ORIGINAL ARTICLE

Neutrophil-lymphocyte ratio and mean platelet volume can be a predictor for severity of acute appendicitis

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ABSTRACT

BACKGROUND: Early diagnosis of perforation in acute appendicitis (AA) allows surgeons to select the most appropriate treatment. The aim of the present study was to determine whether preoperative neutrophil-lymphocyte ratio (NLR) and mean platelet volume (MPV) could predict perforation in AA.

METHODS: Data collected from 413 consecutive patients with AA and 100 healthy controls were analyzed retrospectively. Patients were categorized as having had phlegmonous appendicitis, appendicitis with localized peritonitis, or appendicitis with perforation and/or gangrene. MPV and NLR values were compared among the control group and the 3 groups of patients with AA.

RESULTS: Means values of MPV were 9.3±8 fL for the patient group and 8.5±0.9 fL for the healthy control group (p=0.0005). Mean values of MPV by patient subgroup were 8.8±5.8 for phlegmonous appendicitis, 8.9±5.8 for localized peritonitis, and 12.8±9.7 for appendicitis with perforation and/or gangrene (p=0.005). Cut-off value of MPV was set at 8.92 to differentiate AA with perforation and/or gangrene from other types of AA. Mean NLRs of patients with phlegmonous appendicitis, appendicitis with localized peritonitis, and appendicitis with perforation and/or gangrene were 8.3±5.6, 9.1±6.2, and 10.6±6.4, respectively; p=0.023. The cut-off value for NLR was set at 7.95 to differentiate AA with perforation and/or gangrene from other types of AA.

CONCLUSION: Both NLR and MPV can be useful in predicting severity of AA.

Keywords: Appendicitis; lymphocyte; mean platelet volume; neutrophil; predictive factors.

INTRODUCTION

Acute appendicitis (AA) is one of the most common acute surgical conditions of the abdomen, and has a lifetime risk of approximately 7%.[1] Although urgent appendectomy is still considered the gold standard treatment, recent evidence has shown that AA can be treated conservatively without surgery.[2] However, conservative treatment is likely inconvenient in cases of perforated AA. Therefore, any factor that allows for prediction of perforation in AA contributes significantly to patient-specific treatment. Furthermore, early diagnosis of perforation is likely to improve outcomes, allowing the surgeon to prepare for a relatively troublesome operation, including the selection of laparoscopy or laparotomy, etc. Aside from symptoms and specific physical examination findings, ultrasonography and computed tomography have become the most useful tools in the diagnosis of perforation in AA, prior to surgery. However, these examinations can be very costly.

While it has been reported that raised bilirubin and C-reactive protein (CRP) levels are markers of perforation, they are not sufficiently accurate.[3] Mean platelet volume (MPV) is a marker derived from megakaryocytes during platelet production, associated with platelet function and activation.[4] Its roles in thrombosis and inflammation have been investigated.[5] Neutrophil-lymphocyte ratio (NLR), an inflammatory marker, has been found to be predictive in the prognosis of colorectal cancer and cardiovascular diseases.[6,7]

The predictive powers of NLR and MPV in the diagnosis of AA have been evaluated.[8,9] However, information regarding severity of AA was not included in these studies. The aim of the present study was to determine whether preoperative NLR and/or MPV levels could predict severity of AA.

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MATERIALS AND METHODS

Patients

A prospective database of 434 patients who underwent appendectomies between January 2012 and October 2013 was reviewed. Patients with non-inflamed appendix tissues on final pathology reports were included. Patients who underwent appendectomy as part of another abdominal operation were excluded (n=22). Hence, 413 patients were found to be eligible.

Healthy Volunteers

Healthy volunteers (n=100) admitted to the general surgery outpatient clinic were enrolled for comparison with the patient group. The volunteers were all tumor- and inflammation-free, with no history of malignancy or recent local/systemic inflammation. They were age-matched to the patient population.

Data

In addition to demographic data, complete blood count tests were preoperatively obtained from the patient and control groups to assess leukocyte, neutrophil, lymphocyte, and MPV counts. Laboratory analysis was conducted with an automated hematology analyzer (Coulter® LH 780; Beckman Coulter Inc., Brea, CA, USA). NLRs were then calculated in accordance to complete blood counts. Postoperatively, all appendix specimens were pathologically evaluated. In accordance with per-operative findings, pathology specimens were categorized as phlegmonous appendicitis, appendicitis with localized peritonitis, and appendicitis with perforation and/or gangrene.

Statistical Analysis

Descriptive analysis was performed, and data were presented as mean±SD. Differences among the groups were analyzed using chi-square and analysis of variance (ANOVA) tests. Recommended cut-off values for NLR and MPV were obtained with receiver operating curve (ROC) analysis. Logistic regression test was used for univariate analysis and to calculate odds ratios (OR) with 95% confidence interval (CI). SPSS analysis was performed using SPSS software (version 17.0; SPSS Inc., Chicago, IL, USA), and significance level was set at $p<0.005$.

RESULTS

Demographics

Mean age of the patient group was 32.4 (range 16–82), and mean age of the healthy controls was 42.7 (range 18–83). No statistical significance was found between the patient and healthy control groups (p=0.45). The patient group consisted of 295 males (71.4%), and 118 females (28.6%); the healthy controls consisted of 90 males (89.1%) and 11 females (10.9%). No statistical significance (p=0.82) was found between the patient and healthy control groups (Table 1). Appendix pathology was grouped as phlegmonous appendicitis (n=233; 56.4%), appendicitis with localized peritonitis (n=133; 32.2%), and appendicitis with perforation and/or gangrene (n=47; 11.4%).

Complete Blood Cell Counts

Means of leukocyte counts were 14.4±3.7 x 10^3/µl for the patient group and 7.5±1.7x 10^3/µl for the healthy control group. Statistical significance was found between the patient and healthy control groups (95% CI: 7.2–7.9; 95% CI: 13.9–14.7; p=0.0005, respectively).

The white blood cell (WBC) counts of patients with phlegmonous appendicitis, appendicitis with localized peritonitis, and appendicitis with perforation and/or gangrene were 14.2±3.6 x 10^3/µl, 14.2±3.8 x 10^3/µl, and 15.6±3.8 x 10^3/µl; p=0.06, respectively. Neutrophil counts of patients with phlegmonous appendicitis, appendicitis with localized peritonitis, and appendicitis with perforation and/or gangrene were 11.5±3.6 x 10^3/µl, 11.6±3.7 x 10^3/µl, and 12.7±3.5 x 10^3/µl;

Table 1. The demographic data of the patients with appendicitis and the healthy controls

	Acute appendicitis			Healthy controls			p
	n	%	Mean±SD	n	%	Mean±SD	
Number of patients	413			101			
Mean age (range)	32.4 (16–82)			42.7 (18–83)			0.45
Gender							0.82
Male	295	71.4		90	89.1		
Female	118	28.6		11	10.9		
WBC (x10^3/µl)			14.4±3.7			7.5±1.7	0.0005
NL ratio			8.7±5.9			2.7±2.2	0.009
MPV (Fl)			9.3±8			8.5±0.9	0.0005

SD: Standard deviation; WBC: White blood cell; NL: Neutrophil-lymphocyte; MPV: Mean platelet volume.

Table 2. Relationship between laboratory parameters of patients with different forms of appendicitis

	Flegmonous appendicitis			Appendicitis with localized peritonitis			Appendicitis with perforation or gangrene			p
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
No. of patients	233	56.4		133	32.2		47	11.4		
Mean age			32.7±11.8			31.8±10.8			34.1±13.9	0.42
Gender										
Male	168			91			36			0.34
Female	65			42			11			
WBC (x10^3/µl)			14.2±3.6			14.2±3.8			15.6±3.8	0.06
Neutrophil (x10^3/µl)			11.5±3.6			11.6±3.7			12.7±3.5	0.13
Lymphocyte (x10^3/µl)			1.7±0.7			1.6±0.7			1.7±0.9	0.34
NLR			8.3±5.6			9.1±6.2			10.6±6.4	0.023
MPV (Fl)			8.8±5.8			8.9±5.8			12.8±9.7	0.005

SD: Standard deviation; WBC: White blood cell; NLR: Neutrophil-lymphocyte ratio; MPV: Mean platelet volume.

p=0.13, respectively. Lymphocyte counts of patients with phlegmonous appendicitis, appendicitis with localized peritonitis, and appendicitis with perforation and/or gangrene were 1.7±0.7 x 10^3/µl, 1.6±6.9 x 10^3/µl, and 1.7±9.4 x 10^3/µl; p=0.34, respectively (Table 2).

Mean Platelet Volume

Means of MPVs were 9.3±8 fL for the patient group and 8.5±0.9 fL for the healthy control group. Statistical significance was found between the patient and healthy control groups (95% CI: 8.3–8.5; 95% CI: 8.3–10.1; p=0.0005, respectively). Means of MPVs according to pathologies in the patient group were 8.8±5.8 (range: 6–96) for phlegmonous appendicitis, 8.9±5.8 (range: 6.1–74) for localized peritonitis, and 12.8±9.7 (range 6.7–87) for appendicitis with perforation and/or gangrene. Statistical significance was found among the patient groups (95% CI: 8.5–10.1; p=0.005). According to ROC analysis, the cut-off value in differential diagnosis of AA was set at 8.92, with sensitivity of 73% and specificity of 57% (AUC: 0.57; 95% CI: 0.49–0.62; p=0.0005).

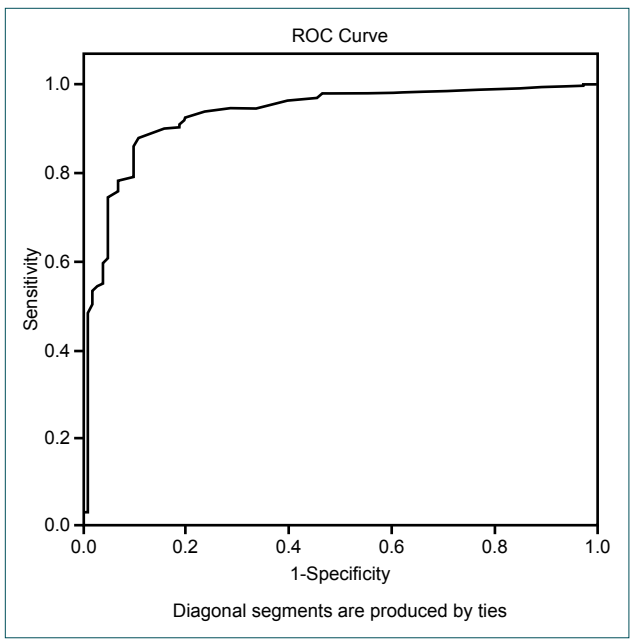

Figure 1. ROC analysis of neutrophil-lymphocyte ratios to set cut-off value for appendicitis with perforation and/or gangrene (AUC: 0.763; 95% CI: 0.66-0.84; sensitivity: 78%; specificity: 67%; p=0.001).

Neutrophil-Leucocyte Ratios

Means of NLRs of patients with phlegmonous appendicitis, appendicitis with localized peritonitis, and appendicitis with perforation and/or gangrene were 8.3±5.6, 9.1±6.2, and 10.6±6.4, respectively, p=0.023. ROC analysis was performed to determine cut-off value to identify patients with perforation and/or gangrene. The cut-off value was set as 7.95 (AUC: 0.763; 95% CI: 0.66-0.84; sensitivity: 78%; specificity: 67%; p=0.001; Fig. 1).

Univariate analysis was performed to determine association between laboratory parameters and appendicitis with perforation and/or gangrene. The analysis demonstrated OR as WBC levels (OR: 1.001; 95% CI: 1.000–1.002; p=0.017), neutrophil counts (OR: 0.999; 95% CI: 0.998–1.000; p=0.018), NLR being over 7.95 (OR: 3.037; 95% CI: 2.458–5.218; p=0.001), and MPV (OR: 1.036; 95% CI: 1.010–1.075; p=0.007; Table 3).

DISCUSSION

Early diagnosis of AA, prior to progression to gangrene and/or perforation, is important in order to minimize morbidity from this common entity. In spite of radiological advances,

Table 3. Univariate analysis of clinical features in relation to appendicitis with perforation or gangrene

Variables	p	Odds Ratio	95% CI
White blood cell	0.017	1.001	1.000–1.002
Neutrophil count	0.018	0.999	0.998–1.000
Lymphocyte count	0.164	0.999	0.998–1.000
Sex (male/female)	0.843	0.929	0.446–1.932
Neutrophil-lymphocyte ratio (≤7.95/>7.95)	0.001	3.037	2.458–5.218
Mean platelet volume	0.007	1.036	1.010–1.075

95% CI, 95% confidence interval.

differentiating subgroups of patients with severe disease may be challenging for the surgeon. As the percentage of perforated appendicitis is 18.3–34%, a test that aids in diagnosis of AA complications may be useful.[3] Leucocyte count was reportedly the earliest test to indicate appendiceal inflammation, with a sensitivity of 82–96%.[10,11] Rises in leucocyte and neutrophil counts were found to be related to severity of AA.[12] The sensitivity of neutrophil count in AA was shown to be 60–87% in prior trials.[13] Hyperbilirubinemia, high erythrocyte sedimentation rates, and high CRP levels were have also been reported as markers of complications in AA.[3,14,15] Raised CRP values have 40–99% sensitivity and 27–90% specificity in the diagnosis of AA.[16]

In the present study, comparison of high leukocyte and neutrophil counts to healthy controls was as expected (p=0.005 and p=0.009, respectively). No statistical significance was observed among the appendicitis groups concerning leucocyte and neutrophil counts (p=0.06 and p=0.13, respectively). These tests are invaluable, not only in the diagnostic work-up, but also in differentiating severe forms of AA.

MPV, a platelet index calculated by automatic cell analyzer, is used for differential diagnosis of both thrombocytosis and thrombocytopenia.[17] MPV is actually a marker of functional status of platelets. It increases with production of young platelets; hence, MPV count indicates platelet activation.[18] MPV is also thought to reflect inflammatory burden in ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, chronic obstructive pulmonary disease, diabetes mellitus, and myocardial infarction.[19–22] Controversy persists regarding MPV response in AA. Studies have shown MPV decrements in AA, compared to healthy controls.[23,24] However, a recent study found higher values of MPV in AA patients, with a cut-off above 7.87 fL, and low sensitivity and specificity (66% and 51%, respectively).[8]

In the present study, higher values of MPV were found in patients with AA, compared to healthy controls (9.3±8 vs 9.3±8, p=0.0005). The aim of the present study was to determine the role of MPV in predicting more severe forms of AA, such as appendicitis with perforation and/or gangrene. The cut-off value to differentiate AA patients with perforation and/or gangrene from other AA patients was 8.92 fL, with a sensitivity of 73% and a specificity of 57%.

Regarding NLR, it was presently demonstrated that a cut-off value of 7.95 could significantly differentiate AA patients with perforation and/or gangrene from those with less-severe AA, with a sensitivity of 78% and a specificity of 67%. A recent trial showed that NLR values >8 demonstrated significant association with gangrenous appendicitis. Lymphocyte counts may fall in severe cases of AA.[25] However, no statistically significant decrease in lymphocyte count was found in cases of appendicitis with perforation and/or gangrene in the present study (p=0.34). According to the present results, NLR values were statistically significant among the AA groups (p=0.023). Thus, both NLR and MPV can aid in the assignment of patients with complications to appropriate subgroups.

The non-operative approach in the treatment of AA, with clinical observation, has the risk of peritonitis and the need for emergency appendectomy in about 8–10% of cases. Therefore, it is an acceptable option in cases of uncomplicated appendicitis.[26,27] Once surgical treatment has been selected, options include open or laparoscopic appendectomy. Abe et al. recently reported that complicated appendicitis and diffuse peritonitis were risk factors of conversion to open during laparoscopic appendectomy.[28] Furthermore, in a comparison of open to laparoscopic appendectomies, the Cochrane review reported a nearly threefold increase in intra-abdominal abscesses following laparoscopic appendectomy, which may lead surgeons to choose open appendectomy in cases of perforated appendicitis.[29]

Conclusion

There is still no single diagnostic tool to determine severity of AA. The choice between clinical observation and emergency surgery depends upon the expertise of the surgeon. Laboratory parameters such as MPV and NLR may aid in the prediction of perforation, and in the choice between follow-up and suitable operative technique.

Conflict of interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Nötrofil-lenfosit oranı ve ortalama trombosit hacminin akut apandisitin şiddetini belirlemedeki rolü

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AMAÇ: Perfore akut apandisitin (AA) erken tanınması zor olabilmektedir. Bu çalışmada, ameliyat öncesi nötrofil-lenfosit oranı (NLR) ve ortalama trombosit hacmi (MPV) ölçümlerinin akut apandisit olgularında perforasyonu belirlemedeki rolü araştırıldı.

GEREÇ VE YÖNTEM: Dört yüz on üç AA'lı olguya ait geriye dönük veriler ile 100 sağlıklı kontrol çalışmaya dahil edildi. Akut apandisitli olgulara ait patolojiler flegmonöz apandisit, lokalize peritonitin eşlik ettiği apandisit ve perforasyonlu ve/veya gangrenöz apandisit olguları olarak üç grupta incelendi. Hastalara ait MPV ve NLR değerleri gruplar içerisinde ve sağlıklı kontrollere ait sonuçlarla karşılaştırıldı.

BULGULAR: Ortalama MPV değeri AA grubunda 9.3±8 FL ve sağlıklı kontrollerde 8.5±0.9 Fl idi (p=0.0005). Ortalama MPV değerleri flegmonöz apandisit grubunda 8.8±5.8, lokalize apandisit grubunda 8.9±5.8 FL ve perforasyonlu ve/veya gangrenöz apandisit grubunda 12.8±9.7 FL olarak saptandı (p=0.005). Perforasyonlu/gangrenöz apandisitli olguları diğer apandisit olgularından ayırmak için ölçülen eşik MPV değeri 8.92 Fl idi. Ortalama NPV değerleri basit apandisit, lokalize apandisit, perforansyonlu/gangrenöz apandisit gruplarında sırasıyla 8.3±5.6, 9.1±6.2 ve 10.6±6.4 olarak saptandı (p=0.023). Perforasyonlu/gangrenöz apandisitli olguları diğer apandisit olgularından ayırmak için ölçülen eşik NPV değeri 7.95 idi.

TARTIŞMA: Nötrofil-lenfosit oranı ve MPV ölçümleri akut apandisitin şiddetini belirlemede klinik tanıya yardımcı olabilir.

Anahtar sözcükler: Apandisit; lenfosir; nötrofil; ortalama platelet hacmi; prediktif faktörler.

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