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Original article

Sarcopenia as a predictor of overall survival after cytoreductive nephrectomy for metastatic renal cell carcinoma

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Abstract

Purpose: Cytoreductive nephrectomy (CN) is a therapeutic consideration in patients with metastatic renal cell carcinoma (mRCC). We hypothesized that sarcopenia, a novel marker of nutritional status, is a predictor of survival after CN.

Materials and methods: Of 105 patients who underwent CN at our institution for mRCC, 93 had preoperative imaging available for analysis. Skeletal muscle index was calculated on axial images at the third lumbar vertebrae, and a threshold skeletal muscle index of $<43\ cm^2/m^2$ in men with a body mass index (BMI) $<25\ kg/m^2$, $<53\ cm^2/m^2$ in men with a BMI $>25\ kg/m^2$, and $<41\ cm^2/m^2$ in women was used to classify patients as sarcopenic vs. nonsarcopenic. This classification was then retrospectively correlated with overall survival (OS).

Results: Overall, 27 patients (29.0%) had sarcopenia before surgery. Sarcopenic patients received neoadjuvant systemic therapy more often ($P = 0.022$), had lower BMI ($P = 0.001$), had a higher incidence of hypoalbuminemia before surgery ($P = 0.035$), received more blood transfusions perioperatively ($P = 0.006$) owing to lower preoperative hemoglobin levels ($P = 0.001$), and had longer length of stay after surgery ($P = 0.02$). Median OS in sarcopenic patients was 7 months (95% CI: 0.8–13.2) vs. 23 months (95% CI: 12.4–33.6) in nonsarcopenic patients. On multivariate analysis, sarcopenia was an independent predictor of OS (hazard ratio = 2.13, 95% CI: 1.15–3.92; $P = 0.016$) in addition to number of metastatic sites >2 (hazard ratio = 2.09, 95% CI: 1.24–3.53; $P = 0.006$).

Conclusions: Sarcopenia can be an important prognostic factor associated with worse OS after CN for mRCC.

Keywords: Sarcopenia; Survival; Metastatic; Renal cell carcinoma; Cytoreductive nephrectomy

1. Introduction

Although prognostic criteria have been developed to predict survival and risk stratify patients with metastatic renal cell carcinoma (mRCC) undergoing cytoreductive nephrectomy (CN), few have concentrated on preoperative nutritional markers [1–4]. However, it is well known that cancer-related cachexia can limit response to therapy and affect survival [5]. Poor nutritional status has also been shown to adversely affect outcomes in the treatment of other abdominal malignancies [6]. Sarcopenia, defined as loss of skeletal muscle mass, is an emerging index of nutritional status that has recently been studied in patients with cancer [7,8]. Sarcopenia can also consistently be determined by measuring the lumbar skeletal muscle index (SMI), which can be calculated using the cross-sectional area of the muscle identified at the third lumbar vertebrae (L3) seen on axial computed tomography (CT) or magnetic resonance (MR) images [9,10].

The purpose of this study was to determine if sarcopenia could be a useful predictor of overall survival (OS) in patients undergoing CN for mRCC. We hypothesize that sarcopenia would serve as an important prognostic tool for OS in this cohort, broadening its usage not only in the

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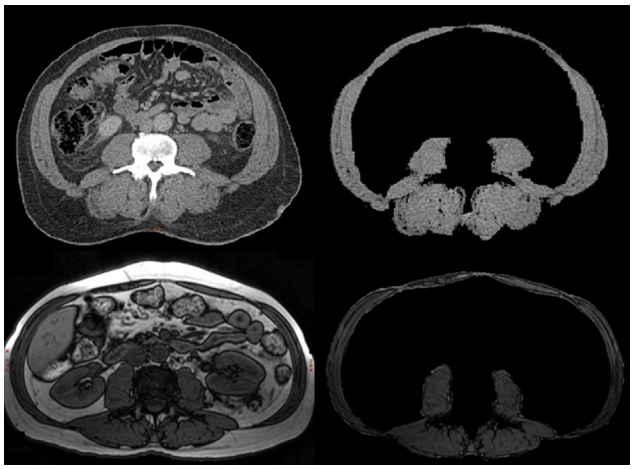

Fig. 1. Skeletal muscle isolation at L3 on an axial CT or MR (T2-weighted) image using attenuation/signal intensity thresholds for segmentation.

pretreatment counseling of patients with mRCC but also in clinical decision making.

2. Methods

2.1. Data collection

After institutional review board approval, we retrospectively identified 105 patients who underwent CN for mRCC at our institution between March 2001 and June 2014. Metastatic disease was confirmed through biopsy or radiographic imaging. Patients with available demographic information, clinical data, postoperative follow-up, and axial CT or MR images 90 days before surgery were included in the analyses. We excluded 12 patients who did not have accessible preoperative imaging or appropriate follow-up, leaving 93 patients in our study population. The median time interval between the date of imaging and the surgical date was 33 days (interquartile range [IQR]: 14–46 d). Preoperative laboratory values were obtained from solitary measurements drawn 1 to 2 weeks before CN. Complications were captured via retrospective medical record review of the patient's postoperative course and subsequent clinic visits within 30 days of surgery.

Clinical node positivity was defined as any retroperitoneal or hilar lymph node more than 1 cm in size on preoperative imaging, and nodal disease was not included as a metastatic site. The Heng score was measured based on the described prognostic criteria with good defined as a score of 0, intermediate defined as a score of 1 to 2, and poor defined as a score ≥ 3 [1]. The Eastern Oncology Cooperative Group (ECOG) performance status in addition to Karnofsky score was identified in a prospective fashion during the patient's initial clinic visit within 2 months before surgery. Usage of neoadjuvant or adjuvant systemic therapy (primarily tyrosine kinase inhibitors) was documented. The Clavien scoring system was used to categorize 30-day complications, and the vital status of each patient at the available follow-up was also noted. Follow-up was defined from the time of surgery until the date of last contact or date of death, and the primary outcome of the study was OS.

2.2. Image analysis

With the guidance of a fellowship-trained radiologist (J.T.C.), we measured the SMI at L3 on axial CT ($n = 74$) or T2-weighted MR ($n = 19$) images for our study group in concordance with prior literature [9–11]. Preoperative images were transferred to and processed on an AW Server software package (version 2.0; General Electric, Fairfield, CT). The software required selection of 4 consecutive axial images to activate the processing tools necessary to calculate skeletal muscle volume. We identified abdominal images centered at the level of L3 which best demonstrated both transverse processes. Image collimation or slice thickness varied from 1 to 15 mm among the available preoperative examination results. From these images, all visible skeletal muscles including the rectus abdominis; internal, external, and lateral obliques; psoas; quadratus lumborum; and erector spinae muscles were selected using attenuation or signal intensity threshold segmentation tools, while excluding all bony and other soft tissue structures such as fat, vasculature, the liver, the bowel, and the spinal cord (Fig. 1). Standard minimum and maximum attenuation or signal intensity thresholds were not used, but rather adjusted manually for each patient to achieve the most accurate muscle segmentation. From this, a 3-dimensional volumetric calculation of skeletal muscle was performed, and this volume was divided by the corresponding slice thickness to measure the cross-sectional area on a single image (Fig. 2).

Lumbar SMI was then calculated by dividing the cross-sectional area (cm^2) by the patient's height (m^2), and it was reported as cm^2/m^2. Using sex-specific definitions of sarcopenia stratified according to body mass index (BMI) and recently validated in more than 1,473 patients with cancer, a threshold SMI of $<43\ cm^2/m^2$ in men with a BMI $<25\ kg/m^2$, $<53\ cm^2/m^2$ in men with a

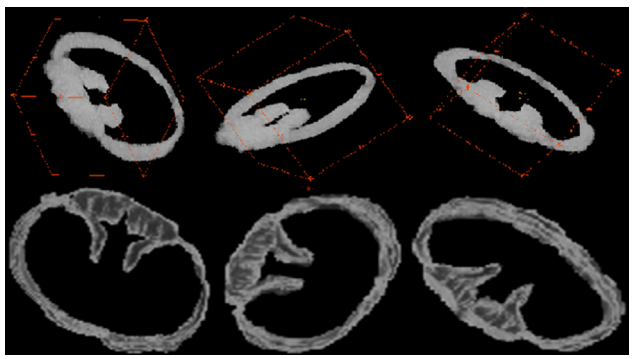

Fig. 2. The 3-dimensional volumetric calculation of isolated skeletal muscle on 4 contiguous axial images at L3.