Translational Oncology
www.transonc.com

Volume 7 Number 5 October 2014 pp. 632–637 632

# The Combination of Platelet Count and Neutrophil Lymphocyte Ratio Is a Predictive Factor in Patients with Esophageal Squamous Cell Carcinoma

**Ji-Feng Feng*,† , Ying Huang‡ and Qi-Xun Chen*,†**

*Department of Thoracic Surgery, Zhejiang Cancer Hospital, Hangzhou 310022, China; †Key Laboratory Diagnosis and Treatment Technology on Thoracic Oncology, Hangzhou 310022, Zhejiang Province, China; ‡Department of Nursing, Zhejiang Cancer Hospital, Hangzhou, China

## Abstract

*OBJECTIVE:* The prognostic value of inflammation indexes in esophageal cancer was not established. In this study, therefore, both prognostic values of Glasgow prognostic score (GPS) and combination of platelet count and neutrophil lymphocyte ratio (COP-NLR) in patients with esophageal squamous cell carcinoma (ESCC) were investigated and compared. *METHODS:* This retrospective study included 375 patients who underwent esophagectomy for ESCC. The cancer-specific survival (CSS) was calculated by the Kaplan-Meier method, and the difference was assessed by the log-rank test. The GPS was calculated as follows: patients with elevated C-reactive protein (>10 mg/l) and hypoalbuminemia (<35 g/l) were assigned to GPS2. Patients with one or no abnormal value were assigned to GPS1 or GPS0, respectively. The COP-NLR was calculated as follows: patients with elevated platelet count (>300 × $10^9$/l) and neutrophil lymphocyte ratio (>3) were assigned to COP-NLR2. Patients with one or no abnormal value were assigned to COP-NLR1 or COP-NLR0, respectively. *RESULTS:* The 5-year CSS in patients with GPS0, 1, and 2 was 50.0%, 27.0%, and 12.5%, respectively ($P < .001$). The 5-year CSS in patients with COP-NLR0, 1, and 2 was 51.8%, 27.0%, and 11.6%, respectively ($P < .001$). Multivariate analysis showed that both GPS ($P = .003$) and COP-NLR ($P = .003$) were significant predictors in such patients. In addition, our study demonstrated a similar hazard ratio (HR) between COP-NLR and GPS (HR = 1.394 *vs* HR = 1.367). *CONCLUSIONS:* COP-NLR is an independent predictive factor in patients with ESCC. We conclude that COP-NLR predicts survival in ESCC similar to GPS.

*Translational Oncology (2014) 7, 632–637*

## Introduction

Esophageal cancer (EC) is the eighth most common cancer worldwide and the sixth leading cause of death from cancer [1]. Squamous cell carcinoma (SCC) comprises about 80% of all ECs worldwide [2]. In China, SCC is the most common pathologic type of ECs, in contrast to the predominance of adenocarcinoma in the Western countries [3,4]. There are important biologic differences between China and Western countries regarding ECs; therefore, a prognostic study that takes into account SCC in China is necessary.

Recently, systemic inflammatory response plays an important role in the progression of cancer [5,6]. Previous studies have shown that serum C-reactive protein (CRP) influenced the prognosis in patients with gastrointestinal cancers [7]. Moreover, the Glasgow prognostic score (GPS) combines serum CRP and hypoalbuminemia and has been demonstrated to be a predictive factor in various cancers, including ECs [8–10]. In addition, there is an increasing evidence

Address all correspondence to: Ji-Feng Feng, MD, Department of Thoracic Surgery, Key Laboratory Diagnosis and Treatment Technology on Thoracic Oncology, Zhejiang Cancer Hospital, No. 38 Guangji Road, Banshan Bridge, Hangzhou 310022, China. E-mail: Jifzhejiang@gmail.com
Received 23 June 2014; Revised 29 July 2014; Accepted 30 July 2014


1936-5233/14
http://dx.doi.org/10.1016/j.tranon.2014.07.009

that platelet count and neutrophil lymphocyte ratio (NLR) can be used for prognostication in several cancers [11,12]. Recently, Ishizuka et al. [13] evaluated a novel inflammation-based prognostic system, termed as the combination of platelet count and NLR (COP-NLR). They demonstrated that COP-NLR is a useful predictor of postoperative survival in patients with colorectal cancer [13]. However, to the best of our knowledge, no studies regarding COP-NLR in patients with EC are available. Therefore, the aim of this study was to investigate and compare the prognostic values of COP-NLR and GPS in patients with esophageal squamous cell carcinoma (ESCC).

## Methods

### *Patients*

From January 2006 to December 2008, a retrospective analysis was conducted in 375 patients with ESCC who underwent curative esophagectomy at Zhejiang Cancer Hospital. All of the patients included in the analysis fit the following criteria: 1) ESCC confirmed by histopathology, 2) surgery with curative esophagectomy, 3) at least six lymph nodes were examined for pathologic diagnosis, and 4) surgery was neither preceded nor followed by adjuvant chemotherapy and/or radiotherapy.

On the basis of the medical records, the following data were collected for each patient: age, gender, laboratory examination, differentiation, tumor length and location, depth of invasion, nodal metastasis, and other miscellaneous characteristics. Ethical approval was obtained from the Ethical Committees of Zhejiang Cancer Hospital. All of the patients included in the study were staged according to the seventh edition of the American Joint Committee on Cancer Cancer Staging Manual [14].

In our institute, patients were followed up in the outpatient department. X-ray or computed tomography of the chest was performed during the follow-up. As this study described the prognosis of patients with ESCC, therefore, a cancer-specific survival (CSS) analysis would be more appropriate. Therefore, the CSS was ascertained in this study. The last follow-up time was November 2011.

### *GPS and COP-NLR Evaluation*

Routine laboratory measurements including the serum levels of CRP, albumin, and blood cell counts were extracted in a retrospective fashion from the medical records. GPS was calculated as follows: patients with elevated CRP (>10 mg/l) and hypoalbuminemia (<35 g/l) were assigned to GPS2. Patients with one or no abnormal value were assigned to GPS1 or GPS0, respectively [8]. COP-NLR was calculated as follows: patients with elevated platelet count level ($>300 \times 10^9$/l) and NLR (>3) were assigned to COP-NLR2. Patients with one or no abnormal value were assigned to COP-NLR1 or COP-NLR0, respectively [13].

### *Statistical Analysis*

Statistical evaluation was conducted with SPSS 17.0 (Chicago, IL). The Pearson Chi-squared test was used to determine the significance of differences. Correlation analysis was performed by Pearson and Spearman correlation analyses. CSS was calculated by the Kaplan-Meier method, and the difference was assessed by the log-rank test. A univariate analysis was used to examine the association between various prognostic predictors and CSS. Possible prognostic factors associated with CSS on univariate analysis were considered in a multivariable Cox proportional hazards regression analysis with the enter method. Moreover, the Akaike information criterion (AIC) and Bayesian information criteria (BIC) were used to identify the statistical model [15,16]. AIC was defined as AIC = −2log(maximum likelihood) + 2 × (the number of parameters in the model). BIC was defined as BIC = −2log(maximum likelihood) + (the number of parameters in the model) × log(sample size). A smaller AIC or BIC value indicates a more desirable model for predicting the outcome. A $P$ value less than .05 was considered to be statistically significant.

## Results

### *Patient Characteristics*

Among the 375 patients with ESCC, 49 (13.1%) were women and 326 (86.9%) were men. The mean age was 59.1 ± 7.8 years, with an age range from 36 to 80 years. All of the clinicopathologic characteristics were comparable between patients grouped by GPS and COP-NLR, as shown in Tables 1 and 2. There were significant differences between the GPS and COP-NLR groups in tumor length ($P<.001$), depth of invasion ($P<.001$), and nodal metastasis ($P<.001$). In addition, an elevated COP-NLR was also associated with higher differentiation ($P=.006$).

### *Cancer-Specific Survival*

The 5-year CSS was 38.1% in our study. The 5-year CSS in patients with GPS0, 1, and 2 was 50.0%, 27.0%, and 12.5%, respectively (GPS0 *vs* GPS1, $P<.001$; GPS1 *vs* GPS2, $P=.035$; Figure 1). The 5-year CSS in patients with COP-NLR0, 1, and 2 was 51.8%, 27.0%, and 11.6%, respectively (COP-NLR0 *vs* COP-NLR1, $P<.001$; COP-NLR1 *vs* COP-NLR2, $P=.005$; Figure 2).

### *Prognostic Factors*

By univariate analysis, we found that seven clinicopathologic variables had significant associations with CSS (Table 3). Then, all of

**Table 1.** The Characteristics of the 375 SCCE Patients Grouped by GPS

| | GPS0 (*n*) | GPS1 (*n*) | GPS2 (*n*) | *P* Value |
|---|---|---|---|---|
| Age (years) | | | | .697 |
| ≤60 | 125 | 63 | 26 | |
| >60 | 87 | 52 | 22 | |
| Gender | | | | .245 |
| Female | 32 | 14 | 3 | |
| Male | 180 | 101 | 45 | |
| Tumor length (cm) | | | | <.001 |
| ≤3 | 71 | 25 | 3 | |
| >3 | 141 | 90 | 45 | |
| Tumor location | | | | .193 |
| Upper | 9 | 7 | 4 | |
| Middle | 93 | 61 | 26 | |
| Lower | 110 | 47 | 18 | |
| Vessel involvement | | | | .101 |
| Negative | 183 | 90 | 37 | |
| Positive | 29 | 25 | 11 | |
| Perineural invasion | | | | .226 |
| Negative | 177 | 92 | 35 | |
| Positive | 35 | 23 | 13 | |
| Differentiation | | | | .273 |
| Well | 32 | 13 | 7 | |
| Moderate | 144 | 75 | 27 | |
| Poor | 36 | 27 | 14 | |
| Depth of invasion | | | | <.001 |
| T1 | 49 | 13 | 1 | |
| T2 | 41 | 17 | 4 | |
| T3 | 108 | 67 | 35 | |
| T4 | 14 | 18 | 8 | |
| Nodal metastasis | | | | <.001 |
| Negative | 128 | 56 | 15 | |
| Positive | 84 | 59 | 33 | |