DIAGNOSTIC VALUE OF THE NEUTROPHIL TO LYMPHOCYTE RATIO AND THE PLATELET TO LYMPHOCYTE RATIO IN PATIENTS WITH GASTRIC ADENOCARCINOMA

ZULFU BAYHAN1, SEZGIN ZEREN2, FATMA EMEL KOCAK3, MEHMET FATIH EKICI4, CUNEYT KAHRAMAN5, CENGIZ KOCAK5, SUKRU AYDIN DUZGUN1

1Department of General Surgery, Faculty of Medicine, Dumlupinar University, Kutahya - 2Department of Biochemistry, Faculty of Medicine, Dumlupinar University, Kutahya - 3Department of General Surgery, Evliya Celebi Training and Research Hospital, Kutahya - 4Department of Internal Medicine, Faculty of Medicine, Dumlupinar University, Kutahya - 5Department of Pathology, Faculty of Medicine, Dumlupinar University, Kutahya, Turkey

Abstract

Background: Gastric adenocarcinoma is the second commonest cause of cancer-related deaths worldwide. Improving this, will depend on earlier diagnosis and treatment. Recently it has been reported that inflammatory markers, particularly the neutrophil / lymphocyte ratio (NLR) and platelet / lymphocyte ratio (PLR), and to a lesser extent the mean platelet volume (MPV), may be useful in the early diagnosis and prognostication of various malignancies.

Objective: To investigate whether the NLR, PLR and MPV may be useful markers for the early diagnosis of gastric adenocarcinoma.

Materials and methods: We retrospectively studied a group of 36 patients with gastric adenocarcinoma, comparing them to healthy age and sex matched controls. Full blood counts were used to obtain various hematological indices, including the MPVs and to calculate the NLRs and the PLRs. Unpaired t-tests were used to determine if these differed between patients and controls.

Results: Hemoglobin concentrations and lymphocyte counts were both significantly lower in patients compared to controls (P < 0.001). Neutrophil counts, NLRs, and PLRs were significantly higher in patients than in controls (P = 0.012, <0.001, and <0.001, respectively). MPVs did not differ significantly between patients and controls (P = 0.320)

Conclusions: Both NLRs and PLRs may be useful markers for the early diagnosis of gastric adenocarcinoma. They are almost universally available and easily obtained.

Key words: Adenocarcinoma, platelets, lymphocytes, neutrophils, gastric neoplasm.

DOI:10.19193/0393-6384_2016_1_17

Received May 30, 2015; Accepted January 02, 2016

Introduction

Despite advances in its treatment, gastric cancer is the second commonest cause of cancer-related deaths in the world(1). Patients are usually diagnosed when the tumor is inoperable and when regional and distant metastatic disease is already present. The 5-year survival rate is <10%(2), and therefore earlier diagnosis and improved treatments are crucial if this is to be improved.

In recent years, there has been interest in the use of inflammatory markers for the early diagnosis of cancer. Inflammation can initiate the onset of cancer and it has an important role in its further progression, including the development of metastases(3). Neutrophils, platelets, and T- and B-lymphocytes all have important functions in tumor-related inflammation and immunology(4). A number of markers of inflammation have been investigated in different cancer types to determine their usefulness for early diagnosis and prediction of prognosis. Examples include the neutrophil / lymphocyte ratio (NLR), the platelet / lymphocyte ratio (PLR), and the mean platelet volume (MPV). PLR, NLR, and MPV have been reported to be increased in patients with a number of cancer types, including
carcinoma of the colon, breast, thyroid and esophagus\(^5\)\(^-\)\(^8\). In this study, we aimed to investigate the utility of these markers in the early diagnosis of gastric adenocarcinoma.

**Materials and methods**

This was a retrospective study performed at the Department of General Surgery, Dumlupinar University, Evliya Celebi Research and Education Hospital, Turkey between May 2013 and January 2015. It was carried out in accordance with the Declaration of Helsinki. Informed written consent was obtained from all participants and patient data was anonymized. We collected data from a cohort of patients diagnosed with gastric adenocarcinoma preoperatively and a similar number of healthy controls. The control group was formed by the people who were admitted to hospital for general examination and diagnosed with any illness.

The exclusion criteria were as follows: patients under the age of 18 years; those with chronic cardiac or lung disease, or chronic renal or liver failure; and those treated with steroid or immunosuppressant medication within the last year. The diagnosis of gastric adenocarcinoma was made by histopathological examination of biopsy specimens obtained endoscopically from the upper gastrointestinal tract. We obtained hematological data from the hospital’s laboratory information system (HLIS), and the results of the following indices were recorded: white blood cell (WBC) count; hemoglobin (Hb) concentration; platelet (PLT) count; neutrophil (Ne) count; lymphocyte (Ly) count; and the mean platelet volume (MPV).

We then derived the NLR and PLR values. In our hospital, samples for full blood counts are obtained from venous blood collected into 2.0 mL dipotassium (K2) ethylene diamine tetraacetic acid (EDTA) vacuum tubes (BD Vacutein® BDPlumouth, UK). Analysis was performed using Coulter Gen-S automated haematology instruments (Beckman Coulter LH 780 Gen-S System; Miami, FL, USA).

Statistical analysis was performed using SPSS version 19.0 (SPSS, Chicago, IL). All data sets were tested for normality using the Kolmogorov-Smirnov test. Differences between groups for all parameters were analyzed using unpaired t-tests. All data were expressed as mean ± SD. A P-value of <0.05 was considered as statistically significant.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Patient</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 36</td>
<td>N = 36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years) ± SD</td>
<td>63.4 ± 9.0</td>
<td>66.5 ± 11.6</td>
<td>0.336</td>
</tr>
<tr>
<td>Gender (number)</td>
<td></td>
<td></td>
<td>0.615</td>
</tr>
<tr>
<td>Female</td>
<td>11</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>WBC (10³/mm³)</td>
<td>8.0 ± 2.0</td>
<td>9.1 ± 4.2</td>
<td>0.128</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>12.9 ± 1.9</td>
<td>11.0 ± 1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLT (10³/mm³)</td>
<td>248.7 ± 62.9</td>
<td>380.9 ± 63.8</td>
<td>0.224</td>
</tr>
<tr>
<td>MPV (fL)</td>
<td>8.3 ± 0.7</td>
<td>8.5 ± 1.3</td>
<td>0.32</td>
</tr>
<tr>
<td>Ne (10⁹/l)</td>
<td>48.7 ± 15.9</td>
<td>67.5 ± 41.6</td>
<td>0.012</td>
</tr>
<tr>
<td>Ly (10⁹/l)</td>
<td>23.9 ± 7.5</td>
<td>15.9 ± 10.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NLR</td>
<td>2.2 ± 1.0</td>
<td>6.5 ± 7.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLR</td>
<td>113.9 ± 43.1</td>
<td>194.0 ± 118.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 1**: Comparison of various parameters between patients and controls.

\*WBC - White blood cell; Hb - Hemoglobin; MPV - Mean platelet volume; Ne - Neutrophil count; Ly - Lymphocyte count; NLR - Neutrophil / lymphocyte ratio; PLR - Platelet / lymphocyte ratio

**Results**

We collected data on 36 patients and 36 controls. They were well matched for sex and age (Table 1).

**Figure 1**: Comparison of neutrophil / lymphocyte ratios between patients and controls.

**Figure 2**: Comparison of platelet / lymphocyte ratios between patients and controls.

Hematological data from the study and control groups are shown in Table 1. Significant differences
were observed in a number of parameters. In particular, the Hb concentrations and the Ly counts were lower and the Ne counts higher in the patient group compared to the controls. Both the NLRs and the PLRs were significantly higher in the patient group than in the control group (Figures 1 & 2). The MPVs were not significantly different in the patient group compared to the control group.

Discussion

Primary treatment of gastric cancer has been accepted as surgery in worldwide. The main objective of the surgery to ensure curability. Curative treatment can be achieved by detecting tumors at an early stage, making the appropriate lymph node dissection and performing the appropriate perioperative treatment and monitoring(9). Early diagnosis is the most important parameter among these parameters. Survival rates are extremely low in cases which there is an absence of an early diagnosis(10). Detection of early gastric cancer rates are higher in some countries like Japan and Western countries than in developing countries(9). Extension, accessibility and feasibility of screening methods for patients in risk groups constitute this difference in developed countries. Because of these reasons, several different and easy accessible parameters have been the subject of research on early detection of gastric adenocarcinoma.

The relationship between the development of cancer and inflammation are well known today. Many types of cancers develop from infection and inflammation areas. Inflammation is also very important stage in cancer progression(11).

It is still not so clear that, which mechanism has increased the number of neutrophils in patients with cancer. Cancer tissue produces myeloid growth factors such as granulocyte colony-stimulating factor, tumor necrosis factor-alpha, interleukin-1 and interleukin-6, that are thought to be caused neutrophil elevation(6). The growth of neutrophil concentration inhibits antitumor immune response by suppressing lymphocyte activity, thus leading to tumor growth and development of metastasis(5-7). According to these studies an imbalance in the NLR value may be related to tumor growth and metastasis. Lots of studies show that there is powerful correlation between inflammation and malignancy and they have investigated the significance of NLR values in malignant diseases(14-16).

Thrombocytosis occurs as a result of stimulation of megakaryocytes by proinflammatory cytokines such as interleukin-1 and interleukin-6. Thrombocytosis is an indicator of severity of the inflammation(17). It has been suggested that platelets play an important role in the progression and metastasis of cancer(18). Activated platelets contribute to tumor angiogenesis and promote tumor formation by secreting angiogenic growth factors(19). In addition to this, tumor cells lead to aggregate other tumor cells and platelets in the circulation. The aggregation of tumor cells and platelets contribute the persistence of tumor cell viability(20). Thus, elevated PLR levels are related with carcinogenesis. Addition to this, MPV is another parameter detecting the platelet activation(21). MPV is an early indicator of platelet activation(22). Platelets demonstrate differences in functional activity and size. Large platelets are relatively young; they are more reactive and produce more thrombogenic factors(23).

Therefore, in cases where increased platelet activation occurs, the rise of young platelets and MPV values is to be expected condition. There are also available studies that determine increased MPV values in a variety of malignancies(24-26).

The main finding of our study was that the NLR and the PLR is significantly higher in patients with gastric adenocarcinoma than in healthy controls. This is the first time this has been reported in this particular patient group, but the finding mirrors similar observations in other solid organ malignancies, when compared to patients with non-malignant disorders of the same organ(27-30), or to healthy controls(31). We did not find a significant difference in MPV in patients compared to controls. This was also reported to be the case in patients with carcinoma of the lung(32). However, NLR, PLR and MPV were all reported to be potential markers for colorectal adenocarcinoma(3).

Studies also suggest that PLR and NLR may be useful as prognostic markers for various cancers. In a study of patients with gastric carcinoma, 5-year survival was poorer in those whose initial NLRs and PLRs were higher(33). It was suggested that the NLR might be an independent prognostic factor in gastric carcinoma. In patients with carcinoma of the liver, higher initial PLRs correlated with lower survival rates, and the PLR was found to be an independent prognostic factor for survival(34).

In our patients, a lower lymphocyte count can explain both the elevated NLRs and PLRs since there was no significant difference in the platelet
counts in patients compared to controls and the neutrophil counts in patients were higher than in controls. This suggests that lower lymphocyte counts in patients with gastric adenocarcinoma may be of significance biologically.

In conclusion, the NLR and PLR may be useful markers in the diagnosis of gastric adenocarcinoma. They may be particularly helpful in patients at risk of gastric carcinoma as a consequence of longstanding dyspeptic complaints. In such patients, an elevated NLR and/or PLR might prompt further investigation into the possibility of a gastric malignancy. Calculating the NLR and PLR is relatively simple, as it only requires a full blood count that is almost universally available. However, our study was limited by its retrospective nature and relatively small sample size. Larger, prospective studies are required to confirm our findings.

References

25) Tuncel T, Ozgun A, Emirzeoglu L, Celik S, Bilgi O, et al. Mean platelet volume as a prognostic marker in...


