The use of platelet indices, plateletcrit, mean platelet volume and platelet distribution width in emergency non-traumatic abdominal surgery: a systematic review

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Abstract

Platelet indices (PI) — plateletcrit, mean platelet volume (MPV) and platelet distribution width (PDW) — are a group of derived platelet parameters obtained as a part of the automatic complete blood count. Emerging evidence suggests that PIs may have diagnostic and prognostic value in certain diseases. This study aimed to summarize the current scientific knowledge on the potential role of PIs as a diagnostic and prognostic marker in patients having emergency, non-traumatic abdominal surgery. In December 2015, we searched Medline/PubMed, Scopus and Google Scholar to identify all articles on PIs. Overall, considerable evidence suggests that PIs are altered with acute appendicitis. Although the role of PI in the differential diagnosis of acute abdomen remains uncertain, low MPV might be useful in acute appendicitis and acute mesenteric ischemia, with high MPV predicting poor prognosis in acute mesenteric ischemia. The current lack of consistency and technical standards in studies involving PIs should be regarded as a serious limitation to comparing these studies. Further large, multicentre prospective studies concurrently collecting data from different ethnicities and genders are needed before they can be used in routine clinical practice.

Key words: platelets; acute appendicitis; acute cholecystitis; acute mesenteric ischemia; platelet indices

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Introduction

Platelets are cytoplasmatic fragments of bone marrow megakaryocytes, with a diameter of 3-5 μm and a volume of 4.5–11 fl (1). A single megakaryocyte releases 1500–2000 of them to the bloodstream, where they circulate for 7–10 days. Inactivated platelets in the blood are discoid shaped and do not contain a nucleus. Their cytoplasm contains three different types of granules (i.e. alpha granules, dense granules, and lysosomal granules), secretory vesicles that contain preformed molecules, and a complex membranous system (1).

Platelets are dynamic blood particles whose primary function, along with the coagulation factors, is haemostasis, or the prevention of bleeding. Platelets interact with each other, as well as with leukocyte and endothelial cells, searching the vascular bed for sites of injury, where they become activated. When stimulated, platelets undergo a shape change, increasing their surface area and bioactive molecules stored within their alpha and dense granules’ molecules are rapidly secreted (2).

In addition to their important role in haemostasis and thrombosis, accumulating evidence demonstrates that platelets contribute to the inflammatory process, microbial host defence, wound healing, angiogenesis, and remodelling (3). Platelets release > 300 proteins and small molecules from
their granules (chemokines, cytokines like interleukin-1β, CD40 ligands, β-thromboglobulin, growth factors etc.), which can influence the function of the vascular wall and circulating immune cells (3-6). Platelets also secrete microbicidal proteins and antibacterial peptides (5,7).

Platelets also mediate leukocyte movement from the bloodstream through the vessel wall to tissues. Platelets are capable of forming reactive oxygen species; the oxidative stress that accompanies inflammation can also activate platelets (8-10). Platelets’ ability to influence other cells means that they can also play many principal roles in the pathophysiology of diseases.

Platelet indices

Complete blood count (CBC) tests with automated haematology analysers are one of the most commonly ordered tests in clinical laboratories. Modern haematology analysers in routine diagnostic use, which measure platelet indices (PIs), use impedance counting or optical light scatter counting techniques. The measurement principle influences the results, and the results from different analysers are not comparable (11).

Platelet count in the blood can be rapidly measured using an automated haematologic analyser. Platelet indices are biomarkers of platelet activation. They allow extensive clinical investigations focusing on the diagnostic and prognostic values in a variety of settings without bringing extra costs. Among these platelet indices, plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) are a group of platelet parameters determined together in automatic CBC profiles; they are related to platelets’ morphology and proliferation kinetics (Table 1).

The volume of platelets in the bloodstream is heterogeneous, and their structures and metabolic functions differ. Typically, the average mean cell volume is 7.2–11.7 fL in healthy subjects (12,13). In MPV, the analyser-calculated measure of thrombocyte volume is determined directly by analysing the platelet distribution curve, which is calculated from a log transformation of the platelet volume distribution curve, to yield a geometric mean for this parameter in impedance technology systems. In some optical systems, MPV is the mode of the measured platelet volume (14). MPV is determined in the progenitor cell, the bone marrow megakaryocyte. The platelet volume is found to be associated with cytokines (thrombopoietin, interleukin-6 and interleukin-3) that regulate megakaryocyte ploidy and platelet number and result in the production of larger platelets (15-17). When platelet production is decreased, young platelets become bigger and more active, and MPV levels increase. Increased MPV indicates increased platelet diameter, which can be used as a marker of production rate and platelet activation. During activation, platelets’ shapes change from biconcave discs to spherical, and a pronounced pseudopod formation occurs that leads to MPV increase during platelet activation.

| Parameter | Description | Unit |
|-----------|-------------|------|
| Mean platelet volume (MPV) | Analyser-calculated measure of thrombocyte volume | femtoliters (fL) |
| Platelet volume distribution width (PDW) | Indicator of volume variability in platelets size | percentage (%) |
| Plateletcrit (PCT) | Volume occupied by platelets in the blood | percentage (%) |
| Mean platelet component (MPC) | Measure of mean refractive index of the platelets | gram/decilitre (g/dL) |
| Mean platelet mass (MPM) | MPM is calculated from the platelet dry mass histogram | picogram (pg) |
| Platelet component distribution width (PCDW) | Measure of the variation in platelet shape | gram/decilitre (g/dL) |
| Platelet larger cell ratio (P-LCR) | Indicator of larger (> 12 fL) circulating platelets | percentage (%) |
| Immature platelet fraction (IPF) | Percentage of immature platelets | percentage (%) |

Table 1. Platelet indices
PDW is an indicator of volume variability in platelets size and is increased in the presence of platelet anisocytosis (17). PDW is a distribution curve of platelets measured at the level of 20% relative height in a platelet-size distribution curve, with a total curve height of 100% (18). The PDW reported varies markedly, with reference intervals ranging from 8.3 to 56.6% (12,19-21). PDW directly measures variability in platelet size, changes with platelet activation, and reflects the heterogeneity in platelet morphology (13,20). Under physiological conditions, there is a direct relationship between MPV and PDW; both usually change in the same direction (20). Meanwhile, there are conflicting reports in the literature about the relationship between platelet volume and numbers, which suggests that they are affected by different mechanisms (5,21-25).

PCT is the volume occupied by platelets in the blood as a percentage and calculated according to the formula $PCT = \text{platelet count} \times \text{MPV} / 10,000$ (25-27). Under physiological conditions, the amount of platelets in the blood is maintained in an equilibrium state by regeneration and elimination. The normal range for PCT is 0.22–0.24% (13,25-27). In healthy subjects, platelet mass is closely regulated to keep it constant, while MPV is inversely related to platelet counts (6,13,27). Genetic and acquired factors, such as race, age, smoking status, alcohol consumption, and physical activity, modify blood platelet count and MPV (27-29).

Platelet larger cell ratio (P-LCR) is an indicator of circulating larger platelets (> 12 fL), which is presented as percentage. The normal percentage range is 15–35%. It has also been used to monitor platelet activity (30).

Mean platelet component (MPC) is a measure of mean refractive index of the platelets by modified two-angle light scatter and it is useful in determining changes in the status of platelet activation. Platelet component distribution width (PCDW) and mean platelet mass (MPM) are new platelet activation parameters measured by the Siemens Advia 120 haematology analyser.

Immature platelet fraction (IPF) indicates the percentage of immature platelets, as a percentage of the total platelet population measured in the reticulocyte/optical platelet channel of the haematology analyser by flow cytometry, in which dye penetrates the cell membrane, staining the RNA in the cytoplasm of immature (or reticulated) platelets on the Sysmex XE-2100 analyser (Sysmex Corporation, Kobe, Japan). The IPF percentage increases as production of platelets increases, and low values indicate suppressed thrombopoiesis (31). The clinical significance, reference values and usefulness of some of these parameters are still under investigation (32).

**Platelet indices as diagnostic and prognostic markers**

Simultaneous measurement of all of the platelet indices will provide us a valid instrument for measuring disease severity and an insight into the potential etiology that resulted in platelets' indices changes. Platelet volume heterogeneity occurs during its production and increases MPV and PDW comparatively, suggesting that bone marrow produces platelets and rapidly releases them into circulation (18). A simultaneous reduction of platelet count and PCT indicates that platelets have been excessively consumed (33).

Platelets play an important role in inflammation, and recently, several additional functions for platelets in the process of inflammation were defined. A substantial number of studies have demonstrated crucial roles for platelets in the pathogenesis of various inflammatory clinical conditions where inflammation is important (34). Numerous research groups have found a relationship between the changes in platelet indices and the activation of the coagulation system, severe infection, trauma, systemic inflammatory reaction syndrome, and thrombotic diseases (34). Platelet indices have been shown to have diagnostic value in certain inflammatory diseases, such as inflammatory bowel diseases, rheumatoid arthritis, ankylosing spondylitis, ulcerative colitis, and atherosclerosis (6,34-39).
MPV acts as a negative or positive acute phase reactant in different inflammatory conditions. High MPV levels are associated with high-grade inflammation owing to the presence of the large platelets in circulation. MPV might decrease in high-grade inflammation due to the consumption and sequestration of these large platelets in the vascular segments of the inflammatory region. Low MPV is associated with low-grade inflammation, like rheumatoid arthritis and attacks of familial Mediterranean fever. MPV decreases and increases in acute and chronic disorders, respectively (6).

MPV shows the activity of disease in systemic inflammation, acute pancreatitis, unstable angina, and myocardial infarction (40-43). MPV can be a modifiable marker in identifying patients with active ankylosing spondylitis and rheumatoid arthritis, which is thought to be due to increased consumption of platelets in the inflammation area and MPV increases with therapy in these patients (37,44).

Sepsis is another example of obvious interaction between the immune and haemostatic system. Since these systems are closely linked, septic patients are observed to have low platelet count due to production of many cytokines, endothelial damage and bone marrow suppression. In patients with septic shock, the rise in MPV, and to a lesser extent an increase in P-LCR and PDW, indicates a worse prognosis (6,45,46).

In the emergency department, surgeons frequently use CBC to determine inflammatory pathologies and as part of routine preoperative assessment. Platelet indices especially MPV, may be a simple way to provide valuable information during routine blood counts without increasing the cost of diagnosis or differentiating non-traumatic abdominal surgery patients.

To date, there has been no published meta-analysis of the potential use of PIs in emergency non-traumatic abdominal surgery. In addition, there has been only one published meta-analysis of the value of MPV as a predictor of cardiovascular risk, by Chu et al. (43). This review aimed to summarize current scientific knowledge of the potential role of PIs as a diagnostic and prognostic marker in emergency non-traumatic abdominal surgery patients, especially those with acute appendicitis, acute cholecystitis and acute mesenteric ischemia.

**Methods**

In December 2015, we searched Medline/PubMed, Scopus and Google Scholar for ‘platelet’, ‘platelet indices’, ‘platelet distribution width’, ‘plateletcrit’, PCT, ‘mean platelet volume’ and ‘MPV’ in combination with ‘surgery’, ‘acute appendicitis’, ‘acute cholecystitis’ and ‘acute mesenteric ischemia’, identifying a number of studies. Then, we sequentially screened titles, abstracts and full-text articles to identify all relevant articles published in English. We reviewed reference lists to identify further literature references to eligible studies. Studies were included in this review if they were published in a peer-reviewed journal and included human subjects. Both retrospective and prospective studies were considered for this review whereas case reports were excluded. We set no age limits. Power analysis has not been performed in any of these studies. All data (from 24 studies) are presented systematically and summarized in Table 2.

**Acute appendicitis and platelet parameters**

Acute appendicitis is defined as inflammation of the of the appendix vermiformis, and usually causes pain in the right lower abdominal quadrant that is the most common cause of acute abdomen in all age groups attending to emergency settings (47). Appendectomy is the most frequently performed surgery in the emergency surgery clinics. It is important to diagnose acute appendicitis before complications occur because diagnostic delay considerably increases the risk of appendicitis perforation.

Although in some patients the symptomatology and examination findings are classic, it is hard to diagnose in patients with less specific signs with abdominal pain; a number of diseases mimic appendicitis. It is often difficult to rule it out on the basis of clinical presentation, and requires further investigation to diagnose correctly. On the other
hand, the entity of negative appendectomies is 14.7% to 8.47% of abdominal exploration surgery, and negative appendectomy is associated with unnecessary risks and costs to patients (47,48). Clinical history, physical exam with ultrasonography, computed tomography, and magnetic resonance imaging have been shown to contribute to diagnostic accuracy in patients with suspected acute appendicitis, but not all the time. There has been much effort to search for biomarkers to identify patients at risk for appendicitis; however, most of them are expensive and unavailable in most emergency departments, and there is difficulty in making an accurate diagnosis of appendicitis (49). Therefore, as cheap and available diagnostic markers, inflammation-related CBC parameters, white blood cell (WBC) count, and neutrophil percentage are the most frequent markers of inflammation used in diagnosis, and are the earliest indicators in showing inflammation of appendicitis (49). None are diagnostic of acute appendicitis and their sensitivity and specificity ranges vary widely and are dependent upon the population under study, symptom time duration and cut-off values used (50,51). Given the limitations of the current inflammatory markers, surgeons are searching for other potential biomarkers for the diagnosis of acute appendicitis to decrease the rate of negative laparotomies in cases with a pre-diagnosis of acute appendicitis, so as to lead to fewer delays in diagnosis and the early prediction of perforation (52,53). In order to increase the accuracy of acute appendicitis detection, some researchers have been directed towards using platelet parameters in addition to WBC, which is easily applicable everywhere, cheap, and non-invasive, and would not cause a loss in diagnostic time.

Studies investigating PIs as biomarkers of acute appendicitis patients

Some of these studies suggested MPV alteration as a valuable diagnostic marker, but the alteration of MPV in acute appendicitis is controversial. Seven retrospective case control studies stated that the MPV was lower in acute appendicitis patients than in healthy controls (54-60), whereas one study reported the opposite finding (61). Two studies showed no significant difference between the two groups in adult patients (62,63). The general properties of these studies are shown in Table 2. All except one were retrospective, and acute appendicitis diagnosis was confirmed histopathologically and the control group was composed of distinct patients with no symptoms, including patients admitted to outpatient centres for routine exams. The analysers used were different, and in some studies, it was not indicated which analyser was used. This may introduce bias into certain study designs.

Yang et al. found that, when groups of patients diagnosed with acute appendicitis were subdivided according to gender, only the male group showed a statistically significant decrease in MPV (P = 0.009) (58). This study was in accordance with Lee et al., which stated that PIs are not useful in distinguishing acute appendicitis from normal populations in female candidates (63).

In the study by Kucuk and Kucuk, control and acute appendicitis group data were obtained from the same patients, and no intra-individual difference between patients in terms of MPV was found. Previous MPV values corresponding to the non-inflammatory state were determined from these patients’ medical records in the hospital database. They found that MPV was significantly lower relative to non-diseased stages. Receiver operating characteristic curve analysis suggested that the optimal cut-off point for the diagnosis of acute appendicitis was 6.10 fL, with a sensitivity of 83% and a specificity of 42% (64).

Kılıç et al. could not find a difference between acute appendicitis and patient groups, and suggested that MPV could have been affected by an inflammatory process other than appendicitis. They considered this the most important factor resulting in no significant difference in MPV between acute appendicitis patients and controls in their study (65).

Meanwhile, a study conducted by Narci et al. suggested that higher MPV values might guide the diagnosis of acute appendicitis, with 66% sensitivity and 51% specificity (61).
Table 2. Summary of studies

| Reference (publication year) | Number of patients and controls (years) | Sample, analyzer, method | Platelet indices | Study design | Comment |
|-----------------------------|-----------------------------------------|--------------------------|------------------|-------------|---------|
| **Acute Appendicitis (adults)** |                                         |                          |                  |             |         |
| Albayrak et al. (2011)      | 226 patients with AA (2.5 ± 15.1) and 206 controls (35.5 ± 14.7) | ND, Beckman Coulter analyzer, impedance | MPV: 7.25 ± 0.85 fL | Decreased* (P < 0.001) | Diagnostic, case-control, prospective |
|                             |                                         |                          | MPV: 9.01 ± 1.33 fL |             | CBC analysed within 2 hours after collection. Best cut-off point for MPV in the diagnosis of AA was ≤ 7.6 fL. |
| Tanrikulu et al. (2014)     | 239 patients with AA and 21 patients with normal appendix were included jointly in the patient group (31.8 ± 12.4); 158 controls (32.2 ± 10.5) | ND | MPV: 7.75 ± 1.24 fL | Decreased* (P < 0.001) | Diagnostic, case-control, retrospective, multicenter study |
|                             |                                         |                          | MPV: 8.49 ± 0.97 fL |             | Best cut-off point for MPV in the diagnosis of AA was ≤ 7.3 fL. |
| Erdem et al. (2015)         | 100 patients with AA (33.6 ± 12.2) and 100 controls (30.8 ± 9.7) | ND | MPV: 7.4 ± 0.9 fL | Decreased* (P < 0.001) | Diagnostic, case-control, retrospective |
|                             |                                         |                          | MPV: 9.1 ± 1.6 fL |             | CBCs analysed 24 hours prior to surgery. Best cut-off point for MPV in the diagnosis of AA was ≤ 7.95 fL. |
| Dinc et al. (2015)          | 295 patients with AA and 100 patients with other intra-abdominal infections; 100 controls (16–94) | EDTA-anticoagulated blood, ND | MPV (fL) in AA patients 8.5 (6.1–14.2); MPV (fL) in patients with intra-abdominal infection 8.9 (6.0–13); PDW (%) in AA patients 18.4 (10.3–62.5); PDW (%) in patients in intra-abdominal infection 40.8 (12.8–87.9) | MPV: 8.9 (6.9–14.5) fL; PDW 49.0 (10.6–86.5)% | Diagnostic, case-control, retrospective |
|                             |                                         |                          | MPV decreased* (P = 0.001); PDW increased† (P < 0.001) |             | All samples analysed within 10 minutes. Diagnostic accuracy for PDW was 96.0%. |
| Yang et al. (2014)          | 196 AA patients (41.8 ± 15.5) and 143 controls (44.0 ± 10.3) | EDTA-anticoagulated blood, Advia 2120 (Siemens Healthcare Diagnostics, Germany), optical method | MPV: 7.82 ± 0.64 fL | Decreased* (P = 0.042) | Diagnostic, case-control, retrospective |
|                             |                                         |                          | MPV: 7.96 ± 0.58 fL |             | CBC analysed within 2 hours after collection. |
| Reference (publication year) | Number of patients and controls (years) | Sample, analyzer, method | Platelet indices | Study design | Comment |
|-----------------------------|----------------------------------------|--------------------------|-----------------|-------------|---------|
| Fan et al. (2015)           | 160 gangrenous AA patients (43.0 ± 12.5) and 160 healthy controls (45.6 ± 19.6) | EDTA-anticoagulated blood, ND | MPV: 9.21 ± 1.38 fL; PDW: 15.25 ± 1.90% | Diagnostic, case-control, retrospective | MPV decreased* (P = 0.000); PDW increased† (P = 0.000) All samples analysed within 10 minutes. Best cut-off point for MPV in the diagnosis of AA was ≤ 9.6 fL. Best cut-off point for PDW in the diagnosis of AA was ≥ 15.1 fL. |
| Narci et al. (2013)         | 503 patients (34.7 ± 14.1) and 121 controls (35.2 ± 8.1) | Celi-Dyne 3700 (Abbott Diagnostics, IL, USA), impedance | MPV: 7.92 ± 1.68 fL | Diagnostic, case-control, retrospective | Increased† (P < 0.001) Best cut-off point for MPV in the diagnosis of AA was ≥ 7.87 fL. |
| Bozkurt et al. (2015)       | Patients operated for appendectomy were divided into three groups: 90 uncomplicated AA; 120 complicated AA and 65 negative appendectomy (17–78) | Sysmex XT-2000i (Sysmex Corporation, Kobe, Japan), impedance and optic | MPV in uncomplicated AA patients 10.40 ± 0.93 fL; MPV in complicated AA 10.27 ± 0.93 fL; MPV in negative appendectomy patients 10.42 ± 1.00 fL | Diagnostic, case-control, retrospective | None Not changed (P = 0.478) Best cut-off point for MPV in the diagnosis of AA was ≥ 10.8 fL. |
| Lee et al. (2011)           | 130 female AA patients (43.4 ± 16.6) and 85 female controls (45.1 ± 12.1) | ND | MPV: 10.58 ± 0.80 fL | Diagnostic, case-control, retrospective | Not changed (P = 0.285) - |
| Kucuk et al. (2015)         | 60 patients (33.15 ± 10.94)             | Celi-Dyne 3700 (Abbott Diagnostics, IL, USA), impedance | MPV in AA patients 7.03 ± 0.8 fL; previous MPV: 7.58 ± 1.11 fL | Diagnostic, case-series, retrospective | Decreased* (P = 0.01) Previous MPV of the same patient was evaluated as control. |
| Kilç et al. (2015)          | 316 AA patients and 316 controls (14–76) | EDTA-anticoagulated blood, LH 780 Analyzer (Beckman Coulter Inc., USA), impedance | MPV: 8.03 (5.53–14.40) fL | Diagnostic, case-control, retrospective | Not changed (P = 0.193) CBC analyses were performed within 2 hours after collection. |
| Aktimur et al. (2015)       | 407 AA patients and 61 patients with normal appendix (range 16–86) | ND | MPV in AA patients 9.6 ± 1.5 fL; MPV in negative appendectomy 9.1 ± 1.5 fL | Diagnostic, case-control, retrospective | Increased (P = 0.018) For cut-off value of 9.6 fL, sensitivity was 57.1% and specificity was 60.7%. |
Table 2. Summary of studies (continued)

| Reference          | Acute appendicitis (pediatric) | Number of patients | Sample, analyzer, method | Platelet indices | Study design | Comment |
|--------------------|--------------------------------|--------------------|--------------------------|------------------|--------------|---------|
| Sexana et al. (2015) | Attempted to define potential thresholds value which is predictive of a diagnosis in 213 AA patients. | 100 AA patients 7.4 ± 3.6 | EDTA-anticoagulated blood; ABX-Pentra, DX 120 | MPV: 8.90 ± 1.29 fL | Diagnostic, case-control, retrospective | ND |
| Bilici et al. (2011) | When they used an MPV cut-off value of ≤ 7.6 fL, they found sensitivity, specificity, of which and was 83.73%, 75%, and 83.56%, respectively | 100 AA patients (8.1 ± 3.4) and 100 controls (8.7 ± 3.6) | EDTA-anticoagulated blood; ABX-Pentra, DX 120 (ABX-Horiba, France), impedance | MPV: 7.55 ± 0.89 fL | Diagnostic, case-control, retrospective | When they used an MPV cut-off value of ≤ 7.6 fL, they found sensitivity, specificity, of which and was 83.73%, 75%, and 83.56%, respectively |
| Uyanik et al. (2012) | In 305 AA patients (9.5 ± 2.9) and 305 controls (9.6 ± 3.1) | 305 AA patients 7.9 ± 0.8 fL | EDTA-anticoagulated blood; ND | MPV: 7.9 ± 0.9 fL | Diagnostic, case-control, retrospective | ND |
| Yilmaz et al. (2015) | In 204 AA patients 7.37 ± 0.9 fL; MPV in negative appendectomy 7.60 ± 1.24 fL; PCT in negative appendectomy 0.208 ± 0.045; PDW in AA patients 16.3 ± 0.5; PDW in negative appendectomy 0.208 ± 0.045 | 204 AA patients (10.4 ± 3.7) and 20 subjects with normal appendix vermiformis (10.9 ± 4.2) | EDTA-anticoagulated blood; Mindray BC-5800 (Mindray BioMedical Electronics Co., Ltd., China), impedance | MPV: 7.37 ± 0.9 fL; MPV in negative appendectomy 7.60 ± 1.24 fL; PCT in negative appendectomy 0.208 ± 0.045; PDW in AA patients 16.3 ± 0.5; PDW in negative appendectomy 0.208 ± 0.045 | Diagnostic, case-control, retrospective | MPV: 7.37 ± 0.9 fL; MPV in negative appendectomy 7.60 ± 1.24 fL; PCT in negative appendectomy 0.208 ± 0.045; PDW in AA patients 16.3 ± 0.5; PDW in negative appendectomy 0.208 ± 0.045 |
| Seker et al. (2013) | In 33 patients with AC (56.4 ± 15.5), 32 patients with CC (51.4 ± 13.8), and 28 controls (54.7 ± 15.3). | 33 patients with AC (56.4 ± 15.5), 32 patients with CC (51.4 ± 13.8), and 28 controls (54.7 ± 15.3) | EDTA-anticoagulated blood; Mindray BC-5800 (Mindray BioMedical Electronics Co., Ltd., China), impedance | MPV: 7.28 ± 0.74 fL | Case-control, retrospective | MPV: 7.28 ± 0.74 fL |

Acute cholecystitis

| Reference          | Number of patients | Sample, analyzer, method | Platelet indices | Study design | Comment |
|--------------------|--------------------|--------------------------|------------------|--------------|---------|
| Seker et al. (2013) | 32 patients with CC (51.4 ± 13.8), 28 controls (54.7 ± 15.3) | EDTA-anticoagulated blood; Mindray BC-5800 (Mindray BioMedical Electronics Co., Ltd., China), impedance | MPV: 7.28 ± 0.74 fL | Case-control, retrospective | 32 patients with CC (51.4 ± 13.8), 28 controls (54.7 ± 15.3) | ND |
| Reference (publication year) | Number of patients and controls (years) | Sample, analyzer, method | Platelet indices | P | Study design | Comment |
|-----------------------------|----------------------------------------|--------------------------|----------------|---|--------------|---------|
| **Acute mesenteric ischemia (AMI)** | | | | | | |
| Türköglu et al. (2015) | 95 patients who underwent emergency surgery for acute mesenteric ischemia (68.4 ± 14.4) and 90 controls (67.1 ± 15.7) | EDTA-anticoagulated blood, Cell-Dyne 3700 (Abbott Diagnostics, IL, USA), impedance | MPV: 9.4 ± 1.1 fL | MPV: 7.4 ± 1.4 fL | (P < 0.001) | Case-control | The best cut-off point for MPV in the diagnosis of AA was > 8.1 fL |
| Altıntoprak et al. (2013) | 30 patients operated for AMI (29–94), two groups according to outcome – non-survivors (group 1) and survivors (group 2) | ND | None | MPV in non-survivors: 9.01 fL; MPV in survivors: 7.80 fL | (P = 0.002) | Prognostic, retrospective | SDs were not given |
| Aktimur et al. (2015) | 62 AMI related laparotomy and/or bowel resection patients (41–93 yrs), 62 AA patients (14–86), 61 negative appendectomy patients (16–73) | ND | None | MPV in AMI patients 10.8 ± 0.9 fL; MPV in AA patients 10.5 ± 0.8 fL; MPV in negative appendectomy patients 9.1 ± 1.5 fL | (P < 0.001) | Retrospective | The median ages were significantly different. CBCs were taken 24 hours prior to surgery. |
| Bilgiç et al. (2015) | 61 patients operated for AMI (40–91); two groups according to outcome: Survivors (53–87) and non-survivors (40–91) | ND | None | Non-survivor MPV: 8.4 (5.5–10.4) fL; survivor MPV: 7.6 (6.6–8.9) fL | (P < 0.01) | Prognostic, retrospective | Cut-off point for mortality in AMI was MPV = 8.1 fL. Sensitivity, specificity, positive and negative predictive values were 60%, 73.1%, 74.7%, and 58%, respectively. |

Age is presented as mean age ± standard deviation or age range. Platelet indices are presented as mean ± standard deviation or mean (range). AA – acute appendicitis; MPV – mean platelet volume; CC – chronic cholecystitis; AMI – acute mesenteric ischemia; CBC – complete blood count; ND – not declared; decreased * – decreased compared to healthy controls; increased † – increased compared to healthy controls.
Some of the studies evaluated the PIs among the groups who underwent appendectomy with a pre-diagnosis of acute appendicitis without including healthy control groups (63,66,67). Aktimur et al. analysed 469 patients who underwent appendectomy; in 408 of the patients, the diagnosis was confirmed by histopathological assessment, and in 61 patients, the appendix were normal. They found that MPV values were higher in the acute appendicitis group compared to negative appendectomies (66).

Bozkurt et al. compared MPV results of uncomplicated acute appendicitis, complicated acute appendicitis (perforated, plastrone, necrotising appendicitis, and appendicitis with peritonitis), and non-appendicitis (normal appendix, reactive lymph node hyperplasia) cases that underwent appendectomy. Although the complicated appendicitis group had a lower MPV value compared to other groups, the levels were not statistically different across the groups (62).

Aydogan et al. separated acute appendicitis patients into two groups according to perforation status. MPV was lower and PDW was higher in the perforated group than in the non-perforated group (67).

Ceylan et al. separated 362 acute appendicitis patients into two groups and found that MPV was lower in subjects without complications compared to subjects with complications and the control group. PDW did not differ between groups (59).

Saxena et al. attempted to define potential threshold values that are predictive of a diagnosis. When they used a cut-off value of MPV < 7.6 fl, they found sensitivity, specificity, and accuracy of 83.73%, 75%, and 83.56%, respectively (68).

Acute appendicitis is the most common surgical condition in children that causes acute abdominal pain, but its diagnosis can be extremely difficult due to its vague signs and symptoms, and is thus at high risk of being misdiagnosed. In addition to limited communication skills, young children pose a diagnostic challenge due the non-specific nature of their symptoms; therefore, more laboratory data are needed to clarify the diagnosis of patients with suspected appendicitis. Platelets as laboratory inflammatory markers have been studied, but the results are contradictory. Bilici et al. found that, in paediatric acute appendicitis patients of 1–15 years old, MPV levels were markedly low compared to the healthy control group (69). On the other hand, Uyanik et al. failed to find a difference in MPV levels between paediatric acute appendicitis patients and the control group (70). They suggested that the destruction of erythrocytes in acute inflammation may cause fragmented cells to be counted as thrombocytes, thus leading to a false MPV decrease. Yilmaz et al. analysed 204 pediatric patients operated on for a preliminary diagnosis of acute appendicitis, of which 20 subjects had normal appendix vermiformis. They found that there is no difference with regard to the PIs between the children with true appendicitis (MPV, PCT, and PDW) and those with a normal appendix (71).

However, a number of issues must be considered when translating measurement of the PIs of appendicitis patients into clinical practice in the emergency setting. PI results are influenced by factors such as the anticoagulant used in the collection tube, the delay in time from sampling to analysis and the individual technologies developed for each type of analyser (72). In light of these findings, we excluded studies that did not report the time from the phlebotomy until the analysis or the analyser on which the PIs were measured. Only five studies fit these reporting criteria. In all of these studies, MPV values were low in acute appendicitis patients compared to healthy controls (54,58,59,65,69).

**Acute cholecystitis**

Acute cholecystitis is an acute inflammatory disease of the gallbladder with an abrupt onset in hours. In most of the cases, the underlying aetiology is gallstone. With early diagnosis and therapy, mortality and morbidity are lowered. Ultrasonography is the most important method in diagnosis, with a sensitivity of 80% to 100% and specificity of 60% to 100%. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and WBC support the diagnosis (73,74). Early diagnosis and treatment of
patients is very important because, if not treated, acute cholecystitis has a high mortality rate (75).

Recently, two retrospective studies investigated MPV as a biomarker of acute cholecystitis. Sayit et al. evaluated 60 patients with a diagnosis of acute cholecystitis, using medical records. Also, the data of 60 age-matched, healthy individuals with normal abdominal ultrasound were evaluated as the control group. They found the MPV levels in patients with acute cholecystitis significantly lower, and PDW and PCT significantly higher in the acute cholecystitis group when compared to the control group (75). Seker et al. analysed 33 patients with acute cholecystitis and 32 patients with chronic cholecystitis, and 28 healthy individuals. MPV values were found to be significantly lower in the acute cholecystitis group when compared to those in the chronic cholecystitis group and control groups (P < 0.05) (74).

Because we found only two retrospective studies, each with a small number of patients, there is a need for larger, prospective, well-designed studies in various settings to measure the potential of PIs in acute cholecystitis patients.

**Acute mesenteric ischemia**

Acute mesenteric ischemia is a syndrome caused by a significant decrease in mesenteric blood flow that results in ischemia and eventual bowel necrosis, with an overall mortality rate of 40–70%. The causes of mesenteric vascular ischemia are embolism, thrombosis and mesenteric venous thrombosis (76,77). Definitive diagnosis can be made by advanced imaging modalities, such as computerized tomography or invasive angiographic evaluations in conjunction with expert radiologic interpretation, but these techniques are not always available in emergency conditions.

Patients with suspected acute mesenteric ischemia are more prone to complications, such as peritonitis and sepsis. Early diagnosis and surgical correction of blood circulation to prevent bowel necrosis and early resection of necrotised intestinal segments as soon as possible prior to sepsis may reduce the hospital mortality rate; this is the best way to decrease the mortality rate in patients with acute mesenteric ischemia (77,78). The survival rate has not improved; the major reason for this is the continuing difficulty in recognizing the condition before bowel infarction occurs; this is due to delayed presentation, nonspecific clinical findings and a lack of routine biochemical markers (77,78).

A number of biochemical parameters are being investigated for early diagnosis, but because they are associated with other diseases and their sensitivities are low, these serum markers are still controversial. There is no sufficiently sensitive or specific marker to guarantee diagnosis of acute mesenteric ischemia. Excessive inflammation and infection in acute mesenteric ischemia has led researchers to investigate inflammation-related CBC parameters to predict acute mesenteric ischemia in suspected patients (79,80). Among them, MPV was studied separately in acute mesenteric ischemia.

Türkoğlu et al. evaluated a total of 95 patients who underwent emergency surgery for acute mesenteric ischemia and 90 healthy volunteers as control group. They found MPV values to be significantly higher in patients with acute mesenteric ischemia than in the controls (81). MPV is evaluated in a number of studies for prediction of prognosis in acute mesenteric ischemia patients. Altintoprak et al. suggested that high MPV can show vascular damage in the liver and kidneys and predisposition to thrombosis, and can be used for re-operation and to discriminate patients with bad thrombosis. They concluded that MPV values at presentation were higher among non-survivors than survivors, and might be beneficial in predicting patients with poor prognosis and in the planning of re-operations. The ready availability of this parameter at no additional cost may encourage its utilization in clinical practice (82). In contrast, Aktimur et al. stated that MPV demonstrated significant prognostic difference in surviving patients with acute mesenteric ischemia. WBC and MPV values were higher in the acute mesenteric ischemia group than the control group with a normal appendix which were operated according to wrong pre-diagnosis as an acute appendicitis. They found higher MPV values in surviving patients in a relatively larger study group (83).
Bilgiç et al. studied 61 acute mesenteric ischemia patients divided into two groups, survivors and non-survivors, according to the outcome, and the two groups were compared in terms of MPV levels and other prognostic factors. They found significantly higher MPV levels in the non-survivor group. ROC curve analysis suggested that the best MPV level cut-off points for acute mesenteric ischemia was 8.1 fL, with sensitivity, specificity, and positive and negative predictive values (PPV and NPV) of 60, 73.1, 74.7, and 58%, respectively. The likelihood ratio was 2.23 (95% CI: 1.1–4.4) for this cut-off MPV level. Their results indicate that an elevated MPV is associated with a worse outcome in patients with acute mesenteric ischemia (84).

According to the studies mentioned above, high MPV levels on admission might explain the increased mortality rate and severity of acute mesenteric ischemia.

**Publication bias and heterogeneity**

The present review has limitations that come from the limitations of the included studies. First, because of the retrospective nature of these studies, the interval between symptom onset and blood testing was not reported in these studies. Additionally, the time between blood collection and analysis time was not standardized between studies. Both are important in the evaluation of PIs. Notably, the method of venipuncture and the degree of accuracy of filling and mixing the sampling tubes may cause platelet activation and result in some of the pre-analytical variables that affect results, which may lead to bias between studies.

Platelet indices change continuously at room temperature depending on the anticoagulant used / the method of analyser (85-89). Most researchers recommend measuring PIs within one hour regardless of anticoagulant, which is not indicated in most of the studies (88). Although ethylenediaminetetraacetic acid (EDTA) is accepted as the reference method in clinical settings (13), it causes time-dependent ultrastructural morphological changes, leading to modification from a discoidal to a spherical shape in platelets (85).

In the literature, discrepancies between PIs come out in the current laboratory practice by a lack of harmonization across the different analysers. The measurement technique (impedance or optical) and the calibration of the haematology analyser can lead to variations (89). When different technologies were compared, there were no significant differences for platelet count, but PIs differed. The current lack of harmonization should be regarded as a serious limitation for comparability of PIs obtained with different haematological analysers.

On the other hand, when advocating the use of PIs as a clinical diagnostic tool in acute appendicitis, the PIs offer several advantages. They do not add any cost for the patient, since it is part of a standard CBC, adds a low testing burden on clinicians and patients.

In conclusion, increasing and convincing evidence shows that use of platelet indices as a marker for non-traumatic abdominal surgery in emergency settings carries some clinical and practical advantages. Although the role of PI in the differential diagnosis of non-traumatic abdominal surgery patients remains uncertain, in addition to other markers, low MPV might be useful in acute appendicitis and acute cholecystitis, and high MPV might be useful in predicting poor prognosis in acute mesenteric ischemia.

Despite the large number of studies and the relative ease with which PIs can be obtained, PIs are not routinely used in clinical practice because, in particular, PIs are not specific for (or predictive of) any particular pathological condition, and there is a considerable bias among studies, revealing a need for more high-quality epidemiological studies. A uniformity of measurement should be used to make the results comparable with each other. Further large, multicentre prospective studies concurrently collecting data from different ethnicities and genders are needed before they can be used in everyday clinical practice.

**Potential conflict of interest**

None declared.
References

1. Hoffbrand AV, Moss PAH, Pettit JE, eds. Essential Haematology. 5th ed. Carlton, Australia: Blackwell publishing Ltd, 2006.

2. Lopez E, Bermejo N, Berna-Erro A, Alonso N, Salido GM, Redondo PC, et al. Relationship between calcium mobilization and platelet α- and δ-granule secretion. A role for TRPC6 in thrombin-evoked δ-granule exocytosis. Arch Biochem Biophys 2015;585:75-81. http://dx.doi.org/10.1016/j.abb.2015.09.012.

3. Golebiewska EM, Poole AW. Platelet secretion: From haemostasis to wound healing and beyond. Blood Rev 2015;29:153-62. http://dx.doi.org/10.1016/j.blre.2014.10.003.

4. Frelinger AL, Torres AS, Caiafa A, Morton CA, Benny-Lang MA, Gerrits A, et al. Platelet-rich plasma stimulated by pulse electric fields: platelet activation, procoagulant markers, growth factor release and cell proliferation. Platelets 2015;19:1-8. http://dx.doi.org/10.3109/09537104.2015.1048214.

5. Mariani E, Filardo G, Canella V, Berlingeri A, Bielli A, Cattini L, et al. Platelet-rich plasma affects bacterial growth in vitro. Cytotherapy 2014;16:1294-304. http://dx.doi.org/10.1016/j.cyt.2014.06.003.

6. Margetic S. Inflammation and haemostasis. Biochem Med (Zagreb) 2012;22:49-62. http://dx.doi.org/10.11613/BM.2012.006.

7. Tang YQ, Yeaman MR, Selsted ME. Antimicrobial peptides from human platelets. Infect Immun 2002;70:6524-33. http://dx.doi.org/10.1128/IAI.70.12.6524-6533.2002.

8. Monteiro PF, Morganti RP, Delbim MA, Calixto MC, Lopes-Pires, ME, Marcondes S, et al. Platelet hyperaggregability in high-fat fed rats: A role for intraplatelet reactive-oxygen species production. Cardiovasc Diabetol 2012;11:5. http://dx.doi.org/10.1186/1475-2840-11-5.

9. Magwensi S, Woodward C, Wraith KS, Aburima A, Raslan Z, Jones H, et al. Oxidized LDL activates blood platelets through CD36/NOX2-mediated inhibition of the cGMP/protein kinase G signaling cascade. Blood 2015;125:2693-703. http://dx.doi.org/10.1182/blood-2014-05-574491.

10. Karimi P, Rashchtizadeh N. Oxidative versus thrombotic stimulation of platelets differentially activates signalling pathways. J Cardiovasc Thorac Res 2013;5:61-5.

11. Lippi G, Pavesi F, Pipitone S. Evaluation of mean platelet volume with four haematological analyzers: harmonization is still an unresolved issue. Blood Coagul Fibrinolysis 2015;26:2335-7. http://dx.doi.org/10.1097/MBC.0000000000000220.

12. Demirin H, Ozhan H, Ucgun T, Celer A, Bulur S, Cil H, et al. Normal range of mean platelet volume in healthy subjects: insight from a large epidemiological study. Thromb Res 2011;128:358-60. http://dx.doi.org/10.1016/j.thromres.2011.05.007.

13. Wiwanitkit V. Plateletcrit, mean platelet volume, platelet distribution width: its expected values and correlation with parallel red blood cell parameters. Clin Appl Thromb Hemost 2004;10:175-8. http://dx.doi.org/10.1111/j.107602960401000208.

14. Senaran H, Ileri M, Altinbas A, Kosar A, Yetkin E, Ozturk M, et al. Thrombopoietin and mean platelet volume in coronary artery disease. Clin Cardiol 2001;24:405-8. http://dx.doi.org/10.1002/clc.4960240511.

15. Larsen SB, Grove EL, Hvas AM, Kristensen SD. Platelet turnover in stable coronary artery disease-influence of thrombopoietin and low-grade inflammation. PLoS One 2014;9:e85366. http://dx.doi.org/10.1371/journal.pone.0085366.

16. Brown AS, Hong Y, de Belder A, Beacon H, Beeso J, Sherwood R, et al. Megakaryocyte ploidy and platelet changes in human diabetes and atherosclerosis. Arterioscler Thromb Vasc Biol 1997;17:802-7. http://dx.doi.org/10.1161/01.ATV.17.4.802.

17. Osselaer JC, Jamart J, Scheiff JM. Platelet distribution width for differential diagnosis of thrombocytosis. Clin Chem 1997;43:1072-76.

18. Sachdev R, Tiwari AK, Goel S, Raina V, Sethi M. Establishing biological reference intervals for novel platelet parameters (immature platelet fraction, high immature platelet fraction, platelet distribution width, platelet large cell ratio, platelet-X, plateletcrit, and platelet distribution width) and their correlations among each other. Indian J Pathol Microbiol 2014;57:231-5. http://dx.doi.org/10.4103/0377-4929.134676.

19. Maluf CB, Barreto SM, Vidigal PG. Standardization and reference intervals of platelet volume indices: Insight from the Brazilian longitudinal study of adult health (ELSA-BRASIL). Platelets 2015;26:413-20. http://dx.doi.org/10.3109/09537104.2014.942620.

20. Vagdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianiou I. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. Hippokratia 2010;14:28-32.

21. Yang A, Pizzulli L, Luderitz B. Mean platelet volume as marker of restenosis after percutaneous transluminal coronary angioplasty in patients with stable and unstable angina pectoris. Thromb Res 2006;117:371-7. http://dx.doi.org/10.1016/j.thromres.2005.04.004.

22. Huczcz Z, Kochman J, Filipiak KL, Horssczarzuk GJ, Gрабowski M, Piatkowski R, et al. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005;46:284-90. http://dx.doi.org/10.1016/j.jacc.2005.03.065.

23. Ates I, Bulut M, Ozkayar N, Dede F. Association between high platelet indices and proteinuria in patients with hypertension. Ann Lab Med 2015;35:630-4. http://dx.doi.org/10.3343/alm.2015.35.6.630.

24. Bessman JD, Williams LJ, Gilmer PR. Mean platelet volume: the inverse relation of platelet size and count in normal subjects, and an artifact of other particles. Am J Clin Pathol 1981;76:289-93. http://dx.doi.org/10.1093/ajcp/76.3.289.

25. Chandrashekar V. Plateletcrit as a screening tool for detection of platelet quantitative disorders. J Hematol 2013;2:22-6. http://dx.doi.org/10.4021/jh70w.
26. Giacomini A, Legovini P, Gessoni G, Antico F, Valverde S, Salvadego MM, et al. Platelet count and parameters determined by the Bayer ADVIA 120 in reference subjects and patients. Clin Lab Haematol 2001;23:181–6. http://dx.doi.org/10.1046/j.1365-2257.2001.00391.x.

27. Adibi P, Faghih Imani E, Talaei M, Ghanei M. Population-based platelet reference values for an Iranian population. Int J Lab Hematol 2007;29:195-9. http://dx.doi.org/10.1111/j.1751-553X.2006.00843.x.

28. Lippi G, Salvagno GL, Danese E, Skafidas S, Tarperi C, Guidi GC, et al. Mean platelet volume (MPV) predicts middle distance running performance. PLoS One 2014;9:e112892. http://dx.doi.org/10.1371/journal.pone.0112892.

29. Hong J, Min Z, Bai-shen P, Jie Z, Ming-ting P, Xian-zhang H, et al. Investigation on reference intervals and regional differences of platelet indices in healthy Chinese Han adults. J Clin Lab Anal 2015;29:21-7. http://dx.doi.org/10.1002/jcla.21721.

30. Hong H, Xiao W, Maита RW. Steady increment of immature platelet mature fraction is suppressed by irradiation in single-donor platelet components during storage. PLoS One 2014;9:e85465. http://dx.doi.org/10.1371/journal.pone.0085465.

31. Briggs C, Kunika S, Hart D, Oguni S, Machin SJ. Assessment of an immature platelet fraction (IPF) in peripheral thrombocytopenia. Br J Haematol 2004;126:93-9. http://dx.doi.org/10.1111/j.1365-2141.2004.04987.x.

32. Kim MJ, Park PW, Seo YH, Kim KH, Seo JY, Jeong JH, et al. Comparison of platelet parameters in thrombocytopenic patients associated with acute myeloid leukemia and primary immune thrombocytopenia. Blood Coagul Fibrinolysis 2014;25:221-5. http://dx.doi.org/10.1097/MBC.0000000000000027.

33. Zhang S, Cui YL, Diao MY, Chen DC, Lin ZF. Use of platelet indices for determining illness severity and predicting prognosis in critically ill patients. Chin Med J 2015;128:1202-18. http://dx.doi.org/10.4103/0366-6999.161346.

34. Thachil J. Platelets in inflammatory disorders: a pathophysiological and clinical perspective. Semin Thromb Hemost 2015;41:572-81. http://dx.doi.org/10.1055/s-0035-1556589.

35. Purnak T, Efe C, Yuksel O, Beyazit Y, Ozaslan E, Altiparmak E. Mean platelet volume could be a promising biomarker to monitor dietary compliance in celiac disease. Ups J Med Sci 2011;116:208-11. http://dx.doi.org/10.3109/03009734.2011.581399.

36. Ozturk ZA, Dag MS, Kuyumcu ME, Cam H, Yesil Y, Yilmaz N, et al. Could platelet indices be new biomarkers for inflammatory bowel diseases? Eur Rev Med Pharmacol Sci 2013;17:334-41.

37. Kim DA, Kim TY. Controversies over the interpretation of changes of mean platelet volume in rheumatoid arthritis. Platelets 2014;15:279-80. http://dx.doi.org/10.3109/09537100903470306.

38. Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, et al. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine 2008;75:291-4. http://dx.doi.org/10.1016/j.jbspin.2007.06.016.

39. Takeyama H, Mizushima T, Iijima H, Shinichiro S, Uemura M, Nishimura J, et al. Platelet activation markers are associated with Crohn’s disease activity in patients with low C-reactive protein. Dig Dis Sci 2015;60:3418-23. http://dx.doi.org/10.1007/s10620-015-3745-2.

40. Beıyat Y, Sayılır A, Turun S, Suvak B, Yesıl Y,TURNAK T, et al. Mean platelet volume as an indicator of disease severity in patients with acute pancreatitis. Clin Res Hepatol Gastroenterol 2012;36:162-8. http://dx.doi.org/10.1016/j.clinre.2011.10.003.

41. Güneş A, Ece A, Şen V, Ulucu U, Aktar F, Tan I, et al. Correlation of mean platelet volume, neutrophil-to-lymphocyte ratio, and disease activity in children with juvenile idiopathic arthritis. Int J Clin Exp Med 2015;11:11337-41.

42. Safak S, Uslu AU, Serdal K, Turker T, Soner S, Lutfi A. Association between mean platelet volume levels and inflammation in SLE patients presented with arthritis. Afr Health Sci 2014;14:919-24.

43. Chu SG, Becker RC, Berger PB, Bhall D, Elkebloom JW, Konkle B, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. J Thromb Haemost 2010;8:148-56. http://dx.doi.org/10.1111/j.1538-7836.2009.03584.x.

44. Yazici S, Yazici M, Erer B, Erer B, Calcý R, Bulur S, et al. The platelet functions in patients with ankylosing spondylitis: anti-TNF-alpha therapy decreases the mean platelet volume and platelet mass. Platelets 2010;21:126-31. http://dx.doi.org/10.1080/09537100903470306.

45. Kim CH, Kim SJ, Lee MJ, Kwon YE, Kim YL, Park KS, et al. An increase in mean platelet volume from baseline is associated with mortality in patients with severe sepsis or septic shock. PLoS One 2015;10:e0119437. http://dx.doi.org/10.1371/journal.pone.0119437.

46. Gao Y, Li Y, Yu X, Gou S, Ji X, Sun T, et al. The impact of various platelet indices as prognostic markers of septic shock. PLoS One 2014;9:e103761. http://dx.doi.org/10.1371/journal.pone.0103761.

47. Emre A, Akbulut S, Bozdag Z, Yilmaz M, Kanlaz M, Emre R, et al. Routine histopathologic examination of appendectomy specimens: retrospective analysis of 1255 patients. Int Surg 2013;98:354-62. http://dx.doi.org/10.9738/INTSURG-D-13-00098.1.

48. Seetahal SA, Noteduro BO, Soonkdeo TC, Oyetunji TA, Greene WR, Frederick W, et al. Negative appendectomy: a 10-year review of a nationally representative sample. Am J Surg 2013;201:433-7. http://dx.doi.org/10.1016/j.amjsurg.2010.10.009.

49. Shogilev DJ, Duros N, Odom SR, Sharpio NL. Diagnosing appendicitis: evidence-based review of the diagnostic approach in 2014. West J Emerg Med 2014;15:859-71. http://dx.doi.org/10.5811/westjem.2014.9.21568.

50. Tucker A, Kostan K, Gartsin I, Verghis R. White cell counts, CRP and appendicitis – is there a role for pre-operative blood tests? A cohort study. J Health Med Inform 2015;6:185. http://dx.doi.org/10.4172/2157-7420.1000185.

51. Bhangar A, Sareide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet 2015;386:1278-87. http://dx.doi.org/10.1016/S0140-6736(15)00275-5.
52. Schellekens DH, Hulsewé KW, van Acker BA, van Bijnen AA, de Jaegere TM, Sastrowijoto SH, et al. Evaluation of the diagnostic accuracy of plasma markers for early diagnosis in patients suspected for acute appendicitis. Acad Emerg Med 2013;20:703-10. http://dx.doi.org/10.1111/acem.12160.

53. Abbas MH, Choudhry MN, Hamza N, Ali B, Ali B, Amin AA, et al. Admission levels of serum Amyloid A and procalcitonin are more predictive of the diagnosis of acute appendicitis compared with C-reactive protein. Surg Laparosc Endosc Percutan Tech 2014;24:488-94. http://dx.doi.org/10.1097/SLE.0000000000000067.

54. Albayrak Y, Albayrak A, Albayrak F, Yildirim R, Aylu B, Uyanik A, et al. Mean platelet volume: a new predictor in confirming acute appendicitis diagnosis. Clin Appl Thromb Hemost 2011;17:362-6. http://dx.doi.org/10.1177/1076029610364520.

55. Tanrikulu CS, Tanrikulu Y, Sabuncuoglu MZ, Karamercan MA, Akkapulu N, Coskun F. Mean platelet volume and red cell distribution width as a diagnostic marker in acute appendicitis. Iran Red Crescent Med J 2014;16:e10211. http://dx.doi.org/10.5812/ircmj.10211.

56. Erdem H, Akkimur R, Cetinkunar S, Reyhan E, Gokler C, Irkorucu O, et al. Evaluation of mean platelet volume as a diagnostic biomarker in acute appendicitis. Int J Clin Exp Med 2015;8:1291–5.

57. Dinc B, Oskay A, Dinc SE, Bas B, Tekin S. New parameter in diagnosis of acute appendicitis: platelet distribution width. World J Gastroenterol 2015;21:1821-6. http://dx.doi.org/10.3748/wjg.v21.i6.1821.

58. Yang JJ, Cho SY, Ahn HJ, Lee HJ, Lee WI, Park TS. Mean platelet volume in acute appendicitis: a gender difference. Platelets 2014;25:226-7. http://dx.doi.org/10.3109/09537104.2013.766923.

59. Ceylan B, Aslan T, Çınar A, Ruhkar Kurt A, Akkoyunlu Y. Can platelet indices be used as predictors of complication in subjects with appendicitis? Wien Klin Wochenschr 2015;128:51. http://dx.doi.org/10.1007/s00508-015-0760-4.

60. Fan Z, Pan J, Zhang Y, Wang Z, Zhu M, Yang B, et al. Mean platelet volume and platelet distribution width as markers in the diagnosis of acute gangrenous appendicitis. Dis Markers 2015;2015:542013. http://dx.doi.org/10.1155/2015/542013.

61. Narci H, Turk E, Karagülle E, Togan T, Karabulut K. The role of mean platelet volume in the diagnosis of acute appendicitis: a retrospective case-controlled study. Iran Red Crescent Med J 2013;15:e11934. http://dx.doi.org/10.5812/ircmj.11934.

62. Bozkurt S, Kose A, Erdogan S, Bosalli GI, Ayrık C, Arpacı RB, et al. MPV and other inflammatory markers in diagnosing acute appendicitis. J Pak Med Assoc 2015;65:637-41.

63. Lee WS, Kim TY. Is mean platelet volume a new predictor in confirming a diagnosis of acute appendicitis? Clin Appl Thromb Hemost 2011;17:E125–6. http://dx.doi.org/10.1177/1076029610389024.

64. Kucuk E, Kucuk I. Mean platelet volume is reduced in acute appendicitis. Turk J Emerg Med 2015;15:23-7. http://dx.doi.org/10.5505/1304.7361.2015.32657.

65. Kölç TY, Yesilaras M, Karaali C, Atilla OD, Sezik S. Diagnostic value of mean platelet volume in acute appendicitis. J Clin Anal Med 2015;1-3.

66. Akkimur R, Cetinkunar S, Yildirim K, Ozdags S, Akkimur SD, Gokakın AK. Mean platelet volume is a significant biomarker in the differential diagnosis of acute appendicitis. Int J Surg 2015;2:930.

67. Aydoğan A, Akkucuk S, Arica S, Motor S, Karakus A, Ozkan OV, et al. The analysis of mean platelet volume and platelet distribution width levels in appendicitis. Indian J Surg 2015;77:495-500. http://dx.doi.org/10.1007/s12262-013-0891-7.

68. Saxena D. Role of mean platelet volume in diagnosis of acute appendicitis. IJBR 2015; 6:235-7. http://dx.doi.org/10.7439/ijbr.v6i4.1918.

69. Bilici S, Sekmenli T, Göksu M, Melek M, Avci V. Mean platelet volume in diagnosis of acute appendicitis in children. Afr Health Sci 2011;11:427.

70. Uyanik B, Kavalcı C, Arslan ED, Yilmaz F, Aslan O, Dede S, et al. Role of mean platelet volume in diagnosis of childhood acute appendicitis. Emerg Med Int 2012;2012:823095. http://dx.doi.org/10.1155/2012/823095.

71. Yilmaz Y, Kara F, Gümüşdere M, Arslan H, Üstebay S. The platelet indices in pediatric patients with acute appendicitis. Int J Res Med Sci 2015;3:1388-139. http://dx.doi.org/10.18203/2320-6012.ijrms20150153.

72. Machin SJ, Briggs C. Mean platelet volume: a quick, easy determinant of thrombotic risk? J Thromb Haemost 2010;8:146-7. http://dx.doi.org/10.1111/j.1538-7836.2009.03673.x.

73. Beliaev AM, Marshall RJ, Booth M. C-reactive protein has a better discriminative power than white cell count in the diagnosis of acute cholecystitis. J Surg Res 2015;198:66-72. http://dx.doi.org/10.1016/j.jss.2015.05.005.

74. Seker A, Incebiyik A, Kucuk A, Terzi A, Yucel Y, Ciftci R et al. Mean platelet volume in patients with acute and chronic cholecystitis. Acta Medica Mediterr 2013;29:515-9.

75. Sayit AT, Gunbey PH, Terzi Y. Is the mean platelet volume a significant biomarker in acute cholecystitis? JCDR 2015;9:5-7. http://dx.doi.org/10.7860/jcdr/2015/12028.6061.

76. Kassahun WT, Schulz T, Richter O, Hauss J. Unchanged high mortality rates from acute occlusive intestinal ischemia: six year review. Langenbecks Arch Surg 2008;393:163-71. http://dx.doi.org/10.1007/s00423-007-0263-5.

77. Klar E, Rahmanian PB, Bücker A, Hauenstein K, Jauch KW, Luther B. Acute mesenteric ischemia: a vascular emergency. Dtsch Arztebl Int 2012;109:249-56.

78. Leoné M, Bechis C, Baumstark K, Ouattara A, Collange O, Augustin P, et al. Outcome of acute mesenteric ischemia in the intensive care unit: a retrospective multicenter study of 780 cases. Inten Care Med 2015;41:667-76. http://dx.doi.org/10.1007/s00134-015-3690-8.

79. Toptas M, Akkoc I, Savas Y, Uzman S, Toptas Y, Can MM. Novel hematologic inflammatory parameters to predict acute
80. Kisaoglu A, Bayramoglu A, Ozogul B, Atac K, Emet M, Atamanalp SS. Sensitivity and specificity of red cell distribution width in diagnosing acute mesenteric ischemia in patients with abdominal pain. World J Surg 2014;38:2770–6. http://dx.doi.org/10.1007/s00268-014-2706-9.

81. Türkoğlu A, Güll M, Oğuz A, Bozdag Z, Ülger BV, Yilmaz A, et al. Mean platelet volume: is it a predictive parameter in diagnosis of acute mesenteric ischemia? Int Surg 2015;100:962-5. http://dx.doi.org/10.9738/INTSURG-D-14-00268.1.

82. Altıntoprak F, Arslan Y, Yaikin O, Uzunoglu Y, Ozkan OV. Mean platelet volume as a potential prognostic marker in patients with acute mesenteric ischemia–retrospective study. World J Emerg Surg 2013;25:49. http://dx.doi.org/10.1186/1749-7922-8-49.

83. Aktimur R, Cetinkunar S, Yildirim K, Aktimur SH, Ugurlucan MH. Neutrophil-to-lymphocyte ratio as a diagnostic biomarker for the diagnosis of acute mesenteric ischemia. Eur J Trauma Emerg Surg 2015;10. http://dx.doi.org/10.1007/s00068-015-0546-4.

84. Bilgic I, Gelecek S, Ozmenc MM, Kasapoglu B. The association of elevated mean platelet volume with the outcome of acute mesenteric ischemia. Blood Coagul Fibrinolysis 2015;26:727-30.

85. Bath PM. The routine measurement of platelet size using sodium citrate alone as the anticoagulant. Thromb Haemost 1993;70:687-90.

86. Macey M, Azam U, McCarthy D, Webb L, Chapman ES, Okrongly D, et al. Evaluation of the anticoagulants EDTA and citrate, theophylline, adenosine, and dipyridamole (CTAD) for assessing platelet activation on the ADVIA 120 system. Clin Chem 2002;48:891-9.

87. Banfi G, Germagnoli L. Preanalytical phase in haematology. J Med Biochem 2008;27:348-53. http://dx.doi.org/10.1007/s00068-015-0546-4.

88. Dastjerdi MS, Emami T, Najafan A, Amini M. Mean platelet volume measurement, EDTA or citrate? Hematology 2006;11:317-9. http://dx.doi.org/10.1080/10245330600954163.

89. Recommendations of the International Council for Standardization in Haematology for Ethylenediaminetetraacetic Acid Anticoagulation of Blood for Blood Cell Counting and Sizing. International Council for Standardization in Haematology: Expert Panel on Cytometry. Am J Clin Pathol 1993;100:371-2. http://dx.doi.org/10.1093/ajcp/100.4.371.

90. Latger-Cannard V, Hoarau M, Salignac S, Baumgart D, Norden P, Lecompte T. Mean platelet volume: comparison of three analysers towards standardization of platelet morphological phenotype. Int J Lab Hematol 2012;34:300–10. http://dx.doi.org/10.1111/j.1751-555X.2011.01396.x.