Impact of sarcopenia on outcome in patients with esophageal resection following neoadjuvant chemotherapy for esophageal cancer

M. Paireder [a], R. Asari [a], I. Kristo [a], E. Rieder [a], D. Tamandl [b], A. Ba-Ssalamah [b], S.F. Schoppmann [a,*]

[a] *Department of Surgery, Upper-GI-Service, Comprehensive Cancer Center GET-Unit, Medical University of Vienna, Vienna, Austria*
[b] *Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria*

Abstract

Background: Nutritional status and body composition parameters such as sarcopenia are important risk factors for impaired outcome in patients with esophageal cancer. This study was conducted to evaluate the effect of sarcopenia on long-term outcome after esophageal resection following neoadjuvant treatment.
Methods: Skeletal muscle index (SMI) and body composition parameters were measured in patients receiving neoadjuvant treatment for locally advanced esophageal cancer. Endpoints included relapse-free survival (RFS) and overall survival (OS).
Results: The study included 130 patients. Sarcopenia was found in 80 patients (61.5%). Patients with squamous-cell cancer (SCC) showed a decreased median SMI of 48 (range 28.4—60.8) cm/m^2 compared with that of patients with adenocarcinoma (AC) of 52 (range 34.4—74.2) cm/m^2, $P < 0.001$. The presence of sarcopenia had a significant impact on patient outcome: HR 1.69 (1.04—2.75), $P = 0.036$. Median OS was 20.5 (7.36—33.64) versus 52.1 (13.55—90.65) months in sarcopenic and non-sarcopenic patients, respectively. Sarcopenia was identified as an independent risk factor: HR 1.72 (1.049—2.83), $P = 0.032$.
Conclusion: Our data provide evidence that sarcopenia impacts long-term outcome after esophageal resection in patients who have undergone neoadjuvant therapy. Assessment of the body composition parameter can be a reasonable part of patient selection and may influence treatment methods.
© 2016 Elsevier Ltd, BASO ~ The Association for Cancer Surgery, and the European Society of Surgical Oncology. All rights reserved.

Keywords: Sarcopenia; Body composition parameter; Esophageal cancer

Introduction

The implementation of multimodal strategies in the treatment of locally advanced esophageal cancer (EC) has improved recurrence rates as well as patient survival.[1,2] Despite this development, EC remains associated with a poor prognosis.[3] Recent studies have emphasized the influence of nutrition and body composition on overall survival in patients with EC.[4,5]

Sarcopenia is the involuntary loss of muscle mass, originally described in the elderly, but now commonly recognized in oncology patients.[6] In various tumor entities, sarcopenia plays an important role as a risk factor for reduced disease-free and overall survival.[5,7,8]

Significant weight loss due to dysphagia and consequent eating habits is a well-documented clinical problem in patients suffering from esophageal cancer. Esophageal cancer patients with signs of sarcopenia have increased complication rates, high treatment drop-out rates, and inferior outcomes.[9—11]

As body composition has come under the focus of clinical studies, the methods of its assessment have changed. Among various tools available, computed tomography

* Corresponding author. Department of Surgery, Upper-GI-Service, Comprehensive Cancer Center GET-Unit, Medical University of Vienna, Spitalgasse 23, 1090 Vienna, Austria. Fax: +43 1 40400 34780.
E-mail address: sebastian.schoppmann@meduniwien.ac.at (S.F. Schoppmann).

(CT) is superior in accuracy and precision for estimating total and fat-free muscle area (FFM).[12] Previous studies showed that CT-assessed sarcopenia is able to predict short-term as well as long-term outcome in various gastro-intestinal malignancies.[13,14] The aim of this study was to investigate the effect of sarcopenia in patients treated by neoadjuvant therapy for locally advanced adenocarcinoma (AC) as well as esophageal squamous-cell cancer (ESCC) prior to esophageal resection and its impact on patients' long-term outcomes.

Patients and methods

Patients

All consecutive patients who underwent esophageal resection for esophageal cancer after neoadjuvant treatment at the Department of Surgery, Medical University of Vienna, Austria, between the years 2006 and 2013 were included in this retrospective analysis. Patients with a missing pre-therapeutic or post-therapeutic CT scan were excluded from this study. Staging laparoscopy was performed only in patients with AEG III tumors. Positron emission tomography (PET) scanning was performed in specially indicated cases.

Clinical data were obtained from an institutional prospective database. Patients were invited to follow-up on a 3-month basis for the first 2 years and every 6 months thereafter until year 5 after surgery. To optimize data accuracy and to reduce the number of patients who may be lost to follow-up, patients were contacted to evaluate their current status if information was missing.

The institutional local ethic commission approved the study.

Image analysis

The CT protocol and image analysis have been extensively described elsewhere.[14] In brief, a single slice on the L3 level was identified and total skeletal muscle (TMA) and subcutaneous and visceral fat were measured. The skeletal muscle index (SMI) is calculated as follows: TMA/height (m) x height (m). Sarcopenia is defined as a reduced skeletal muscle index of ≤ 39 cm^2/m^2 for women and ≤ 55 cm^2/m^2 for men.[7] We performed image analysis on the pre-therapeutic (staging) as well as the post-therapeutic (re-staging) CT scan.

Statistical analysis

SPSS (Version 21.0, SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

All variables are shown as median and range or 95% confidence intervals (95% CIs). Variables were compared between the subgroups using the Mann−Whitney U test for two subgroups. Correlations were calculated using the Pearson rank correlation test. P-values < 0.05 were considered significant.

Survival analysis was performed using a Cox proportional hazards regression model, and hazard ratios (HRs) with 95% CIs were used for data presentation. For the purpose of multivariate analysis, a Cox proportional hazards model with backward elimination was used. All variables with $P < 0.05$ on the univariate analysis were entered into the model. Age, gender, BMI and histology were used to correct for potential factors associated with sarcopenia.

Results

Patients

During the study period 229 patients underwent esophageal resection for esophageal cancer; 99 patients were excluded because of missing above-mentioned eligibility criteria. Thus 130 patients − 106 (81.5%) of whom were males − were included in this study. All patients had received neoadjuvant chemotherapy (CTH). Seven patients (5.4%) had received additional radiotherapy. Eighty-seven patients (66.9%) were treated for AC (71 AEG I, 11 AEG II, 4 AEG III by Siewert classification), whereas 43 patients (33.1%) were diagnosed with ESCC.[15] Seventeen patients (13.1%) had a positive microscopic resection margin. Median follow-up was 21.25 (0.3−99.4) months. In total, signs of sarcopenia were found in 80 patients (61.5%); 55 patients (42.3%) showed sarcopenia before chemotherapy and 75 (57.7%) thereafter. Individuals with sarcopenia showed a significantly lower median BMI (23.7, range 15.4−35.3) than patients without sarcopenia (26.5, range 16.3−36.8), $P = 0.009$. Obesity was found significantly more often in patients without sarcopenia (BMI > 30 kg/m^2: 14 (28%) versus 7 (8.8%), $P = 0.004$. For further demographics and tumor-related details see Table 1.

Influence of sarcopenia on morbidity

Thirty-seven patients (28.5%) had postoperative complications, including anastomotic leakage (n = 17, 13.1%), conduit necrosis (n = 5, 3.8%) and pneumonia (n = 15, 11.5%). Postoperative complications did not show any significant difference among patients with sarcopenia (18, 22.5%) and without sarcopenia (10, 20%), $P = 0.457$. Analysis of complication subgroups of leakage and pneumonia individually did not show any significance. Interestingly, all conduit necrosis occurred in sarcopenic patients ($P = 0.024$). Further information on the influence of sarcopenia on morbidity is delineated in Table 2.

Change of body composition parameters during chemotherapy

During neoadjuvant CTH we found significant changes in various body composition parameters (BCPs) exclusively