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Original Article

Diagnostic value of platelet/lymphocyte ratio and neutrophil/lymphocyte ratio in investigations for helicobacter pylori gastritis

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Abstract: Helicobacter pylori (HP) can cause many diseases and malignant conditions. In the stomach, HP causes mucosal injury and inflammation. We determined the association of the platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) with HP-positive and HP-negative gastritis severity. We retrospectively reviewed 234 patients who had undergone upper gastrointestinal endoscopy for the investigation of dyspepsia and reflux symptoms. The patients were divided into three groups according to the results of the histopathologic evaluation: HP-negative gastritis group, HP-positive gastritis group and control group (neither HP positivity nor gastritis). We routinely collected laboratory data, including complete blood count, from all the patients. The mean neutrophil count was higher and the mean lymphocyte count was lower in the HP-positive gastritis group than in the other groups. The mean platelet count was increased in all groups, but the lowest increase was seen in the HP-positive gastritis group. Both the NLR and PLR were higher in the HP-positive gastritis group than in the other groups. This is first study to determine that the PLR is a biomarker for HP-positive gastritis. Moreover, the PLR is superior to the NLR in patients with HP-positive gastritis.

Keywords: Endoscopy, helicobacter pylori, dyspepsia, platelet/lymphocyte ratio, neutrophil/lymphocyte ratio

Introduction

Helicobacter pylori (HP) is a common pathogen that can lead to a wide range of diseases as well as malignant conditions, including atrophic gastritis, gastroduodenal ulcer, chronic gastritis, intestinal metaplasia, gastric carcinoma, lymphoma, iron deficiency anemia, vitamin B12 deficiency and idiopathic thrombocytopenic purpura [1]. The pathogenesis of HP infection and HP gastritis is still unclear. HP leads to gastric mucosal inflammation and injury, which is the first step in the pathogenesis of HP-related diseases. This is followed by a systemic immune response [2, 3]. Colonization with HP can lead to severe conditions, and therefore, the detection of HP infection and the associated inflammation is important. Invasive HP-detection tests such as histopathologic evaluation and the rapid urease test are reliable, but necessitate upper gastrointestinal endoscopy. Stool tests and breath tests to detect HP are also available, but these are not as reliable as histopathologic evaluation. Hence, a rapid, non-invasive, simple method for the detection of HP infection and the associated inflammation is required.

The neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) are novel, reliable, inexpensive, simple markers for evaluating systemic inflammation and malignancies [4, 5]. In this study, we determined whether the PLR and NLR were associated with HP infec-

Table 1. Laboratory and demographic data of the study patients

Variable	Control n = 79	HP (-) n = 73	HP (+) n = 82	P
Age (years)	39 (30-52)	47 (37-54)	43 (36-50)	0.055
Gender (%)				
Female	57	56	60	0.927
Male	43	44	40	0.903
WBC ($10^3/mm^3$)	7.4 (6.4-9.1)	7.5 (5.9-9.7)	8.1 (6.3-10.3)	0.317
HB (g/dL)	12.4 (11.5-13.9)	12.1 (10.9-13.3)	11.8 (10.4-12.8)[a]	0.014*
PLT ($10^3/mm^3$)	247.0 (197.0-284.0)	240.0 (185.0-281.0)	234.0 (197.0-285.0)	0.615
MPV (fL)	8.3 (8.1-8.7)	8.2 (7.4-9.1)	8.5 (7.4-9.1)	0.333
Neutrophils ($10^9/L$)	47.0 (36.0-56.0)	42.0 (33.8-58.0)	63.1 (52.1-78.5)[a,b]	< 0.001*
Lymphocytes ($10^9/L$)	23.0 (18.0-30.0)	25.0 (18.2-35.5)	11.3 (8.4-16.0)[a,b]	< 0.001*
NLR	2.1 (1.4-2.9)	1.6 (1.3-2.3)	5.8 (3.7-6.9)[a,b]	< 0.001*
PLR	104.1 (79.6-127.0)	90.1 (58.1-147.4)	204.6 (176.3-265.7)[a,b]	< 0.001*

HP: *Helicobacter pylori,* WBC: White blood cell count, HB: Hemoglobin, PLT: Platelet, MPV: Mean platelet volume, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio. $P^a < 0.05$ compared to control group, $P^b < 0.05$ compared to HP (-) group. *: $p < 0.05$ is significant.

tion. This is the first study to show that both the PLR and NLR are elevated in patients with HP-positive gastritis.

Materials and methods

We retrospectively reviewed the data of 538 patients who had undergone upper gastrointestinal endoscopy, for the investigation of dyspepsia and reflux symptoms, in the endoscopy center of the General Surgery Department of Evliya Celebi Hospital, Dumlupınar University between May 2013 and May 2015.

This is a retrospective study. The personal information of the patients was not revealed in the article. *Informed consent* was obtained from all individual participants included in the study. This article does not contain any studies with human participants or animals performed by any of the authors.

At least one biopsy specimen was collected from the antrum and corpus in all patients. Patients who were diagnosed with a malignancy in the upper gastrointestinal system and those with a history of steroid treatment, radiotherapy, chemotherapy or systemic disorders such as diabetes mellitus, rheumatologic disorders, hypertension, ischemic heart diseases and neurological disorders were excluded from the study, because all these conditions can alter the PLR and NLR.

Thus, we finally investigated the data of 233 patients in this study. The subjects were divided into three groups: patients with neither HP positivity nor gastritis (control group), HP-negative gastritis patients and HP-positive gastritis patients. Before the endoscopy, we routinely performed tests for complete blood count (CBC), biochemical parameters and coagulation parameters. So we collected the data from CBC parameters of the patients who had upper GI endoscopy.

The following data were recorded for each patient: age, sex, white blood cell count (WBC), hemoglobin (HB), platelet count, mean platelet volume, neutrophil count, lymphocyte count, NLR and PLR.

Statistical analyses were performed using SPSS software (version 19, SPSS Inc., Chicago, IL). Normality was analyzed using the Shapiro-Wilk test. Since whole data were not normally distributed, data were presented as median and interquartile ranges (IQRs) and nonparametric statistical tests were used. Noncategorical quantitative data were tested using the Kruskal-Wallis analysis of variance on ranks, and the Dunn's method was used for post hoc testing. Categorical data were tested using the Chi-square test. In addition, ROC analysis was performed to evaluate diagnostic value of NLR and PLR. A *P* value less than 0.05 was considered statistically significant.

Results

In this study, we evaluated a total of 234 patients. The demographic and clinical features

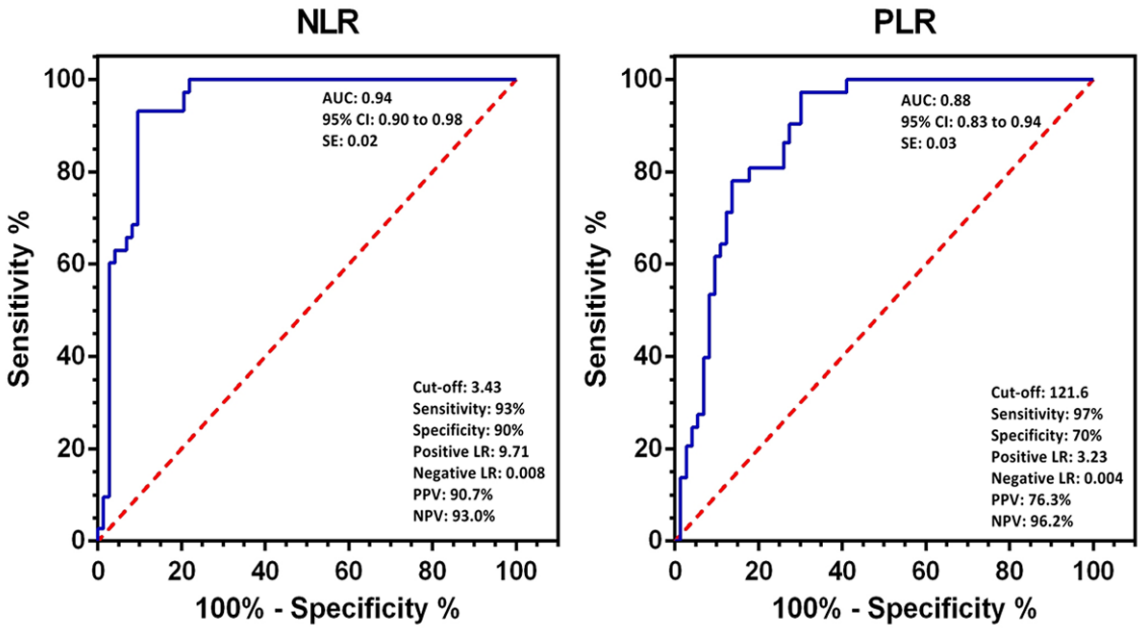

Figure 1. ROC curves for NLR and PLR as diagnostic tests for the differential diagnosis between *H.pylori* (-) and *H.pylori* (+) gastritis.

of the patients were shown in **Table 1.** The control group, HP-negative gastritis group and HP-positive gastritis group consisted of 79 (33.9%), 73 (31.3%) and 82 (35.1%) patients, respectively. No statistical significance were found between groups for age, gender, WBC, PLT, and MPV levels (**Table 1**).

The HP-positive gastritis group had a markedly higher neutrophil level and a lower lymphocyte and HB levels compared to the other groups ($P < 0.001$, $P < 0.001$, $P = 0.014$, respectively). The platelet levels were increased in whole groups, but this increase was lowest in the HP-positive gastritis group. Furthermore, there was no significant differences for platelet levels between study groups. Both the NLR and PLR were remarkably higher in the HP-positive gastritis group compared to the other groups ($P < 0.001$, **Table 1**). In our study, we also observed that PLR and NLR were higher in the HP-positive gastritis group.

Using NLR values, the area under the ROC curve for the differential diagnosis between *H.pylori* (-) and *H.pylori* (+) gastritis was 0.94 (95% confidence interval, CI: 0.90 to 0.98; standart error, SE: 0.02). The cut-off value of NLR for the differential diagnosis between *H.pylori* (-) and *H.pylori* (+) gastritis was 3.43, sensitivity was 93% (95% CI: 84.7% to 97.7%), and specificity was 90% (95% CI: 81.2% to 96.0%), positive likelihood ratio was 9.71, negative likelihood ratio was 0.08, positive predictive value (PPV) 90.7%, negative predictive value (NPV) 93.0% (**Figure 1**). Using PLR values, the area under the ROC curve for the differential diagnosis between *H.pylori* (-) and *H.pylori* (+) gastritis was 0.88 (95% confidence interval, CI: 0.83 to 0.94; standart error, SE: 0.03). The cut-off value of PLR for the differential diagnosis between *H.pylori* (-) and *H.pylori* (+) gastritis was 121.6, sensitivity was 97% (95% CI: 90.5% to 99.7%), and specificity was 70% (95% CI: 58.0% to 80.1%), PLR was 3.23, NLR was 0.04, PPV 76.3%, NPV 96.2% (**Figure 1**).

Discussion

HP is a major cause of gastritis, gastric ulcer, duodenal ulcer and gastric carcinoma. Furthermore, it has been associated with chronic conditions such as stroke, glaucoma, Alzheimer disease, rosacea, diabetes and thyroid disease [6]. Therefore, the accurate detection and prompt treatment of HP infection are of great clinical significance. It is estimated that more than 50% of the global population is infected with HP [1]. HP directly infects the gastric mucosa by invading the gastric mucosal cells

and duplicating in the cytoplasm. This stimulates the release of interleukin (IL)-8, a neutrophil chemotactic factor, which rapidly induces neutrophils and granulocytes. Thus, the neutrophil count is slightly increased. IL-8 also stimulates vascular endothelial growth factor (VEGF), which is activated by platelets. VEGF stimulation leads to an increase in the platelet count. All these steps result in chronic inflammation, which leads to chronic gastritis. The severity of the gastric injury depends on several factors, including bacterial subtype, host genetic factors, duration of infection and environmental factors [4, 7-9].

Since HP infection can lead to premalignant lesions, it must be rapidly detected and eradicated [9]. The NLR and PLR have been suggested to be reliable markers of chronic inflammatory conditions, such as cardiac disorders, malignant diseases, neurological disorders, vertigo, renal failure and systemic diseases such as diabetes mellitus, rheumatologic disorders and hypertension [10-13]. We hypothesized that since HP can cause chronic inflammation, it should be associated with an increase in the levels of systemic inflammatory markers, including the PLR and NLR. Some studies have indicated the effectiveness of the PLR and NLR in predicting the prognosis and survival of patients with malignant or chronic disorders [14, 15]. Thus, we consider that these parameters may be used as diagnostic biomarkers for HP-positive gastritis.

An experimental animal study by Gros et al. indicated that glycoprotein VI plays a role in both neutrophil induction and platelet secretory function. Our analysis showed that the NLR and PLR were higher in the HP-positive gastritis group than in the HP-negative gastritis group. However, the PLR and NLR in the HP-positive gastritis group were remarkably higher as in the literature [16].

Unal et al. reported that PLR was a novel prognostic biomarker for non-small cell lung cancer [14]. In our study, although both the PLR and NLR were higher in the HP-positive gastritis group, the PLR was higher than the NLR. In our study, dyspeptic symptoms were significantly more common among HP-positive gastritis patients than among HP-negative gastritis patients. Therefore, the PLR and NLR can be used as both a diagnostic tool and as a marker for HP in follow-up examinations, which is consistent with the literature [17]. Farah and Khamisy-Farah examined only the NLR in HP-positive gastritis patients [17]. We found that both the PLR and NLR can be used to detect HP in gastritis patients. Furthermore, in the study by Farah and Khamisy-Farah [17], the sample was limited to 50 patients with HP-positive gastritis and 50 patients with HP-negative gastritis. Our sample consisted of 234 patients divided into three groups. We think that our study is more unique to evaluate NLR. In addition to this, we performed ROC analysis for determining diagnostic value of both PLR and NLR has diagnostic value. In fact, the sensitivity and specificity of NLR is superior to PLR.

To the best of our knowledge, this is the first study to evaluate the association of the PLR and NLR with HP-positive and HP-negative gastritis. Likewise, this is the first study to determine that PLR is an independent biomarker for HP-positive gastritis. Further studies with larger samples of patients with HP-positive gastritis are needed.

Conclusion

Our study indicates that both the PLR and NLR can be used as biomarkers for the diagnosis and follow-up of HP infection in gastritis patients. The PLR is superior to the NLR in patients with HP-positive gastritis, but the NLR is more useful in patients with HP-negative gastritis. Also when we evaluated with ROC analysis, NLR is more usable in clinical practice because of its' high sensitivity and specificity. The major limitation of this study is its retrospective nature Prospective studies investigating the follow-up period after the eradication of HP infection in patients with HP-positive gastritis are required.

Disclosure of conflict of interest

None.

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