ was associated

with better median OS of 10.9, 10.9, and 11.2 mo, respectively, allowing clinicians to better sub-stratify the majority of mRCCt patients (Fig.1). Furthermore, we noted improvement in the predictive accuracy of survival after surgery for the seven risk factors identified in this study model versus traditional models [6–8]. When selecting mRCCt patients for CN with thrombectomy, NLR >4, Hgb <LLN, LDH > ULN, absolute neutrophil count > ULN, systemic symptoms, thrombus level, and retroperitoneal adenopathy may help better characterize outcomes after CN.

NLR elevation is a combination of neutrophilia and lymphopenia signaling a systemic inflammatory response to malignancy, and it has been the focus of multiple retrospective RCC studies. Pretreatment NLR elevation has been reported as an independent predictor of OS and recurrence-free survival for localized RCC [23–26]. Similarly, elevated NLR is independently associated with progression-free survival, OS, and response to systemic therapy for mRCC [3–5]. Our study is congruent with several previous studies focused on the value of NLR for patients undergoing CN [9,11,27]. Day et al [27] used a cut point of NLR = 5.0 and reported improved OS for 46 CN patients with NLR <5. Survival benefit was noted for CN versus nonsurgical management irrespective of NLR. Ohno et al. [9] used an NLR cut point of 4.0 in 48 CN patients and reported significantly longer median OS for patients with NLR <4 (36.5 vs 10.2 mo, $p = 0.002$). In general, prior studies have used NLR values between 3.0 and 4.0 [3,9,23–26]. Our optimal 4.0 cut point is consistent with an evaluation of NLR specific to CN for mRCC [11]. An inflammatory microenvironment is a hallmark of patients with metastatic disease; thus, a higher NLR cut point may better select patients with more inflammation [28]. Prior publications assessing NLR have not exclusively examined mRCCt patients.

One must consider the patient population used to develop predictor models prior to generalizing their application for all mRCC patients. Traditional models such as MSKCC and IMDC were developed using clinical trial patients receiving systemic therapy with or without CN [6,7,18]. Only the MDACC model focused on CN patients compared with non-CN patients. Patients with more than four adverse risk variables had similar OS of approximately 9 months compared with those receiving medical therapy alone [8]. Similarly, our analysis suggests that mRCCt patients with more than four risk factors have remarkably poor survival (8.0 months) and may be better served with systemic therapy alone. Table 3 summarizes the patient cohorts and independent predictors of OS for our study and the aforementioned models. Recent work expanded upon the MDACC model to develop a nomogram based on 601 CN patients, suggesting that the most important risk factors include albumin and LDH [29]. However, this cohort does not account for patients with tumor thrombus, a described marker of poor survival [15], and 23% of these patients were pT2 [29].

The model described in our study includes laboratory and clinical preoperative variables that are easily obtained. The model can redistribute risk for this selected patient population and may aid surgeons in selecting patients for complex, high-risk CN with concomitant thrombectomy (Fig. 2). The prognostic accuracy of the model was comparatively better than that of MSKCC, IMDC, and MDACC models for survival after CN (Fig. 3 and Supplementary Fig. 2). Although far from a perfect prognosticator, our seven-factor model

AUC = 0.755 was comparable to other published models in the era of CN and targeted therapy [6,30]. The curve differences may be related to the specific population being examined. As seen in Table 3, patient cohorts used to create risk criteria are heterogeneous. For example, CN was not performed in 17% and 35% of patients constituting IMDC and MSKCC risk criteria, respectively [6,7]. The MDACC population exclusively examined patients undergoing CN for mRCC but lacked data on tumor thrombus patients [8]. Interestingly, inflammation indicators were prognostic signatures only in our model and the IMDC model. These factors were not included in the MDACC analysis. Given that prior studies consistently report lower NLR values for nonmRCC [23–26], we speculate that mRCCtt may enhance cytokine release and systemic inflammation. CN with tumor thrombectomy is a challenging surgery, with potential significant morbidity. NLR appears to be an important marker, and our proposed model may assist in selecting and counseling patients with regards to this complex operation.

Limitations of this study are inherent to its retrospective, observational design and associated biases. Although multivariable models were used to establish independent predictors of OS, unaccounted for differences between institutions may exist. Missing data limited the number of patients used in the final multivariable analysis. It is important to note that we did not collect detailed information on type and duration of postoperative systemic therapy which certainly influences survival. Only OS was available in this dataset instead of cancer-specific survival. Also, given the relative rarity of mRCCtt patients, our model was not externally validated. The next steps certainly include external validation. However, to the best of our knowledge, this remains a large series of mRCCtt patients evaluating the utility of NLR. Although we suggest that NLR and the six other risk factors could help identify patients who will survive longer following CN, our data does not specifically predict the benefit of CN because a non-CN control arm was not included. Ultimately, the decision to perform CN with thrombectomy should be considered on an individual patient basis.

5. Conclusions

Our data show that an NLR >4 is independently associated with decreased OS in mRCCtt patients and highlights the relationship of systemic inflammation and survival. NLR >4 can further stratify non-poor-risk patients in previously reported risk classifications systems. We present seven preoperative risk factors that may better predict OS for this high-risk patient population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Charles Christopher Peyton certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

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Fig. 1 –.

Kaplan-Meier curves for overall survival of (A) MSKCC intermediate-risk group, (B) IMDC intermediate-risk group, and (C) MDACC favorable-risk group stratified by NLR. IMDC = International Metastatic Renal-Cell Carcinoma Database Consortium; MDACC = M.D. Anderson Cancer Center; MSKCC = Memorial Sloan Kettering Cancer Center; NLR = neutrophil-lymphocyte ratio.

0 - 1 risk factors	74	56	41	25	19	10
2 - 3 risk factors	182	108	69	43	26	16
≥ 4 risk factors	76	21	8	2	2	2

Fig. 2 –.
Kaplan-Meier analysis of overall survival of metastatic renal cell carcinoma patients with venous tumor thrombus undergoing cytoreductive nephrectomy based on number of significant independently predictive risk factors established in the current series (log-rank test $p < 0.001$).

Fig. 3 –.

Receiver operator characteristic curves comparing predictive accuracy of overall survival at 12 months after cytoreductive nephrectomy for the current series of seven risk factor multivariable study model (AUC 0.755), MDACC (AUC 0.688), MSKCC (AUC 0.643), and IMDC (AUC 0.586) models.

AUC = area under the curve; IMDC = International Metastatic Renal-Cell Carcinoma Database Consortium; MDACC = M.D. Anderson Cancer Center; MSKCC = Memorial Sloan Kettering Cancer Center.

Table 1 –
Univariate and multivariable Cox proportional hazard regression analysis of overall survival.

	Univariate			Multivariate		
	<i>n</i>	HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value	
Age, yr (median)	332	1.01 (0.99–1.02)	0.26	-	-	-
BMI						
>30	98	0.66 (0.94–0.89)	0.006	0.86 (0.6–1.23)	0.41	
<30	227	Ref		-	-	-
Sex						
Female	147	1.19 (0.94–1.5)	0.15	-	-	-
Male	300	Ref		-	-	-
Race						
Non-Caucasian	207	Ref		-	-	-
Caucasian	123	0.78 (0.59–1.01)	0.06	-	-	-
Smoke ever						
Yes	140	1.09 (0.83–1.43)	0.53	-	-	-
No	156	Ref		-	-	-
Local symptoms						
Present	228	1.13 (0.85–1.5)	0.40	-	-	-
Absent	104	1.0		-	-	-
Systemic symptoms						
Present	155	1.82 (1.40–2.35)	<0.001	1.54 (1.53–2.13)	0.01	
Absent	177	Ref		Ref		
Metastatic symptoms						
Present	60	1.17 (0.85–1.62)	0.34	-	-	-
Absent	272	Ref		-	-	-
Karnofsky performance status						
<80	28	2.12 (1.28–3.77)	0.005	1.7 (0.83–3.49)	0.15	
80	304	Ref		Ref		
Hemoglobin						
<LLN 13 g/dl (M) and 11.5 g/dl (F)	221	1.52 (1.16–1.99)	0.003	1.59 (1.12–2.24)	0.009	

	Univariate		Multivariate	
	<i>n</i>	HR (95% CI)	<i>p</i> value	HR (95% CI)
>LLN	111	Ref		Ref
Corrected serum calcium				
>10 mm/dl	83	1.40 (1.04–1.88)	0.025	1.0 (0.68–1.48)
10 mm/dl	229	Ref		Ref
Serum LDH				
>ULN	82	1.83 (1.36–2.48)	<0.0001	1.74 (1.23–2.45)
ULN	168	Ref		Ref
Albumin				
<LLN	75	1.68 (1.24–2.28)	0.001	1.16 (0.79–1.69)
LLN	229	Ref		Ref
Absolute platelet count				
>ULN	101	1.26 (0.96–1.66)	0.091	-
ULN	230	Ref		-
Absolute neutrophil count				
>ULN	52	1.43 (1.02–2.0)	0.038	1.78 (1.13–2.78)
ULN	280	Ref		-
NLR				
>4.0	157	1.45 (1.12–1.88)	0.004	1.46 (1.05–2.03)
4.0	175	Ref		-
1 cm retroperitoneal adenopathy				
Present	145	1.39 (1.07–1.8)	0.013	1.41 (1.03–1.95)
Absent	187	Ref		Ref
1 cm supradiaphragmatic adenopathy				
Present	99	0.82 (0.61–1.11)	0.20	-
Absent	233	Ref		-
Liver metastasis				
Present	33	0.99 (0.63–1.58)	0.99	-
Absent	299	Ref		-
Thrombus level				
0 = renal vein only	99	Ref		Ref
				0.024

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	<i>n</i>	Univariate		Multivariate	
		HR (95% CI)	<i>p</i> value	HR (95% CI)	<i>p</i> value
1 = IVC 2 cm	42	1.16 (0.76–1.77)	0.49	1.05 (0.63–1.73)	0.87
2 = IVC >2 cm	109	0.89 (0.64–1.23)	0.47	0.88 (0.6–1.3)	0.52
3 = IVC below diaphragm	50	1.25 (0.84–1.84)	0.27	0.9 (0.54–1.49)	0.68
4 = IVC above diaphragm	32	1.62 (1.01–2.59)	0.044	2.4 (1.32–4.34)	0.004

CI = confidence interval; HR = hazard ratio; IVC = inferior vena cava; LLN = lower limit of normal; NLR = neutrophil lymphocyte ratio; Ref = referent; ULN = upper limit of normal.

Table 2 –

Cox proportional hazard ratios for overall survival and median survival in months for cumulative identified risk factors and grouped risk factors.

No. risk factors	n (%)	HR (95% CI)	p value	Median OS (IQR)	Log-rank, p value
0	19 (5.7)	Ref		40.9 (26.5–65.5)	<0.001
1	55 (16.6)	1.1 (0.58–2.1)	0.77	33.7 (21.0–59.4)	
2	91 (27.4)	1.35 (0.74–2.5)	0.33	29.6 (16.1–54.3)	
3	91 (27.4)	2.34 (1.29–4.24)	0.005	14.2 (5.1–35.5)	
4	51 (15.4)	3.92 (2.08–7.38)	<0.001	8.8 (4.5–16.5)	
5	20 (6.0)	4.67 (2.17–10.11)	<0.001	3.1 (2.2–22.4)	
6	5 (1.6)	10.59 (3.71–30.23)	<0.001	1.2 (1.3–5.8)	
Grouped risk factors					
0–1	74 (22.3)	Ref		33.8 (22.3–65.5)	<0.001
2–3	182 (54.8)	1.61 (1.15–2.27)	0.006	23.8 (7.7–42.8)	
4	76 (22.9)	3.96 (2.65–5.9)	<0.001	8.0 (3.7–16.3)	

CI = confidence interval; HR = hazard ratio; IQR = interquartile range; OS = overall survival.

Table 3 –

Summary of current and prior study characteristics predicting overall survival for metastatic renal cell carcinoma patients.

	Current study	MSKCC	IMDC	MDACC
Study population	332 patients with mRCC + tumor thrombus who underwent CN	670 clinical trial patients for mRCC receiving systemic therapy; CN and nonsurgical patient included	645 mRCC patients treated with anti-VEGF therapy; CN and nonsurgical patient included	470 mRCC patients who underwent CN
KPS <80		✓	✓	
Hgb <LLN	✓	✓	✓	
Corrected calcium >10 mm/dl		✓	✓	
LDH > ULN	✓	✓ ^a		✓
Albumin <LLN				✓
Metastasis symptoms				✓
Systemic symptoms	✓			
Prior nephrectomy		✓		
NLR >4.0	✓			
Absolute neutrophil count > ULN	✓		✓	
Platelet count > ULN			✓	
<1 yr diagnosis to treatment			✓	
Level IV thrombus	✓			
T3 or T4 tumor				✓
Liver metastasis				✓
1 cm retroperitoneal adenopathy	✓			✓
1 cm supradiaphragmatic adenopathy				✓

CN = cytoreductive nephrectomy; Hgb = hemoglobin; IMDC = International Metastatic Renal-Cell Carcinoma Database Consortium; KPS = Karnofsky performance status; LDH = lactate dehydrogenase; LLN = lower limit of normal; MDACC = M.D. Anderson Cancer Center; MSKCC = Memorial Sloan Kettering Cancer Center; mRCC = metastatic renal cell carcinoma; NLR = neutrophil-lymphocyte ratio; ULN = upper limit of normal; VEGF = vascular endothelial growth factor.

^aMSKCC criteria required LDH >1.5 × ULN.