

Original Article

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Accuracy of Mean Platelet Volume (MPV) and Red Cell Distribution Width (RDW) for the Diagnosis of Acute Appendicitis: Evaluation of Possible New Biomarkers

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Abstract

Introduction: Acute appendicitis is the most common cause of the abdominal pain in surgery. Despite its significant prevalence, the diagnosis is associated with many problems in some cases, which leads to false appendectomy.

Objective: The aim of this study was to determine the validity of diagnostic tests of mean platelet volume (MPV) and red cell distribution width (RDW), as a new possible tool in the diagnosis of acute appendicitis.

Methods: In this study, all patients who referred to the emergency department of Besat Hospital, Hamadan, Iran, in 2015, with abdominal pain and first impression of acute appendicitis, undergone appendectomy, were evaluated. The diagnostic markers of pre-operative and post-operative pathology and the validity of MPV and RDW were determined in diagnosis of acute appendicitis.

Results: Laboratory and clinical data from 438 patients, presenting the signs and symptoms of acute appendicitis with the mean age of 26.51 ± 13.9 years, were examined (55.6% men). The sensitivity, specificity, positive and negative predictive value of MPV in the diagnosis of acute appendicitis were 59.77, 98.66, 99.5 and 34.26 percent, and for the RDW were 57.79, 56.00, 86.07 and 21.98 percent, respectively. The area under the receiver operating characteristic (ROC) curve for RDW and MPV was 0.61 and 0.90, respectively. The mean of MPV in patients with normal pathologic outcome was 9.52 ± 1.60 and in patients with acute appendicitis was 7.51 ± 1.22 . There was a significant difference between the mean MPV in both groups ($p < 0.001$). The mean of RDW in patients with normal pathology were 13.42 ± 1.97 and 13.05 ± 1.09 , in patients with acute appendicitis. There was a significant difference between the mean RDW of the two groups ($p = 0.009$).

Conclusion: MPV and RDW indexes have the potential to be used by the surgeons in diagnosis of acute and perforated appendicitis, especially in adults, in order to reduce unnecessary appendectomy, but MPV is more valid in screening acute appendicitis, compared to the RDW.

Key words: Appendicitis; Biomarkers; Diagnosis; Erythrocyte Indices; Mean Platelet Volume

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INTRODUCTION

Acute appendicitis is still one of the most common causes of emergency surgeries, with mortality of about 3%, and in the case of perforation, it reaches about 6%. The probability of appendectomy, over the lives of men and women is 25% and 12%, respectively. Approximately, 7% of the general populations undergo appendectomy during their lifetime with acute appendicitis diagnosis (1). It occurs mainly in the second and fourth decades of life, and its incidence is greater in males than females (1.2 to 1.3 to 1). Despite the use of ultrasound and CT scan in recent years, the error detection rate is still between 3 and 15% (2). The

rate of misdiagnosis in women is higher than men. The cases of false appendectomy in women in reproductive age are about 23.2 %, most of which are also at the age of between 40 and 49 years. Overall, the highest false appendectomies in women are reported over 80 years (around 35 %) (3). Acute appendicitis is still the most common cause of abdominal pain and the most widespread critical, abdominal surgery condition. The total mortality rate is 0.3 %, which considerably increases in cases of perforation (6.5 %), elderly patients (5.5 %) or newborns (80%). The advanced bacterial peritonitis due to appendiceal

perforation can have a high degree of mortality even up to 80% (4). The prevalence of appendicitis and the high rate of false appendectomy between 9–44 percent urged us to find a new diagnostic method with high sensitivity and specificity. Despite several available diagnostic tools, the diagnosis of acute phase is still based on the clinical history and physical examinations (5). The platelet count is a part of standard complete blood count (CBC) and is routinely performed in laboratories. Three parameters in the CBC are associated with platelet, including plateletcrit (PCT), mean platelet volume (MPV) and red blood cell distribution width (RDW). MPV is a marker of activity and function of platelets (6). MPV level rises when thrombocyte production increases (7). Various studies have shown low levels of MPV in acute appendicitis. RDW shows the variety of erythrocytes sizes. Inflammation may result in increased RDW via incomplete maturation of the RBC through membrane damage. Some studies showed an increased level of RDW in acute appendicitis (8), while some reported a decline (9, 10). Despite the significant prevalence, the detection and diagnosis are accompanied by many problems in some cases (11). Considering the high prevalence of acute appendicitis and the necessity of fast diagnosis, especially in some age groups, in the case of the use of available and inexpensive paraclinical methods and remarks, the rate of false cases may be reduced. Avoiding unnecessary surgical procedure, the cost, and also the associated complications are the most prominent issues to be solved. Therefore, in this study, the validity of diagnostic tests of MPV and RDW was investigated in acute appendicitis.

METHODS

Study design

The current study was performed during the period of between October 2015 and March 2015, at the emergency department of Besat Hospital Hamadan, Iran. The study was approved as a research project by the Ethics Committee of Hamadan University of Medical Sciences. In this study, there was no intervention, and the surplus cost of the routine diagnosis and treatment process for patients, was not imparted. The checklist was designed anonymously, so moral considerations were followed.

Study Population

All the patients who referred with abdominal pain and diagnosed with appendicitis based on the history and clinical tests, or suggested as one of the differential diagnosis. Patients with chronic

obstructive pulmonary disease, systemic diseases, diabetes mellitus and myocardial infarction were excluded from the study.

Data gathering

The results of the CBC, MPV and RDW tests from the Bioethics Laboratory of Besat Hospital, and the results of pathologic samples from the pathology laboratory, were extracted and recorded in a researcher-made checklist. In this study, the results of the CBC, MPV and RDW tests were considered as a screening test, and the result of pathology as a Gold Standard test. In the case of RDW, the cutoffs were determined as about 13, and the patients were divided into two groups of less than the cutoff, and equal or greater than cutoff point. The same classification was applied to the MPV based on the cutoff point of 7.7, and the two groups of patients were assessed based on the MPV cutoff (5).

Statistical analysis

We first checked the normality of distribution, using the Kolmogorov-Smirnov test. The one-way ANOVA test was applied to compare the mean of RDW and also MPV, in term of the different pathologies of appendicitis. *Tukey's post hoc* test for pairwise comparisons was also used. At the end, the characteristics of patients presented in the 2×2 tables, and the sensitivity, specificity and predictive value of each test were calculated separately, according to the specified formulas. To plot the Receiver operating characteristic (ROC) curve, using SPSS software, the sensitivity was plotted as a function of 1-specificity, and the area under the curve (AUC) was calculated. The results in the 95% confidence interval, and p-values of less than 0.05, were considered statistically significant. The cutoff point for the MPV and RDW values, and the accuracy indexes (sensitivity, specificity and predictive values) for the cutoff points, were calculated

RESULTS

In this study, 428 patients with the mean age of 26.5 ± 13.9 years, and ages ranging from 1 to 83 years, were participated. About 55.5% were males and 44.4% females. The final diagnosis of acute appendicitis was confirmed by pathology in 353 (82.5%) cases. The mean values of MPV in patients with normal pathologic outcome and those with acute appendicitis was significantly different and the mean of MPV in patients with acute appendicitis was lower, compared to the subjects with a normal pathology (9.52 ± 1.60 fL vs. 7.51 ± 1.22 fL; $p < 0.001$). The mean of RDW in patients with normal pathology and acute

Table 1: Analysis of variance (ANOVA) for comparison of the mean of RDW and MPV values in terms of subgroups

Lab tests subgroups	Number (%)	Mean ± SD	95% Confidence Interval		p	
			Lower limit	Upper limit		
MPV	Normal	75 (17.5)	9.52 ± 1.06	9.27	9.76	<0.001
	Acute appendicitis	154 (36.0)	8.38 ± 0.96	8.23	8.53	
	Suppurative appendicitis	119 (27.8)	7.23 ± 0.85	7.08	7.38	
	Gangrenous appendicitis	80 (18.7)	6.24 ± 0.78	6.07	6.42	
	Total	428 (100.0)	7.86 ± 1.42	7.73	7.99	
RDW	Normal	75 (17.5)	13.41 ± 1.08	13.17	13.66	0.037
	Acute appendicitis	154 (36.0)	13.09 ± 0.09	12.93	13.25	
	Suppurative appendicitis	119 (27.8)	12.95 ± 1.13	12.74	13.15	
	Gangrenous appendicitis	80 (18.7)	13.13 ± 1.22	12.86	13.40	
	Total	428 (100.0)	13.11 ± 1.09	13.01	13.22	

appendicitis were 13.42±1.97 and 13.05±1.09, respectively. There was a significant difference between the mean RDW of the two groups (p=0.009). The mean value of RDW in patients with acute appendicitis was lower, compared to those with normal pathologic outcomes.

The result of analysis of variance (ANOVA) demonstrated that there is a significant difference between the mean MPV and RDW in different groups (p<0.05). The mean MPV in patients with acute suppurative appendicitis and gangrenous appendicitis was lower than the rest. The RDW means in the group of patients with acute suppurative appendicitis was lower than others (Table 1). A significant difference was seen in the result of the post hoc Tukey follow-up test for all the subgroups for the MPV. However, in the case of RDW, a statistical significant difference existed only between the subgroup of normal people, and the patients with acute suppurative appendicitis.

Of the 428 patients, diagnosed with acute

appendicitis based on the MPV value, the final diagnosis was confirmed in 353 patients (82.5%), after surgery and performing a pathological examination. The results of MPV screening for diagnosis of acute appendicitis identified the number of true positive (211 cases), false positive (1 case), true negative (74 cases) and the false negative (142 cases). The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of MPV in detecting acute appendicitis were 59.77, 98.66, 99.5 and 34.26 percent, respectively.

Of the 428 patients, diagnosed with acute appendicitis based on the RDW value, the final diagnosis of appendicitis was confirmed in 353 patients (47.82%), after surgery and performing a pathological examination. The results of MPV screening for the diagnosis of acute appendicitis showed 204, 33, 42 and 149 cases of true positive, false positive, true negative and false negative, respectively. The sensitivity, specificity, positive

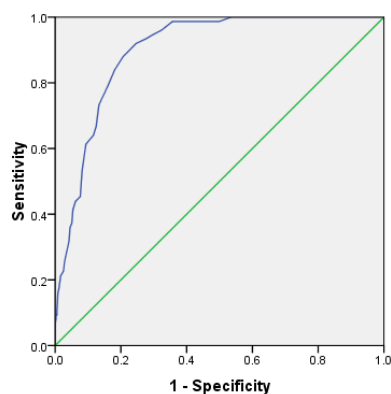


Figure 1: The ROC curve of MPV for detecting appendicitis

Cutoff	Appendicitis	Normal	Total
	N		
< 7.7	211	1	212
≥ 7.7	142	74	216
Total	353	75	428

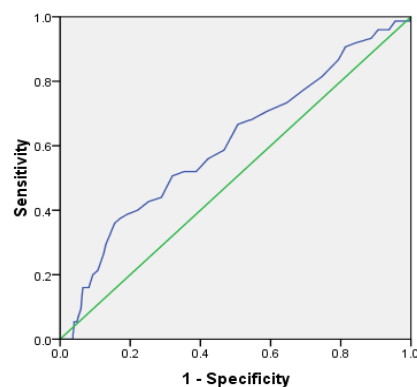


Figure 2: The ROC curve of RDW for detecting appendicitis

Cutoff	Appendicitis	Normal	Total
	N		
< 13	204	33	237
≥ 13	149	42	191
Total	353	75	428

and negative predictive value of RDW for diagnosis of acute appendicitis were 57.79, 56.00, 86.07 and 21.98 percent, respectively.

In the ROC analysis, designed for defining the sensitivity and specificity of the MPV test, the AUC was 0.90; (95% confidence interval (CI), 0.89; 0.93), the standard error was 0.01, ($p < 0.001$). Moreover, in case of the RDW test, the AUC was 0.61, with standard deviation (SD) of 0.37 (95% confidence interval (CI), 0.53; 0.68), respectively ($p = 0.004$). The ROC curves of MPV and RDW for detecting appendicitis are shown in figures 1 and 2.

DISCUSSION

Despite the technical advances in recent years, the improvement in sensitivity and accuracy of diagnostic tests for acute appendicitis has not been remarkable. The CBC, C-reactive protein (CRP), MPV and RDW have been among the markers studied in this matter, which have been used for a long time, along with the clinical symptoms for diagnosis of appendicitis (8, 10, 21-24, 26-30). However, these tests are not specific in the distinctive diagnosis of appendicitis, and may also increase in other inflammatory conditions.

In our study, the mean MPV value in patients with acute appendicitis was lower than those with positive pathology results. Of the 428 patients, who undergone appendectomy with a diagnosis of acute appendicitis, 353 patients (82.47%) had pathologic results in favor of acute appendicitis. This means that 17.53% were mistakenly undergone appendectomy. The rate of MPV markers was found to be lower than normal (7.7 fl), in 77.79% of those whose illness was correctly diagnosed.

In Dinc et al. (9) and Aydogan et al. (11) studies, and some other similar studies (13, 14, 23, 24), MPV has been reported less than normal rate in patients with acute appendicitis, compared to the control group (healthy subjects). Our findings are consistent with the results of the above-mentioned studies.

However, in the study of Uyanik et al. (12), there was no significant difference between the mean MPV of patients with acute appendicitis and the control group. Our findings were not consistent with the results of this study, however, the target group was children in this study. Some studies have shown that although the patient has clinical symptoms in favor of acute appendicitis, especially in children under the age of ten (31, 32), the results of their tests may be normal, suggesting that the diagnostic value of experiments is not valid (29).

In our study, the sensitivity, specificity, positive and negative predictive value of MPV in detecting

acute appendicitis was 59.77, 98.66, 99.5 and 34.26 percent, respectively. Different percentages and rates of sensitivity and specificity are reported in various studies for the MPV, which vary between 66 and 87 percent for sensitivity, as well as, attribute values for the MPV between 35 to 75 percent have been reported (10, 22, 25). The results of our study showed that MPV sensitivity was approximately the same as other study findings. However, in comparison with the above studies, higher specificity was found in our study. This difference was due to cross-sectional survey with no healthy control group.

In our study, the mean rate of RDW in patients with acute appendicitis was lower than those with positive pathology results, and this value was lower than normal, in 57.89% of those who had undergone appendectomy. In the study of Tanrikulu et al. (7), Narci et al. (10) and, Glucin et al (9), RDW in subjects with confirmed appendicitis was significantly lower than those in the control group. Our study results were consistent with these findings.

However, in the study of Dinc et al. (20), there was no significant difference between RDW rates in patients with acute appendicitis and in control group (9); our findings contradicted the results of their study. The findings of the present study were similar to those of the Tanrikulu study for RDW sensitivity and specificity.

Here, in the present study, we showed that in the ROC curve plotted for the RDW sensitivity and specificity, the AUC was 0.61. In a study conducted by Narci et al. the AUC was less than 0.5. Although our result was greater than that of Narci's study, but this value in percentage is not a specific indicator for decision-making. Nonetheless, the AUC was about 0.90 in the ROC curve designed for calculating the sensitivity and specificity of the MPV test. This value is very significant and this variable could be a good indicator for the distinction of the acute phase of appendicitis.

Almost all studies have confirmed the low accuracy of these diagnostic tests, especially its low specificity. Some researchers have suggested that, in order to increase their sensitivity and specificity, two or more variables should be considered simultaneously in combination. Among them, Stefanutti et al. and Rozkark et al., have reported an increase in the sensitivity of the test as 96% by combining the results of CRP and white blood cell (WBC) (32, 33).

It is suggested to compare the MPV and RDW values in patients with clinical symptoms, to discriminate the acute from the perforated

appendicitis, compared to a healthy control group in an analytical study. Surgeons can increase the sensitivity and specificity of diagnostic tests by combining two or more biomarkers along with clinical signs, and by taking into account the age and other conditions, in order to prevent unnecessary appendectomy.

Limitations

Timing maybe an important effective factor that not measured its roll in current study. It may be possible that the time interval between starting the symptoms and presentation of the patients to the ED can effect on the values of RDW and MPV, and the later a patient comes in, the higher the markers, and vice versa. Therefore, it is highly recommended to assess this important factor in further studies on this topic.

CONCLUSIONS

MPV and RDW indices have the potential to be used by the surgeons for the distinction of acute and

perforated appendicitis, especially in adults, and reducing unnecessary appendectomy, however, the validity of MPV in screening acute appendicitis is higher than RDW, which may be considered as a diagnostic marker along with other clinical and para-clinical findings.

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AUTHORS' CONTRIBUTION

All the authors met the standards of authorship based on the recommendations of the International Committee of Medical Journal Editors.

CONFLICT OF INTEREST

None declared.

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