Baseline measure of health-related quality of life (Functional Assessment of Cancer Therapy-Esophagus) is associated with overall survival in patients with esophageal cancer

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ABSTRACT

Objective: Functional Assessment of Cancer Therapy-Esophagus is a health-related quality of life instrument validated in patients with esophageal cancer. It is composed of a general component and an esophageal cancer subscale. Our objective was to determine whether the baseline Functional Assessment of Cancer Therapy-Esophagus and esophageal cancer subscale scores are associated with survival in patients with stage II and III cancer of the gastroesophageal junction or thoracic esophagus.

Methods: Data from 4 prospective studies in Canadian academic hospitals were combined. These included consecutive patients with stage II and III esophageal cancer who received neoadjuvant therapy followed by surgery or chemoradiation/radiation alone. All patients completed baseline Functional Assessment of Cancer Therapy-Esophagus. Functional Assessment of Cancer Therapy-Esophagus and esophageal cancer subscale scores were dichotomized on the basis of median scores. Cox regression analyses were performed.

Results: There were 207 patients treated between 1996 and 2014. Mean age was 61 ± 10.6 years. Approximately 69.6% of patients (n = 144) had adenocarcinoma. All patients had more than 9 months of follow-up. In patients with stage II and III, 93 deaths were observed. When treated as continuous variables, baseline Functional Assessment of Cancer Therapy-Esophagus and esophageal cancer subscale were associated with survival with hazard ratios of 0.89 (95% confidence interval [CI], 0.81-0.96; $P = .005$) and 0.68 (95% CI, 0.56-0.82; $P < .001$), respectively. When dichotomized, they were also associated with survival with a hazard ratio of 0.58 (95% CI, 0.38-0.89; $P = .01$) and 0.43 (95% CI, 0.28-0.67; $P < .001$), respectively.

Conclusions: In patients with stage II and III esophageal cancer being considered for therapy, higher baseline Functional Assessment of Cancer Therapy-Esophagus and esophageal cancer subscale were independently associated with longer survival, even after adjusting for age, stage, histology, and therapy received. Further study is needed, but Functional Assessment of Cancer Therapy-Esophagus may be useful as a prognostic tool to inform patient decision-making and patient selection criteria for studies. (J Thorac Cardiovasc Surg 2016;151:1571-80)
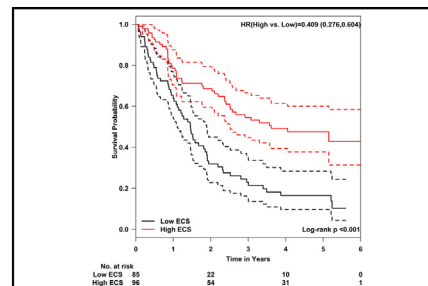
Lower baseline HRQOL (FACT-E) is associated with poorer survival.

Central Message

In patients with stage II and III esophageal cancer, lower HRQOL before therapy is associated with worse survival.

Perspective

In patients with stage II and III esophageal cancer before therapy, higher baseline HRQOL (FACT-E) is associated with higher overall survival. This association persists even after controlling for stage and treatment. Further study is needed, but FACT-E may be a useful prognostic tool to inform patient decision-making and selection criteria for studies.

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Abbreviations and Acronyms
CI = confidence interval
ECS = esophageal cancer subscale
EORTC = European Organization for Research and Treatment of Cancer
FACT-E = Functional Assessment of Cancer Therapy-Esophagus
FACT-G = Functional Assessment of Cancer Therapy-General
HR = hazard ratio
HRQOL = health-related quality of life
QLQ = Quality of Life Questionnaire

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Esophageal cancer has a significant effect on health-related quality of life (HRQOL).[1] Dysphagia is the primary symptom leading the patient to seek medical attention. In addition to the physical problem of difficulty swallowing or the weight loss that may result, social isolation may occur because the inability to swallow comfortably or the risk of food regurgitation may lead to increasing withdrawal from social situations. Poor HRQOL has been shown to be associated with poorer long-term survival in several cancers,[1-7] primarily in those with lung and breast cancer, but there is also evidence demonstrating that poor HRQOL is associated with poorer long-term survival in patients with esophageal cancer.[2,3,5,6] However, these studies were based on post-treatment HRQOL or changes of HRQOL over the course of treatment.[2,3,5,6] Given that esophageal cancer initially may present with significant HRQOL issues, it seems likely that baseline HRQOL may be an especially important prognostic tool in this patient population.

The Functional Assessment of Cancer Therapy-Esophagus (FACT-E) is an HRQOL instrument validated in patients with esophageal cancer. It is composed of a general component (FACT-G) and an esophageal cancer subscale (ECS). Our objective was to determine whether the baseline FACT-E or the baseline ECS alone is associated with overall survival in patients with stage II and III cancer of the gastroesophageal junction or thoracic esophagus.

MATERIALS AND METHODS
Patient Population
Data from 4 prospective, nonrandomized studies in 3 large Canadian academic hospitals (Toronto General Hospital, Princess Margaret Cancer Centre, The Ottawa Hospital) were combined. Table 1 provides a brief description of these studies. The current study and all 4 studies were approved by institutional ethics boards.[8,9] These studies included consecutive eligible patients with clinical stage II or IV cancer of the gastroesophageal junction or thoracic esophagus who received chemotherapy (mostly with cisplatin and irinotecan for up to 3 cycles) and concomitant radiation (typically 50 Gy in 25 fractions) as neoadjuvant therapy or as part of bimodality therapy without surgery. For the purposes of this current study, patients were classified as having received chemotherapy or radiation therapy if they completed at least 50% of the intended therapy. In 1 of the 4 studies, adjuvant sunitinib was used. Sunitinib is a broad-spectrum orally available multitargeted tyrosine kinase inhibitor with antiangiogenic and antitumor activity.[10] For the purposes of this current study, patients were classified as having used adjuvant sunitinib if they had at least 6 months of sunitinib therapy.

The surgical techniques used included McKeown esophagectomy, Ivor-Lewis resection, left thoracoabdominal approach with a left neck incision, minimally invasive esophagectomy, and transhiatal esophagectomy. En bloc resection of overlying mediastinal pleura, a cuff of the diaphragmatic crura, and mediastinal fat was recommended. Recommended lymphadenectomy included lower mediastinal and abdominal lymph nodes. Proximal and distal margins, measured in the operating room, were more than 5 cm beyond the macroscopic tumor. Clinical follow-up after surgery or definitive chemoradiation therapy occurred every 3 months until 2 years postoperatively followed by every 6 months until 5 years postoperatively. Radiologic follow-up occurred with at least yearly computed tomography or chest x-ray for 5 years. Staging was defined according to the 7th edition of the American Joint Committee on Cancer TNM staging system. Pathologic stage was used to describe those who underwent surgery, and clinical stage was used to describe those who did not undergo surgery.

Health-Related Quality of Life Instrument
The FACT-G is a general HRQOL instrument that has been validated for use in any cancer; it consists of 28 questions covering the domains of physical well-being, functional well-being, social well-being, and emotional well-being using a 5-point Likert scale.[9] A disease-specific module, the ECS was validated and added to the FACT-G to result in the FACT-E for esophageal cancer.[9] The ECS consists of 17 items addressing eating, swallowing, enjoyment of food, voice, dry mouth, appetite, cough, choking, and pain; each of these is evaluated using a 5-point Likert scale to generate a summary score of esophageal-specific concerns.[9] Higher scores denote better quality of life. All patients completed FACT-E at baseline; surveys were self-administered at the time of the first consultation with the thoracic surgeon or medical or radiation oncologist before initiation of any therapies.

Statistical Analysis
For univariate analysis, normally distributed continuous data were reported as means with standard deviations and analyzed using independent sample t tests. Data that were not normally distributed were reported as medians with interquartile ranges and analyzed using the Mann–Whitney U test. Fisher exact tests were used for univariate analysis of categoric data. Multivariate time-to-event analyses were performed using Cox regression analyses. FACT-E and ECS were our main predictors of interest. We performed separate Cox regression analyses including only 1 HRQOL for each model (ECS or FACT-E). A forced-entry method was used to control for the following variables: age, stage, histology (adenocarcinoma vs nonadenocarcinoma), year of treatment, and whether the patient received surgery, chemotherapy, radiation, or adjuvant sunitinib therapy. The variable "curative intent" was used to distinguish those patients who received chemoradiation therapy as a curative modality (ie, in select patients with squamous cell cancer) from those who received it on a palliative basis (ie, unresectable or metastatic disease). The FACT-E