

# The correlation between laboratory markers and computed tomography severity index in acute appendicitis



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## The correlation between laboratory markers and computed tomography severity index in acute appendicitis

*AM:* This study aimed to evaluate and to investigate the association of some laboratory markers with the stage of the acute appendicitis.

*MATERIAL AND METHODS:* The hematological parameters (white blood cell count, red cell distribution width, platelet distribution width, mean corpuscular volume, and mean platelet volume values) and tomography scans of 200 patients who admitted to the emergency department with abdominal pain were retrospectively reviewed. Computed tomography grading about the severity of the cases was carried out by two radiologists, as grade 0 for normal appendix to grade 3 for perforated appendicitis. The hematological results of the patients were recorded for each severity group and were compared to detect whether there was a change in the hematological parameters as the severity in CT increases.

*RESULTS:* There was no difference in white blood cell count and red cell distribution width levels but mean platelet volume seemed to decrease as the tomography severity index increased.

*CONCLUSIONS:* Our data suggests that the most reliable instrument to detect appendicitis in the emergency environment is the computed tomography.

**KEY WORDS:** Acute appendicitis, Computed tomography, RDW, PDW, MPV, MCV

## Introduction

Acute appendicitis is one of the most common surgical conditions<sup>1</sup>. The diagnosis remains challenging because it may sometimes represent in atypical features or overlap with other conditions<sup>2</sup>. Although it is obviously necessary to stay away from any unnecessary operations, an estimated 15 percent of negative laparotomies is commonly accepted as appropriate to avoid perforations because they are associated with a higher rate of complications<sup>3</sup>. Despite the fact that, it is a very common situation encountered in emergency department and

many studies have been made for a better diagnosis, there may still be room for improvement for a better and more accurate diagnosis of acute appendicitis.

Some inflammatory serum markers have been studied calprotectin, serum amyloid A, C-reactive protein, and white blood cell count (WBC) and found to be significantly elevated in patients with acute appendicitis even though no certain cutoff points could be determined<sup>4</sup>. Red cell distribution width (RDW), platelet distribution width (PDW), mean corpuscular volume (MCV) and mean platelet volume (MPV) have been shown to be useful as a prognostic marker in various conditions. For example, increased RDW is also believed to be closely associated with the risk of cardiovascular morbidity and mortality in patients with previous myocardial infarction. Also, an elevated RDW is associated with the risk of depression among cardiac patients<sup>5</sup>. Some studies have shown RDW changes in acute appendicitis, although no cutoff value could be determined. Therefore, still the role of RDW in acute appendicitis remains controversial.

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A number of studies have reported that computed tomography (CT) findings are significantly correlated with surgical-pathological severity<sup>6,7</sup>. However, to the best of our knowledge, no study has been performed on the relationship between the CT findings of acute appendicitis and laboratory markers as RDW and MPV. Therefore, we undertook this retrospective study to evaluate and to investigate the association of RDW, PDW, MCV and MPV with the stage of the disease.

## Material and Methods

After ethics committee approval was obtained; CT images of patients were retrospectively reviewed by two radiologists who have experience on abdominal imaging. Two radiologists evaluated and scored (using a 0, 1 or 2 point scales) the severities severities based on CT-determined appendiceal diameters, appendiceal wall changes, caecal changes, periappendiceal inflammatory stranding and phlegmon or abscess formation. Initially they scored all patients blinded to the other researcher and in the cases of 12 patients they rescored the patients reaching a consensus. After scoring was carried out, we searched whether CT findings were significantly related to elevated hematological parameters and thus, investigated the relations of WBC, RDW, PDW, MCV and MPV levels with CT severity scores.

During a twelve month period 200 adult patients (aged 15 years and above) who attended to the emergency

department went to abdominal CT scanning because they were suspected of appendicitis, and they had gone under ultrasonographic examination which failed to give a specific diagnosis. Sixty-five patients who were found to have nonsurgical conditions were discharged within 24 hours after a negative CT scan. Thus, 135 patients (65 men, 70 women; age range 15-85; mean age 38 years) were enrolled in this study and one investigator reviewed the emergency medical charts of these selected patients. All of these patients underwent appendectomy within 12 hours of CT scanning and were pathologically proven to have appendicitis.

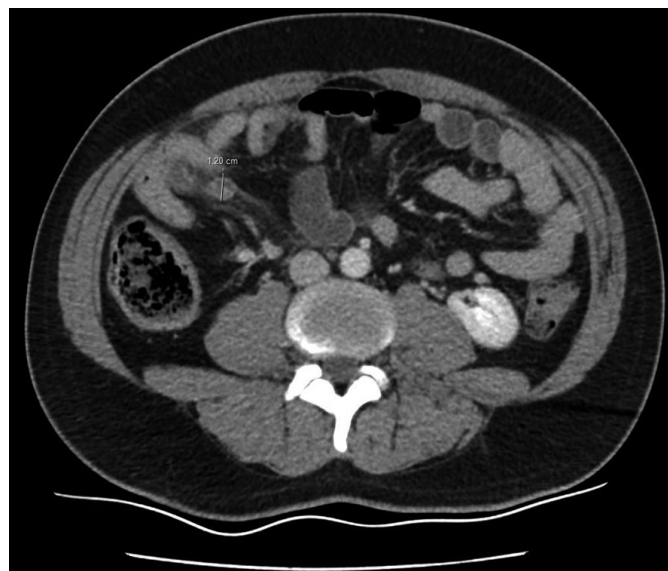


Fig. 2: Axial image shows a fluid-filled appendix of diameter 12 mm with moderate periappendiceal stranding.

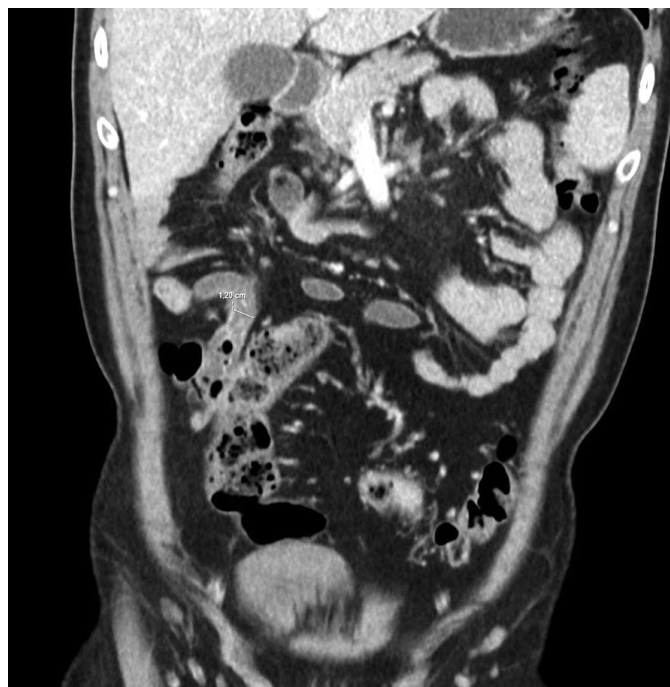


Fig. 1: Coronal reformation image shows a fluid-filled appendix (arrows) of diameter 12 mm. The appendiceal wall shows enhancement with mild periappendiceal stranding.



Fig. 3: Axial image shows a perforated appendix (arrow) with periappendiceal fluid (F).

TABLE I - CT grades of acute appendicitis

CT Classification	CT findings
Grade 0 normal appendix	Normal appendix, <6mm in diameter
Grade 1 mild appendicitis	Fluid-filled appendix, >6 mm in diameter and enhancing wall thickening, mild periappendiceal fat stranding
Grade 2 appendicitis with localised peritonitis	Moderate to severe periappendiceal fat stranding, there is no defect in appendiceal wall
Grade 3 perforated appendicitis	Defect in enhancing appendiceal wall with/without phlegmon or abscess

The CT scans were obtained in the emergency department with intravenous contrast used. All CT examinations were taken with the same 128-slice device (Optima CT660, General Electric Healthcare Systems, Milwaukee, USA). CT technical parameters were as follows: collimation 0.625 mm; pitch 1.014; rotation time 0.5 s; and voltage 120 kV (peak). Post-contrast scans of entire abdomens were performed with a 70 s delay after starting the infusion of 120 ml of non-ionic contrast material. Oral contrast was not given to these patients who were suspected of acute appendicitis. The raw data set was reconstructed at a thickness of 1,5 mm. Peripheral blood samples were all confirmed to be taken within 3 hours before the CT scan was taken.

All CT scans were reviewed by two radiologists dedicated to CT imaging. The reviewers were unaware of the laboratory tests or the physical examinations while they were reviewing the images but they were informed about a suspected appendicitis. The reviewers subjectively evaluated CT findings of appendicitis according to the following scheme: appendiceal diameter, appendiceal wall changes, caecal changes, periappendiceal inflammatory stranding and periappendiceal phlegmon or abscess for-

mation. Based on these findings, the reviewers decided on a CT grade score from 0 to 3 for each patients: Grade 0, normal; Grade 1, mild appendicitis (Fig. 1); Grade 2, appendicitis with localised peritonitis (Fig. 2) and Grade 3, perforated appendicitis (Fig. 3). This is in concert with a previously described grading system<sup>8</sup> (Table I).

#### STATISTICAL ANALYSIS

WBC, MCV, RDW, MPV and PDW values are given as mean and standard deviation. Differences in the aforementioned parameters between groups of CT grades of appendicitis were analysed by one-way analyses of variance and once a significant relationship was observed, a post-hoc test was conducted. Each grade (1,2,3) of CT severity scores for each individual parameter was compared with the control group (grade 0) for each individual parameter with Mann-whitney U test. A *p*-value of <0.05 was considered statistically significant.

#### Results

135 of 200 patients in our study were classified into three grades considering the CT findings. 60 patients who had normal abdominal tomography scans were graded as zero. 10 patients had to be reclassified as a consequence of disagreement on the first evaluation. They were reclassified by the two reviewers in agreement. Of the 200 patients, 60 were graded as 0 and grade 1,2,3 as 65, 45, 30, respectively. The mean maximum and standard deviation of each sub-group CT severity score for every parameter are listed down (Table II).

When the patients with pathologically proven acute appendicitis were analyzed, sex and age was not related to the inflammation of the appendix. Appendiceal diameter was correlated to the inflammation of the appendix ( $P = 0.001 < 0.05$ ). The patients with acute appendicitis had a mean appendiceal diameter of 9 mm (range, 6-15) whereas the patients with normal appendix had a mean appendix diameter of 4,5 mm (range, 3-5) (Table II).

TABLE II - The mean level and standard deviation of each sub-group CT severity score for every parameter

	Grade 0 sub-group (N=60) Mean Level (standard deviation)	Grade 1 sub-group (N=65) Mean Level (standard deviation)	Grade 2 sub-group (N=45) Mean Level (standard deviation)	Grade 3 sub-group (N=29) Mean Level (standard deviation)
WBC	12.2800 (3.91403)	12.6446 (3.80674)	14.4378 (3.01725)	13.19310 (5.166163)
RDW	14.1617 (1.43008)	14.4600 (1.98430)	13.8178 (1.29813)	13.3241 (.97162)
MPV	8,7417 (1,17838)	8,2446 (,74163)	8,1089 (,89717)	7,5724 (,57501)
PDW	16,7767 (,48130)	16,5662 (,56962)	16,6711 (,56312)	16,62 (,292)
MCV	84,9633 (7,28935)	82,6277 (8,48952)	85,2711 (4,18094)	87,6655 (3,80435)

## Discussion

Acute appendicitis still remains a challenge in the emergency department. Up to one third of patients may represent with atypical clinical features<sup>9</sup>. Despite the increased use of imaging modalities negative appendectomies may be as high as 15%<sup>10</sup>. Many laboratory tests have been studied in order to help the diagnosis so as to decrease the negative laparotomy rates. Leucocyte count, neutrophil percentage, MPV and CRP in diagnosing acute appendicitis have been studied as well as RDW, a recently emerging diagnostic marker.

Acute appendicitis starts with the obstruction of the lumen that causes the elevation of intraluminal pressure because of ongoing mucous secretion and progresses to mucosal ischemia and obstruction in venous return. This leads to enlargement of appendix and engorged appendix becomes infected as well<sup>11</sup>. As inflammation proceeds changes in the inflammatory parameters are likely to occur. As for inflammatory parameters; WBC, RDW and MPV were chosen for this study. These are cheap and available diagnostic markers and easy to obtain in the emergency department settings.

Several studies have displayed relationship between severity of appendicitis and elevated WBC counts<sup>12</sup>. However in other studies, proportion of gangrenous and perforated appendicitis in the patients with a normal WBC count was found to be the same as in the patients with an elevated WBC count, and therefore WBC could not be trusted as an indicator of severity<sup>13</sup>.

In our study only 7 people among 140 patients with pathologically confirmed appendicitis had normal WBC. However, in the group with a CT determined normal appendix (grade 0) the mean WBC was also elevated and there was no significant difference in the WBC levels compared to the non-appendicitis group (grade 0) and the three other groups, except the grade 2 group which had higher WBC levels. However there was no difference between the grade 0 and grade 3 in terms of the WBC counts. In pairwise comparison the grade 2 patients had higher WBC counts which was significantly different from the grade 1 and 0 patients. Considering these data we can not conclude that severity may rise with a higher WBC count.

RDW is a simple and inexpensive parameter and measures of the heterogeneity of volume/size of the red blood cells. It is used to differentiate types of anemia<sup>14</sup>. The normal reference range of RDW spans between 11% and 14%. However it has been found predictive in various health conditions such as cardiovascular disease, venous thromboembolism, cancer, diabetes, community-acquired pneumonia, chronic obstructive pulmonary disease, liver and kidney failure, as well as in some other acute or chronic conditions<sup>15</sup>.

In a study, a pediatric group with histologically proven acute appendicitis were found to have higher RDW than children without appendicitis, but the diagnostic value

of RDW was not found to be superior to WBC or CRP in children with acute appendicitis nor for perforated appendicitis<sup>16</sup>. In our study group the mean RDW value was  $14,14 \pm 2,180$  in the appendicitis group. The RDW values did not differ from the non-appendicitis group except the third grade appendicitis group in the pairwise comparison ( $p < 0.05$ ). A lower RDW may point to a complicated appendicitis.

MPV is a part of routine blood count which generally does not attract much attention. It is associated with platelet function and activation and is decided by megakaryocyte volume<sup>17</sup>. MPV is an independent predictor of the risk of stroke among individuals with a history of stroke or transient ischemic attack<sup>18</sup>. MPV is an independent risk factor for myocardial infarction but not for coronary artery disease<sup>19</sup>. MPV was found to be significantly lower in patients with acute appendicitis<sup>20</sup>. The best MPV level cutoff point for acute appendicitis was 7.6 fL, with a sensitivity, specificity, positive predictive value, and negative predictive value of 73%, 84%, 84%, and 74%, respectively<sup>21</sup>.

Bioactive molecules, found in the alpha and dense granules of the trombocytes, are the reason for the proinflammatory properties of the thrombocytes<sup>22</sup>. These molecules are secreted immediately after activation. During activation, platelets transform from biconcave discs to spherical, and subsequent pseudopod formation increases MPV during activation<sup>23</sup>. Danese et al speculated that the reduced MPV could be due to the consumption or sequestration of the large activated platelets in the intestinal vasculature<sup>24</sup>.

Saxena found platelet volume value to be significantly lower in acute appendicitis. They defined a cut-off value of MPV  $< 7.6$  fL and they found that it was positive for %82,6 (175 of 209) of the pathologically proven appendicitis cases<sup>25</sup>.

We observed a decrease in MPV as the grade of severity increases and found the afore mentioned cut-off point as a median for grade 3 appendicitis. MPV seems rather interesting because contrary to WBC levels between our control and appendicitis group, there was significant difference between the non-appendicitis group and the graded groups as a whole.

The PDW, which represents trombocyte immaturity, reflects the heterogeneity of trombocyte volume. Under physiological conditions, there is a direct relationship between MPV and PDW; both usually change in the same direction<sup>26</sup>. A higher level of PDW is associated with alzheimers disease, recurrent micarriages, acute ST-segment elevation myocardial infarction, severe preeclampsia<sup>27-30</sup>.

There are several studies that investigate the relationship between PDW and acute appendicitis. Aydogan et al. separated the acute appendicitis patients into two groups according to whether they are perforated or not and studied the platelet markers. Age, leukocyte, platelet, mean platelet volume, and PDW were higher in cases

with perforation as a comparison with non-perforated cases<sup>31</sup>. Albayrak et al, also found an increase in PDW in appendicitis<sup>21</sup>.

Ceylan *et al.* divided 362 acute appendicitis patients into two groups and further divided the appendicitis group into two: with complications and without. They found out that, MPVs were lower in subjects of appendicitis without complication when compared to the subjects of appendicitis with complication and the control group<sup>32</sup>. The PDW levels did not differ between the three groups. A study by Fan et al, they beheld an increase in the PDW in patients with acute appendicitis and a further increase in the PDW in patients with acute gangrenous appendicitis. They reached a cut off value of PDW as  $15.1 \times 10^9$  /L with a sensitivity of 76.3% with predictivity %93,1. They found that MPV is reduced and PDW is increased in acute gangrenous appendicitis<sup>33</sup>. This is also in agreement with our conclusion about MPV above.

In our study group there was significant difference between the appendicitis and nonappendicitis group ( $p=0,006$ ). However when we look at the subgroups there was only significant difference in the PDW parameter between the grade 1 and grade 0 group while there was no difference in the other subgroups with the control group.

The other parameter we studied was MCV. In a study by Acar et al, when they compared the hematological parameters of renal colic and acute appendicitis patients, there was no significant difference in the acute appendicitis groups considering MCV. However, it was found significantly higher in the renal colic group<sup>34</sup>. In our study we found no difference between the subgroups and the control group as well as the appendicitis and non-appendicitis group.

## Conclusion

With regards to the inflammatory parameters, there was no statistically significant difference between the appendicitis and the non-appendicitis groups, considering the WBC, RDW, PDW, MCV parameters except the MPV parameter. Our control group was a group of patients who admitted to the emergency department with abdominal pain, and went under a CT scan. They were compared with the group of patients who were diagnosed to have acute appendicitis. Both groups had mostly high levels of inflammatory markers which makes the diagnosis challenging. Our data may suggest that the most reliable instrument to detect appendicitis in the emergency environment is the CT.

## Riassunto

Scopo di questo studio è quello di indagare l'associazione di alcuni dati di laboratorio con lo stadio di acuzie dell'appendicite.

Lo studio è stato condotto retrospettivamente su 200 pazienti ricoverati nel dipartimento di emergenza con dolore addominale controllando i parametri ematologici (conta dei globuli bianchi, distribuzione volumetrica delle emazie e delle piastrine, volume corpuscolare medio, e valore medio del volume piastrinico) e la CT.

La gravità sulla base della CT è stata valutata da due radiologi, indicando come grado 0 per appendice normale e grado 3 per appendicite perforata. I risultati ematologici sono stati correlati con ciascun gruppo di gravità e confrontati tra loro per stabilire se ci fosse una variazione dei parametri ematologici con l'incremento di gravità alla CT.

Non è risultata alcuna differenza nella conta dei globuli bianchi né nella distribuzione volumetrica delle emazie, ma il volume medio piastrinico sembra diminuire inversamente alla gravità degli indici della CT.

Questi risultati suggeriscono che l'elemento più affidabile per individuare l'appendicite nell'ambito dell'emergenza è la CT chirurgica

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