Prognostic value of the sarcomatoid component in bladder cancer: A propensity score matching study

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Abstract. Sarcomatoid carcinoma of the bladder is rare, and little is known about the prognostic impact of the proportion of sarcomatoid components of the bladder. The present study aimed to assess the prognostic value of the proportion of sarcomatoid components with regard to death and recurrence rates in patients with bladder cancer (BC), and to validate the worse survival results of sarcomatoid carcinomas of the bladder using propensity score matching. Patients with sarcomatoid carcinoma of the bladder who were treated at the Affiliated Hospital of Qingdao University between August 2010 and May 2021 were included in the study. A 1:2 propensity score matching system based on age, sex and pathological T stage was used for sarcomatoid and non-sarcomatoid carcinoma matching. Finally, 114 patients with BC were included. Patients with sarcomatoid carcinoma had worse 5-year cancer-specific survival (CSS) (69.1 vs. 86.9%; log-rank P=0.008) and recurrence-free survival (RFS) (64.1 vs. 83.6%; log-rank P=0.001) rates compared with patients with non-sarcomatoid carcinoma, as had the subgroup with muscle invasion. Multivariate analysis revealed sarcomatoid carcinoma as an independent prognostic factor. Patients with a low proportion of sarcomatoid components (1-50%) had a better prognosis than patients with a high proportion (>50%), and no significant difference was found compared with the non-sarcomatoid group. Overall, a proportion of sarcomatoid components >50% was a predictor of CSS and RFS. Sarcomatoid components markedly increased the risk of death and recurrence in muscle-invasive BC, but not in non-muscle-invasive BC. A higher proportion of sarcomatoid components was significantly associated with poorer survival.

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Introduction

Although modern medicine has advanced greatly, bladder cancer (BC) still occurs in an increasing number of people, with 573,278 cases in 2020 globally, while the number of deaths has not reduced either, with 212,536 cases in this same year (1,2). Sarcomatoid carcinoma is a rare type of BC that has both mesenchymal and epithelial characteristics (3); however, it is essentially an epithelial-derived cancer (4-6). Sarcomatoid carcinoma can be found in tumours of every system, and its presence means that metastases occur quickly, even after radical surgery (7,8). The median survival time for bladder sarcomatoid carcinoma ranges from 13.4 to 18.5 months (9,10). It is reported that this histopathological type is not sensitive to systemic treatment, such as chemotherapy, and the pathological response to chemotherapy is often not optimistic (11). Therefore, a number of studies analyzing prognostic factors and treatment efficacy have excluded sarcomatoid carcinoma to reduce selection bias (12-14).

Despite this, some patients with sarcomatoid carcinoma can still survive for a long time or even be cured. Identification of these individuals can help with the implementation of more aggressive medical treatment. To the best of our knowledge, to date, few studies have focused on sarcomatoid carcinoma of the bladder (11,15). One study found that lower stages of the cancer may be associated with better survival time (15). Smaller tumour diameter, lower percentage of sarcomatoid components, absence of lymph node invasion and distant metastasis, and absence of tumour necrosis are associated with a prolonged survival time, although this has been found in sarcomatoid carcinoma of organs other than the bladder (16-19). To the best of our knowledge, prognostically relevant variables in sarcomatoid carcinoma of the bladder have not been investigated.

The purpose of the present study was to summarise the clinicopathological features and prognosis of sarcomatoid carcinomas of the bladder, and to confirm the prognostic value of the proportion of sarcomatoid components.

Patients and methods

Patients. The present study included 38 patients with sarcomatoid carcinoma of the bladder and 76 patients with non-sarcomatoid bladder cancer who were treated at the

Department of Urology, The Affiliated Hospital of Qingdao University (Qingdao, China), between August 2010 and May 2021. The inclusion criteria were as follows: i) pathologically diagnosed surgical specimens; and ii) pT staging ≥T1. Patients with carcinosarcoma and sarcoma, which are two pathological types that differ from sarcomatoid carcinoma, were excluded. All patients diagnosed with other cancer types at the same time were excluded. The patients underwent radical cystectomy or transurethral resection, performed by experienced urologists, and volunteered to participate in this study. The Affiliated Hospital of Qingdao University Ethics Committee approved the study (approval number, AHQU-MAL 20210110). All methods were performed in accordance with the relevant guidelines and regulations, such as the Declaration of Helsinki.

Patient details, such as age at diagnosis, sex, body mass index, smoking status, alcohol consumption, diagnosis of diabetes mellitus, presence of hypertension, type of surgery, and documentation of adjuvant regimens of chemotherapeutic agents and immune checkpoint inhibitors, were obtained from the medical records or telephone follow-up. Imaging data were reviewed to determine whether distant metastases were present at the time of surgery. The pathology reports included immunohistochemical information, proportion of sarcomatoid components, pathological T stage, regional lymph node invasion, tumour necrosis, lymphovascular invasion and vascular tumour thrombus. Pathological staging was on the basis of the eighth edition of the TNM staging criteria of the Union for International Cancer Control (20). Lymphovascular invasion implied the invasion of endothelium-lined spaces of microvessels and lymphatics (21). The subgroup analysis was performed, and the patients were divided into two groups, namely, muscle-invasive BC and non-muscle-invasive BC, according to whether the tumour invaded the muscle.

Follow-up. Patients were followed up every 3 months for 2 years and annually thereafter. Recurrence or metastasis was detected using computed tomography and/or magnetic resonance imaging. The primary outcomes were cancer-specific survival (CSS) and overall survival (OS), defined as death from BC and all causes, respectively, or the end of follow-up. Another outcome was recurrence-free survival (RFS), defined as disease recurrence, newly detected metastasis or death from all causes.

Propensity score matching. To balance the confounders of sarcomatoid and non-sarcomatoid BC, propensity score matching was applied. The logistic regression model was performed according to age, sex and pathological T stage. The matching algorithm was 1:2 nearest neighbour matching with a 0.1 calliper width.

Statistical analysis. The Wilcoxon rank-sum test, χ^2 test and Fisher's exact test were used to compare the continuous and categorical variables of the patients. The Kaplan-Meier method was used to obtain survival rates and the log-rank test was used to compare survival curves. The association between the sarcomatoid components and other variables and the survival outcomes were calculated by Cox proportional hazard regression models and summarised using hazard ratios (HRs) and 95% confidence intervals (CIs). Collinearity diagnosis was used to test for multi-collinearity. The optimal cut-off value of the proportion of sarcomatoid components for prognostic value was determined through the receiver operating characteristic curve. Statistical analysis was performed using R 3.5.0 software (R Foundation) and SPSS version 26.0 (IBM Corp.). A two-sided P-value of <0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics. A total of 38 patients with sarcomatoid carcinomas of the bladder were identified from the hospital database. Another 76 patients with non-sarcomatoid BC were selected as the control group after matching by propensity score. The median follow-up time was 46 months. The patients with sarcomatoid and non-sarcomatoid carcinoma of the bladder were mostly male (76 vs. 78%, respectively; P=0.875). The median age at diagnosis was 72 years (range, 65-79 years) and 71 years (range, 64-76 years), respectively (P=0.658). The majority of patients with stage T1 BC underwent transurethral resection of the bladder (88 vs. 84%, respectively; P>0.999). By contrast, most patients with muscle-invasive BC underwent radical cystectomy (82 vs. 96%, respectively; P=0.090). Muscle-invasive BC accounted for the majority of sarcomatoid and non-sarcomatoid carcinomas (58 vs. 58%, respectively; P=0.921) (data not shown). The proportion of patients with regional lymph node invasion (11 vs. 11%, respectively; P>0.999) and lymphovascular invasion (13 vs. 26%, respectively; P=0.109) was low. A sarcomatoid component proportion of >50% was observed in 45% of the patients with sarcomatoid carcinoma. A single patient with sarcomatoid carcinoma used tyrosine kinase inhibitor anlotinib after the discovery of lung metastases (data not shown). Patient characteristics after matching were not significantly different and are listed in Table I.

Prognosis and independent prognostic factors. A total of 11 patients with sarcomatoid carcinoma and 9 with non-sarcomatoid carcinoma died of cancer during the follow-up. Significant differences were found between the sarcomatoid and non-sarcomatoid carcinoma groups in terms of 1-year CSS rate (80.2 vs. 100%, respectively), 3-year CSS rate (73.4 vs. 96.4%, respectively) and 5-year CSS rate (69.4 vs. 86.9%, respectively) (log-rank P=0.008) (Fig. 1A). After stratification by depth of invasion, non-muscle-invasive BC with sarcomatoid carcinoma components did not confer a worse CSS rate (5-year CSS rate: 100 vs. 91.8%, respectively; log-rank P>0.05) (Fig. 1C). Among the patients with muscle-invasive BC, sarcomatoid carcinomas had a significantly worse median CSS (38 vs. >120 months, respectively), with a 5-year CSS rate of 39.1% compared with 81.8% for non-sarcomatoid carcinomas (log-rank P<0.001) (Fig. 1E). A total of 15 patients with sarcomatoid BC and 12 with non-sarcomatoid BC experienced recurrence. The common metastatic sites of sarcomatoid carcinoma of the bladder were the bones (n=4), lungs (n=3), liver (n=2) and pelvic cavity (n=2). The 5-year RFS rates of the sarcomatoid and non-sarcomatoid carcinoma groups were 64.1 and 83.6%, respectively (log-rank P=0.001) (Fig. 1B). The 5-year RFS rates with and without sarcomatoid differentiation were 93.8 and 96.2%, respectively, in the non-muscle-invasive subgroup (Fig. 1D). The patients with sarcomatoid carcinoma

Table I. Patient characteristics of the sarcomatoid and non-sarcomatoid groups.

Feature	Sarcomatoid (n=38)	Non-sarcomatoid (n=76)	P-value
Median age (IQR), years	72 (65-79)	71 (64-76)	0.658
Male, n (%)	29 (76)	59 (78)	0.875
Median BMI (IQR)	25.2 (21.8-27.5)	23.7 (20.8-26.0)	0.336
Hypertension, n (%)	12 (32)	25 (33)	0.888
Diabetes mellitus, n (%)	6 (16)	11 (14)	0.924
Smoking, n (%)	16 (42)	37 (49)	0.545
Alcohol, n (%)	6 (16)	32 (42)	0.005
ECOG ≥1, n (%)	7 (18)	10 (13)	0.457
Type of surgery, n (%)			
Radical cystectomy	20 (53)	47 (62)	0.346
Transurethral resection	18 (47)	29 (38)	
Median tumor size (IQR), cm	3.5 (2.6-4.4)	3.0 (2.1-4.5)	0.356
pT stage, n (%)			
pT1	16 (42)	32 (42)	0.921
pT2	10 (26)	21 (28)	
pT3	9 (24)	18 (24)	
pT4	3 (8)	5 (7)	
pN1, n (%)	4 (11)	8 (11)	>0.999
LVI, n (%)	5 (13)	20 (26)	0.109
Coagulative tumor necrosis, n (%)	8 (21)	6 (8)	0.086
Multifocal, n (%)	8 (21)	24 (32)	0.238

Values were calculated using the Wilcoxon rank-sum test for continuous and categorical variables, and the χ^2 and Fisher exact tests for unordered categorical variables. BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; LVI, lymphovascular invasion; IQR, interquartile range; pT, pathological tumor; pN, pathological node.

had a worse median RFS time (11 vs. >120 months) in the muscle-invasive subgroup (Fig. 1F).

On multivariate analysis, larger tumour diameter, pT stage ≥T2, regional lymph node invasion and sarcomatoid carcinoma were independent prognostic factors for cancer-specific death. pT stage ≥T2, regional lymph node invasion and sarcomatoid carcinoma increased the risk of disease recurrence in the patients with BC. Independent predictors of OS were BMI, tumor size, pT stage and sarcomatoid carcinoma. Multivariate analysis showed that sarcomatoid carcinoma of the bladder was significantly associated with worse CSS (HR, 6.19; 95% CI, 2.31-16.6; P<0.001), RFS (HR, 4.44; 95% CI, 2.03-9.71; P<0.001) and OS (HR, 3.04; 95% CI, 1.39-6.66; P=0.005) (Table II).

Analysis of the sarcomatoid component. Among the patients with sarcomatoid carcinoma, 11 had pure sarcomatoid carcinomas and 27 had mixed component carcinomas (sarcomatoid and non-sarcomatoid carcinoma). No significant difference in pathological stage (P=0.5), CSS and RFS was observed between the two groups, but both groups had higher CSS and RFS rates than the non-sarcomatoid group (Fig. S1A and B). According to the receiver operating characteristic curve, 45% sarcomatoid components was identified as the optimal cut-off score (Fig. S1C). The area under the curve was 0.68. Finally, 50% was used for the comparison of sarcomatoid components to achieve higher specificity. No significant differences in characteristics were found between patients with a sarcomatoid component >50% and patients with a sarcomatoid component ≤50% (Table SI), with the exception that tumours were larger in patients with a sarcomatoid component >50% (4 vs. 3 cm; P=0.009). The 5-year CSS and RFS rates for patients with a sarcomatoid component >50% were lower than those for patients with a low proportion (≤50%) of sarcomatoid component and patients with non-sarcomatoid BC (CSS: 53.5 vs. 80.6 vs. 89.2%, respectively; log-rank P<0.001; Fig. 2A; RFS: 47.4 vs. 78.5 vs. 83.6%, respectively; log-rank P<0.001; Fig. 2B). In the subgroup of muscle-invasive BC, patients with a sarcomatoid component >50% similarly had worse 5-year CSS and RFS rates (CSS: 22.9 vs. 37.9 vs. 81.8%, respectively; log-rank P<0.001; Fig. 2E; RFS: 23.3 vs. ns (indicating <5 years of follow-up) vs. 71.6%, respectively; log-rank P<0.001; Fig. 2F). In the non-muscle-invasive BC subgroup, in the >50% and ≤50% sarcomatoid component, and non-sarcomatoid groups, there was no significant difference in CSS (100.0 vs. 100.0 vs. 96.0%, respectively; log-rank P=0.3; Fig. 2C) but there was a significant difference in RFS (85.7 vs. 100.0 vs. 96.2%, respectively; log-rank P=0.003; Fig. 2D). Multivariate analysis showed that a sarcomatoid component >50%, pT stage ≥T2 and tumour size >3.5 cm predicted cancer-specific death. Independent predictors of recurrence were a higher proportion of sarcomatoid component, higher T stage, regional lymph node invasion and larger tumour size. Tumour T stage,

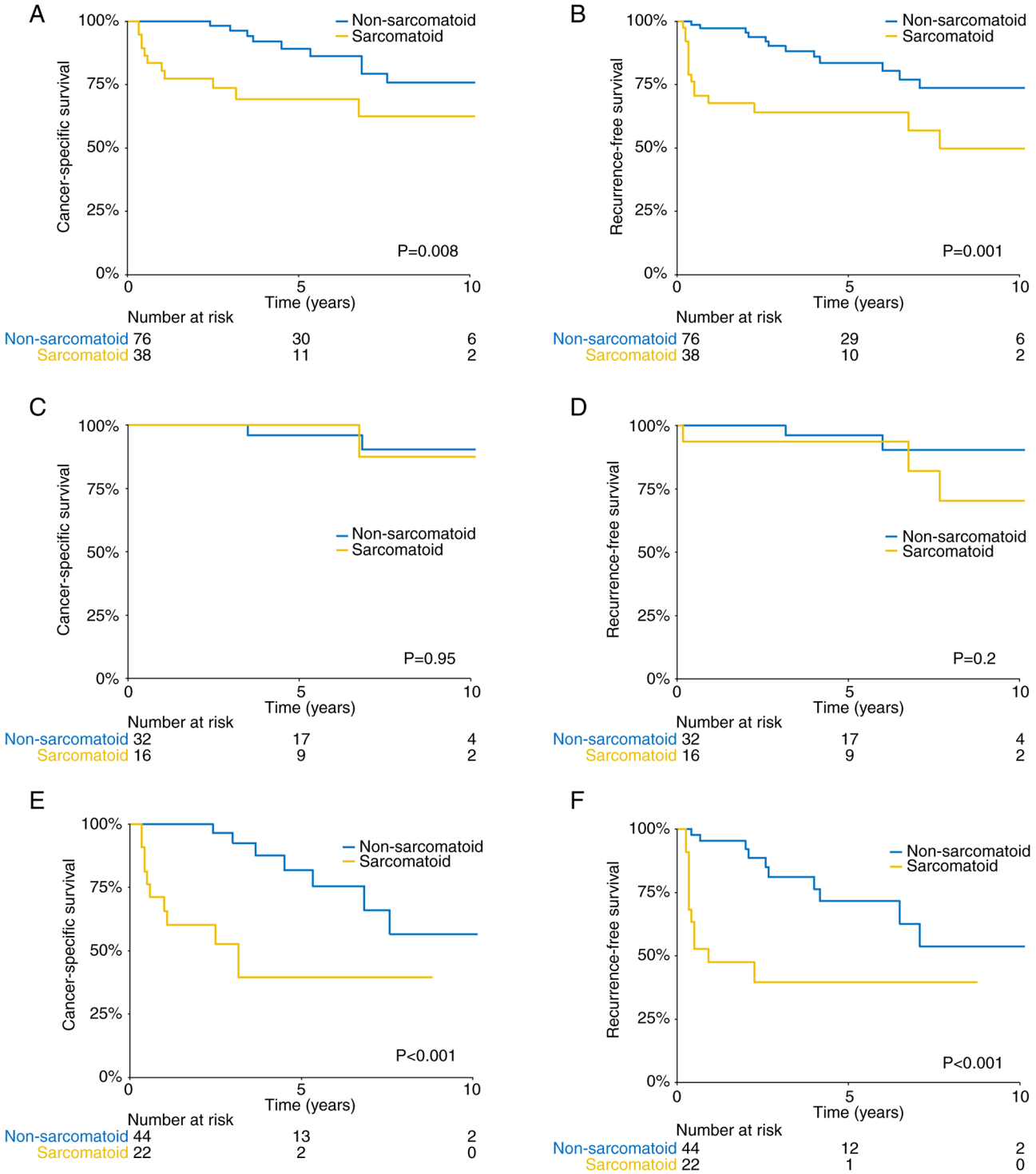

Figure 1. Kaplan-Meier curves showing survival differences between patients with sarcomatoid and non-sarcomatoid carcinoma, stratified by muscle invasion. (A) CSS of all patients. (B) RFS of all patients. (C) CSS of patients with NMIBC. (D) RFS of patients with NMIBC. (E) CSS of patients with MIBC. (F) RFS of patients with MIBC. CSS, cancer-specific survival; MIBC, muscle-invasive bladder cancer; NMIBC, non-MIBC; RFS, recurrence-free survival.

tumour size, and Eastern Cooperative Oncology Group score were predictors of OS (Table III). No multi-collinearity was observed between variables in all regression analyses.

Discussion

Sarcomatoid carcinoma is a rare pathological type of BC, accounting for 0.07-2.4% of BCs (22,23). In the present study, 38 out of 5,196 patients with BC had final pathological confirmation of sarcomatoid carcinoma, representing ~0.73% of the cases. To the best of our knowledge, this is the first study to compare sarcomatoid and non-sarcomatoid carcinoma of the bladder using propensity score matching and assessing the prognostic value of the proportion of sarcomatoid components.

The prognosis of sarcomatoid carcinoma of the bladder remains controversial, with some studies concluding that

Table II. Univariate and multivariate Cox regression analyses of all patients for CSS, RFS and OS.

	CSS				RFS				OS			
	Univariate		Multivariate[a]		Univariate		Multivariate[a]		Univariate		Multivariate[b]	
Feature	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (per 10-year increase)	0.98 (0.58-1.65)	0.870		-	0.94 (0.60-1.47)	0.762		-	1.32 (0.88-1.99)	0.221		-
Sex (male vs. female)	0.62 (0.23-1.73)	0.367		-	0.79 (0.32-1.95)	0.624		-	0.83 (0.36-1.92)	0.702		-
ECOG (≥1 vs. 0)	1.28 (0.37-4.34)	0.697		-	1.17 (0.40-3.37)	0.801		-	1.45 (0.60-3.49)	0.371		-
Hypertension (yesvs. no)	0.36 (0.11-1.21)	0.098		-	0.58 (0.23-1.42)	0.224		-	0.50 (0.22-1.15)	0.052		-
DM (yes vs. no)	2.33 (0.85-6.37)	0.010		-	1.50 (0.57-3.95)	0.437		-	1.39 (0.58-3.35)	0.537		-
Smoking (yes vs. no)	0.88 (0.37-2.10)	0.772		-	0.78 (0.37-1.65)	0.477		-	1.20 (0.61-2.36)	0.571		-
Alcohol (yes vs. no)	0.58 (0.22-1.49)	0.256		-	0.89 (0.41-1.93)	0.751		-	0.71 (0.35-1.45)	0.326		-
BMI (per 5-kg/m^2 increase)	0.96 (0.54-1.73)	0.868		-	1.35 (0.82-2.28)	0.278		-	1.00 (0.42-2.41)	0.026	0.54 (0.32-0.94)	0.030
Surgery (RC vs. TUR)	3.42 (0.43-27.11)	0.212		-	3.20 (1.34-7.66)	0.010		-	3.43 (1.58-7.43)	0.002		-
Tumor size (>3.5 vs. ≤3.5 cm)	3.57 (1.46-8.72)	0.005	2.64 (1.01-6.89)	0.047	3.08 (1.43-6.65)	0.004		0.101	3.42 (1.72-6.80)	<0.001	2.59 (1.28-5.26)	0.008
pT stage (≥T2 vs. T1)	5.93 (1.96-17.03)	0.002	6.50 (1.92-22.08)	0.003	4.71 (1.87-11.75)	0.001	4.73 (1.74-12.91)	0.002	4.71 (2.10-10.55)	<0.001	4.85 (2.02-	<0.001
pN stage (N1 vs. N0)	5.83 (1.97-17.21)	0.001	3.48 (1.13-10.75)	0.032	7.35 (3.04-17.84)	<0.001	5.58 (2.20-14.18)	<0.001	4.79 (2.00-11.50)	<0.001		0.125
LVI (yes vs. no)	1.41 (0.46-4.31)	0.544		-	1.37 (0.54-3.46)	0.458		-	2.43 (1.14-5.20)	0.018		0.786
Necrosis (yes vs. no)	2.21 (0.64-7.62)	0.210		-	2.48 (0.93-6.59)	0.074		-	2.36 (0.90-6.15)	0.079		-
Multifocal (yes vs. no)	1.38 (0.57-3.33)	0.474		-	1.29 (0.59-2.79)	0.455		-	0.84 (0.40-1.76)	0.638		-
Sarcomatoid differentiation (yes vs. no)	2.89 (1.23-6.82)	0.020	6.19 (2.31-16.62)	<0.001	2.98 (1.42-6.27)	0.004	4.44 (2.03-9.71)	<0.001	1.59 (0.81-3.12)	0.156	3.04 (1.39-6.66)	0.005

[a]Adjusted for tumor size, pT stage and pN stage; [b]adjusted for tumor size, pT stage, pN stage, BMI and LVI. CSS, cancer-specific survival; RFS, recurrence-free survival; OS, overall survival; DM, diabetes mellitus; BMI, body mass index; RC, radical cystectomy; TUR, transurethral resection; LVI, lymphovascular invasion; HR, hazard ratio; pT, pathological tumor; pN, pathological node; ECOG, Eastern Cooperative Oncology Group.

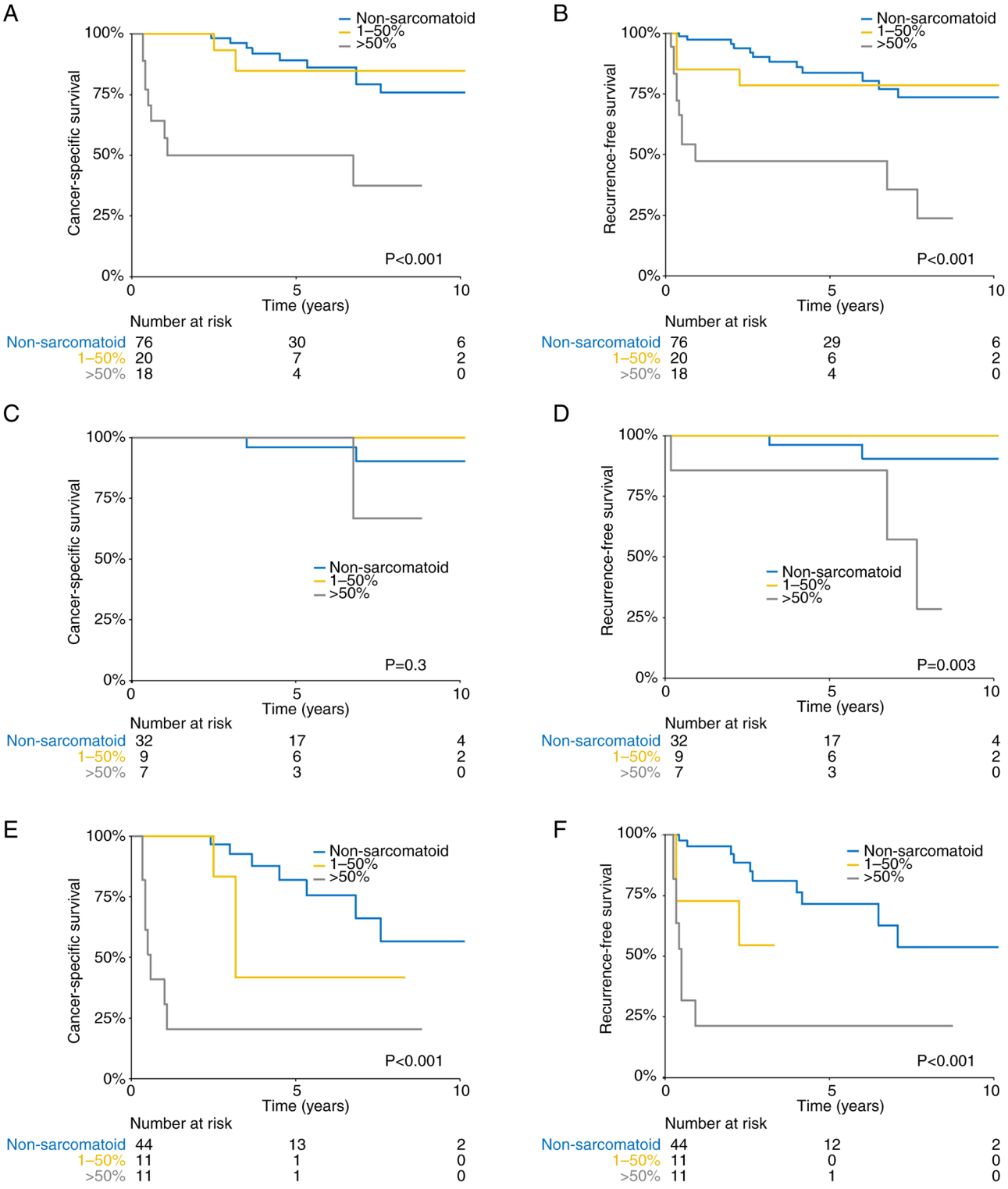

Figure 2. Survival differences in the sarcomatoid carcinoma (>50%), sarcomatoid carcinoma (1-50%) and non-sarcomatoid carcinoma groups, stratified by muscle invasion. (A) CSS of all patients. (B) RFS of all patients. (C) CSS of patients with NMIBC. (D) RFS of patients with NMIBC. (E) CSS of patients with MIBC. (F) RFS of patients with MIBC. CSS, cancer-specific survival; MIBC, muscle-invasive bladder cancer; NMIBC, non-MIBC; RFS, recurrence-free survival.

the sarcomatoid component was not significantly associated with survival (10,23-26) and others arguing for a markedly increased risk of death (11,27). Most of these studies were from the SEER database, case series, and studies with a too short follow-up time (<6 months) or a too small number of cases (<20) (10,23-27), which resulted in a high risk of bias. There was an interaction between sarcomatoid differentiation and advanced stage. Therefore, the worse prognosis in sarcomatoid carcinoma compared with non-sarcomatoid carcinoma might be explained by a higher proportion of patients with muscle invasion, invasion outside the bladder and regional lymph node invasion (11,28). The present study matched sarcomatoid

Table III. Univariate and multivariate Cox regression analyses of patients with sarcomatoid carcinoma for CSS, RFS and OS.

	CSS				RFS				OS			
	Univariate		Multivariate[a]		Univariate		Multivariate[a]		Univariate		Multivariate	
Feature	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (per 10-year increase)	0.70 (0.42-1.16)	0.168		-	0.80 (0.51-1.28)	0.354		-	0.90 (0.55-1.48)	0.678		-
Gender (male vs. female)	0.38 (0.11-1.30)	0.124		-	0.41 (0.14-1.22)	0.110		-	0.53 (0.17-1.72)	0.293		-
ECOG (≥1 vs. 0)	1.40 (0.29-6.66)	0.673		-	1.71 (0.47-6.23)	0.417		-	3.13 (0.93-10.49)	0.07	5.77 (1.26-26.5)	0.024
Hypertension (yes vs. no)	0.45 (0.10-2.10)	0.310		-	0.72 (0.23-2.26)	0.569		-	0.32 (0.07-1.45)	0.140		-
DM (yes vs. no)	5.14 (1.48-17.81)	0.010		0.478	2.96 (0.92-9.48)	0.068		0.419	3.49 (1.08-11.29)	0.037		0.762
Smoking (yes vs. no)	1.16 (0.35-3.81)	0.810		-	0.69 (0.24-2.01)	0.494		-	1.38 (0.48-3.98)	0.557		-
Alcohol (yes vs. no)	1.05 (0.22-4.90)	0.955		-	1.10 (0.30-3.97)	0.888		-	0.73 (0.16-3.30)	0.681		-
BMI (per 5-kg/m^2 increase)	0.83 (0.42-1.65)	0.588		-	1.26 (0.64-2.49)	0.511		-	0.60 (0.33-1.10)	0.096		0.122
Surgery (RC vs. TUR)	4.33 (1.11-16.93)	0.035		-	2.15 (0.72-6.41)	0.169		-	4.28 (1.30-14.08)	0.017		-
Tumor size (>3.5 vs. ≤3.5 cm)	9.25 (1.97-43.50)	0.005	10.60 (1.65-67.48)	0.013	3.88 (1.29-11.70)	0.016	5.59 (1.46-21.39)	0.012	5.20 (1.60-16.88)	0.006	4.47 (1.17-18.7)	0.029
pT stage (≥T2 vs. T1)	14.2 (1.74-115.04)	0.013	17.93 (1.76-182.89)	0.015	6.01 (1.54-23.36)	0.010	4.71 (1.05-21.11)	0.043	8.81 (1.90-40.84)	0.006	10.50 (1.96-56.1)	0.006
pN stage (N1 vs. N0)	6.95 (1.64-29.46)	0.009	3.48 (1.13-10.75)	0.182	7.44 (2.18-25.37)	0.001	9.41 (1.58-56.02)	0.014	4.85 (1.24-19.01)	0.023		0.510
LVI (yes vs. no)	0.041 (0.00-127.18)	0.436		-	0.50 (0.06-3.82)	0.500		-	0.62 (0.08-4.76)	0.647		-
Necrosis (yes vs. no)	1.31 (0.28-6.14)	0.729		-	1.30 (0.36-4.60)	0.689		-	1.73 (0.47-6.31)	0.407		-
Multifocal (yes vs. no)	1.35 (0.36-5.10)	0.658		-	1.16 (0.37-3.65)	0.800		-	1.45 (0.46-4.65)	0.528		-
Sarcomatoid proportion (>50 vs. 1-50%)	4.57 (1.21-17.33)	0.025	5.18 (1.18-22.82)	0.030	2.99 (1.02-8.78)	0.046	4.35 (1.07-17.66)	0.040	3.08 (1.03-9.24)	0.045	4.03 (0.82-19.91)	0.087

[a]Adjusted for DM, tumor size, pT stage and pN stage; [b]adjusted for ECOG, DM, BMI, tumor size, pT stage, pN stage, BMI and LVI. CSS, cancer-specific survival; RFS, recurrence-free survival; OS, overall survival; DM, diabetes mellitus; BMI, body mass index; RC, radical cystectomy; TUR, transurethral resection; LVI, lymphovascular invasion; HR, hazard ratio; pT, pathological tumor; pN, pathological node; ECOG, Eastern Cooperative Oncology Group.

and non-sarcomatoid carcinoma well for pathological T stage by propensity score matching, and found that sarcomatoid carcinoma conferred worse survival time and exhibited more aggressive behaviour. After being adjusted by T stage, N stage and tumour size, the same conclusion was still reached. Results were consistent with a study that investigated patients with sarcomatoid carcinoma at the Memorial Sloan Kettering Cancer Center (11). After stratification for T stage, the results were the same for muscle-invasive sarcomatoid carcinoma. Due to the limited number of patients, the prognostic value of sarcomatoid carcinoma in non-muscle invasive BC should be studied in a larger sample.

The 5-year CSS rate for patients with sarcomatoid carcinoma in the Affiliated Hospital of Qingdao University was higher than that in previous studies (37-64%) (10,23-26). This may be due to the different inclusion criteria in the previous studies. Inclusion of patients who underwent radical cystectomy or muscle invasion meant a higher stage, or inclusion of patients who also had carcinosarcoma resulted in a significantly worse prognosis compared with that for patients with sarcomatoid carcinoma. In the present multivariate analysis of patients with bladder sarcomatoid carcinoma, the proportion of sarcomatoid components, pathological T stage and tumour size were predictors of cancer-specific death. Diamantopoulos *et al* (15) found that American Joint Committee on Cancer stage and an age ≥85 years increased the risk of cancer-specific death. Sui *et al* (9) found that stage ≥T3 and Charlson Comorbidity Index ≥1 were prognostic factors for all-cause mortality. The proportion of sarcomatoid components of the bladder has not been reported to be of prognostic value and, to the best of our knowledge, the present study showed for the first time that a high proportion of sarcomatoid components is an independent prognostic factor. Reporting on the percentage of sarcomatoid carcinoma components is recommended to improve risk stratification and predict survival of patients with BC.

Currently, no uniform consensus guidelines are available for the standard treatment of patients with sarcomatoid carcinoma (29,30). In the present study, patients with non-muscle-invasive BC mostly underwent transurethral resection (87.5%), while radical cystectomy was the main treatment option for muscle-invasive BC (81.8%). The present study showed no significant survival benefit from radical cystectomy for non-muscle-invasive BC presenting with sarcomatoid carcinoma components. Therefore, stage T1 bladder sarcomatoid carcinoma is less aggressive, and additional radical cystectomy will only increase the likelihood of surgical complications, with no evidence of a survival benefit. No patients with sarcomatoid carcinoma received neoadjuvant chemotherapy. A total of 2 patients were treated with tyrosine kinase inhibitors and radiotherapy, respectively, only after the discovery of lung metastases. Previous studies have found no significant survival benefit from neoadjuvant or adjuvant chemotherapy in patients with sarcomatoid differentiated urothelial carcinoma of the bladder (9,10,31,32). In the study by Almassi *et al* (11) consisting of 131 patients with sarcomatoid carcinoma, it was concluded that there was no significant difference in the reduced recurrence rate with neoadjuvant chemotherapy. As muscle-invasive bladder sarcomatoid carcinoma has a worse prognosis and insensitivity to chemotherapy, more treatment options should be explored.

The present study had several limitations. The study was a single-centre, retrospective study, and patients' baseline characteristics were imbalanced. Propensity score matching only controlled for partially important confounders; therefore, partial selection bias still existed. As sarcomatoid carcinoma is rare, the sample size of this study was inevitably small. Therefore, further prospective study in a large-scale population should be undertaken to validate the results.

In conclusion, the present study showed that patients with BC containing sarcomatoid components had poorer survival and higher recurrence rates than those with non-sarcomatoid carcinoma of the bladder. No difference in prognosis was found between patients with pure sarcomatoid components and those with mixed sarcomatoid components. A sarcomatoid carcinoma component accounting for >50% of a tumour is a predictor of death and recurrence, and can be used as a valuable cut-off point. Pathologists should report the proportion of sarcomatoid carcinoma components, and patients with sarcomatoid carcinoma >50% should be brought to the attention of clinicians.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

GZ and LS conceived and designed the study. SL, YY and ZW collected and analyzed the data. SL and LS wrote the manuscript. LS revised the statistical analysis and revised the manuscript. All authors have read and approved the final manuscript. GMZ, SL, YY, JCM and LJS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The study was performed in accordance with the relevant guidelines and regulations of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of The Affiliated Hospital of Qingdao University (Qingdao, China). All patients involved in the present study provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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