Archives of Medical Research 46 (2015) 557–563

Archives of Medical Research

ORIGINAL ARTICLE

Increased Neutrophil-Lymphocyte Ratio Is a Poor Prognostic Factor in Patients with Esophageal Cancer in a High Incidence Area in China

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Received for publication April 9, 2015; accepted September 7, 2015 (ARCMED-D-15-00223).

Background and Aims. Neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) have been assumed to be a marker to predict the survival of patients with different types of cancer. We undertook this study to verify the prognostic value of the NLR and the PLR for predicting the survival rate of patients with esophageal cancer in a high incidence area in China.

Methods. In total, 820 cases from a high incidence area that had pathologically confirmed esophageal cancers initially diagnosed at the Fourth Hospital of Hebei Medical University from 2007–2008 were analyzed. The medical record system was used to collect patient information regarding personal details, cancer type, treatment, and routine blood examinations at the time of admission. Follow-up evaluations were conducted by the established follow-up system at the hospital. We used Kaplan-Meier method to calculate overall survival (OS) rate. We used Cox regression analysis to analyze the factors that may affect the OS rate of the patients. SPSS 13.0 and Excel software packages were used for statistical analysis.

Results. In total, 864 cases were consistent with the inclusion criterion. At the end of the study, 820 cases received follow-up evaluation. Follow-up rate was 94.91%. Among the 820 cases, 334 died of esophageal cancer, whereas 486 remain alive as of March 15, 2014. Five-year OS rate of the patients with esophageal cancer was 40.66%. Patients in the NLR $\geq$3.5 group demonstrated shorter OS than patients in the NLR $<$3.5 group (53.2 vs. 33.4 months, $p = 0.001$). Multivariate analysis indicated that age, pathological type, TNM stage, surgery and NLR were all independent risk factors for esophageal cancer. OR of NLR $\geq$3.5 group was 1.287 (1.049–1.580).

Conclusions. NLR may be an independent prognostic factor for esophageal cancer in high incidence areas.

Key Words: Esophageal cancer, Neutrophil-lymphocyte ratio (NLR), Platelet-lymphocyte ratio (PLR), Prognosis, Survival rate.

Introduction

Esophageal cancer is one of the most common cancers worldwide with an estimated 456,000 cases and 400,000 deaths in 2012. More than 80% of esophageal cancer cases and deaths occur in developing countries. The incidence of esophageal cancer has a high geographical diversity and ranges from 3/100,000 individuals per year in low incidence areas to >100/100,000 individuals per year in high incidence regions. China has the highest incidence and mortality rate of esophageal cancer, accounting for 52.8% of new cases and 49.3% of deaths due to esophageal cancer worldwide (1). Cixian and Shexian in Hebei Province, which border Linxian in Henan Province, are the areas with the highest incidence of esophageal cancer in China and worldwide. The incidence rate of esophageal cancer in Cixian was 176.87/100,000 men and 108.75/100,000 women in

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0188-4409/$ - see front matter.
http://dx.doi.org/10.1016/j.arcmed.2015.09.003

2012 (2). Increasing evidence suggests that genetic susceptibility, lifestyle-related risk factors and prognostic factors differ between high- and low-incidence areas (3).

Although advances have been made in multidisciplinary treatments for esophageal cancer, this cancer continues to have a poor prognosis, with a 5-year OS rate of ~21% because of a general lack of symptoms until reaching an advanced stage (4). The 5-year OS rate was 18% in Cixian from 2000–2002 (5). The prognosis of esophageal cancer is based on the pathological stage, histological type, pathogenic sites, biological behaviors and treatment measures; however, specific factors have not yet been elucidated (6,7). Due to the discrepant results within the same stage, there is an urgent demand for new parameters especially serum predictive biomarkers to complement TNM staging to accurately predict the prognosis and to provide an appropriate preoperative patient counseling. Recently, increasing evidence has shown that a systemic inflammatory response is of prognostic value in various cancers (8,9). The neutrophil-lymphocyte ratio (NLR), which can comprehensively reflect the inflammatory and immune status in patients with cancer, has been assumed to be an easily available and reliable marker to predict the survival of patients with different types of cancer such as lung cancer (10), colorectal cancer (11), liver cancer (12), breast cancer (13), and renal cell carcinoma (14). In addition, many studies have confirmed that the platelet-lymphocyte ratio (PLR) has significant prognostic value in patients with malignant tumors (15–19). However, results regarding esophageal cancer have been contradictory (20–22) and there is no study about high-risk areas of esophageal cancer. The present study was conducted to verify the hypothesis that an elevated NLR might prove to be a clinically available prognostic indicator of the OS rate of patients with esophageal cancer in high incidence areas.

Materials and Methods

Patients

This retrospective analysis was conducted using data from 864 consecutive patients from high incidence areas in Hebei Province with histologically confirmed esophageal cancer who were treated at the Fourth Hospital of Hebei Medical University (also known as the Tumor Hospital of Hebei Province, a large and comprehensive hospital with the rank of level three and grade A) from January 1, 2007–December 31, 2008. Inclusion criterion was that patients must have received a pathological diagnosis of primary esophageal cancer. Exclusion criteria were as follows: transfusion history, active bleeding during the preceding 2 months, bleeding diathesis, hyper- or hypothyroidism, severe infections, diffuse intravascular coagulation, heparin therapy, anti-inflammatory treatment during the past week or connective tissue diseases. Eventually, 864 cases were included in the analysis; 575 cases were male (66.6%) and 289 cases were female (33.4%).

Data Collection

Personal patient data were extracted from the medical records and included gender, age, occupation and family history. Tumor data consisted of the pathogenic site, pathological type, TNM stage and surgical situation. Laboratory data including hemoglobin (HGB) levels, neutrophil count, lymphocyte count, and platelet count were obtained on the first day the patients were hospitalized. Then, NLR was calculated as a simple ratio of the absolute neutrophil count and the absolute lymphocyte count; similarly, the PLR was defined as the ratio between the absolute platelet count and the absolute lymphocyte count.

Follow-up Studies

Follow-up evaluations were performed according to the standard follow-up system of the hospital every 6 months after patients were discharged from the hospital. The deadline for follow-up evaluations was March 15, 2014. The survival period was measured from the date of admission to the date of death or to the date of the follow-up deadline.

Statistical Analysis

SPSS 13.0 and Excel software packages were used for the statistical analysis. We used χ^2 tests or Fisher's exact probability method to study the relationship between the NLR, PLR and patient information variables (i.e., gender, age, family history, pathological type, TNM stage, surgery incidence). OS rate was calculated by the Kaplan-Meier method. OS rates of patients in the different groups were compared by the log-rank χ^2 test (inspection level = 0.05). Uni- and multivariate Cox regression models were conducted to analyze the factors that influence the OS rate.

Results

Patient Characteristics

In total, 864 cases from January 2007–December 2008 met the inclusion criterion, but only the 820 cases with follow-up evaluations were included in the study. The follow-up rate was 94.91%. Among the 820 cases, 334 died of esophageal cancer, whereas 486 remain alive by March 15, 2014. Follow-up period ranged from 8–87 months, and the median follow-up period was 31 months. Overall, 526 (64.1%) cases were male, and 294 (35.9) were female; the median age was 60.0 ± 9.3 years (range 38–74). In total, 626 (76.3%) patients underwent surgery.