



Original article

Is sarcopenia and sarcopenic obesity associated with clinical and pathological outcomes in patients undergoing radical nephroureterectomy?

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Abstract

Purpose: To investigate the association between sarcopenia and sarcopenic obesity on clinical, perioperative, and oncologic outcomes in patients with upper-tract urothelial carcinoma (UTUC) undergoing radical nephroureterectomy (RNU).

Methods: Retrospective review of our institutional UTUC database was performed to identify all patients who underwent radical nephroureterectomy from 2002–2016. Skeletal Muscle Index (SMI) was measured at the L3 vertebral level and standardized according to patient height (cm^2/m^2). Sarcopenia was defined as $<55 \text{ cm}^2/\text{m}^2$ for men and $<39 \text{ cm}^2/\text{m}^2$ for women. Sarcopenic obesity was also assessed in patients with BMI $>30 \text{ kg}/\text{m}^2$. Unadjusted logistic regression and Wilcoxon rank sum tests examined the relationship between sarcopenia and variables.

Results: A total of 100 patients (66 men and 34 women) with a mean age of 68 years, BMI of 30, Charlson comorbidity index of 4.0, tumor size of 3.5, and SMI of $50.8 \text{ cm}^2/\text{m}^2$ were included. Furthermore, 42 patients (42%) were sarcopenic, and 18 patients (18%) had sarcopenic obesity. Median EBL was 150 ml, OR duration was 322 minutes, and length of stay was 5.0 days. Sarcopenia was associated with several clinical factors including decreasing BMI, male sex, and coronary artery disease, albeit without association with any perioperative or oncologic outcomes. Sarcopenic obesity was similarly associated with several clinical variables including male sex, diabetes mellitus, hyperlipidemia, as well as increased EBL ($P = 0.047$) and non-bladder cancer disease relapse ($P = 0.049$).

Conclusions: This contemporary cohort of patients undergoing RNU highlights the association of nonmodifiable risk factors with sarcopenia and disease relapse with sarcopenic obesity. Larger studies are necessary to further validate these observations. © 2017 Elsevier Inc. All rights reserved.

Keywords: Upper-tract urothelial carcinoma; Sarcopenia; Obesity; Radical nephroureterectomy

1. Introduction

Upper-tract urothelial carcinoma (UTUC) is an uncommon disease that comprises 5% to 10% of all urothelial

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tumors [1]. The National Cancer Institute's Surveillance Epidemiology and End Results (SEER) database collectively refers to kidney and renal pelvis cancer as a single entity [2]; however, upper-tract cancers are pathologically distinct tumors that require an entirely separate therapeutic approach. The incidence of UTUC has steadily increased for both renal pelvic and ureteral lesions [3], and high-grade or invasive disease is associated with a poor prognosis. Although radical nephroureterectomy (RNU) remains the gold standard for management of nonmetastatic renal pelvic

and proximal UTUC, it is an invasive procedure with increased potential postoperative morbidity, particularly for the elderly or patients with advanced disease. The reliability of current stratification systems for identifying higher-risk surgical patients, including the American Society of Anesthesiologists (ASA) score, Charlson comorbidity index (CCI), and Eastern Cooperative Oncology Group (ECOG) performance status, has recently been questioned [4,5], and ultimately prompting recent investigations toward alternative preoperative measures to assess patient frailty.

Sarcopenia, defined as degenerative wasting of skeletal muscle mass, is a novel potential risk marker for predicting postoperative outcomes [6]. In patients with urothelial carcinoma, women with sarcopenia who underwent radical cystectomy have been shown to have an increased risk of major complications [7]. Reports of worsened overall survival and disease-specific survival have been previously reported in the general surgery literature [4,8,9]. Those patients with sarcopenia associated with obesity, recognized independently as “sarcopenic obesity,” likewise have an associated increased risk of mortality [6].

To date, few data exist regarding the association of sarcopenia and sarcopenic obesity on perioperative and oncologic outcomes in patients undergoing RNU. The aim of the present study, therefore, is to better determine whether sarcopenia or sarcopenic obesity in a contemporary Western UTUC population may serve as a clinical marker for adverse perioperative events or oncologic outcomes.

2. Methods

A retrospective review of the prospectively maintained UTUC database at Penn State Health Milton S. Hershey Medical Center identified 133 patients who underwent RNU from 2002 to 2016. Clinical variables for analysis included age, sex, race, BMI, ECOG score, ASA classification, CCI, presenting symptoms, and select comorbidities. Complications were annotated by the Clavien-Dindo grading system with distribution of complications previously published. Patients were excluded from the cohort if perioperative imaging, postoperative data, or oncologic follow-up were incomplete for review. With such criteria, our final cohort of analysis was 100 patients.

Skeletal muscle area (SMA, cm^2) was determined from pre- or early postoperative abdominal CT scans utilizing the Aquarius iNtuition software (Version 4.4.11, TeraRecon, Inc., San Mateo, CA). Available cross-sectional imaging closest to the day of surgery was preferentially selected. SMA measurements were performed at the L3 mid-vertebral level by manually outlining the circumferential abdominal and lumbar muscle groups (Fig.). Imaging measurements were performed independently by 2 investigators (N.J.K., S.B.) after completing a quality analysis/quality control (QA/QC) standardized exercise prepared by a third investigator (N.S.) with concordant results

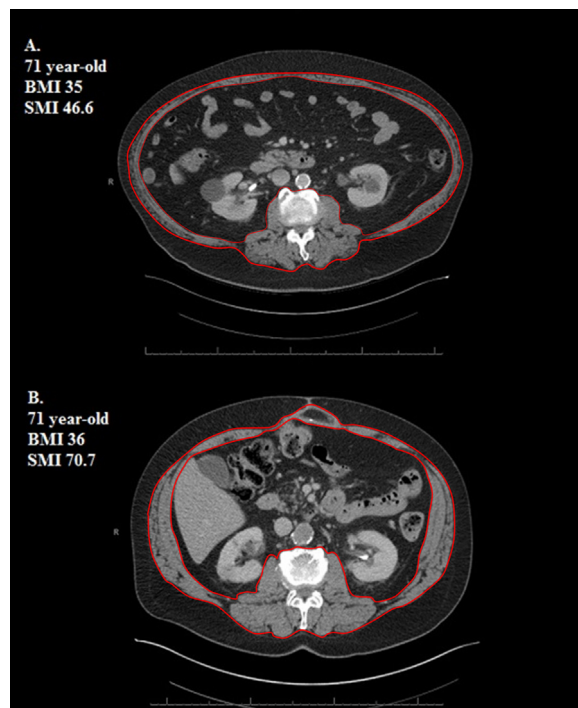


Fig. Comparison of sarcopenic (A) vs. nonsarcopenic (B) skeletal muscle mass at the L3 mid-vertebral level in male patients with similar age and BMI. (Color version of figure is available online.)

(concordance index 0.90). The Hounsfield Unit attenuation threshold ranged from -29 to $+150$ in order to incorporate skeletal muscle density [10]. The Skeletal Muscle Index (SMI, cm^2/m^2) was calculated from SMA and normalized to patient height squared. Sarcopenia was defined as $\text{SMI} < 55 \text{ cm}^2/\text{m}^2$ for men and $< 39 \text{ cm}^2/\text{m}^2$ for women according to international consensus reference values [11]. Sarcopenic obesity was defined based on WHO criteria for obesity ($\text{BMI} \geq 30$) in those patients with sarcopenia [12].

For oncologic outcomes, patients were followed every 3 to 4 months for the first year following RNU, every 6 months from the second through the fifth year, and annually thereafter. Follow-up consisted of a history, physical examination, routine blood work and serum chemistry studies, urinary cytology, chest radiography, cystoscopic evaluation of the urinary bladder, and radiographic evaluation of the contralateral upper urinary tract. Elective bone scans, chest computerized tomography (CT), or magnetic resonance imaging were performed when clinically indicated. Non-bladder cancer relapse includes urothelial cancer recurrence in liver, lung, bone, brain, retroperitoneum, and any other sites outside the urinary bladder. Mean length of follow-up was 31.2 months (range: 5.0–122.0).

Descriptive statistics were utilized to summarize all variables. Comparisons between patients with and without sarcopenia or sarcopenic obesity were performed using several methods depending on the outcome variable. Logistic regression was used for patient-specific and

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