MPV and other inflammatory markers in diagnosing acute appendicitis

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Abstract

Objective: To investigate whether mean platelet volume can be used as an inflammatory marker for the diagnosis of acute appendicitis, and to determine the role, if any, of white blood cell count, C-reactive protein and neutrophil count in this regard.

Methods: The retrospective study was conducted at Mersin University (MEU) Health Research and Application Center, Emergency Department, Mersin, Turkey, and included medical record of patients having gone appendectomy between April 2012 to July 2013. Based on pathology examination, the cases were grouped as uncomplicated, complicated, and non-appendicitis cases. Preoperative white blood cell, neutrophil, C-reactive protein and mean platelet volume were noted. SPSS 16 was used for statistical analysis.

Results: Records of 275 patients were studied. Overall, 90(32.7%) patients were uncomplicated, 120(43.7%) complicated, and 65(23.6%) were non-appendicitis cases. The first two groups had a significantly higher white blood cell (p=0.001) and neutrophil (p<0.001) counts than the third one. Mean platelet volume levels were not statistically different (p=0.478).The neutrophil count had a sensitivity of 76.19%, specificity of 56.92%, positive predictive value of 85.11%, and negative predictive value of 42.53%; white blod cell count had sensitivity 68.10%, specificity 61.54%, positive predictive value 85.12%, and negative predictive value 37.38%; mean platelet volume level had sensitivity 74.76%, specificity 35.38%, positive predictive value 78.89%, and negative predictive value 30.26%; and C-reactive protein level had sensitivity 84.29%, specificity 30.77%, positive predictive value 79.73%, and negative predictive value 37.74%.

Conclusion: Elevated white blood cell and neutrophil counts may be used as diagnostic tests in cases of acute appendicitis, while C-reactive protein and mean platelet volume levels were not useful as diagnostic markers.

Keywords: Acute appendicitis, Mean platelet volume, C-reactive protein, Leucocyte count. (JPMA 65: 637; 2015)

Introduction

Acute appendicitis (AA) is the most common cause of urgent abdominal operations and it is still difficult to diagnose despite its classical signs and symptoms being well known.[1,2] A delay in diagnosis is associated with perforation and increased complication rate.[3] In AA the negative laparotomy rate is generally around 20%.[2] Therefore, distinguishing nonspecific abdominal pain from AA is of paramount importance. The value of various parameters — C-reactive protein (CRP), white blood cell (WBC) count, lymphocyte/leucocyte ratio, interleukin-6 (IL-6), IL-10, IL-4, IL-5, IL-12, tumour necrosis factor alpha (TNF), endotoxin, erythrocyte sedimentation rate (ESR), procalcitonin, fibrinogen, alpha 2-macroglobulin, alpha 1- antitrypsin, D-lactate — for diagnosis of AA have been studied.[4] However, they have proved non-superior to clinical history, physical examination, and usual laboratory studies in diagnosing AA at an early stage.[5]

Mean platelet volume (MPV) is a measure of thrombocyte size provided by complete blood count (CBC) analysers as a routine part of CBC and it is usually overlooked by clinicians.[6] Elevated MPV levels have been reported in chronic obstructive lung disease (COPD), myocardial infarction (MI), diabetes, and high altitude.[3] On the other hand, some studies have reported that MPV levels decrease in rheumatoid disorders such as rheumatoid arthritis and ankylosing spondylitis, ulcerative colitis, and acute pancreatitis.[6-9] Furthermore, there are studies that have showed that MPV is affected by inflammation.[3,6-9] There are only a few studies examining the relationship between MPV and AA and their results are variable.[1,3,4]

The current study was planned to examine whether MPV level can be used as an inflammatory marker in non-appendicitis, uncomplicated appendicitis and complicated appendicitis cases. In addition, we planned to determine if there was any difference between the groups with respect to WBC, CRP and neutrophil count.

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Patients and Methods

The retrospective study was conducted at Mersin University (MEU) Health Research and Application Center, Emergency Department, Mersin, Turkey, and included medical record of patients having gone appendectomy between April 2012 and July 2013. After approval from the ethics committee of Mersin University Faculty of Medicine, Turkey, data pertaining to patients aged at least 17 years who had presented to the emergency department (ED) with abdominal pain and had undergone appendectomy after a diagnosis of acute appendicitis on pathological basis was studied. Those excluded were patients with acute cerebrovascular disease, MI, pregnancy, heart failure, peripheral vascular disease, COPD, haematological disorder, diabetes mellitus, acute or chronic disorders, cancer, or liver disease; those using anticoagulants or non-steroidal anti-inflammatory drugs (NSAIDs); or those who had no leucocyte, neutrophil, MPV, CRP levels measured or ultrasonography performed the same day prior to the operation. Based on the pathology results, data was divided into 3 groups: uncomplicated AA (uncomplicated; AA without peritonitis or phlegmonous appendicitis); complicated appendicitis (perforated, plastrone, necrotising appendicitis and appendicitis with peritonitis); and non-appendicitis (normal appendix, and reactive lymph node hyperplasia) cases. Preoperative WBC, neutrophil, MPV, and CRP levels were recorded. CBC analysis had been performed with Sysmex XT-2000I (Roche, Istanbul, Turkey) and CRP analysis with Cobas integra 800 (Roche, Istanbul, Turkey) device. The reference intervals for MPV and CRP levels and WBC and neutrophil counts were set by the local hospital's laboratory (WBC: 4.5-11 x10³/μL; neutrophil: 1.5-6.7 x10³/ μL; MPV: 7.4-10.4 fL; CRP: <5 mg/L). Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and cut-off value of WBC, neutrophil counts and MPV and CRP levels were calculated. The likelihood ratios were calculated as positive (LR+) and negative (LR-).

SPSS 16.0 was used for statistical analysis. Normality of data for continuous variables was analysed using Shapiro Wilk test. Age and CRP levels did not have normal distribution. Inter-group differences were analysed with one-way analysis of variance (ANOVA) for normally distributed parameters and with Kruskal-Wallis test for non-normally distributed parameters. Paired comparisons were done with Bonferroni test. Descriptive statistics included mean and standard deviation (mean±SD) for normally distributed parameters and minimum, maximum, median, and 25-75% percentiles for non-normally distributed parameters. Pearson's Chi-Square test was used for categorical variables. Frequencies and percentages were presented as descriptive statistics. A receiver operating curve (ROC) analysis was performed for sensitivity, specificity, LR+ and LR- values for the cut-off points belonging to continuous variables. Uncomplicated and complicated AA cases were merged into a single group and designated as the AA group when performing ROC analysis. Hence, ROC analysis was performed between the cases of AA and non-appendicitis. A p value less than 0.05 was considered statistically significant.

Results

Records of 363 patients were studied, but 88(24.24%) were left out on the basis of exclusion criterion or missing data. The records of the remaining 275(75.75%) patients represented the final sample. Of them, 90(32.7%) patients were uncomplicated, 120(43.7%) complicated, and 65(23.6%) were non-appendicitis cases.

Male gender had a higher rate of acute appendicitis (p<0.001). While 69(76.7%) uncomplicated cases and 79(65.8%) complicated appendicitis cases were male, 41(63.1%) non-appendicitis cases were female (Table-1). Of the male patients, 69(40.1%) were diagnosed to have uncomplicated appendicitis and 79(45.9%) were diagnosed with complicated appendicitis. Besides,

Table-1: Pathological diagnostic groups by gender.

Gender	Uncomplicated Appendicitis	Complicated Appendicitis	Non-Appendicitis	p
Male	69(76.7)	79 (65.8)	24 (36.9)	<0.001
Female	21(23.3)	41 (34.2)	41 (63.1)	

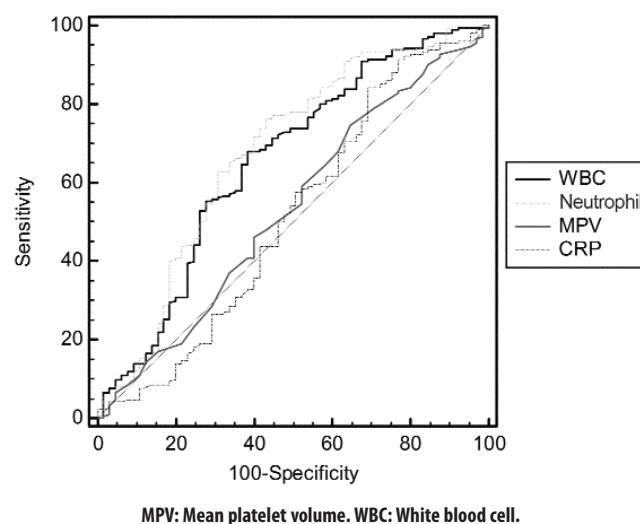**MPV: Mean platelet volume. WBC: White blood cell.**

Figure: Receiver Operating Curve (ROC) of MPV, WBC, Neutrophil and CRP.

Table-2: Comparison of CRP and Age parameters.

	Uncomplicated Appendicitis (n=90)		Complicated Appendicitis (n=120)		Non-Appendicitis (n=65)		p
	Min-Max	Median [25-75% percentiles]	Min-Max	Median [25-75% percentiles]	Min-Max	Median [25-75% percentiles]	
Age	17-78	31 [23-40]	17-76	33 [25-42]	17-69	34 [25.5-42.5]	0.270
CRP	0-341.66	13.05 [3.21-39.65]	0.10-431.80	17.76 [3.62-52.35]	0.16-443.00	17.65 [2.24-70.78]	0.555

Note: Test values were expressed as median (25th/75th percentile) range.
CRP: C-reactive protein.

Table-3: Comparison of MPV, neutrofil and WBC parameters between pathological diagnosis groups.

	Uncomplicated Appendicitis (n=90)	Complicated Appendicitis (n=120)	Non-Appendicitis (n=65)	p
WBC	14.048 ± 3.735	14.333 ± 3.727	12.112 ± 4.467*,†	0.001
Neutrofil	10.945 ± 3.73	11.227 ± 3.399	8.891 ± 4.328*,†	<0.001
MPV	10.402 ± 0.934	10.272 ± 0.935	10.423 ± 1.000	0.478

MPV: Mean platelet volume
WBC: White blood cell.
*Differences with uncomplicated appendicitis, †: Differences with complicated appendicitis.

Table-4: ROC analysis.

	Cut-off	AUC (p)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy	LR+	LR-
MPV	10.8	0.532 (0.4455)	74.76 [68.32 - 80.49]	35.38 [23.92 - 48.23]	78.89 [72.56-84.35]	30.26 [20.25-41.87]	65.45	1.16	0.71
CRP	59.41	0.514 (0.7627)	84.29 [78.65-88.93]	30.77 [19.91-43.45]	79.73 [73.83-84.81]	37.74 [24.67-52.25]	71.64	1.22	0.51
Neutrophil	8.23 x10³/ μL'	0.677 (<0.0001)	76.19 [69.84 - 81.78]	56.92 [44.04 - 69.15]	85.11 [79.20-89.87]	42.53 [31.99-53.59]	71.64	1.77	0.42
WBC	12.51 x10³/ μL'	0.654 (0.0002)	68.10 [61.33 - 74.34]	61.54 [48.64 - 73.35]	85.12 [78.82-90.13]	37.38 [28.18-47.31]	66.54	1.77	0.52

Note: Test values were expressed 95% Confindence interval.
MPV: Mean platelet volume. CRP: C-reactive protein. WBC: White blood cell. PPV: Postive predictive value. NPV: Negative predictive value. ROC: Receiver operating curve. AUC: Area under the curve.

24(14%) males and 41(39.8%) females were ultimately found to have no appendicitis.

There were no significant differences among the groups with respect to age and CRP level (Table 2).

WBC (p=0.001) and neutrophil (p<0.001) counts were higher in uncomplicated and complicated appendicitis cases compared to non-appendicitis cases. MPV levels were not significantly different across the groups (p=0.478) (Table 3).

ROC analysis found that neutrophil and WBC measurements were significant, and, as such, a neutrophil value above 8.23 x10³/μL was allowed to diagnose AA (p<0.0001). The sensitivity, specificity, PPV, and NPV of neutrophil count for diagnosing AA were found to be 76.19%, 56.92%, 85.11%, and 42.53%, respectively. A WBC level above 12.51 x10³/μL was allowed to diagnose AA (p=0.0002). WBC level had sensitivity 68.10%, specificity 61.54%, PPV 85.12%, and NPV 37.38%. Values above 10.8 fL for MPV and above 59.41 mg/L for CRP were able to diagnose AA, albeit statistically non-significant (p>0.05).

MPV had a sensitivity, specificity, PPV, and NPV of 74.76%, 35.38%, 78.89%, and 30.26%, respectively. MPV level was lower in the complicated appendicitis patients, although it did not reach statistical significance (p>0.05). CRP level had sensitivity 84.29%, specificity 30.77%, PPV 79.73%, and NPV 37.74%. The likelihood of neutrophil and WBC counts for differentiation of true patients was high (Table-4, Figure).

Discussion

Debate surrounding the benefit of laboratory tests in diagnosing AA still continues.[10] In this study we planned to investigate the results of MPV, leucocyte, neutrophil and CRP values based on the pathology results in patients undergoing appendectomy with an early diagnosis of AA.

It is believed that there is a link between thrombocyte activation, thrombosis and the pathophysiology of the diseases with a tendency for inflammation. Many thrombocyte markers, including MPV, have been related to thrombosis and inflammation.[11] In a study, cases with acute pancreatitis had lower MPV levels.[6] Another study

reported that cases with ankylosing spondylitis and rheumatoid arthritis had a lower MPV level compared to control group.[7] One study found that during an ulcerative colitis attack, MPV level decreased and MPV could be used for diagnosis of that disease.[8] Similarly, one study showed that MPV level was unchanged compared to the control group outside the attacks, but was significantly reduced during attacks, which was associated with lower morbidity.[12] There are a few studies regarding the role of MPV in AA diagnosis in children and adults, albeit with variable results.[1,3,4,13] A study comparing a healthy adult control group and an adult patients group with AA found significantly lower MPV level. It reported a cut-off MPV value of 7.6 for AA, a sensitivity of 73%, specificity 84%, PPV 84%, and specificity 74%. It also stated that MPV level should not be overlooked in cases with suspected AA.[3] One study reported a significant reduction in MPV level in patients with AA. It found a cut-off level of 7.55, sensitivity 87%, and specificity 60% for MPV.[13] One study did not find any relationship between paediatric appendicitis and MPV levels.[1] Another found a significantly higher MPV level in cases with AA compared to the control group. It reported a cut-off value of 7.87, sensitivity 66%, and specificity 51% for MPV.[4] In our study, the cut-off level of MPV was 10.8ft, sensitivity 74.76%, specificity 35.38%, PPV 78.89%, and NPV 30.26%. There was no significant difference between the appendicitis cases (complicated or uncomplicated) and non-appendicitis cases with respect to MPV levels. However, the complicated appendicitis group had a lower MPV measurement value compared to other groups. The reduction in MPV levels was explained as the sequestration of larger thrombocytes in the vascular segments of the inflamed intestines.[9] However, as there are not many studies on this subject, it is clear that further studies should be conducted in this field.

Leucocyte count is a commonly employed test in AA diagnosis. Many studies have reported use of increased leucocyte level in early diagnosis of appendicial inflammation since AA cases continue commonly with leucocytosis. Neutrophil is usually associated with bacterial infections. Earlier studies reported WBC sensitivities 67-97.8%, specifities 31.9-90.8%, NPV 77.9-82%, and PPV 42-91.8%.[2,10,13-17] An increased neutrophil count has been reported to have sensitivity 68.6-98.9%, specificity 33.1-91%, PPV 84.7-89.21%, and NPV 53-71.5%.[2,3,10,13,16] In agreement with the literature, we found higher WBC and neutrophil counts in complicated and uncomplicated appendicitis compared to the non-appendicitis cases. The WBC count had a higher specificity and PPV value compared to other parameters. The WBC parameter had a cut-off level of 12.51 x10^3/μL, sensitivity

68.10%, specificity 61.54%, PPV 85.12%, and NPV 37.38%. The neutrophil parameter had a cut-off value of 8.23 x10^3/μL, sensitivity 76.19%, specificity 56.92%, PPV 85.11%, and NPV 42.53%.

CRP is an acute phase protein and can be used as a marker and diagnostic tool in some inflammations and attacks of some disorders.[18] A meta-analysis exploring the diagnostic accuracy of CRP revealed a very wide range of sensitivity and specificity (47-74%, and 55-89%, respectively).[19] Other studies investigating the role of CRP in diagnosing AA have reported sensitivities ranging between 76.5% and 95.6%, specifities ranging between 26.1% and 77.7%, and PPV 95.6.[2,10] The cut-off level of CRP was 59.41mg/dl, sensitivity 84.29%, specificity 30.77%, PPV 79.73%, and NPV 37.74% in our study. Furthermore, CRP values had a higher sensitivity but lower specificity compared to other parameters. A large body of studies has shown that CRP levels increase in parallel with the severity of the inflammatory response in AA.[2,10,16,18,20] A study found that there was not any definite level of CRP that will diagnose AA, but its elevated level may suggest abscess formation in AA cases.[16] One study reported that the mean CRP level was higher in perforated appendix compared to normal appendix, but there were no significant differences between uncomplicated appendicitis and non-appendicitis cases.[10] This study found no difference between the groups with respect to CRP level. The sensitivity of CRP was higher, but its specificity was lower compared to those of other parameters. CRP level was within normal limits in some AA cases in this study. This condition may be explained by the fact that CRP level starts to increase 12-24 hours after the symptom onset.[18] We additionally observed that CRP concentration was also higher in cases having no appendicitis. A study made the same observation that the cases with normal appendix had an elevated CRP level.[16] In our study, the patients who had an elevated CRP level but had no appendicitis had no signs of acute infection, an additional pathology in ultrasonography, or any other intraabdominal pathology after appendectomy either. CRP elevation in patients with no appendicitis may be associated with the presence of other acute inflammatory disorders remaining undiagnosed.

Conclusion

There was no statistically significant difference between patients with appendicitis (complicated or uncomplicated) and those having no appendicitis with respect to MPV level. However, the complicated appendicitis group had a lower MPV value compared to other groups. WBC and neutrophil counts were observed to be increased in AA cases, and more so in complicated

appendicitis cases. CRP levels did not significantly differ across the groups. Considering the largely varied results reported in literature, it is essential to conduct large-scale prospective studies in future.

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