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Sarcomatoid differentiation and cumulative risk assessment in metastatic renal cell carcinoma: a Korean multicenter study Running Title: Sarcomatoid Differentiation in RCC

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Article

Keywords: Carcinoma, Neoplasm metastasis, Prognosis, Renal cell carcinoma, Sarcomatoid differentiation

Posted Date: October 27th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11230884/v1

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Additional Declarations: No competing interests reported.

Abstract

Sarcomatoid differentiation is an aggressive histologic transformation of renal cell carcinoma (RCC) associated with poor prognosis. We retrospectively analyzed 1,013 patients with metastatic RCC from the Korean Renal Cancer Study Group database, comparing clinicopathologic features and survival by sarcomatoid differentiation status and constructing a cumulative risk model combining sarcomatoid differentiation with other adverse factors. Overall and cancer-specific survival were estimated using the Kaplan–Meier method, and independent prognostic factors were identified using Cox proportional hazards models. Sarcomatoid differentiation was present in 206 patients (20.3%) and was associated with higher Fuhrman grade, more advanced pathologic stage, and higher rates of tumor necrosis and renal vein invasion (all $p < 0.01$). Median overall survival was shorter with sarcomatoid differentiation than without (18.8 vs 33.5 months; $p < 0.001$), as was cancer-specific survival (18.1 vs 33.1 months; $p < 0.001$). Sarcomatoid differentiation independently predicted poorer overall survival (hazard ratio 1.36, 95% confidence interval 1.08–1.73) and cancer-specific survival (hazard ratio 1.39, 95% confidence interval 1.10–1.77). The cumulative risk model showed a stepwise decline in cancer-specific survival, from a median of 36.0 months with 0–1 adverse factors to 10.0 months with four or more. These findings support incorporating sarcomatoid differentiation into cumulative risk stratification for metastatic RCC.

Introduction

Renal cell carcinoma (RCC) accounts for approximately 2–3% of adult malignancies and remains a major contributor to global cancer mortality[1]. Although the early detection rate has increased due to widespread use of cross-sectional imaging, a substantial proportion of patients still present with locally advanced or metastatic disease at the time of diagnosis[1,2]. Histologically, RCC represents a heterogeneous group of malignancies, with clear-cell RCC comprising approximately 75% of all cases[3].

In Korea, urologic cancers constitute an increasing proportion of the national cancer burden. A recent nationwide analysis using the Korea National Cancer Incidence Database reported continuous increases in the incidence of kidney cancers over the last two decades[4]. These trends indicate an increasing clinical burden of RCC in the Korean population.

However, regardless of the histologic subtype, a subset of tumors can undergo sarcomatoid dedifferentiation, characterized by spindle-shaped malignant cells resembling soft-tissue sarcoma[5,6]. Sarcomatoid differentiation reflects an aggressive transformation driven by an epithelial-to-mesenchymal transition and is associated with aggressive tumor biology and poor clinical outcomes[7–9].

Previous studies have demonstrated that sarcomatoid RCC (sRCC) is associated with a higher nuclear grade, extensive necrosis, microvascular invasion, and advanced pathologic stage at the time of presentation[7,8]. In addition, the proportion of a sarcomatoid component within the tumor has been correlated with an increasing risk of disease progression and cancer-specific mortality, even after

accounting for tumor stage and grade[9]. These pathologic features contribute to the characteristically poor survival outcomes in sRCC, with historical studies reporting a median overall survival (OS) of < 1 year in metastatic cases and significantly inferior survival even among patients undergoing nephrectomy[7,10].

Despite its clinical importance, sarcomatoid differentiation remains relatively understudied in Asian and Korean populations. Most available data originate from Western cohorts, where registry-based and large-institution studies have documented the prognostic impact of sarcomatoid features[11]. In Korea, where RCC incidence continues to rise[4], evidence regarding the real-world prevalence and prognostic relevance of sarcomatoid differentiation has been sparse. Further, prior studies have often been limited by small sample sizes, single-institution designs, or incomplete adjustment for competing clinical variables.

This study aimed to evaluate the prognostic significance of sarcomatoid differentiation in a large, multicenter Korean cohort of patients undergoing nephrectomy for RCC. Through a detailed assessment of clinical characteristics, pathologic features, and oncologic outcomes, we sought to clarify the role of sarcomatoid differentiation as an independent determinant of patient survival and to provide region-specific evidence to support risk-adapted management strategies in RCC.

Results

Among the 1,013 patients included in the analysis, 206 (20.3%) demonstrated sarcomatoid differentiation. Baseline demographic variables—including age, sex, body mass index, smoking status, and ECOG performance status—did not differ significantly between patients with and without sarcomatoid features (Table 1). Conversely, patients with sarcomatoid differentiation were more likely to present with adverse disease characteristics. A significantly higher proportion of patients belonged to the poor-risk MSKCC category (41.7% vs. 31.0%, p = 0.005). Advanced pathologic stage (pT3–4) and nodal involvement (pN1) were more frequently observed in the sarcomatoid compared with the non-sarcomatoid group (76.7% vs. 65.6% and 37.9% vs. 29.7%, respectively; p = 0.031). Sarcomatoid tumors exhibited markedly aggressive pathologic features compared with non-sarcomatoid tumors, including a significantly higher prevalence of Fuhrman grade 4 disease (77.7% vs. 24.2%, respectively; p < 0.001), extensive tumor necrosis (63.1% vs. 28.6%, respectively; p < 0.001), and renal vein invasion (32.0% vs. 25.0%, respectively; p = 0.052) (Table 2).

Table 1
Patient Characteristics

Variable	Non-sarcomatoid (n = 807)	Sarcomatoid (n = 206)	p-value
Age, years	57.4 ± 11.9	56.6 ± 10.6	0.384
BMI, kg/m²	23.4 ± 3.6	23.1 ± 3.1	0.290
Sex			
- Male	624 (77.3%)	159 (77.2%)	1.000
- Female	183 (22.7%)	47 (22.8%)	
Smoking Status			0.089
- Never	446 (55.3%)	115 (55.8%)	
- Former	190 (23.5%)	60 (29.1%)	
- Current	138 (17.1%)	28 (13.6%)	
- Unknown	33 (4.1%)	3 (1.5%)	
ECOG Performance Status			0.658
– 0	389 (48.2%)	92 (44.7%)	
– 1	380 (47.1%)	104 (50.5%)	
- ≥2	38 (4.7%)	10 (4.9%)	
Comorbidities			
Diabetes mellitus	146 (18.1%)	39 (18.9%)	0.859
Hypertension	326 (40.4%)	77 (37.4%)	0.478
Chronic kidney disease	25 (3.1%)	8 (3.9%)	0.729
Cerebrovascular accident	12 (1.5%)	3 (1.5%)	1.000
Heart disease	11 (1.4%)	4 (1.9%)	0.771
MSKCC Risk Group			0.005
- Favorable	18 (2.2%)	1 (0.5%)	
- Intermediate	539 (66.8%)	119 (57.8%)	
- Poor	250 (31.0%)	86 (41.7%)	
Clinical T stage			0.005
- cT1	202 (25.0%)	34 (16.5%)	
- cT2	164 (20.3%)	58 (28.2%)	

Variable	Non-sarcomatoid (n = 807)	Sarcomatoid (n = 206)	p-value
- cT3	267 (33.1%)	79 (38.3%)	
- cT4	174 (21.6%)	35 (17.0%)	

Table 2
Pathological and Metastatic Outcomes

Variable	Non-sarcomatoid (n = 807)	Sarcomatoid (n = 206)	p-value
Pathologic T stage			0.002
- pT1	158 (19.6%)	20 (9.7%)	
- pT2	120 (14.9%)	28 (13.6%)	
- pT3	454 (56.3%)	128 (62.1%)	
- pT4	75 (9.3%)	30 (14.6%)	
Nodal Involvement (N1)	240 (29.7%)	78 (37.9%)	0.031
Metastatic Profile			1.000
- M0	9 (1.1%)	2 (1.0%)	
- M1	798 (98.9%)	204 (99.0%)	
Common Metastatic Sites			
- Lung	519 (64.3%)	144 (69.9%)	0.154
- Liver	47 (5.8%)	14 (6.8%)	0.719
- Lymph node	237 (29.4%)	78 (37.9%)	0.023
- Bone	179 (22.2%)	35 (17.0%)	0.125
- Brain	23 (2.9%)	7 (3.4%)	0.848
- Other	106 (13.2%)	30 (14.6%)	0.659
Fuhrman grade			< 0.001
– 1	5 (0.6%)	0 (0.0%)	
– 2	106 (13.1%)	8 (3.9%)	
– 3	472 (58.5%)	30 (14.6%)	
– 4	195 (24.2%)	160 (77.7%)	
– 5	29 (3.6%)	8 (3.9%)	
Histology code*	1.3 ± 1.2	1.6 ± 1.7	0.019
Tumor necrosis	231 (28.6%)	130 (63.1%)	< 0.001
Renal vein invasion	202 (25.0%)	66 (32.0%)	0.052
IVC invasion	44 (5.5%)	7 (3.4%)	0.305
Positive surgical margin	23 (2.9%)	10 (4.9%)	0.220

Survival outcomes also differed significantly. The results of Kaplan–Meier curve analysis demonstrated considerably shorter OS and CSS durations in patients with sarcomatoid differentiation compared with those without it. The median OS duration was 18.8 months in the sarcomatoid group, compared with 33.5 months in the non-sarcomatoid cohort. A similar pattern was observed for CSS durations in patients with and without sarcomatoid differentiation (18.1 vs. 33.1 months, respectively), with both comparisons showing statistical significance ($p < 0.001$). (Fig. 1).

In multivariate Cox regression analysis, sarcomatoid differentiation remained an independent predictor of poor OS (HR 1.36, 95% CI 1.08–1.73, $p = 0.010$) and CSS (HR 1.39, 95% CI 1.10–1.77, $p = 0.007$) after adjustment for established prognostic variables. (Fig. 2).

Other independent predictors of worse CSS included the higher MSKCC risk category, renal vein invasion, nodal involvement, and advanced pathologic T stage (Table 3). Similar results were observed in analyses of OS duration.

Table 3
Multivariable Cox Proportional Hazards Analysis for Cancer-Specific Survival

Variable	HR	95% CI	p-value
Sarcomatoid differentiation	1.39	1.10–1.77	0.007
Age	1.01	1.01–1.03	< 0.001
BMI	0.93	0.91–0.95	< 0.001
Smoking status			
- Former smoker	1.25	1.01–1.54	0.043
- Current smoker	0.83	0.64–1.07	0.143
MSKCC risk group			
- Intermediate	3.25	1.30–8.11	0.011
- Poor	4.78	1.89–12.13	0.001
Pathological T stage (pT3/4 vs. pT1/2)	1.42	1.01–1.99	0.044
Fuhrman grade (3/4 vs. 1/2)	2.10	1.52–2.96	< 0.001
Nodal involvement (N1 vs. N0)	1.31	1.09–1.57	0.004
Renal vein invasion	1.31	1.06–1.60	0.011

Kaplan–Meier analysis according to the cumulative number of adverse factors demonstrated progressively worse cancer-specific survival with increasing risk burden (Fig. 3). Median CSS was 36.0 months in patients with 0–1 factors, 28.0 months in those with 2 factors, 16.0 months in those with 3 factors, and 10.0 months in those with ≥ 4 factors. Patients with ≥ 4 adverse factors had the poorest

outcomes, whereas those with 0–1 factors had the most favorable survival (log-rank p < 0.001). In multivariable Cox regression adjusted for age, body mass index, and smoking status, the adjusted risk of cancer-specific mortality increased stepwise with the number of adverse factors (2 factors: HR 1.376, 95% CI 1.137–1.666; 3 factors: HR 2.143, 95% CI 1.719–2.672; ≥4 factors: HR 2.617, 95% CI 2.042–3.354; all p ≤ 0.001)(Table 4).

Table 4
Cumulative Risk Model for Cancer-Specific Survival According to the Number of Adverse Factors; sarcomatoid differentiation, pathologic T stage ≥pT3, nodal involvement (pN1), Fuhrman grade 4–5, and MSKCC poor-risk status.

Number of adverse factors	Patients, n	CSS events, n	Median CSS, months	Adjusted HR	95% CI	p-value
0–1	404	252	36.0	1.00	Reference	—
2	310	224	28.0	1.38	1.14–1.67	0.001
3	176	135	16.0	2.14	1.72–2.67	< 0.001
≥ 4	122	93	10.0	2.62	2.04–3.35	< 0.001

Additionally, sarcomatoid differentiation was more frequently observed in patients with lymph node metastasis compared to those without, whereas no significant differences were observed across other metastatic sites (Table 2).

Additionally, the distribution of adverse clinicopathologic features according to sarcomatoid differentiation is illustrated in Supplementary Fig. 1. Patients with sarcomatoid differentiation demonstrated a higher burden of concurrent high-risk features, indicating the coexistence of multiple adverse features.

Discussion

Sarcomatoid differentiation has long been recognized as an aggressive histologic variant of RCC, and our current findings from this multicenter Korean cohort study support its significant prognostic implications. Patients with sarcomatoid RCC consistently demonstrated poorer OS and CSS duration, even after adjusting for major clinicopathologic factors. These findings are in line with observations from Western cohorts and help clarify the behavior of sarcomatoid RCC in Asian patients[11].

In our present study, tumors with sarcomatoid differentiation showed a high frequency of adverse pathologic features, including advanced pT stage, lymph-node metastasis, renal vein invasion, and substantial tumor necrosis. Approximately 78% of sarcomatoid tumors we analyzed were Fuhrman grade 4, which is compatible with their well-known dedifferentiated appearance. Previous studies have also demonstrated similar correlations between sarcomatoid change and aggressive pathology[5–8].

An important finding of the present study is that sarcomatoid differentiation was not only an independent prognostic factor but also closely associated with the accumulation of multiple adverse clinicopathologic features. Survival worsened progressively with increasing numbers of adverse factors (Fig. 3), supporting a cumulative risk effect. These findings suggest that the cumulative burden of adverse clinicopathologic features may provide additional risk stratification among patients with metastatic RCC. Sarcomatoid differentiation should be interpreted within a broader context of risk accumulation rather than as an isolated binary variable. In addition, sarcomatoid differentiation frequently co-occurred with other high-risk features and was more commonly associated with lymph node metastasis, suggesting a non-random pattern of adverse characteristics and a nodal-dominant pattern of tumor dissemination. These findings support the view that sarcomatoid differentiation reflects a biologically aggressive phenotype and should be considered in risk-adapted treatment strategies. The clustering of adverse features observed in Supplementary Fig. 1 further supports this interpretation and is consistent with shared biological processes driving tumor progression[12].

Specifically, de Peralta-Venturina et al.[5] observed that sarcomatoid features are predominantly found in tumors with advanced pathological stages (pT3 or pT4) and are frequently associated with distant metastases at the time of diagnosis across all RCC subtypes. Cheville et al.[6] reported a poor median survival duration of only 8 months for patients with sRCC, emphasizing that the sarcomatoid component is a potent predictor of mortality independent of the underlying histology. Mian et al.[7] documented that approximately 77% of patients with sRCC presented with synchronous metastatic disease, while Leibovich et al.[8] identified sarcomatoid differentiation as a major driver of extensive tumor necrosis that carried a significantly elevated risk of cancer-specific mortality compared with non-sarcomatoid high-grade tumors.

These findings are biologically plausible. Sarcomatoid transformation is thought to reflect an epithelial-to-mesenchymal transition that is driven by genomic instability and transcriptional alterations[7,8]. Molecular analyses have frequently identified mutations involving TP53, CDKN2A/B, and other pathways related to rapid tumor progression and resistance to therapy[9,10]. Loss of chromatin-remodeling genes such as PBRM1 and BAP1 has also been associated with disease progression and poorer survival in metastatic clear-cell RCC, supporting the concept that underlying molecular alterations contribute to the aggressive clinical course of high-risk tumors[13]. Such genomic alterations may contribute to the aggressive clinical course observed across various cohorts, including the one analyzed in this study.

Consistent with prior research, sarcomatoid differentiation remained an independent predictor of OS and CSS in multivariate regression models. This result supports the view that sarcomatoid change provides prognostic information beyond traditional staging or grading of tumors. Although some studies have suggested that the proportion of the sarcomatoid component in tumors may offer additional prognostic value[8,14], sarcomatoid-specific proportional data were not available in our cohort. Leibovich et al.[8] reported a dose-response relationship in which an increasing percentage of the sarcomatoid component was associated with a progressive decline in cancer-specific survival. Similarly, Zhang et al.[14]

incorporated the sarcomatoid percentage into a novel prognostic model, demonstrating that higher proportions of these features significantly correlated with an increased risk of distant metastasis. Notably, the presence of any sarcomatoid element was sufficient to identify a high-risk group with significantly worse outcomes.

The prevalence of sarcomatoid differentiation in our cohort (20.3%) was slightly higher than the 5–15% commonly reported in Western institutional cohort-based studies[5,6]. Several factors may explain this difference, including selection patterns at tertiary centers, heterogeneity in surgical volume, or improvements in pathologic detection. It is also possible that biological or population-specific factors may play a role.

In recent years, immune checkpoint inhibitor (ICI)-based therapy has changed the treatment landscape of sarcomatoid RCC[15–18]. Trials such as CheckMate-214 have demonstrated high response rates with nivolumab plus ipilimumab in patients with sarcomatoid histology, showing responses that were not typically observed with VEGF-targeted therapy alone[15]. Similarly, pembrolizumab-based and cabozantinib-based combinations have shown improved outcomes for these patients[16–19]. Although our present study did not include systemic therapy information, the poor outcomes observed in sarcomatoid RCC support early use of systemic therapy, particularly for patients with high-risk pathology such as pT3/pT4 tumors or tumor necrosis.

Whether sarcomatoid differentiation should directly influence surgical management or decisions regarding adjuvant therapy remains uncertain. Future prospective Korean cohort studies evaluating perioperative or adjuvant immunotherapy specifically for sarcomatoid RCC would help clarify these issues. Given the responsiveness of sarcomatoid RCC to ICI-based regimens, future research incorporating molecular and immunologic profiling may provide more individualized treatment strategies. These findings suggest that patients with sarcomatoid differentiation, particularly those with multiple concurrent adverse features, may benefit from early initiation of systemic therapy rather than a surgery-first approach.

This study has several strengths. It represents one of the largest multicenter Korean cohort studies evaluating sarcomatoid differentiation and includes extensive clinicopathologic data covering multiple institutions. However, the limitations of the current study should also be noted. The retrospective study design introduced potential selection and information biases. In addition, the inclusion of patients from tertiary referral centers may have resulted in selection bias, potentially enriching the cohort with more advanced or complex cases. Furthermore, inter-institutional variability in pathological assessment may have influenced the classification of sarcomatoid differentiation. Additionally, we were unable to evaluate the proportion of the sarcomatoid component or incorporate systemic therapy data, especially regarding ICI exposure. Molecular or genomic analyses were not available, limiting further biological insight into this subgroup. Although the cumulative risk model demonstrated a stepwise association with cancer-specific survival, external validation and formal assessment of model discrimination and calibration are required before clinical implementation. Despite these limitations, our findings contribute

meaningful evidence regarding sarcomatoid RCC in a Korean population. Future studies should aim to integrate molecular profiling, radiologic biomarkers, and real-world immunotherapy outcomes to better understand the biology and improve management strategies for this high-risk subset. In conclusion, sarcomatoid differentiation in RCC is strongly linked with aggressive clinicopathologic features and independently predicts inferior OS and CSS. Sarcomatoid differentiation status should be considered in clinical decision-making.

Methods

This study was conducted by employing the centralized, multi-institutional database of the Korean Renal Cancer Study Group (KRoCS), which prospectively collects standardized clinicopathologic data from major tertiary referral hospitals across Korea. We performed a retrospective cohort analysis of patients who underwent radical or partial nephrectomy for histologically confirmed RCC between January 2005 and December 2022.

Eligible patients were identified through the pathology archives and surgical registries of each institution and were subsequently merged into the KRoCS central repository after data harmonization and quality verification. Patients were excluded if they had benign renal tumors, insufficient histopathologic information, or incomplete survival data. After applying these criteria, 1,013 patients were included in the final analytic cohort. Given the retrospective design, no formal sample size calculation was performed.

Sarcomatoid differentiation was defined according to standardized pathologic criteria used in prior KRoCS-based studies, namely the presence of any spindle-cell morphology consistent with a sarcomatoid transformation on microscopic examination, irrespective of the percentage involved. Clinical variables extracted from electronic medical records included demographic characteristics (age, sex, body mass index), smoking status, and comorbidities such as hypertension, diabetes mellitus, chronic kidney disease, cerebrovascular accident, and cardiovascular disease. Performance status was assessed using the Eastern Cooperative Oncology Group (ECOG) scale.

Pathologic variables were abstracted from formal pathology reports and included tumor size, histologic subtype, Fuhrman nuclear grade, presence of coagulative tumor necrosis, renal vein or inferior vena cava invasion, surgical margin status, and pT and pN stages based on the American Joint Committee on Cancer staging system. The extent and location of metastases observed at the time of initial diagnosis—including in lungs, liver, bone, lymph nodes, and brain—were recorded when applicable. For patients with metastatic disease, a risk stratification was conducted using the Memorial Sloan Kettering Cancer Center (MSKCC) criteria.

Survival status and cause of death were verified through institutional electronic medical records and cross-checked with national death registry data. Overall survival (OS) was defined as the time from diagnosis to death from any cause, whereas cancer-specific survival (CSS) was defined as the time from diagnosis to death attributable directly to RCC.

OS and CSS values were estimated using the Kaplan–Meier method and compared between groups using the log-rank test. Survival time was calculated from the date of RCC diagnosis to the date of death or last follow-up. Cancer-specific mortality was determined based on cause-of-death information from institutional medical records and national death registry data.

To identify independent prognostic factors, multivariate Cox proportional hazards regression analyses were performed. Covariates were selected a priori based on clinical relevance and prior literature and included age, body mass index, smoking status, diabetes mellitus, ECOG performance status, MSKCC risk group, pathologic T stage (≥ pT3 vs. <pT3), nodal involvement (pN1), renal vein invasion, and presence of sarcomatoid differentiation. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported. Proportional hazards assumptions were assessed using Schoenfeld residuals.

Additional analyses were performed to evaluate the cumulative impact of adverse clinicopathologic factors on cancer-specific survival.

A composite risk score was generated by summing the number of predefined adverse factors, including sarcomatoid differentiation, pathologic T stage ≥pT3, nodal involvement (pN1), Fuhrman grade 4–5, and MSKCC poor risk group.

Patients were categorized into four groups based on the number of adverse factors (0–1, 2, 3, and ≥ 4). Survival outcomes were compared using Kaplan–Meier analysis and multivariable Cox proportional hazards models adjusted for age, BMI, and smoking status.

Missing data were handled using complete-case analysis, and the proportion of missing values for each variable was assessed.

All statistical analyses were conducted using R software (version 4.3.1), and a two-sided p value < 0.05 was considered statistically significant.

In addition, potential sources of bias were carefully considered. Given the retrospective nature of the study and the inclusion of patients from tertiary referral centers, selection bias toward more advanced or complex cases may have been present. These limitations were taken into account during data interpretation. This retrospective multicenter study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. 2602-148-1721). The study was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived by the Institutional Review Board because of the retrospective nature of the study. Generative AI tools were used during manuscript preparation to assist with formatting, statistical cross-checks, and regeneration of Figs. 2 and 3 and Supplementary Fig. 1 from the authors' own dataset and pre-specified analyses; all AI-assisted output was reviewed by the authors for factual accuracy, and the authors take full responsibility for the final content.

Declarations

Competing interests

The authors declare no competing interests.

Funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contribution

Conceptualization: HDY, SHC, JKK. Methodology: HDY, JHH. Data collection or management: MHK, HDY, SHC, JC, CK, JJO, TGK, SHJ, SHL, JKN, WSK, BCJ, JYL, SHH, WKH, WSH, YGL, YSL, SYP, YEY, SGK, SHK, JKK, MK, SIS, CHL, YHK, JS, CS, JYP, SB, HHL, JKIJ, JWC, CC, ECH. Data analysis: MHK, HDY, SHC, JKK. Visualization: HDY. Manuscript writing/editing: MHK, HDY, SHC, JKK. Supervision: HDY, SHC, JHH, JC, CK, JKK. All authors contributed to the study conception and design, revised the manuscript critically for important intellectual content, and approved the final manuscript.

Acknowledgments

The authors thank the Department of Biostatistics at Seoul National University Hospital for their valuable advice and support in statistical analysis. The authors also acknowledge the support of the clinical research staff at Korean Renal Cancer Study Group for assistance with data collection and management.

Data Availability

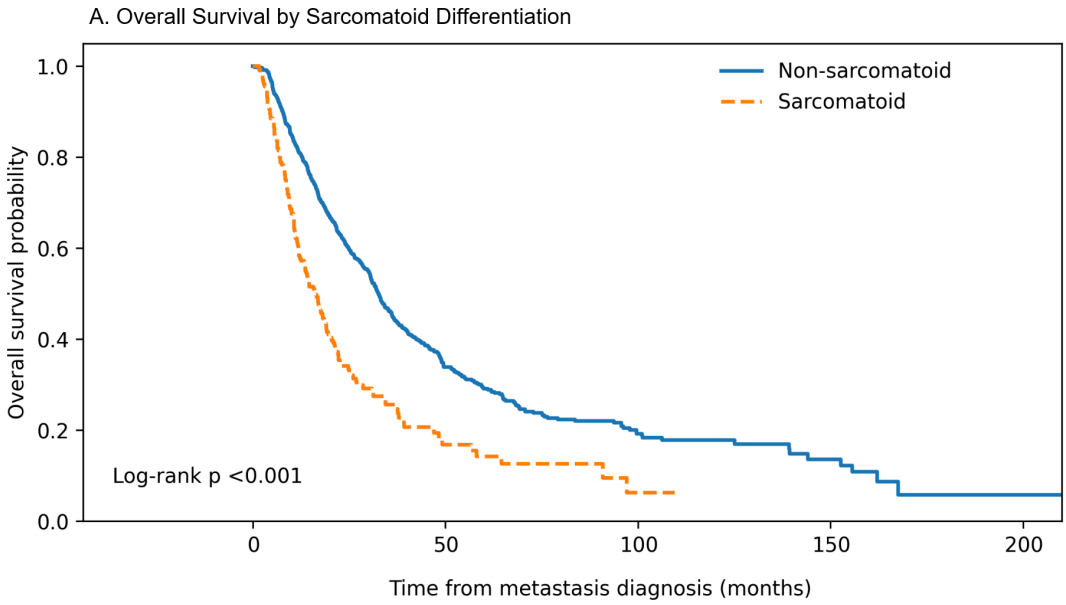
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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Figures



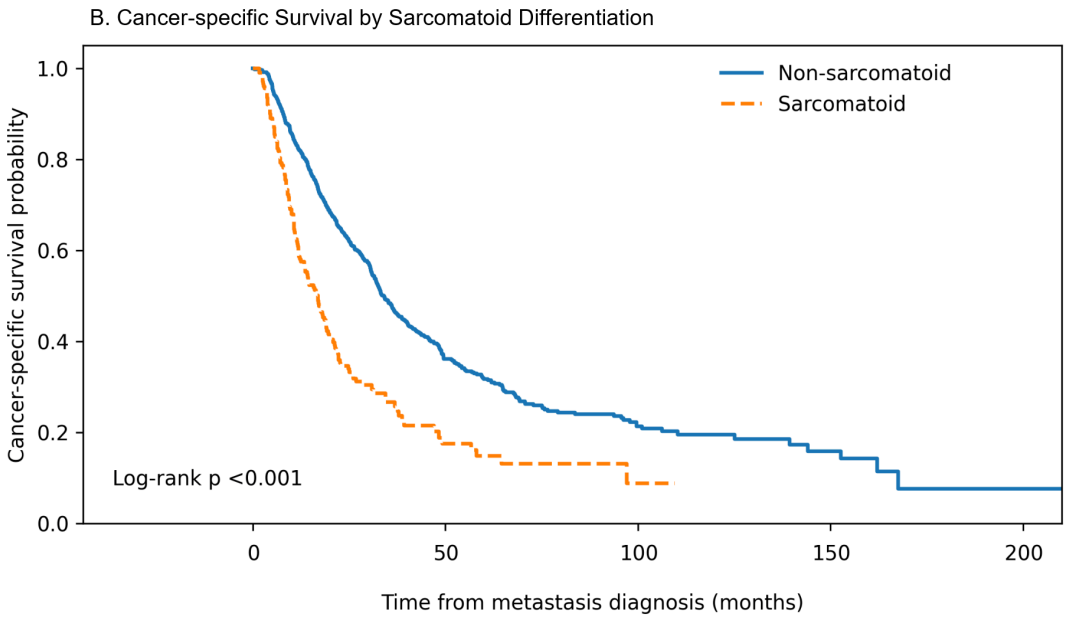


Figure 1

Kaplan–Meier curves for survival according to sarcomatoid differentiation.
(a) Overall survival was significantly worse in patients with sarcomatoid differentiation than in those without sarcomatoid differentiation (log-rank p<0.001).

(b) Cancer-specific survival was also significantly worse in patients with sarcomatoid differentiation than in those without sarcomatoid differentiation (log-rank p<0.001).

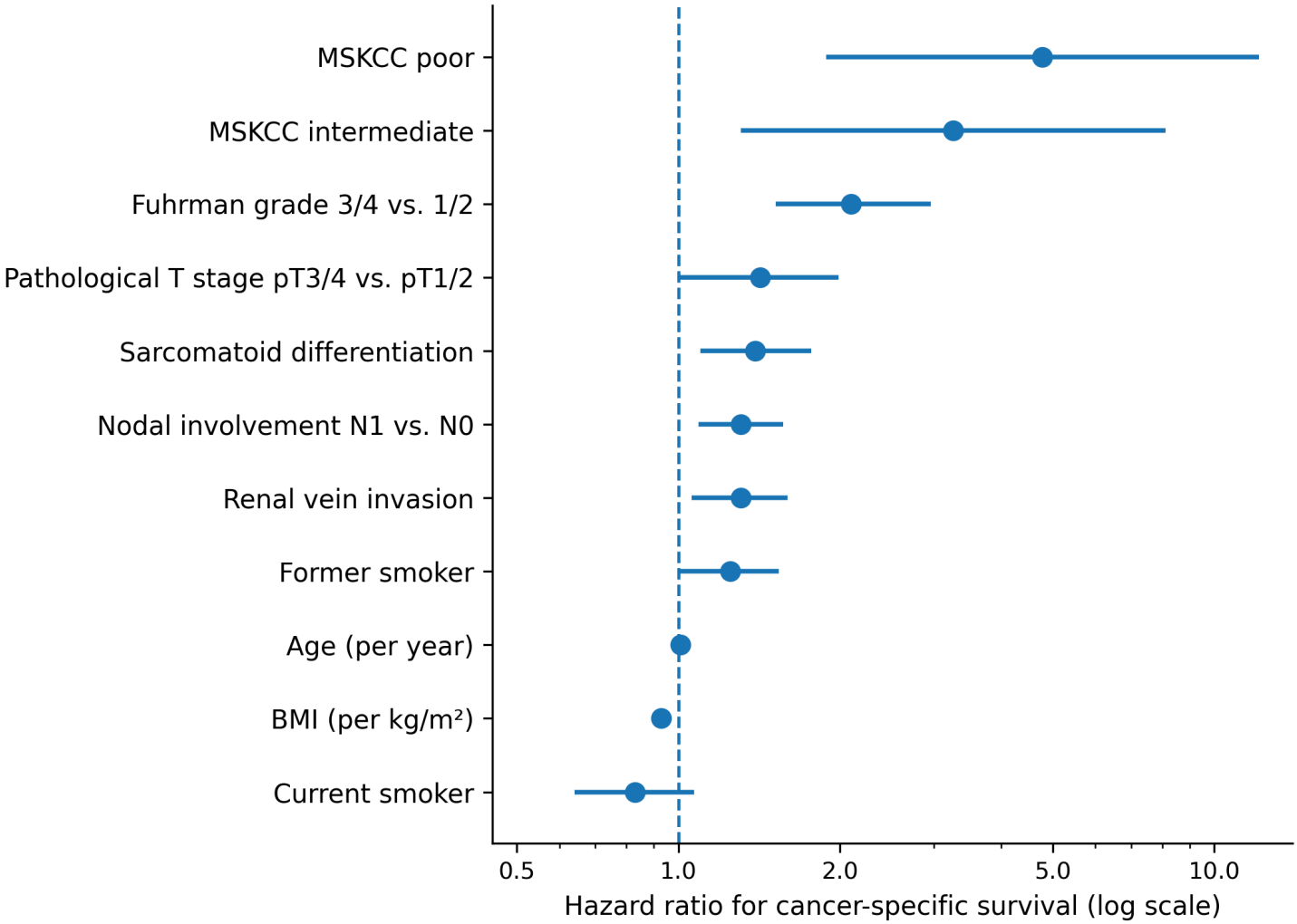
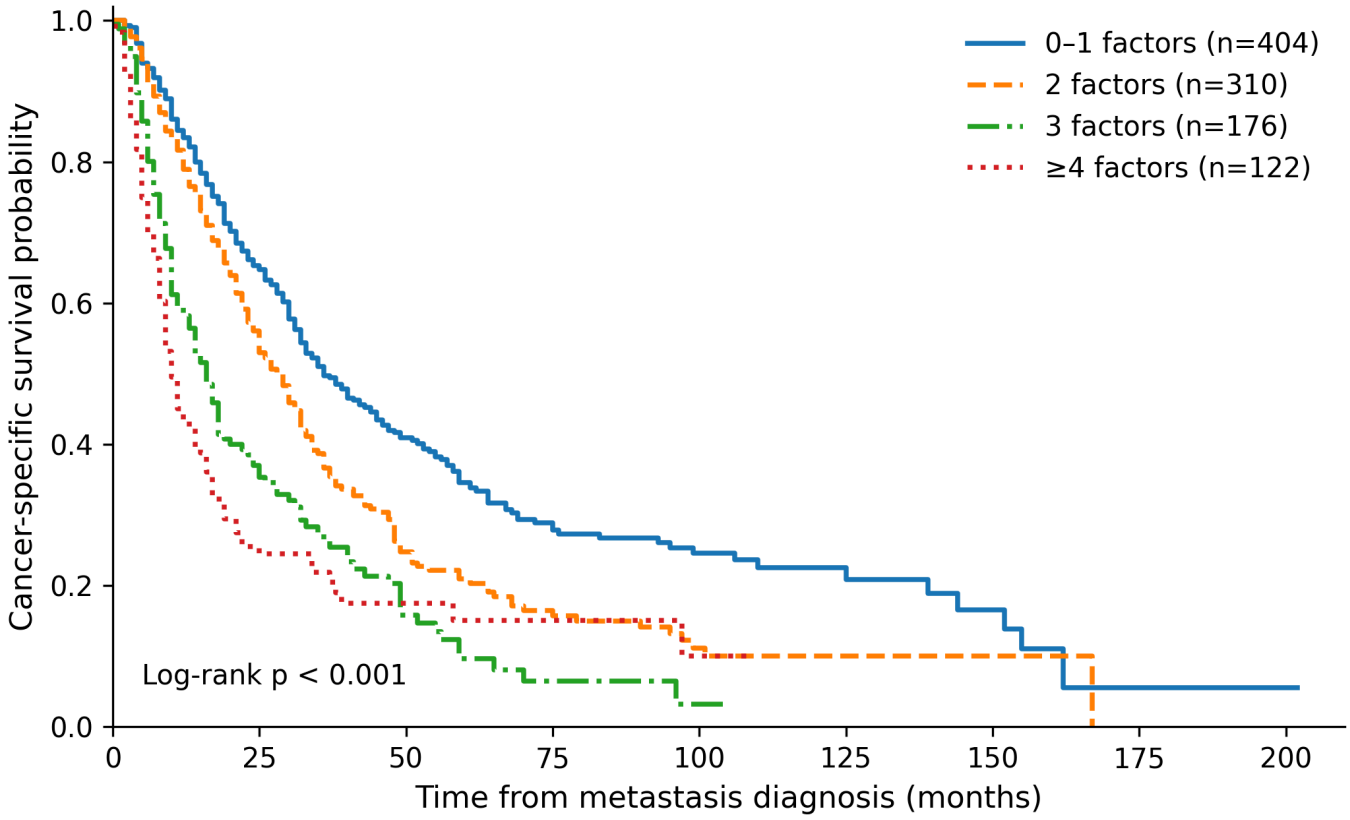


Figure 2

Forest plot of independent prognostic factors for cancer-specific survival. Sarcomatoid differentiation demonstrated a prognostic impact comparable to other established adverse clinicopathologic features, supporting its role as a clinically meaningful independent risk factor.



No. at risk									
0–1	404	220	110	57	32	13	6	1	1
2	310	145	48	24	10	4	2	0	0
3	176	46	14	4	1	0	0	0	0
≥4	122	24	7	6	1	0	0	0	0

Figure 3

Kaplan–Meier curves for cancer-specific survival according to the number of adverse risk factors.

Patients with increasing numbers of adverse factors demonstrated a stepwise deterioration in survival outcomes, supporting a cumulative risk effect. (log-rank p<0.001).

Supplementary Files

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- SupplementaryFigure1300DPI.tif