Review

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.

Table 1. Platelet indices

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 (%)

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 = platelet count $\times$ 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 *at 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		P	Study design	Comment
			Patients	Controls			
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	MPV: 9.01 ± 1.33 fL	Decreased* (P < 0.001)	Diagnostic, case-control, prospective	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	MPV: 8.49 ± 0.97 fL	Decreased* (P < 0.001)	Diagnostic, case-control, retrospective, multicenter study	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	MPV: 9.1 ± 1.6 fL	Decreased* (P < 0.001)	Diagnostic, case-control, retrospective	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)%	MPV decreased* (P = 0.001); PDW increased† (P < 0.001)	Diagnostic, case-control, retrospective	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	MPV: 7.96 ± 0.58 fL	Decreased* (P = 0.042)	Diagnostic, case-control, retrospective	CBC analysed within 2 hours after collection.

Table 2. Summary of studies (continued)

Reference (publication year)	Number of patients and controls (years)	Sample, analyzer, method	Platelet indices		P	Study design	Comment
			Patients	Controls			
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%	MPV: 10.91 ± 2.72 fL; PDW: 12.5 ± 1.93%	MPV decreased* (P = 0.000); PDW increased† (P = 0.000)	Diagnostic, case-control, retrospective	All samples analysed within 10 minutes. Best cut-off point for MPV in the diagnosis of AA was ≤ 9.6fL. Best cut-off point for PDW in the diagnosis of AA was ≥ 15.1fL.
Narci *et al*. (2013)	503 patients (34.7 ± 14.1) and 121 controls (35.2 ± 8.1)	Cell-Dyne 3700 (Abbott Diagnostics, IL, USA), impedance	MPV: 7.92 ± 1.68 fL	MPV: 7.43 ± 1.34 fL	Increased† (P < 0.001)	Diagnostic, case-control, retrospective	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	None	Not changed (P =0.478)	Diagnostic, case-control, retrospective	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	MPV: 10.04 ± 0.83 fL	Not changed (P = 0.285)	Diagnostic, case-control, retrospective	-
Kucuk *et al*. (2015)	60 patients (33.15 ± 10.94)	Cell-Dyne 3700 (Abbott Diagnostics, IL, USA), impedance	MPV: in AA patients 7.03 ± 0.8 fL; previous MPV: 7.58 ± 1.11 fL	None	Decreased* (P = 0.01)	Diagnostic, case-series, retrospective	Previous MPV of the same patient was evaluated as control.
Kılıç *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	MPV: 8.10 (5.70–13.90) fL	Not changed (P = 0.193)	Diagnostic, case-control, retrospective	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	None	Increased (P = 0.018)	Diagnostic, case-control, retrospective	For cut-off value of 9.6 fL, sensitivity was 57.1% and specificity was 60.7%.

Table 2. Summary of studies (continued)

Reference (publication year)	Number of patients and controls (years)	Sample, analyzer, method	Platelet indices		P	Study design	Comment
			Patients	Controls			
Sexana D *et al.* (2015)	Attempted to define potential thresholds value which is predictive of a diagnosis in 213 AA patients.	ND	ND	None		Diagnostic retrospective	When they used an MPV cut-off value of ≤ 7.6 fL, they found sensitivity, specificity and accuracy of which was 83.73%, 75% and 83.56%, respectively
Acute appendicitis (pediatric)							
Bilici S *et al.* (2011)	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	MPV: 8.90 ± 1.29 fL	Decreased* (P = 0.001)	Diagnostic, case-control, retrospective	CBC was analyzed 2 hours after blood collection. Specificity was 54% and sensitivity was 87% for MPV at ≤ 7.4 fL.
Uyanik *et al.* (2012)	305 AA patients (9.5 ± 2.9) and 305 controls (9.6 ± 3.1)	EDTA-anticoagulated blood, ND	MPV: 7.9 ± 0.9 fL	MPV: 7.7 ± 0.8 fL	Not changed (P > 0.05)	Diagnostic, case-control, retrospective	CBC analyses were performed within 1 hour after collection.
Yilmaz *et al.* (2015)	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), iImpedance	MPV in AA patients 7.37 ± 0.9 fL; MPV in negative appendectomy 7.60 ± 1.24 fL; PCT in AA patients 0.220 ± 0.057; PCT in negative appendectomy 0.208 ± 0.045; PDW in AA patients 16.3 ± 0.5; PDW in negative appendectomy 16.4 ± 0.7	None	Not changed (P > 0.05) for MPV, PCT and PDW	Diagnostic, case-control	The number of patients with normal appendix vermiformis was too small.
Acute cholecystitis							
Seker *et al.* (2013)	33 patients with AC (56.4 ± 15.7), 32 patients with CC (51.4 ± 13.8), 28 controls (54.7 ± 9.61)	ND	MPV in AC patients 6.38 ± 0.88 fL; MPV in CC patients 7.78 ± 0.75 fL	MPV: 7.88 ± 0.74 fL	Decreased* (P < 0.05)	Case-control Retrospective	The number of patients was too small.

Table 2. Summary of studies (continued)

Reference (publication year)	Number of patients and controls (years)	Sample, analyzer, method	Platelet indices		P	Study design	Comment
			Patients	Controls			
Acute mesenteric ischemia (AMI)							
Türkoğlu *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 Retrospective	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	MPV in non-survivors: 9.01 fL; MPV in survivors: 7.80 fL	None	(P = 0.002)	Prognostic, retrospective	SDs were not given
Aktimur *et al* (2015)	62 AMI related laparotomy and/or bowel resection patients (41–93), 62 AA patients (14–86), 61 negative appendectomy patients (16–73)	ND	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	None	(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	Non-survivor MPV: 8.4 (5.5 –10.4) fL; survivor MPV: 7.6 (6.6–8.9) fL	None	(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. Yılmaz *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 cholecy stitis 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.

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