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Sarcopenia is not associated with morbidity, mortality, or recurrence after esophagectomy for cancer

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ABSTRACT

Background: Sarcopenia is associated with increased morbidity and mortality in hepatic, pancreatic and colorectal cancer. We examined the effect of sarcopenia on morbidity, mortality, and recurrence after resection for esophageal cancer.
Methods: Retrospective review of consecutive esophagectomies from 2010 to 2015. Computed tomography studies were analyzed for sarcopenia. Morbidity was analyzed using Fischer's test and survival data with Kaplan Meier curves.
Results: The sarcopenic group ($n = 127$) had lower BMI, later stage disease, and higher incidence of neoadjuvant radiation than those without sarcopenia ($n = 46$). There were no differences in morbidity or mortality between the groups ($p = .75$ and $p = .31$, respectively). Mean length of stay was similar ($p = .70$). Disease free and overall survival were similar ($p = .20$ and $p = .39$, respectively).
Conclusion: There is no association between sarcopenia and increased morbidity, mortality and disease-free survival in patients undergoing esophagectomy for cancer. Sarcopenia in esophageal cancer may not portend worse outcomes that have been reported in other solid tumors.

1. Introduction

Esophageal cancer is rising in incidence and remains a challenging disease to treat.[1] Although the five-year survival has improved over recent years, as screening and therapy continue to evolve, morbidity and mortality from the disease and its treatment is substantial. Not surprisingly, there is a growing interest and emphasis on identifying pre-treatment risk factors that may be modified to improve outcomes after treatment.

Sarcopenia is a clinical condition including loss of skeletal muscle mass and an associated decreased functional ability, due to aging or an induced catabolic state.[2–4] Skeletal muscle mass can be objectively quantified. Computed tomography (CT) has been validated as a tool to measure core skeletal muscle volume.[2,5] Sarcopenia has been associated with poor outcomes in a variety of surgical and oncologic procedures. Very few studies have investigated the impact of sarcopenia in patients undergoing esophagectomy for esophageal cancer, and adverse outcomes have not reliably been demonstrated.

Our aim was to determine if sarcopenia was associated with increased length of stay (LOS), morbidity, mortality, or decreased survival in patients undergoing esophagectomy for esophageal cancer in a single, large volume academic medical center.

2. Material and methods

2.1. Patient selection

We performed a retrospective review of a prospective database of esophageal diseases at a single National Cancer Institute-designated center. Consecutive esophagectomies for malignancy from January 2010 to December 2015 performed by a single team of foregut and thoracic surgeons were extracted for analysis. Inclusion criteria included patients undergoing esophagectomy for squamous cell carcinoma (SCC), esophageal adenocarcinoma (EA), or

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high-grade dysplasia (HGD), as well as age greater than 18 years and computed tomography (CT) imaging performed within three months prior to surgery. Patients were excluded from study if there was incomplete clinical documentation, no CT scan within three months prior to surgery, or if the entirety of their body was not encapsulated on the CT image due to body mass limitations.

Complete preoperative workup with a history and physical exam was collected for all study patients. Standard preoperative laboratory data (complete blood count, basic metabolic panel, and albumin) were also documented. Preoperative medical comorbidities were tracked and recorded, and an age-adjusted Charlson Comorbidity Index (CCI) was calculated for each patient.

2.2. Measurement of skeletal muscle index and sarcopenia

CT images in our institutional radiology system were exported to an encrypted external hard drive and imported into OsiriX (Pixmeo SARL, Geneva, Version 9.0) software. Images were analyzed with the same technique as that used in the majority of previous sarcopenia and esophageal cancer studies.[6–10] The third lumbar vertebrae, where the transverse processes were visible, was used as a landmark axial level. Two consecutive images were chosen to measure muscle cross-sectional area. The psoas, paraspinal, oblique, and rectus muscle areas were quantified with dedicated renderings as a region of interest (ROI), using a Hounsfield unit (HU) threshold of −30 to +150 to select skeletal muscle but exclude fat, bone, and vasculature. Any ROI automatically selected that was not skeletal muscle was manually removed. Cross-sectional areas were averaged and corrected for height to calculate the muscle index expressed in cm^2/m^2. Previously defined international consensus muscle index cutoff values for sarcopenia were used to define limits for men at less than 52.4 cm^2/m^2 and for women less than 38.5 cm^2/m^2 (Figs. 1 and 2).[11,12]

2.3. Outcomes and statistical analysis

The prevalence of sarcopenia was evaluated, and standard descriptive statistics of baseline characteristics for patients with and without sarcopenia were summarized. Differences in baseline characteristics between patients with and without sarcopenia were evaluated with a combination of F-tests for continuous variables and with Chi-square tests, Fisher's Exact tests, and the Freeman-Halton Fisher Exact test for categorical variables. The association between sarcopenia and clinical stage, presence of complications during hospital stay, and outcomes after hospital discharge were evaluated with Chi-square testing. Primary outcomes of interest were length of stay, inpatient mortality, and inpatient morbidity (pneumonia, unstable arrhythmia, heart attack/failure, stroke, pulmonary embolism, respiratory, renal failure, infection requiring therapy, or gastroesophageal anastomotic complications). Secondary outcomes included disease-free survival (DFS) and overall survival (OS), measured with the Kaplan-Meier method. Results at $\alpha \leq 0.05$ were considered significant.

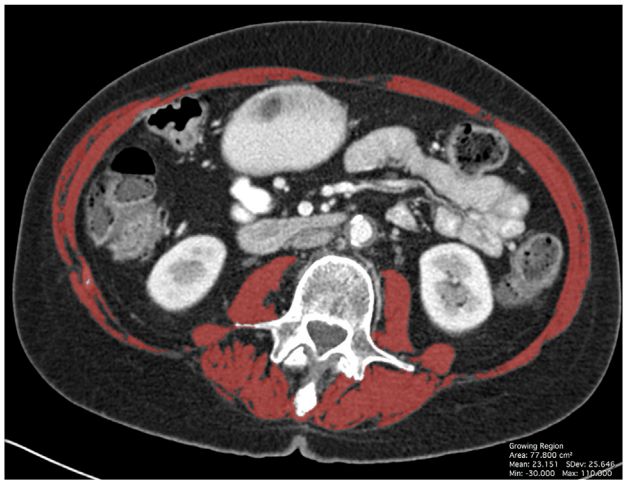

Fig. 1. CT Scan of a Female Sarcopenic Patient- Preoperative CT scan of a female sarcopenic patient *(muscle area = 77.8* cm^2*; muscle index = 31.9* cm^2/m^2*)*. The paucity of abdominal wall and paraspinous musculature is highlighted in red. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

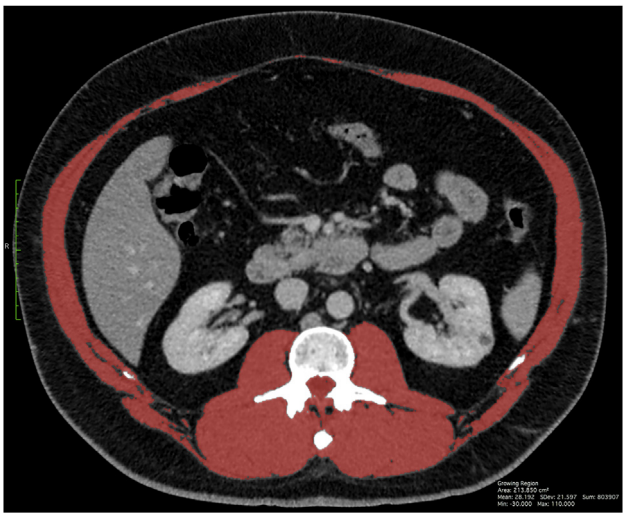

Fig. 2. CT Scan of a Male Non-sarcopenic Patient- Preoperative CT scan of a male non-sarcopenic patient *(muscle area = 213.9* cm^2*; muscle index = 76.6* cm^2/m^2*)*. The large volume of abdominal wall and paraspinous musculature is highlighted in red. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3. Results

One hundred-seventy three patients met study inclusion criteria. Eighty-three percent were male, with an average age of 66 years and body mass index (BMI) of 26.6 kg/m^2. Two patients had high-grade dysplasia (1.2%), 21 patients (12.1%) had squamous cell carcinoma, and the remaining 150 patients (86.7%) had a diagnosis of adenocarcinoma. Neoadjuvant chemoradiotherapy (CRT) was administered to 143 patients (82.7%). The mean CCI of the overall cohort was 4.9. There were no differences between groups with regard to age, gender, other comorbidities, or laboratory markers of nutrition (Table 1). The mean follow-up time of the study was 27.6 months. Three patients were lost to follow-up.

Sarcopenia was identified in 127 patients (73%). The sarcopenia group (SP) had a significantly lower BMI and later stage disease than those without sarcopenia (NS) ($p = .02$). There was a higher utilization of neoadjuvant radiation among patients with sarcopenia (88% vs. 74%, $p = .03$), but the use of neoadjuvant chemotherapy was not statistically different between groups (88% vs. 76%, $p = .06$). The SP patients were more likely to undergo a three-field esophagectomy, compared to an Ivor-Lewis or transhiatal approach ($p = .04$, Table 1). Open and minimally invasive approaches were similar between those with and without sarcopenia ($p = .28$).

In-hospital morbidity occurred in 47% ($n = 60$) of sarcopenic patients and 50% ($n = 23$) of those without objective sarcopenia, although this was not statistically different between groups