Central European Journal of Urology

ORIGINAL PAPER

UROLOGICAL ONCOLOGY

Sarcopenia is an independent predictor of survival in patients undergoing radical cystectomy for bladder cancer: a single-centre, retrospective study

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Citation: Erdik A, Cimen HI, Atik YT, et al. Sarcopenia is an independent predictor of survival in patients undergoing radical cystectomy for bladder cancer: a single-centre, retrospective study. Cent European J Urol. 2023; 76: 81-89.

Article history
Submitted: Jan. 17, 2023
Accepted: April 15, 2023
Published online: May 5, 2023

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Introduction This study aimed to determine whether sarcopenia is a predictor of overall survival (OS) and cancer-specific survival (CSS) in patients with bladder cancer (BC) undergoing radical cystectomy (RC).
Material and methods Patients who underwent radical cystectomy for BC between September 2016 and June 2022 were retrospectively reviewed. Patients underwent digital computed tomography (CT) scans of the abdomen and pelvis. The skeletal muscle index (SMI) was used to assess sarcopenia using CT images. OS and CSS were estimated using Kaplan-Meier curves. Predictors of CSS and OS were analysed using univariate and multivariate Cox regression models.
Results Of the 84 reviewed patients, 45 (53.6%) had sarcopenia. The median follow-up period for survivors was 70 months. Patients with sarcopenia were older and had a lower BMI, but other preoperative clinical and laboratory parameters were similar to those of patients without sarcopenia. During follow-up, 57 (67.9%) patients died, 39 (46.4%) due to BC. In addition, patients with sarcopenia had worse 5-year OS (24.4% vs 41.0%, p = 0.036) and CSS (35.6% vs 61.5%, p = 0.012) than non-sarcopenic patients. The findings indicate that sarcopenia is an independent predictor of increased CSS (HR, 2.841; p = 0.003) and overall mortality (HR, 2.465; p = 0.004) in multivariate analysis.
Conclusions The results of this study support the view that sarcopenia is an important risk factor for predicting CSS and OS in BC patients undergoing RC.

Key Words: bladder cancer ‹› frailty ‹› radical cystectomy ‹› sarcopenia ‹› survival

INTRODUCTION

Radical cystectomy (RC) with pelvic lymph node dissection, preceded by cisplatin-based neoadjuvant chemotherapy in suitable patients, remains the gold standard treatment for muscle-invasive bladder cancer (MIBC) and high-risk, non-muscle-invasive urothelial carcinoma of the bladder (UCB) resistant to intravesical therapy [1]. Despite surgical and medical advances, in recent studies, early complications and postoperative mortality within 90 days are still high in RC, ranging from 49 to 64% and 4 to 11%, respectively [2, 3].

The indication for RC is generally based on the patient's age, comorbidities, and performance status [4, 5]. Higher age and comorbidities of the operated patients, and an increase in complications and perioperative morbidity observed after RC have been demonstrated in large case reports [6]. Although these factors are essential measurements of overall health, they do not enable precise preoperative clinical decisions. Therefore, a preoperative prognostic factor capable of adequately stratifying patients for proper preoperative management is required [7].

Sarcopenia is characterized by a paucity of muscle mass, which is a key component of frailty. Frailty is a clinical syndrome that suggests decreased physiological reserve. Muscle mass reduction is directly associated with functional impairment, loss of strength, increased likelihood of falling, and loss of autonomy [8]. Data from a prior study suggest that frailty is associated with impaired mobility, disability, poor endurance, and prolonged hospitalization [9].

In addition to comorbidity, frailty and sarcopenia are of specific interest in oncological patients. Sarcopenia is associated with markedly worse survival in patients with several different types of cancer, such as lung, melanoma, breast, renal, and gastrointestinal (pancreatic, colorectal, and hepatobiliary) [10–13]. A recent study reported that sarcopenia is a new predictor of prognosis and risk of postoperative complications [14].

These studies support the notion that it may be difficult to predict which patients will experience inadmissible morbidity or mortality after radical surgery. As such, indicators of functional decline, frailty, sarcopenia, and poor performance may help prepare vulnerable patients for high-risk curative therapies. Therefore, we explored the value of sarcopenia in patients with bladder cancer (BC) who underwent RC.

MATERIAL AND METHODS

Characteristics of patients and surgical intervention

This single-centre, retrospective study was approved by the Institutional Review Board of the Ethics Committee of Sakarya University (approval number: 050.01.04-39877-352). The need for informed consent was waived by the Institutional Review Board of our hospital because of the retrospective design of the study.

We retrospectively reviewed 136 patients who underwent RC with a diagnosis of BC (high-risk or invasive) in our clinic between September 2012 and June 2020. Of these, 10 patients were excluded because they had no axial computed tomography (CT) images for the evaluation of sarcopenia within 90 days before surgery or because they did not have complete data available; 6 patients with other histology of transurethral resection-bladder tumour (TURBT) specimens (3 patients with squamous cell carcinoma and 3 patients with small cell carcinoma) were excluded. In addition, 36 patients with a follow-up period of less than 60 months who were alive were excluded from the study. To assess for possible bias introduced by missing digital imaging, clinicopathologic features and survival of patients with missing data were compared with patients in the study cohort. Hence, the final study cohort consisted of 84 patients for whom CT-based sarcopenia assessment could be performed. Clinical T stage was determined according to the 2009 International Union Against Cancer tumour, node, and metastasis classification system of bladder tumours.

Baseline characteristics and laboratory data, such as age, gender, body mass index (BMI), performance status, Charlson comorbidity index (CCI), operation time (OT), estimated blood loss (EBL), hospital stay (HS), preoperative haemoglobin, albumin, and creatinine levels, and pathological tumour stage and grade were collected.

Surgical technique and follow-up

Low-molecular-weight heparin was started in the evening before the surgery and continued until the 30th postoperative day. Anaerobic antibiotics, third-generation cephalosporins, and elastic compression stockings were used as prophylaxis for infections and thromboembolic events. Open radical cystectomy and extended pelvic lymphadenectomy were performed on the patients using the standard procedure. An ileal conduit was performed on the patients.

Postoperative routine daily examinations and routine laboratory and imaging follow-ups of the patients were performed as standard. The patients were called for control during the RC follow-up in the first and third months. Apart from the follow-ups, readmission status up to 30 days and mortality and complications observed up to the 90th postoperative day were recorded according to the Clavien-Dindo (CD) scoring system [15]. According to the CD classification, major complications were defined as grades 3–5 and minor or no complications were defined as grades 0–2.

Image analysis (preoperative CT-based muscle measurement)

One radiologist (O.F.A) blindly assessed the cross-sectional skeletal muscle surface (cm^2) at the level of the transverse process of L3 on CT images before treatment [16]. Measurements were performed using Osirix™ version 7.0 (32-bit; http://www.osirix-viewer.com). The "Grow Region (2D/3D Segmentation)" tool automatically selected all skeletal muscle mass in one transversal CT image. The distinction between different tissues is based on Hounsfield units (HU). A threshold range of -30 to +110 HU

was used for the skeletal muscle [16]. The psoas, paraspinal, transverse abdominal, external oblique, internal oblique, and rectus abdominis muscles were measured (Figure 1). Manual adjustment of the selected areas was performed if necessary. The averages of the 2 measurements were used for calculations. Intra-interobserver reliability was evaluated, and the median value was used for further analysis.

Clinical assessments

In the present study, according to the definition by Martin et al., sarcopenia was defined as a skeletal muscle index (SMI) <43 cm^2/m^2 for men with BMI <25 kg/m^2, SMI <53 cm^2/m^2 for men with BMI ≥25 kg/m^2, and SMI <41 cm^2/m^2 for women [17].

Statistical analysis

The significance tests used to compare patients with and without sarcopenia were the Mann-Whitney U test for continuous variables and the chi-squared test for categorical variables. The primary outcomes of interest were cancer-specific survival (CSS) and overall survival (OS). CSS and OS were estimated using the Kaplan-Meier method and compared using the log-rank test. Disease recurrence was defined as local pelvic tumour recurrence or distant metastasis occurring >30 days after RC, excluding metachronous upper tract cancers. Associations between time to death from any cause and death from UCB were evaluated using univariate and multivariate Cox proportional hazards regression models and summarized with hazard ratios (HR) and 95% confidence intervals (95% CIs). All features that were found to be statistically significant predictors on univariate analysis for both outcomes of interest were included in the final multivariable models. Statistical analyses were conducted with SPSS (version 26, Chicago, IL, USA). All tests were 2-sided, with a p-value <0.05 considered statistically significant.

RESULTS

Cohort

A total of 84 patients, 78 (92.9%) of whom were male, were enrolled in this study. The median age of the patients was 69 (min–max 48–92) years. Median SMI was 46.89 (min–max 27.18–69.39) cm^2/m^2 in men and 39.02 (min–max 22.46–58.02) cm^2/m^2 in women. The overall prevalence of sarcopenia within the population in the current study was 45 of 84 (53.6%) according to the Martin criteria [17], including 66.7% of women (4 of 6 women) and 52.6% of men (41 of 78 men).

Sarcopenia patients were significantly older (median preoperative age of 72 years vs 64 years; p = 0.043) but were otherwise similar regarding gender, preoperative laboratory measurements, CCI, American Society of Anaesthesiologists score (ASA), tumour node metastasis stage (TNM), presence of positive soft tissue surgical margin, history of intravesical therapy, perioperative or postoperative complications, lymphovascular invasion (LVI), administration of neoadjuvant or adjuvant chemotherapy, HS, EBL, presence of postoperative blood transfusion, OT, drain removal time, and oral food intake (p >0.05 for all, Table 1).

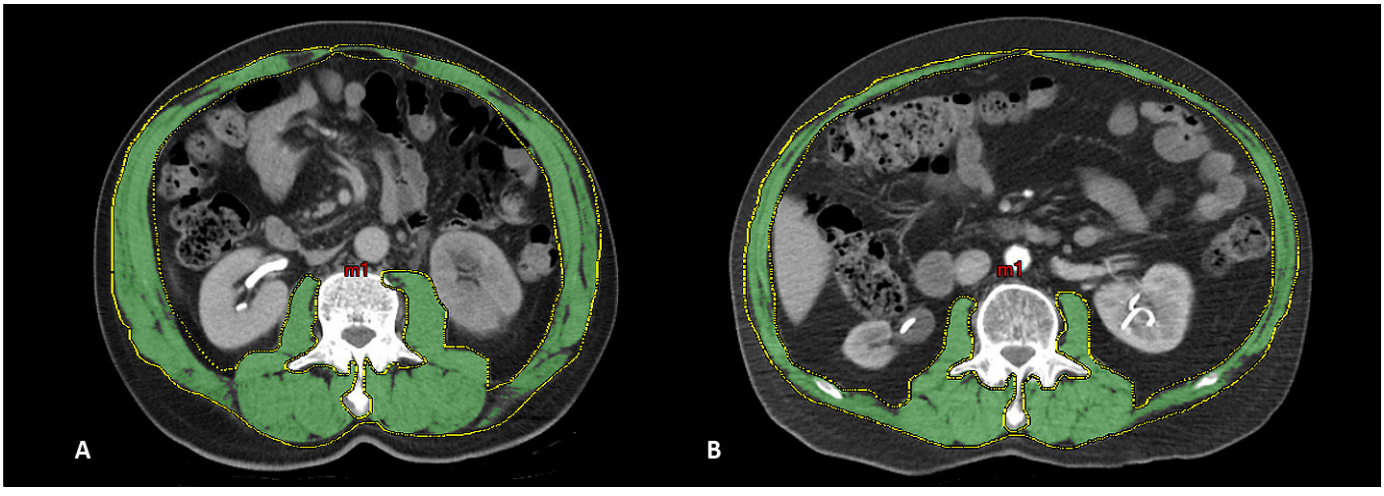

Figure 1. *Axial CT images at the third lumbar vertebra region with skeletal muscle highlighted in green. Figure A represents a male non-sarcopenic patient with a skeletal muscle index (SMI) of 58.1, and Figure B represents a sarcopenic male patient with an SMI of 38.7. The green regions represent the skeletal muscle, identified by attenuation limits of -29 to +110 Hounsfield units (HU). The SMI is calculated by dividing the cross-sectional skeletal muscle area (cm^2) by the patient's height squared (m^2).*

In addition, the median BMI was significantly lower in sarcopenic patients compared with their counterparts (25.00 vs 28.40 kg/m^2; p <0.001, respectively). For OS, within 90 days after surgery, there was a significant difference between the sarcopenic and non-sarcopenic groups. Within 90 days, 14 (16.7%) patients died, of whom 11 (11/45, 24.4%) were sarcopenic and 3 (3/39, 7.7%) were non-sarcopenic. Patient characteristics are summarized in Table 1.

Table 1. *Demographic and clinicopathological characteristics of the patient cohort with and without sarcopenia*

Variables	Entire Cohort (n = 84)	Sarcopenic patients (n = 45)	Non-sarcopenic patients (n = 39)	p-value
Median age at RC, years (min-max)	69 (48–92)	72 (48–84)	64 (48–92)	0.043[a]
Sex, no. (%)				
Female	6 (7.1)	4 (8.9)	2 (5.1)	0.681[b]
Male	78 (92.9)	41 (91.1)	37 (94.9)	
Median BMI (kg/m^2) (min–max)	25.10 (19.2–36.0)	25.00 (19.4–28.5)	28.40 (22.6–36.0)	<0.001[a]
Median preoperative albumin, g/dL (min–max)	3.50 (2.3–4.4)	3.50 (2.3–4.4)	3.70 (2.3–4.4)	0.137[a]
Median preoperative creatinine, mg/dL (min–max)	1.08 (0.50–3.50)	1.09 (0.50–3.50)	1.08 (0.63–2.93)	0.497[a]
Median preoperative haemoglobin, g/dL (min–max)	11.95 (8.40–15.60)	11.70 (8.40–15.60)	12.10 (9.00–15.00)	0.504[a]
Charlson comorbidity index, no. (%)				
≤2	8 (9.5)	4 (8.9)	4 (8.9)	0.066[b]
3–4	48 (57.1)	21 (46.7)	27 (59.2)	
≥5	28 (33.3)	20 (44.4)	8 (20.5)	
ASA score, no. (%)				
≤2	38 (45.2)	19 (42.2)	19 (48.7)	0.551[b]
≥3	46 (54.8)	26 (57.8)	20 (51.3)	
Clavien–Dindo				
0	32 (38.1)	14 (31.1)	18 (46.2)	0.341[b]
1–2	28 (33.3)	16 (35.6)	12 (30.8)	
≥3	24 (28.6)	15 (33.3)	9 (23.1)	
Neoadjuvant chemotherapy, no. (%)	4 (4.8)	3 (6.7)	1 (2.6)	0.620[b]
Adjuvant chemotherapy, no. (%)	25 (29.8)	13 (28.9)	12 (30.8)	0.851[b]
Pathologic tumour stage, no. (%)				
≤pT1	14 (16.7)	6 (13.3)	8 (20.5)	0.440[b]
pT2	24 (28.6)	11 (24.4)	13 (33.3)	
pT3	26 (31.0)	17 (37.8)	9 (23.1)	
pT4	20 (23.8)	11 (24.4)	9 (23.1)	
Pathologic N classification, no. (%)				
pN0/x	56 (66.7)	30 (66.7)	26 (66.7)	0.787[b]
pN1	17 (20.2)	10 (22.2)	7 (17.9)	
≥pN2	11 (13.1)	5 (11.1)	6 (15.4)	
History of intravesical therapy				
Present	16 (19.0)	6 (13.3)	10 (25.6)	0.152[b]
Absent	68 (81.0)	39 (86.7)	29 (74.4)	
Lymphovascular invasion, no. (%)	36 (42.9)	20 (44.4)	16 (41.0)	0.752[b]
Perioperative complication, no. (%)	7 (8.3)	4 (8.9)	3 (7.7)	0.843[b]
Postoperative complication, no. (%)	52 (61.9)	31 (68.9)	21 (53.8)	0.157[b]
Presence of positive soft tissue surgical margin, no. (%)	14 (16.7)	8 (17.8)	6 (15.4)	0.769[b]
Operative time (minutes) (min–max)	320 (169–598)	320 (169–598)	320 (200–490)	0.809[a]
Estimated blood loss (ml) (min–max)	700 (250–4500)	700 (250–4500)	700 (250–2100)	0.939[b]
Hospital stay (days) (min–max)	11 (4–49)	12 (6–49)	10 (4–32)	0.200[a]
Oral food intake (days) (min–max)	4 (1–18)	4 (2–18)	4 (1–9)	0.208[a]
Drain removal (days)	9 (3–44)	9 (3–44)	9 (3–22)	0.658[a]
Presence of postoperative blood transfusion, no (%)	46 (54.8)	21 (46.7)	25 (64.1)	0.109[b]
30-day readmission, no. (%)	16 (19.0)	8 (17.6)	8 (20.5)	0.750[b]
90-day readmission, no. (%)	17 (20.2)	12 (26.7)	5 (12.8)	0.115[b]
90-day mortality, no. (%)	14 (16.7)	11 (24.4)	3 (7.7)	0.040[b]

[a]Mann-Whitney U test, [b]chi-square test
ASA – American Society of Anaesthesiologists; BMI – body mass index; RC – radical cystectomy; no – number of patients

Patients' risk of death (all-cause) and bladder cancer after radical cystectomy

The median follow-up period for survivors was 70 months (min–max 60–111 months). The median overall follow-up period was 20.50 months (min–max 1–111 months). Fifty-seven (67.9%) patients died, 39 (46.4%) due to UCB. In addition, patients with sarcopenia had significantly decreased 5-year OS (24.4% vs 41.0%, p = 0.036) and CSS (35.6% vs 61.5%, p = 0.012, Figure 2) than non-sarcopenic patients.
On univariate analysis, the presence of sarcopenia and higher CCI, pathological T classification, preoperative creatinine level, LVI, presence of perioperative

Table 2. *Univariate and multivariable Cox regression models addressing prediction of overall survival after radical cystectomy for urothelial carcinoma of the bladder*

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.022 (0.995–1.050)	0.115	–	–
Gender (ref. men)	1.498 (0.468–4.975)	0.496	–	–
BMI	0.968 (0.913–1.027)	0.286	–	–
Sarcopenia (ref. absence)	1.737 (1.020–2.958)	0.042	2.465 (1.327–4.578)	0.004
CCI				
CCI: 3–4 (ref. <3)	1.244 (0.653–2.372)	0.507	1.075 (0.528–2.189)	0.842
CCI: ≥5 (ref. <3)	3.282 (1.734–6.214)	<0.001	2.789 (1.304–5.964)	0.008
ASA score ≥3 (ref. ≤2)	1.576 (0.927–2.679)	0.093	–	–
pT stage				
pT2 (ref. ≤pT1)	3.460 (1.001–11.959)	0.050	4.320 (1.176–15.872)	0.028
pT3 (ref. ≤pT1)	6.890 (2.044–23.218)	0.002	5.444 (1.487–20.213)	0.011
pT4 (ref. ≤pT1)	10.801 (3.125–37.331)	<0.001	5.653 (1.353–23.607)	0.018
pN stage				
pN+ stage (reference: pN0/x)	1.696 (0.995–2.893)	0.052	–	–
Preoperative albumin	0.802 (0.536–1.201)	0.284	–	–
Preoperative creatinine	1.867 (1.200–2.906)	0.006	1.409 (0.872–2.274)	0.161
Preoperative haemoglobin	0.884 (0.750–1.042)	0.143	–	–
Adjuvant chemotherapy (reference: not administered)	1.153 (0.663–2.005)	0.614	–	–
Presence of LVI (ref. absence)	2.825 (1.665–4.822)	<0.001	1.569 (0.793–3.102)	0.196
Perioperative complication (ref. absence)	2.880 (1.221–6.793)	0.016	1.744 (0.610–4.987)	0.300
Positive STSM (ref. absence)	2.685 (1.400–5.147)	0.003	1.700 (0.779–3.714)	0.183
Postoperative blood transfusion (ref. absence)	0.911 (0.538–1.514)	0.727	–	–

CI – confidence interval; CCI – Charlson comorbidity index; LVI – lymphovascular invasion; STSM – soft tissue surgical margin; BMI – body mass index; OR – odds ratio; ASA – American Society of Anaesthesiologists

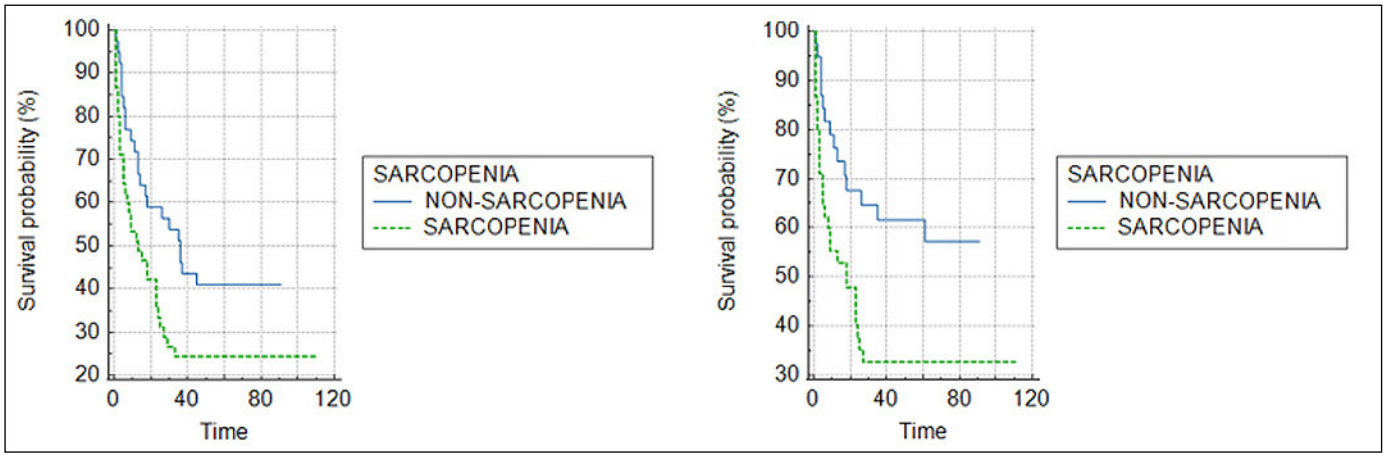

Figure 2. *Kaplan-Meier curves depicting overall survival (left) and cancer-specific survival (right) are shown in patients with and without sarcopenia.*

Table 3. *Univariate and multivariable Cox regression models addressing the prediction of cancer-specific survival after radical cystectomy for urothelial carcinoma of the bladder*

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age	1.015 (0.983–1.047)	0.357	–	–
Gender (ref. men)	1.109 (0.343–3.584)	0.863	–	–
BMI	0.961 (0.897–1.029)	0.254	–	–
Sarcopenia (ref. absence)	2.155 (1.153–4.028)	0.016	2.841 (1.425–5.664)	0.003
CCI				
CCI: 3–4 (ref. <3)	0.666 (0.253–1.752)	0.410	–	–
CCI: ≥5 (ref. <3)	1.018 (0.373–2.781)	0.972		
ASA score ≥3 (ref. ≤2)	1.816 (0.981–3.361)	0.058	–	–
pT stage				
pT2 (ref. ≤pT1)	3.377 (0.739–15.425)	0.116	3.259 (0.698–15.218)	0.133
pT3 (ref. ≤pT1)	7.100 (1.629–30.942)	0.009	4.571 (0.991–21.073)	0.051
pT4 (ref. ≤pT1)	12.754 (2.873–56.622)	0.001	8.059 (1.550–41.990)	0.013
pN stage				
pN+ stage (reference: pN0/x)	1.747 (0.881–3.462)	0.110	–	–
Preoperative albumin	0.966 (0.603–1.548)	0.886	–	–
Preoperative creatinine	1.381 (0.791–2.413)	0.256	–	–
Preoperative haemoglobin	0.924 (0.767–1.112)	0.403	–	–
Adjuvant chemotherapy (reference: not administered)	1.274 (0.688–2.359)	0.441	–	–
Presence of LVI (ref. absence)	2.979 (1.612–5.504)	<0.001	1.794 (0.882–3.648)	0.107
Perioperative complication (ref. absence)	2.882 (1.120–7.416)	0.028	2.051 (0.743–5.659)	0.165
Positive STSM (ref. absence)	2.792 (1.353–5.761)	0.005	1.624 (0.709–3.722)	0.252
Postoperative blood transfusion (ref. absence)	1.040 (0.574–1.984)	0.897	–	–

CI – confidence interval; CCI – Charlson comorbidity index; LVI – lymphovascular invasion; STSM – soft tissue surgical margin

complications, and positive soft tissue surgical margin (STSM) were found to be significantly associated with a patient's risk of death – from overall survival (Table 2). Although LVI, presence of perioperative complications, positive STSM, and preoperative creatinine level approached statistical significance in the univariate analysis, they were not found to be significant in the multivariable model. In multivariable analysis, higher CCI, pathological T classification, and the presence of sarcopenia were significantly associated with increased all-cause mortality after RC (HR, 2.465; 95%Cl 1.327–4.578; p = 0.004) (Table 2).
In univariate Cox analysis, sarcopenia, higher pathological tumour (pT) stage, LVI, positive STSM, and the presence of perioperative complications were significantly associated with decreased CSS after RC for UCB. On multivariable analysis using a Cox proportional hazards regression model, clinical T stage and presence of sarcopenia (HR, 2.841; 95%Cl 1.425–5.664; p = 0.003) were significantly associated with CSS in patients undergoing RC (Table 3).

DISCUSSION

Sarcopenia comprises a loss of skeletal muscle, and it can be defined as primary or secondary [18]. Sarcopenic patients have lower nutritional and swallowing functions than non-sarcopenic patients [19].
The present study was designed to determine the intensity of sarcopenia and its effect on survival in a cohort of patients undergoing RC for UCB. First, we defined that in this cohort of patients with UCB who underwent surgery, 53.6% were classified as sarcopenic preoperatively, according to Martin et al. [17]. The prevalence of sarcopenia in the United States and Europe has been reported to be 5–13% in the 7th decade and 11–50% in those over 80 years old [20]. A possible explanation for this might be that the high prevalence of sarcopenia in this UCB cohort, combined with the high percentage pT3 and pT4 grade patients and high overall CCI and ASA score, had a negative impact on the health of patients with UCB undergoing RC.
Prior studies have shown that the 90-day mortality rates were 4–11.2% [3, 21]. In this RC cohort, 14 patients (16.7%) died within 90 days of surgery. There are several possible explanations for this finding. First, only 28.6% (n = 24) of patients who underwent surgery for muscle-invasive bladder tumours had pathological stage pT2. Additionally, 31.0% (n = 26) of the patients were upstaged to pT3, and 23.8% (n = 20) to pT4. Second, of the 84 patients, one-third

had an overall CCI score of 5 or higher and over half (54.8%) had an ASA score of 3 or more.

Although our 90-day mortality rate was high and not comparable to that of previous studies, all patients experienced complicated postoperative events (myocardial infarction, pulmonary embolism, infectious complications, etc.). The primary cause of death in 11 of the 14 patients in the current study was rapid progression of BC. Therefore, the mortality rate of patients was relatively high. May et al. revealed that 35% of patients diagnosed with pT1 had their pathology upstaged after radical cystectomy [22]. Therefore, it is noted that patients in the high-risk group may have non-organ-confined UBC and should be operated promptly. In addition, these findings may help us understand the potential significance of using SMI to risk-stratify patients before surgery.

Also, the most important finding was that sarcopenia was independently associated with increased risks of postoperative CSS (HR, 2.841; 95%CI, 1.425–5.664; p = 0.003) and overall mortality (HR, 2.465; 95%CI, 1.327–4.578; p = 0.004). These results are consistent with those of previous studies. Several studies have investigated the effects of sarcopenia on survival. A study by Mayr et al. indicated that sarcopenia was associated with worse 5-year OS (38.3% vs 50.5%; p = 0.002) and 5-year CSS (49.5% vs 62.3%; p = 0.016). Moreover, sarcopenic patients had a 1.43-fold greater risk of cancer-related death within 5 years after RC (HR, 1.42; 95%CI, 1.00–2.02; p = 0.048). Sarcopenic patients had a 1.42-fold greater risk of death within 5 years after RC than non-sarcopenic patients (HR, 1.43; 95%CI 1.09–1.87; p = 0.01) [23]. Psutka et al. analysed the data from 205 patients followed for 6.7 years and concluded that sarcopenia was associated with worse 5-year OS (39 vs 70%; p = 0.003) and CSS (49 vs 72%; p = 0.003) compared with non-sarcopenic patients. Similarly, sarcopenia was an independent predictor of OS (HR, 1.93; 95%CI 1.23–3.00; p = 0.004) and CSS (HR, 2.14; 95%CI 1.24–3.71; p = 0.007) [14]. In a retrospective single-centre cohort of 136 patients, Hirasawa et al. revealed that sarcopenia was an independent predictor of CSS (HR, 2.3; 95%CI 1.2–4.4; p = 0.015) [7]. Contrary to previously published studies, Smith et al. reported no significant difference between sarcopenia and one-year or 2-year OS [24]. However, this analytical method has several limitations. The median follow-up duration of this study was relatively low at 16 months, and sarcopenia was evaluated by total psoas area (TPA), which lacks standardized reference values. Another study failed to demonstrate any significant differences in survival between patients with TPA. Ahmadi et al. found a significant relationship between TPA and 6-month and one-year OS in a univariate analysis. However, TPA did not seem to be an independent predictor of survival after multivariate analysis [25].

Several studies have described the role of survival with comorbidity scores (ACE-27, CCI, etc.) after RC for UBC [26, 27]. The present study findings suggest that sarcopenia is a predictor of survival in UCB, independently of the severity of comorbidity, ASA score, and performance status (such as ECOG). Clinicians can evaluate sarcopenia and SMI using free software and CT images, without special training [23]. The decrease in skeletal muscle mass is potentially reversible; therefore, sarcopenia has gained prominence in clinical practice [18]. Resistance training and sufficient protein and calorie intake are essential components in managing patients with sarcopenia [28, 29]. Alternatively, anabolic steroids, such as oxandrolone, have demonstrated some benefit in preventing, delaying, or reversing sarcopenia with minimal toxicity and have been approved by the US Food and Drug Administration [30].

The findings of this study have some limitations. First, we collected data from 136 patients in a non-consecutive fashion owing to the retrospective nature of the study. Second, 10 patients who underwent RC during this surgery did not have digital CT scans available for body composition analysis and were therefore excluded from the study. A likely explanation is that the study institution is a tertiary referral centre in our region; the referring hospital may have provided imaging, and referral centres had only digital imaging reports. In addition, because the study centre was a referral hospital, a small group of patients were excluded from the study because they were followed up by the referral hospital. Third, in observational studies, the potential for bias from the loss of patients with MIBC is likely to be associated with the disease. To avoid this bias, the clinicopathological characteristics and survival of patients with missing data were compared with those of patients in the study cohort to determine the potential for bias due to loss of patients. No significant differences were found between the clinicopathological features, CCI or CD scores, and postoperative outcomes of the 2 groups. Finally, considering its retrospective nature, this study was unable to demonstrate that SMI correlates with other frailty metrics such as performance status on patient questionnaires and nutritional status.

CONCLUSIONS

The current data highlight the importance of sarcopenia as an essential risk factor for predicting CSS

and all-cause mortality in patients with UCB undergoing RC. These findings will help other researchers to design preoperative regulations to modify skeletal muscle swallowing, which may result in improved outcomes after RC.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

The present study protocol was reviewed and approved by the Institutional Review Board of Sakarya University College of Medicine (approval number: 050.01.04-39877-352). Informed consent was obtained from all subjects when they were enrolled.

AUTHORS' CONTRIBUTIONS

Research conception and design: AE, HIC. Data acquisition: AE, DG. Statistical analysis: AE, YTA. Data analysis and interpretation: HIC, OK. Drafting of the manuscript: AE, FH. Critical revision of the manuscript: HIC, HSS. Administrative, technical, or material support: OFA. Supervision: OK, HSS. Approval of the final manuscript: HIC, OK, FH, HSS.

All authors have read and approved the manuscript.

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