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Original Article

The predictive value of neutrophil-lymphocyte ratio and mean platelet volume in patients with colorectal carcinoma

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Abstract

Aim: This study aimed to investigate neutrophil-lymphocyte ratio (NLR) and mean platelet volume (MPV) for predicting colorectal cancer (CRC).

Material and Methods: We investigated retrospectively patients who underwent colonoscopy. The study consisted of 75 patients with CRC and 91 study participants with normal colonoscopy as control group, and MPV and NLR were compared between groups. MPV and NLR were also investigated for tumor stage and metastasis.

Results: Among the CRC patients the mean NLR value (3.09 vs 2.26) and PLT count (287080 vs 251857) were significantly higher, whereas the mean MPV (9.62 vs 10.68 fL) and hemoglobin level (11.62 vs 14.18 g/dl) were significantly lower in the CRC group. WBC count was not significantly different between the groups. Mean NLR in metastatic patients and non-metastatic patients were 3.56 and 2.73, respectively (p:0.01).

Conclusion: We showed that high NLR and low MPV are associated with CRC. Elevated NLR is related with presence of CRC and it can be used for risk prediction. Although we found lower MPV levels, conflicting results about MPV in CRC prevents it from using as a marker in CRC.

Keywords: Colon polyp; colonoscopy; colorectal cancer; mean platelet volume; metastasis; neutrophil-lymphocyte ratio

INTRODUCTION

Among various cancer types, colorectal cancer (CRC) is one of the most common causes of cancer mortality worldwide (1). Various markers have been evaluated in patients with CRC, but all of these markers have low ability in detecting CRC (2,3). Although CEA has value in the follow-up management of patients with CRC, The American Society of Clinical Oncology did not recommend using CEA, CA 19-9 or another marker as a screening test for CRC (2).

Mean platelet volume (MPV), lymphocyte and neutrophil counts are routinely measured parameters by complete blood count (CBC) analyzers. MPV is the average size of platelets, which predicts the platelet production rate (4). Evidence suggest that MPV may be used as an inflammation marker for disease activity in several chronic inflammatory diseases including ulcerative colitis, rheumatoid arthritis (RA), ankylosing spondyloarthritis (AS) and familial Mediterranean fever (5-9). In these conditions the MPV value was detected low (6-9), but other trials showed elevated MPV levels among RA and AS patients, and found also a drop after medical therapy (10,11). Coronary artery diseases, cerebrovascular diseases, deep vein thrombosis, acute pancreatitis, nonalcoholic fatty liver disease and malignancies such as pancreatic adenocarcinoma, hepatocellular carcinoma, and gastric cancer are other disease examples for high levels of MPV (12-20). Also NLR was investigated in various cancers, and data showed that NLR was a significant prognostic factor in some gastrointestinal system cancers (21-27).

In this retrospective study, we compared MPV and NLR values in patients with CRC and control group. Our aim

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was to investigate predictive values of NLR and MPV in CRC. Moreover, significance of these values were also evaluated in patients with metastatic CRC.

MATERIAL and METHODS

We investigated retrospectively patients who underwent colonoscopy for various indications. All patients underwent prompt colonoscopy using Olympus video-endoscopes (GIF type-160 and 180). Seventy-five patients with CRC and 91 age and gender matched subjects with normal total colonoscopy were included in this retrospective study. The patients' demographic features, endoscopic and laboratory findings were investigated. The endoscopic and laboratory data was extracted from the computerized database. Patients with hematological diseases, heart failure, chronic infections, rheumatic diseases, hepatic disorders, renal disease, other known cancer, leukocytosis or leucopenia were not included in the study. Patients with colon polyps were excluded from the control group either.

Total leukocyte (WBC), lymphocyte and neutrophil counts, Hemoglobin (Hb), MPV value and Platelet (PLT) levels were determined on samples obtained from peripheral blood. Dividing the serum absolute neutrophil count to the serum absolute lymphocyte count resulted as NLR. The total cell counts were measured by Sysmex XE-2100. At our hospital, normal MPV value ranges between 7.2 and 11.1 fL.

Local Ethics Committee approval was obtained before the beginning of the study.

The data were analyzed with Statistical Package for the Social Sciences version 20.0 (SPSS Inc., Chicago, USA) and MedCalc version 15.2.1 statistical software. The Kolmogorov-Smirnov test was applied to evaluate the normal distribution of the variables. Values were expressed as mean ± standard deviation (SD) for normally distributed variables, and as median and 25th%-75th% percentiles for not normally distributed variables. Variables were compared using the independent t-test and Mann–Whitney U-test for normally and non-normally distributed data, respectively. The chi-square test was used for categorical data. To evaluate the independent association of variables with colon cancer and metastases, logistic regression analysis was performed. The optimal cut-off values of MPV and NLR variables for detection of colorectal cancer and metastases was calculated using receiver operating characteristic (ROC) curve analysis with 95% confidence intervals (CI). The specificity, sensitivity, negative predictive rate (NPR), positive predictive rate (PPR), positive likelihood (+LR), negative likelihood (-LR) and kappa value were calculated to determine the diagnostic accuracy. P values less than 0.05 were considered to be statistically significant.

RESULTS

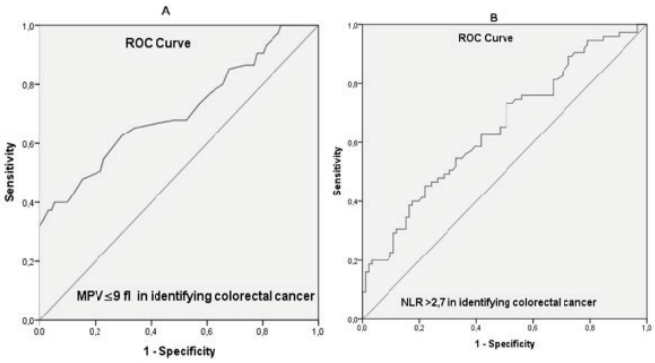
The sociodemographic features and laboratory values are summarized in Table 1. Seventy-five patients were in the CRC group, and the mean age was 62.9 years. Forty-seven (63%) of the cases were male and 28 (37%) were female. The control group included 57 men and 34 women, whose mean age was 62.3 years. Age and gender were not statistically different between two groups.

Among the CRC patients the mean NLR value and PLT count were higher (p<0.001 and p:0.01, respectively) whereas the mean MPV and Hb level were lower compared to the control group (p<0.001 each). Mean WBC count did not differ between groups (Table 1).

Table 1. Comparison of clinical and laboratory parameters between control and colorectal cancer groups

	Colorectal cancer group, n: 75 (45.2%)	Control group, n: 91 (54.8%)	P
Age (years)†	62.89 (±12.6)	62.31 (±11.6)	0.75
Male/Female(%)‡	47 /28 (63/37)	57 /34 (63 / 37)	0.99
WBC (x103)†	7.34(±1.91)	7.12 (±1.58)	0.40
Hb (gr/dl)†	11.62 (±2.17)	14.18 (±1.55)	< 0.001
PLT (x103)†	287.08 (±88.64)	251.86 (±86.13)	0.01
MPV (fl)§	9.61 (±1.64)	10.68 (±0.87)	< 0.001
NLR§	3.1 (±1.72)	2.26 (±0.94)	0.001

WBC: White Blood Count; NLR: Neutrophil to Lymphocyte Ratio; MPV: Mean Platelet Value; Hb: Hemoglobin



MPV: Mean platelet volume, NLR: Neutrophil to lymphocyte ratio

Figure 1. Comparison of receiver operating characteristic curves of mean platelet value and neutrophyl to lymphocyte ratio values in identifying colorectal cancer. For colorectal cancer area under receiver operating characteristic (ROC) curves were 0.69 (%95CI: 0.61-0.76) and 0.65 (%95CI: 0.57-0.72) for MPV and NLR, respectively

A cut-off value of MPV for diagnosing CRC was found as ≤9 fL by ROC analysis [Sensitivity: 37.3%, specificity: 95.6%, AUC: 0.69 (0.61–0.76) p:<0.001] and the cut-off value of NLR was 2.7 [Sensitivity: 46.7%, specificity: 75.8%, AUC: 0.65 (0.57–0.72) p:0.01] (Figure 1, Table2). NLR and MPV were independent predictive factors for determining CRC in the logistic regression analysis (OR=1.77, 95% CI: 1.29–2.43; OR=0.40, 95% CI: 0.27-0.60, respectively).

Table 2. Statistical diagnostic measures of MPV and NLR variables in the detection of colon cancer and metastases

	Variables in the detection of colon cancer		Variables in the detection of metastasis	
Diagnostic measures	**MPV (≤ 9 fl)**	**NLR (>2.7)**	**MPV (≤10fl)**	**NLR (>2.6)**
AUC (95% CI)	0.69 (0.61-0.76)	0.65 (0.57-0.72)	0.59 (0.46-0.70)	0.66 (0.54-0.77)
SEN (95% CI)	37.3 (26.4–49.3)	46.7 (35.1-58.6)	75.8 (57.7–88.9)	66.7 (48.2-82.0)
SPE (95% CI)	95.6 (89.1–98.8)	75.8 (65.7–84.2)	38.1 (23.6–54.4)	64.3 (48.0–78.4)
PPR (95% CI)	87.5 (71.0-96.5)	61.4 (47.6-74.0)	49.0 (34.8-63.4)	59.5 (42.1-75.2)
NPR (95% CI)	64.9 (56.2-73.0)	63.3 (53.5-72.3)	66.7 (44.7-84.4)	71.1 (54.1-84.6)
$^{+}$LR (95% CI)	8.5 (3.1–23.1)	1.93 (1.2-3.0)	1.2 (0.9–1.7)	1.87 (1.2-3.0)
$^{-}$LR (95 %CI)	0.66 (0.5-0.8)	0.7 (0.6-0.9)	0.64 (0.3-1.3)	0.52 (0.3-0.9)
AR (%)	69	61	52	65
Kappa test (P value)	**<0.001**	**0.01**	0.53	**0.01**
Kappa test (k value)	0.30	0.21	0.07	0.31

MPV: Mean Platelet Value; NLR: Neutrophil To Lymphocyte Ratio; AUC: Area Under The Roc Curve; SEN: Sensitivity; SPE: Specifity; PPR: Positive Predictive Rate; NPR: Negative Predictive Rate; AR: Accuracy Rate; $^{+}$LR: Positive Likelihood Ratio; $^{-}$LR: Negative Likelihood Ratio

Table 3. Comparison of clinical and laboratory parameters between metastatic and non-metastatic colorectal cancer groups

	Metastatic, n: 33, (44%)	Non-metastatic, n: 42 (56%)	P
Age (years)†	61.82 (±12.11)	63.74 (±12.05)	0.75
Male/Female(%)‡	21 /12 (64/36)	26 /16 (62/38)	0.87
WBC (x103)†	7.54 (±1.76)	7.19 (±2.02)	0.43
Hb (gr/dl)†	11.60 (±2.13)	11.64 (±2.23)	0.94
PLT (x103)†	287.73 (±76.2)	286.57 (±98.22)	0.95
MPV (fl)§	9.31 (±1.86)	9.85 (±1.42)	0.15
NLR§	3.56 (±1.91)	2.73 (±1.48)	0.01

†: Mean (±Standard deviation)
‡: Case number (%)
§: Median (25th-75th percentiles)
WBC: White Blood Count; NLR: Neutrophil to Lymphocyte Ratio; MPV: Mean Platelet Value; Hb: Hemoglobin

Among 75 CRC patients 33 had metastatic CRC and 42 had no metastasis (Table 3). Mean NLR in metastatic patients and non-metastatic patients were 3.56 and 2.73, respectively (p:0.01). Metastasis did not influence the mean MPV, Hb level, PLT and WBC counts. The cut-off value of MPV for detecting metastasis was found to be ≤10 fL by ROC analysis [Sensitivity: 75.8%, specificity: 38.1%, AUC: 0.9 (0.46–0.70) p:0.53] and the NLR for detection of metastases was 2.6 [Sensitivity: 66.7%, specificity: 64.3%, AUC: 0.66 (0.54–0.77) p:0.01] (Figure 1). NLR was an independent predictive factor for the presence of metastasis in CRC patients (OR=1.37, 95% CI: 1.007–1.866) but MPV was not an independent predictive factor (Table 2).

Thirty-eight patients had rectum cancer and 37 had colon cancer in different segments of the colon. Patients with colon cancer had a lower Hb level than patients with rectum cancer (10.95 vs 12.28 g/dl; p<0.01). NLR, MPV, PLT and WBC counts were not significantly different among colon and rectum cancer.

DISCUSSION

Patients with CRC may present with various symptoms, but it is also detected in asymptomatic individuals by routine screening. In a report from Kaiser Permanente, over 30 percent of all CRCs are asymptomatic (28). Data show that the CRC incidence and mortality declines over time, possibly thanks to early detection through screening and improved treatment (29). Colonoscopy is the gold standard for CRC diagnosis, but it is an operator-skill dependent modality. The high cost, complications, patient discomfort and unwillingness are major problems about colonoscopy (30).

An ideal CRC screening program should have high sensitivity and specificity, with low cost and safety. Serum markers like CEA and CA 19-9 are non-invasive tests with low cost and no complication, but their sensitivity and specificity for CRC are low (2,3,31). Because of these reasons, we aimed to investigate the predictive value of MPV and NLR in patients with CRC.

Although there is a marked relationship of chronic inflammation with carcinogenesis arising in patients with inflammatory bowel diseases (32), data linking chronic inflammation with colorectal carcinogenesis is conflicting (33). CRP, as an inflammatory marker was investigated for CRC. In some studies there was an inverse association between CRP and CRC incidence (34), whereas other studies showed exactly opposite results (33). Elevated WBC was detected in patients with colon cancer and WBC levels were related to mortality in a large cohort study, but no statistically significant difference was detected for rectum cancer (35). Besides, trials showed that aspirin and NSAID use reduce the risk of CRC (34,36). All these data supports the hypothesis that inflammation is a risk factor for CRC, or CRC causes inflammation.

CBC is a routinely performed health examination, even in asymptomatic patients. Neutrophil and lymphocyte counts and MPV value are components of the CBC, without additional expense. NLR is associated with systemic inflammatory burden, and despite some opposite data MPV decreases in inflammatory disorders (6-9). Our findings show that CRC patients have higher NLR and lower MPV values, which is thought to show the inflammatory reaction. Li et al. evaluated MPV and NLR as potential biomarkers for CRC and they found that NLR was increased in patients with CRC (37). High NLR values are indicators for poor prognosis in CRC (24,25), and the treatment of CRC decreases NLR values in CRC (38). Our study showed that NLR was higher in metastatic patients, which supports the prognostic value of NLR in CRC.

The aforementioned study showed also an increase in MPV value in patients with CRC (37). Also MPV values decrease after treatment of CRC (38), and because MPV values decrease after therapy one can expect that MPV values should be higher in CRC patients. Our results are conflicting with these findings. Our study showed a lower mean MPV among CRC compared with control group. Similar contradiction was also found in RA and AS patients. Some trials showed an increase in MPV among AS and RA patients (10,11), whereas another study showed a decrease (8). In our opinion, because of these conflicting results one cannot suggest MPV for predicting CRRC or a prognostic factor for CRC.

Patients with rectum cancer have a lower Hb level compared to colon cancer. This is an expected finding because colon cancer tends to be more asymptomatic and causes more iron deficiency anemia from unrecognized blood loss (39). It is known that patients with right sided colon carcinomas lose more blood than patients with CRC at other colonic parts (40). In the present study NLR and MPV were similar between colon and rectum cancers.

CONCLUSION

Our study determined that high NLR and low MPV are associated with CRC, but these tests are non-specific to be suitable for predicting CRC. Elevated NLR may potentially support risk prediction, and using NLR along with other screening modalities may increase its efficiency. Additionally NLR is higher among metastatic patients and could be used as a prognostic marker either. Because of the conflicting results MPV should rather not be used for CRC prediction.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: The local ethic committee of Yıldırım Beyazit University, Faculty of Medicine approved the study protokol. The approval date is 15/10/2014 and the number is 160.

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