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ScienceDirect

EJSO 41 (2015) 1308–1315

EJSO the Journal of Cancer Surgery

www.ejso.com

Impact of inflammation-based prognostic score on survival after curative thoracoscopic esophagectomy for esophageal cancer

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Accepted 9 July 2015
Available online 30 July 2015

Abstract

Background: Despite recent improvements in early detection, progress in surgical techniques, and development of chemoradiation therapies, prognosis of esophageal cancer remains poor. The aim of the present study was to assess whether Glasgow Prognostic Score (GPS), an inflammation-based prognostic score, has prognostic value independent of conventional clinicopathological criteria in patients undergoing curative resection for esophageal cancer, even in elderly patients.

Methods: We retrospectively reviewed the database of 141 consecutive patients with histologically verified esophageal squamous cell carcinoma who underwent potentially curative surgery in our institute, between January 2006 and December 2014. GPS and neutrophil lymphocyte ratio (NLR) were calculated.

Results: On multivariate analysis, TNM stage ($p < 0.0001$) and GPS ($p = 0.041$) were independently associated with worse prognosis in overall patients with esophageal cancer.

Multivariate analysis evaluated the prognostic factors in two different patient groups: patients younger than 70 years (non-elderly) and those aged 70 years or more (elderly).

Multivariate analysis demonstrated that TNM stage ($p = 0.0003$) was an only independent risk factor for a worse prognosis among non-elderly group. Meanwhile, multivariate analysis demonstrated that TNM stage ($p = 0.001$) and GPS ($p = 0.043$) were the independent risk factor for a worse prognosis among elderly group.

Conclusion: The present study demonstrated that GPS is associated with prognosis and can be considered as an independent prognostic marker in patients who underwent esophagectomy. Moreover, the GPS has the advantage of being simple to measure, routinely available and well standardized. But the present study failed to confirm the NLR as a significant predictor of survival following resection for esophageal cancer.

Keywords: Esophageal cancer; Glasgow Prognostic Score; Neutrophil lymphocyte ratio; Prognosis

Introduction

Despite recent improvements in early detection, progress in surgical techniques, and development of chemoradiation therapies, prognosis of esophageal cancer remains poor worldwide. Surgery is the mainstay treatment for esophageal cancer, but an appreciable proportion of patients with advanced esophageal cancer develop recurrence, even after curative resection. Therefore, accurately predicting the prognosis is needed to improve patient survival and to provide an appropriate preoperative patient counseling.

Host-related factors including performance status, weight loss, smoking, and comorbidity, in addition to tumor pathology, play an important role in cancer outcomes.[1] However, the use of weight loss as a prognostic factor remains problematic since it is often not well defined and subject to bias.[2,3] Furthermore, performance status is recognized to be subjective.[4]

There has been an increasing evidence that the cancer-associated systemic inflammatory response has a great

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http://dx.doi.org/10.1016/j.ejso.2015.07.008

influence on disease-related outcomes for many cancer sites.[5,6] Recent several studies have indicated that the systemic inflammatory response may be associated with poor outcome in patients with advanced cancer.[7–9] In particular, the GPS, an inflammation-based prognostic score that includes only the serum levels of C-reactive protein (CRP) and albumin, is one of the most useful scoring systems for prognostication of patients with various advanced cancers.[10–13] The GPS is simple, convenient and can be calculated easily at the time of admission. Moreover, recent reports have demonstrated the utility of NLR, which is calculated from the neutrophil count divided by the lymphocyte count.[14] NLR is also a measure of systematic inflammation and an elevated NLR was found to predict poor survival in breast cancer patients.[15]

The aim of the present study was to assess whether GPS, an inflammation-based prognostic score, has prognostic value independent of conventional clinicopathological criteria in patients undergoing a potentially curative resection for esophageal cancer, even in elderly patients.

Patients and methods

Patients

We retrospectively reviewed the database of 141 consecutive patients with histologically verified esophageal squamous cell carcinoma who underwent potentially curative esophagectomy with R0 resection in our institute, between January 2006 and December 2014. R0 resection was defined as a complete resection without microscopic involvement of margins. Thoracoscopic subtotal esophagectomy with a three-field lymph node dissection was performed in all patients, followed by laparoscopic gastric surgery with an elevation of gastric conduit to the neck via the posterior mediastinal pathway or retrosternal pathway with an end-to-end anastomosis of the cervical esophagus and gastric conduit. The patient's clinical characteristics, laboratory data, treatment, and pathological data were obtained from a retrospective review of the records. No patients had clinical signs of infection or other systemic inflammatory conditions preoperatively.

Permission to perform this retrospective study was obtained from the ethical board of our institution.

Inflammation-based prognostic scores

Laboratory measurements including the serum levels of CRP, albumin and total cholesterol, white blood cell (WBC) count, neutrophil count, and lymphocyte count were performed on the day of admission. GPS and NLR were calculated based on these clinical data. The GPS was constructed as previously described.[16] Briefly, patients with both an elevated C-reactive protein (>1.0 mg/dl) and hypoalbuminemia (<3.5 g/dl) were allocated a score of 2. Patients in whom only one of these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0. NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count.[14] For the purposes of analysis, an NLR of ≧2.5 is allocated a score of 1, and <2.5 a score of 0.

TNM stage

The pathological classification of the primary tumor, the degree of lymph node involvement and the presence of organ metastasis were determined according to the TNM classification system (7th edition of the cancer staging manual of the American Joint Committee on Cancer[17]).

Statistical analysis

Means and standard deviations were calculated and differences were identified using Student's t test. Differences between categories were identified using the Chi-square test. Survival curves were produced using the Kaplan–Meier survival method. Two groups were compared with a two-sided log-rank test. Hazard ratios were calculated and univariate and multivariate analyses were performed using Cox proportional hazards regression models. The potential prognostic factors for esophageal cancer were as follows: age (<70 vs. ≧70); gender (male vs. female); albumin concentration (<3.5 g/dl vs. ≧3.5 g/dl), CRP (<1.0 mg/dl vs. ≧1.0 mg/dl), pStage (1, 2 vs. 3), tumor size (<3 cm vs. ≧3 cm), operation time (<600 min vs. ≧600 min), intraoperative blood loss (<500 ml vs. ≧500 ml), GPS (GPS 0 vs. GPS 1–2), and NLR (0 vs. 1). Medical records were retrospectively reviewed to examine these factors.

All statistical analyses were performed using IBM SPSS Statistics version 21 for Windows (IBM Corporation, Armonk, NY, USA), and a p values of less than 0.05 was considered statistically significant.

Results

Relationships between GPS and clinicopathological features in esophageal cancer

Relationships between GPS and clinicopathological features are shown in Table 1. Significant correlations were observed between GPS and such factors as neutrophil count ($p = 0.016$), albumin concentrations ($p < 0.0001$), C-reactive protein ($p < 0.0001$), depth of tumor ($p = 0.002$), TNM stage ($p = 0.04$), and NLR ($p = 0.001$).

Prognostic factors for survival in esophageal cancer

The univariate analysis demonstrated that albumin concentrations ($p = 0.003$), TNM stage ($p < 0.0001$), tumor size ($p = 0.007$), and GPS ($p = 0.003$) were the significant risk factor for a worse prognosis (Table 2).