ORIGINAL ARTICLE

EVALUATION OF THE RESULTS OF HEMATOLOGICAL PARAMETERS OF PATIENTS WITH GASTRIC CANCER

Mide Kanserli Hastaların Hematolojik Parametre Sonuçlarının Değerlendirilmesi

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ABSTRACT

Objective: Gastric cancer is a major health concern which fourth leading cause of cancer death and fifth most common cancer. It has difficulties such as having a poor prognosis and diagnoses at an advanced stage. There are studies to find prognostic indicators that are easily and less invasively obtained in gastric cancer and hematological tests are one of them. In this study, we aimed to investigate the relation between hematological test and gastric cancer.

Material and Methods: 48 patients diagnosed with gastric cancer and 45 healthy adults in the control group were examined prospectively. All participants' demographic data and laboratory results were obtained from the hospital database and recorded.

Results: In the gastric cancer group compared to the healthy control group, while red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean cell hemoglobin concentration (MCHC), platelet distribution width (PDW), lymphocyte (LYM), eosinophil (EO) values were statistically lower, mean corpuscular hemoglobin (MCH), red cell distribution width-standard deviation, red cell distribution width-coefficient of variation (RDW-CV), nucleated red blood cells (NRBC), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) values were observed statistically higher ($p<0.05$). RBC, HGB, HCT, LYM, RDW-SD, RDW-CV, NLR, PLR, and MLR exhibited considerably higher area under the curve (AUC) values in the receiver operating characteristic (ROC) analysis of these parameters ($p<0.001$).

Conclusion: RBC, HGB, HCT, LYM, RDW-SD, RDW-CV, NLR, PLR, and MLR levels can be used as a supportive test to eliminate endoscopic delays in gastric cancer diagnosis.

Keywords: *Stomach; Adenocarcinoma; Laparoscopic Gastrectomy; Blood Cell Count*

ÖZET

Amaç: Mide kanseri, kansere bağlı ölümlerde dördüncü ve en sık görülen kanserlerde beşinci sırada yer alan önemli bir sağlık sorunudur. Prognozun kötü olması ve ileri evrede tanı konması gibi güçlükleri vardır. Mide kanserinde kolay ve daha az invaziv olarak elde edilen prognostik göstergeleri bulmaya yönelik çalışmalar vardır ve hematolojik testler bunlardan biridir. Bu çalışmada hematolojik test sonuçları ile mide kanseri arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntemler: Bu çalışmada mide kanseri tanısı almış 48 hasta ve kontrol grubunda yer alan 45 sağlıklı yetişkin retrospektif olarak incelendi. Tüm katılımcıların demografik verileri ve laboratuvar sonuçları hastane veri tabanından elde edildi ve kaydedildi.

Bulgular: Mide kanserli grupta sağlıklı kontrol grubuna göre; kırmızı kan hücreleri (RBC), hemoglobin (HGB), hematokrit (HCT), ortalama hücre hemoglobin konsantrasyonu (MCHC), trombosit dağılım genişliği (PDW), lenfosit (LYM), eozinofil (EO) değerleri istatistiksel olarak daha düşüktü, ortalama eritrosit hemoglobin (MCH), kırmızı hücre dağılım genişliği-standart sapma, kırmızı hücre dağılım genişlik-varyasyon katsayısı (RDW-CV), çekirdekli kırmızı kan hücreleri (NRBC), nötrofil lenfosit oranı (NLR), trombosit lenfosit oranı (PLR) ve monosit lenfosit oranı (MLR) değerlerinin istatistiksel olarak daha yüksek olduğu gözlendi ($p<0,05$). RBC, HGB, HCT, LYM, RDW-SD, RDW-CV, NLR, PLR ve MLR, bu parametrelerin alıcı çalışma karakteristiği (ROC) analizinde oldukça yüksek eğri altı alan (AUC) değerleri sergiledi ($p<0,001$).

Sonuç: RBC, HGB, Hct, LYM, RDW-SD, RDW-CV, NLR, PLR ve MLR seviyeleri mide kanseri tanısında endoskopik gecikmeleri ortadan kaldırmak için destekleyici test olarak kullanılabilir.

Anahtar Kelimeler: *Mide; Adenokarsinom; Laparoskopik Gastrektomi; Kan Hücre Sayımı*

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INTRODUCTION

Gastric cancer (GC) is one of the most common type of cancer and is an aggressive disease which is front row cause of cancer-related death (1-2). While the incidence of GC decreases due to some factors such as early diagnosis, healthy life and reduced incidence of disease-causing bacteria, but still there is an increase in mortality rates and incidence of the disease in some geographies (3). GC development affected by both genetic and environmental factors (4). Various genetic changes such as mutations at the cytogenetic level in the somatic cell or loss of function of the DNA mismatch repair system in some types of GC have been shown in the occurrence of the disease (5-7). Environmental and nutritional factors play a role in the development of the disease. Consumption of salty and salt-preserved foods, nitrates or pickled foods have been associated with an increased risk of developing stomach cancer (8-9). Content of the diet, eating habits and smoking can increase the risk of disease (9-10). The early stages of the disease may be asymptomatic or have minimal symptoms, so the disease is difficult to diagnose and constantly diagnosed at an advanced stage (11).

Currently, the gold standard method for detecting GC is upper endoscopy with tissue biopsy. However, these methods have disadvantages such as being invasive, costly and time-consuming. Therefore, rapid, economical, non-invasive method researches continue. Studies on genetic, biochemical and hematological parameters that have the potential to one of the biomarkers on blood, urine, saliva and gastric juice are in progress. However, although some results are very promising, further studies with larger sample sizes with larger numbers of healthy patients are needed (12-14). The prognostic significance of some hematology test results, such as leukocyte and platelet count, and mean platelet volume, has been demonstrated in various malignancies (15-16). We aimed to investigate the status of hematological tests in evaluating hematological changes associated with GC, as well as other medical tests and imaging modalities, regarding the diagnosis or treatment of GC.

MATERIAL AND METHODS

This study was based on retrospective analysis of 48 patients diagnosed with GC and 45 healthy adults. A patient group was formed from individuals who underwent curative laparoscopic (assisted) gastrectomy and diagnosed with gastric adenocarcinoma in Sabuncuoğlu Şerefeddin Training and Research Hospital between January 2021 and January 2023. An informed consent form was obtained from the individuals before the laparoscopic (assisted) gastrectomy procedure. For both groups, individuals with chronic diseases, ongoing infections, diabetes mellitus, autoimmune disease, under the age of 18, and blood transfusions were excluded. Amasya University Rectorate Non-Invasive Clinical Research Ethics Committee (Jan 2023 Number of Meeting 02 Decision Number 2023/05).

Laboratory values of white blood cell (WBC), red blood cells (RBC), hemoglobin (HGB), hematocrit (HCT), mean cell hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet (PLT), red cell distribution width-standard deviation (RDW-SD), red cell distribution width-coefficient of variation (RDW-CV), platelet distribution width (PDW), mean platelet volume (MPV), plateletcrit (PCT), nucleated red blood cells (NRBC#), nucleated red blood cells (NRBC), neutrophil (NEUT#), lymphocyte (LYMPH#), monocyte (MONO#), eosinophil (EO #), basophil (BASO#), LYMP, MONO, NEUT, EO and BASO measured in Sysmex XN-1000 analyzer and demographics and data were extracted from the hospital database records.

SPSS 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) software was used for statistical analysis of data. First of all, Kolmogorov-Smirnov test was used to determine the data distribution, and Independent Samples t-test was used for pairwise comparison of parametric tests for data showing normal distribution according to this test, and Mann Whitney-U test, which is one of the nonparametric tests, was used for data that did not show normal distribution. Evaluating the discrimination of these analyzes between the patient group and the healthy group was evaluated with the Receiver Operating Characteristic (ROC) test. $p<0.05$ was considered statistically significant.

RESULTS

Demographic data of the patient and control groups included in the study are given in Table 1. Accordingly, there was no difference between the mean age of the

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Table 1. Demographic data of Control and Patient Groups

	Control (n=45)	Patient (n=48)
Age (year)	62.22±11.85	65.812±9.55
Gender (Woman/Man)	9/39	11/34

Table 2. Levels of Hematological Values in Control and Patient Groups

	Control (n=45)	Patient (n=48)	p values
RBC ($x10^6$)	4.786±0.542	3.948±0.669	.000
WBC ($x10^3$)	7.054±1.085	8.157±4.470	.863
PLT ($x10^6$)	227.555±46.256	206.062±91.826	.162
HGB (g/dL)	14.000±1.498	11.320± 2.058	.000
HCT	37.866±2.0108	35.025± 5.781	.000
NEU ($x10^3$)	3.948±0.867	5.945±4.352	.056
MCH	29.226±1.850	28.816±2.900	.442
MCHC	33.091±1.233	32.054±2.186	.007
RDW-CV	13.444±1.092	16.477±4.176	.000
RDW-SD	42.264±2.650	53.904±14.25	.000
NRBC	0.000±0.002	0.014±0.040	.000
PDW	12.306±2.233	11.172±2.553	.005
PCT	0.235±0.052	0.212±0.068	.030
LYMPH ($x10^3$)	2.279±0.657	1.227±0.769	.000
EO ($x10^3$)	0.186±0.186	0.116±0.159	.000
LYM%	32.404±8.080	16.836±10.906	.000
MONO%	8.295±2.067	6.872±4.888	.003
NEUT%	55.917±7.851	69.630±19.532	.000
EOS%	2.400±1.133	1.563±1.743	.000
BASO%	0.544±0.298	0.371±0.321	.006
NLR	1.922±0.878	6.9123±6.773	.000
PLR	108.063±40.191	224.027±174.241	.000
MLR	0.280±0.162	0.567±0.478	.007

red blood cells (RBC), white blood cell (WBC), platelet (PLT), hemoglobin (HGB), hematocrit (HCT), neutrophil (NEUT#), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), red cell distribution width-coefficient of variation (RDW-CV), red cell distribution widt-h-standard deviation (RDW-SD), nucleated red blood cells (NRBC), platelet distribution width (PDW), plateletcrit (PCT), lymphocyte (LYMPH), eosinophil (EO), lymphocyte percentile (LYM%), monocyte percentile (MONO%), neutrophil percentile (NEUT%), eosinophil percentile (EOS %), basophil percentile (BASO%), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) P<0.05 statistically significant

patient group and the mean age of the control group (p= 0.110).

In the GC group compared to the healthy control group, RBC, HGB, HCT, mean cell MCHC, PDW, LYM, EO values were statistically lower, MCH, RDW-SD, RDW-CV, NRBC, neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR) values were observed statistically higher (p<0.05). On the other hand, no difference was observed in MCH, PLT and WBC values between the two groups. (Table 2 presents hematological data.) RBC, HGB, HCT, MCHC, PDW, PCT, LYM, EO, RDW-SD, RDW-CV, NLR, PLR, and

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Figure 1. ROC analysis curves of hematological data

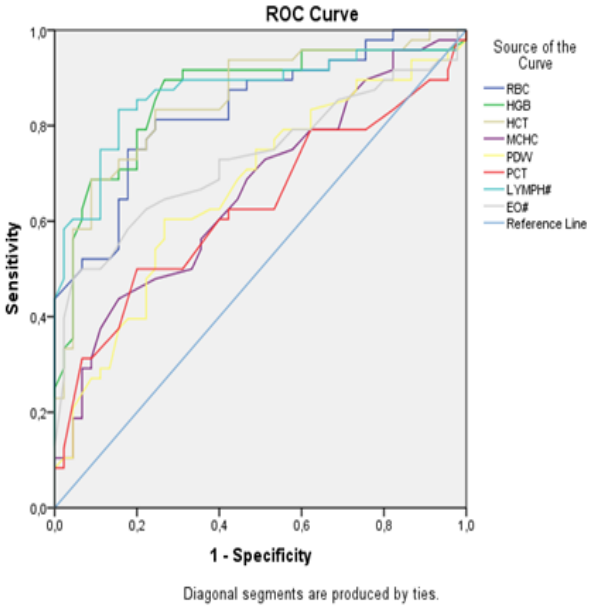

Figure 2. ROC analysis curves of hematological data

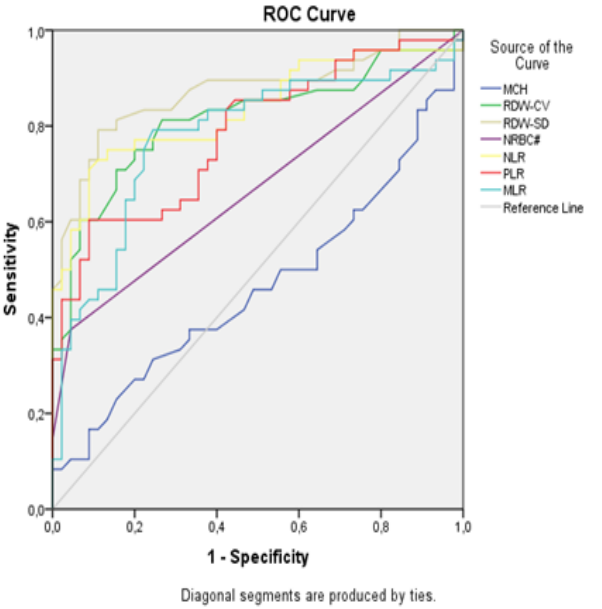

Table 3. ROC analysis data for hematological testing

	AUC	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
RBC	.834	.041	.000	.752	.915
HGB	.862	.040	.000	.784	.941
HCT	.854	.040	.000	.777	.932
MCHC	.663	.056	.007	.554	.773
PDW	.669	.056	.005	.559	.780
PCT	.631	.058	.030	.516	.745
LYMPH	.871	.039	.000	.794	.947
EO	.732	.053	.000	.628	.836
MCH	.465	.061	.564	.347	.584
RDW-CV	.814	.046	.000	.724	.904
RDW-SD	.872	.038	.000	.797	.947
NRBC#	.669	.056	.005	.558	.779
NLR	.834	.043	.000	.750	.919
PLR	.783	.047	.000	.691	.876
MLR	.778	.050	.000	.679	.876

red blood cells (RBC),hemoglobin (HGB), hematocrit (HCT), mean cell hemoglobin concentration (MCHC), platelet distribution width (PDW), plateletcrit (PCT), lymphocyte (LYMPH), eosinophil (EO), mean cell hemoglobin (MCH),red cell distribution width-coefficient of variation (RDW-CV), red cell distribution width-standard deviation (RDW-SD), nucleated red blood cells (NRBC),lymphocyte percentile (LYM%), monocyte percentile (MONO%), neutrophil percentile (NEUT%), eosinophil percentile (EOS %), basophil percentile (BASO%), neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR) and monocyte lymphocyte ratio (MLR)

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MLR exhibited considerably higher area under the curve (AUC) values ($p<0.001$) in the receiver operating characteristic (ROC) analysis of these parameters. (Figure 1, Figure 2 and Table 3 show ROC analysis data.)

DISCUSSION

In this study, we examined the whole blood hematology results of GC patients and healthy individuals. Because recent studies and new data on GC are needed. Due to the nature of the disease, it is difficult to diagnose the disease in the early stages. In addition, current methods used in diagnosing the disease are expensive and laborious (14). The tumor microenvironment is associated with a tumor-associated systemic state of inflammation, thereby accelerating tumor progression (17). Although recent studies suggest that cytokines secreted by inflammatory cells in the tumor microenvironment affect tumor cell proliferation and migration, the exact mechanisms are still unknown (18-19). Some genetic tests, such as the application of cfDNA use, is difficult to study for early GC detection due to the low level in early stage of GC and technical difficulties in its detection (20).

The NLR and PLR are indicator of systemic inflammation. In line with our results, Fang et. all, found that the systemic inflammatory markers NLR and PLR were higher in GC cancer and showed diagnostic sensitivity (21). Furthermore, they indicate NLR and PLR were more valuable for the diagnosis of GC than the traditional tumor markers CEA and CA19-9. Zhao et al. noted that both preoperative high NLR and PLR collected from routine blood tests are associated with poor overall survival, but they emphasized that only NLR can be an independent prognostic marker in patients with metastatic GC. Consequently, they reported that high NLR and PLR levels may contribute to adverse anti-tumor function (22). Lian et al., showed that preoperative PLR and NLR levels were significantly higher in patients with GC than in healthy individuals, and they stated that they could provide important diagnostic and prognostic results in patients with resectable GC (23).

RDW is predictor of inflammation and related with erythrocyte volume variability and erythrocyte homeostasis (24). It has been shown RDW associated with many diseases, and in studies on GC, Wang et al. suggested that high pre-treatment RDW level may be a negative predictor for cancer prognosis (25). And parallel with our RDW-CV results, Pietrzyk et all. showed that GC patients higher mean RDW values than healthy individuals (26). In cancer-induced inflammation, the survival of red blood cells is short. The number of immature red blood cells increases, resulting in high RDW. Therefore, high RDW is often seen in GC patients (27).

Aksoy et al. found that HGB, MLR and WBC results were significantly different in the GC patient group. HGB and MLR results are consistent with our results, while WBC results are not. Because according to our data, there was no significant difference in WBC between the groups (28). In their study on patients with GC who received neoadjuvant chemotherapy, Cheng et al. showed similar results and stated that MLR can be used as a convenient and inexpensive prognostic marker (29). Song et al., reported that MLR may be biomarkers to predict overall survival in patients with advanced GC (30).

It has been shown that PDW may be effective as an indicator of inflammation, and there is a close relationship between PDW, white blood cell count and serum C-reactive protein level (31). In parallel with our results, Cheng et al. showed decreased PDW associated with GC, but Saito et al. showed opposite to our results increased PDW increases in GC patients. They explained that this may be due to differences in diagnosis and different analysis methods chosen among studies, such as median value cut-off and optimal cut-off (27-32).

CONCLUSION

In our study, there were limitations such as being subject to bias, because it was retrospective, and the small number of patients included in our study. However, among the findings we obtained regarding the hematological parameters we examined, the RBC, HGB, HCT, MCHC, PDW, LYM, EO values were statistically lower in patients with GC compared to the control group. The fact that it is higher than the mean value indicates that endoscopic intervention can be evaluated as a prognostic marker in the diagnosis of GC. We believe that our findings will contribute to further research to be conducted.

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