Surgery Open Science 19 (2024) 166–171

Contents lists available at ScienceDirect

Surgery Open Science

journal homepage: www.journals.elsevier.com/surgery-open-science

Research Paper

Predicting the dynamics of organ failure in patients with acute pancreatitis depending on the mean platelet volume

Heorhii Levytskyi *, Volodymyr Sheiko

Department of Surgery No. 2, Poltava State Medical University, Poltava, Ukraine

HIGHLIGHTS

- An MPV level ≥11.8 fL in the first 72 h of AP may indicate early organ failure.
- MPV ≥11.8 fL indicates a higher risk of developing persistent OF or multisystem OF.
- Patients with AP aged over 55, obese, or with IHD or diabetes have elevated MPV levels.

ARTICLE INFO

Keywords:
Acute disease
Inflammation
Mean platelet volume
Multiple organ failure
Pancreatitis, acute necrotizing
Logistic models

ABSTRACT

Background: The aim of this study is to determine the correlation between the blood serum mean platelet volume (MPV) and the dynamics of the OF course during the early phase in patients with moderately severe and severe acute pancreatitis (AP).

Methods: The predetermined criterion was the presence of the OF according to the revised Atlanta criteria 2012 for moderately severe and severe AP. A prospective sample of patients was stratified by severity, and two groups were defined based on MPV. Demographic indicators, comorbidities and clinical outcomes were compared between these groups. Multifactorial analysis determined whether an elevated MPV is independently associated with early OF and other unfavorable outcomes.

Results: Out of 108 patients, 20 had moderately severe AP and 88 had severe AP. The blood serum MPV, measured within 72 h of the onset of AP symptoms was lower 11.8 fL in 32 patients and equal to or greater 11.8 fL in 76 patients. Patients with elevated MPV were older (63 vs. 48 years), had obesity (59.2 % vs. 25 %), diabetes mellitus (DM) (51.3 % vs. 12.5 %), ischemic heart disease (70.8 % vs. 28.1 %) and more frequently experienced persistent OF (93.4 % vs. 53.1 %) compared to those with MPV lower 11.8 fL. The incidence of early OF increased proportionally with the severity of MPV (81.6 % vs. 34.4 % in the group with MPV lower 11.8 fL, Ptrend < 0.0001). In multifactorial analysis, adjusted for body mass index and DM, MPV equal to or greater 11.8 fL was independently associated with early OF.

Conclusions: Elevated blood serum MPV of patients with AP are independently and proportionally correlated with early organ failure in patients with alcoholic and idiopathic etiology of AP.

Key message: The study provides an evaluation of MPV as a prognostic marker for organ failure within the initial 7 days following the onset of acute pancreatitis symptoms. Additionally, alterations in MPV were identified in patients with acute pancreatitis who had diabetes or ischemic heart disease within the first 24 h of hospitalization.

Introduction

Acute pancreatitis (AP) is the most widespread among abdominal cavity diseases. The incidence of AP is reported to be 77 cases per 100,000 population in Ukraine [1] and tends to increase globally, primarily due to its severe course [2]. Severe AP is characterized by the presence of persistent organ failure (OF) and is accompanied by a high level of complications and mortality. Approximately 50 % of the total

* Corresponding author at: Department of Surgery No. 2, Poltava State Medical University, 23 Shevchenko Street, Poltava 36011, Ukraine.
E-mail address: h.levytskyi@pdmu.edu.ua (H. Levytskyi).
URL: https://www.instagram.com/drheorhiilevytskyi?igsh=dXV5dGN1Mmt1bHFm (H. Levytskyi).

https://doi.org/10.1016/j.sopen.2024.04.011
Received 28 December 2023; Received in revised form 2 April 2024; Accepted 28 April 2024
Available online 10 May 2024

mortality comprises patients who developed the OF in the early phase of AP, within the first 7 days from the onset of symptoms [3,4]. It is crucial to promptly identify risk factors for the development of early OF. It is crucial to promptly identify risk factors for the development of early OF, including those associated with the involvement of multiple systems.

Mean Platelet Volume (MPV) is an indicator of the average size and activity of platelets. Platelets that are larger in size are generally younger. Young platelets are more reactive and produce more prothrombotic factors, such as thromboxane A2 [5]. In a retrospective study, a correlation was found between MPV and the severity of AP, with AP patients having significantly lower levels of MPV compared to healthy individuals [6]. Some studies have identified a correlation between MPV and the severity of AP, specifically in relation to the presence of the OF [7,8], although the results of other studies have been contradictory [9].

Considering the evident impact of the degree of inflammation on the MPV [10], it can be hypothesized that an increase in MPV after the onset of AP serves as a prognostic marker for systemic complications, particularly the development of the OF. There are studies that evaluated MPV in AP patients within the first 72 h of hospital admission, demonstrating that MPV >12 femtoliters (fL) plays an independent predictive role in the risk of developing OF [7]. However, insufficient number of prospective studies examining the prognostic role of MPV in assessing the dynamics of the OF in AP patients has been found.

The aim of this study is to determine the correlation between the blood serum MPV and the dynamics of the OF course during the early phase in patients with moderately severe and severe AP.

Methods and material

This study was carried out by the staff of Department of Surgery No. 2 at Poltava State Medical University (PSMU), formerly known as the Ukrainian Medical Stomatological Academy (UMSA), in Poltava, Ukraine. It was conducted at the Center for Thoracoabdominal Surgery of the 'M.V. Sklifosovsky Poltava Regional Clinical Hospital,' a Communal Enterprise of the Poltava Regional Council. This observational research is part of the department's ongoing scientific work, entitled 'Prediction and Prevention of Complications in Acute Abdominal Surgical Pathology' (State registration number 0111U006299). Approval was obtained from the PSMU Ethics Committee. Informed consent was obtained from each patient before the start of the study.

A prospective study was conducted, analyzing the medical histories of 108 patients with moderately severe and severe AP from December 2019 to December 2023. Our study excluded patients with mild acute pancreatitis because the majority of them did not require prolonged hospitalization or surgical treatment. The study involved patients aged 18 and older, without a current or past history of pregnancy, and those who could provide informed consent (or in compliance with the requirements of the Helsinki Declaration of the World Medical Association, "Ethical Principles for Medical Research Involving Human Subjects").

Patients with hypertriglyceridemia (HTG), biliary etiology of AP, as well as those with concurrent malignancies and known immunological deficits, were excluded from the study. The step-up approach to managing biliary AP, which significantly differs from treatment strategies for AP of other etiologies, was a determining factor in excluding these patients from our study. Given that an elevated blood bilirubin level is a criterion for biliary AP, we excluded these patients. HTG AP is rare in Ukraine; no cases were identified in our observation period from 2019 to 2023.

Observations were executed for patients until discharge, including data from subsequent hospitalizations. Relevant demographic, laboratory, imaging data and clinical outcomes were documented for each patient. The sample also included patients who were referred from other hospitals and data for this subset were obtained during the analysis of discharge summaries, in accordance with the study requirements.

Characteristics of patients with AP, etiology, local complications, interventions performed, organ failure, clinical outcomes such as the presence of persistent OF, onset of the OF in the early phase within the first seven days from the onset of AP symptoms, length of hospital stay, duration and need for intensive care unit (ICU) admission, mortality and the level of readmission were determined according to the 2019 World Congress of Emergency Surgery guidelines for the management of severe acute pancreatitis [11], BMJ Best Practice–Acute Pancreatitis [12], as well as Revised Atlanta Classification (RAC) [13]. Patients without an obvious etiology of AP were classified as idiopathic.

Key characteristics, complications and outcomes are presented in Table 1. The majority were male patients (76 (70.4 %)). In 53 (49.1 %) patients, the body mass index (BMI) was ≥30. Upon admission, 43 (39.8 %) patients had diabetes mellitus (DM) and 60 patients (55.6 %) had ischemic heart disease. The primary etiology was identified as previous alcohol use in 63 (58.3 %) patients, followed by idiopathic causes in 33 (30.6 %) patients, and other etiologies in 12 (11.1 %) patients. Early OF was observed in 73 (67.6 %) patients. In terms of duration, transient OF was detected in 20 (18.5 %) patients, and persistent OF in 88 (81.5 %) patients. A higher percentage was established in single organ failure (83 (76.9 %) patients), while multiple OF was observed in 25 (23.1 %)

Table 1
Patient characteristics, complications and outcomes.

Characteristics	*N* (%)
Total number of patients	108 (100 %)
Men	76 (70.4 %)
Mean age in years (IQR)	57 (43–68)
Referred from other hospitals	90 (83.3 %)
Patients who underwent CT scan	107 (99.1 %)
BMI ≥30	53 (49.1 %)
Diabetes mellitus at admission	43 (39.8 %)
Ischemic heart disease at admission	60 (55.6 %)

Etiology	*N* (%)
Alcoholic	63 (58.3 %)
Idiopathic	33 (30.6 %)
Other	12 (11.1 %)

Complications	*N* (%)
Peripancreatic necrosis	85 (78.7 %)
Sterile *peripancreatic necrosis*	67 (62.0 %)
Infected *peripancreatic necrosis*	18 (16.7 %)
OF	108 (100 %)
Transient OF	20 (18.5 %)
Persistent OF	88 (81.5 %)
Single organ failure	83 (76.9 %)
Multiple OF	25 (23.1 %)
Early OF (within the first 7 days)	73 (67.6 %)
Heart failure	14 (13.0 %)
Renal failure	58 (53.7 %)
Respiratory failure	65 (60.2 %)

Outcomes	
Categorical	*N* (%)
Mortality	16 (14.8 %)
ICU admission	104 (96.3 %)
Need for interventions	97 (89.8 %)

Continuous	Median (IQR)
ICU stay	11 (5.7)
Hospital stay	23 (7.0)

ICU, intensive care unit; IQR, interquartile range; OF, organ failure.

patients. Among the evaluated organ systems, a higher percentage of patients had respiratory failure (65 (60.2 %)), followed by renal failure (58 (53.7 %)), and cardiovascular failure was observed in a significantly smaller percentage of patients (14 (13.0 %)).

The patients were assigned into two groups: those with moderately severe or severe AP, based on the duration of OF and the presence of local complications according to the RAC [13–15].

OF was determined using the modified Marshall Multiple Organ Dysfunction Score (MODS), as presented in the RAC classification. In MODS, OF is defined with a score of two or more in one of the three organ systems: respiratory, cardiovascular or renal [13]. Early OF was the primary endpoint, considering its significant role in mortality during the first week from the onset of initial symptoms of the disease. Additionally, patients with persistent OF and multiple OF were considered as the secondary endpoints.

MPV measurement

MPV is a standard parameter included in the complete blood count panel for all patients at our hospital. It is measured using automatic hematological analyzers MINDRAY BC-5150 or BC-3000 plus, manufactured by Shenzhen Mindray Bio-Medical Electronics Co. The MPV measurement was routinely performed for all patients in the ICU and the Surgical Unit within the first 24 h of hospitalization. If more than one measurement of MPV was available during this time, the analysis included the highest deviating value Given the lack of a significant correlation between the MPV and the number of platelets among patients with AP within the first 24 h of hospitalization, the number of platelets was not included in the current study. A threshold value for MPV was established for the groups based on the severity of AP. Based on this threshold, two groups were defined, categorized as low and high MPV, with corresponding evaluations of key clinical characteristics and outcomes.

Statistical analysis

The entire statistical analysis was performed using XLSTAT 2021 (Addinsoft, Paris, France) [16]. Categorical variables were described using frequencies and percentages. Continuous variables were described using means and standard deviations or medians and interquartile ranges, depending on the distribution of the variables. Pairwise testing between severity grades in the classification system was conducted using the Fisher's exact tests and Mann-Whitney *U* tests for binary and continuous data, respectively.

The threshold level of MPV corresponding to moderately severe and severe courses of AP was determined by the ROC analysis. Groups stratified by MPV levels were compared with clinical characteristics and outcomes using univariate analysis (Table 3). The association between clinical outcomes and MPV groups was assessed using Cochran-Armitage trend test for binary data and Kendall's trend test for continuous data.

Binary and multinomial logistic regression models were used to evaluate the relationship between input clinical characteristics, including MPV, and early OF and other outcomes. Variables with *p*-value <0.35 in univariate analysis were included in the *multivariate model*. Interaction and collinearity between characteristics were verified. The model was adjusted for BMI $\geq$ 30 and DM as relevant risk factors for early OF. A statistically significant association was considered with a *p*-value <0.05.

Results

Clinical characteristics of patients by severity of AP

Patients were categorized into severity groups. Severe AP was determined in 88 patients according to the RAC classification, and 20 patients had moderately severe AP. None of the patients in the moderately severe AP group died, whereas 16 (18.2 %) patients died in the severe AP group. In the moderately severe AP group, 16 (80 %) patients received ICU support during hospitalization. In the severe AP group, all patients spent some time in the ICU. The median duration of ICU stay was 8 [4–11] and 12 (8.7–15) for moderately severe and severe AP, respectively. Almost all patients (87 (98.9 %)) in the severe AP group underwent surgical interventions, while only half of the patients (10 (50 %)) required it in the moderately severe AP group. The length of hospital stay for patients in the moderately severe AP group was 21 [18–23] days, and for the severe AP group, it was 25 [20–28] days (Table 2).

We determined the optimal threshold value for MPV in moderately severe and severe AP using the ROC analysis. The optimal threshold level for MPV was 11.8 fL with a sensitivity of 0.773, specificity of 0.800 and accuracy of 0.778. The area under the curve was 0.816 (Fig. 1).

The MPV value of 11.8 fL was used to stratify groups based on clinical characteristics, outcomes and complications. Blood serum MPV was measured in all patients within 24 h of hospitalization. Out of 108 patients, 32 (29.6 %) had an MPV lower 11.8 fL, while in 76 (70.4 %) patients, MPV was equal to or greater 11.8 fL. In the group with high MPV, BMI $\geq$30 was in 45 (59.2 %) patients compared to 8 (25 %) patients with MPV $<$11.8 fL ($P = 0.001$). Significantly higher age was observed in patients with MPV $\geq$11.8 fL (average age 63 years vs. 48; $P < 0.0001$) compared to patients with MPV lower 11.8 fL. Additionally, the proportion of patients with ischemic heart disease at hospital admission was significantly higher in the group with high MPV (70.8 % vs. 28.1 %; P $<$ 0.0001) and DM (51.3 % vs. 12.5 %; $P < 0.0002$). No significant association was found between the etiology of AP and low or high MPV within the first 24 h of hospitalization (alcoholic: 71.9 % vs. 52.6 %; $p = 0.064$; idiopathic: 18.8 % vs. 35.5 %; $P = 0.084$) and patient referral from another hospital (78.1 % vs. 85.5 %; $P = 0.346$).

Clinical outcomes

Clinical outcomes between patients with MPV $\geq$11.8 fL and patients with blood serum MPV lower 11.8 fL significantly differed, as shown in Table 3. Early OF developed in 62 (81.6 %) patients out of 76 in the group with MPV $\geq$11.8 fL, significantly indicating a distinction compared to 11 (34.4 %) patients in the group with low MPV. Considering the identified MPV 11.8 fL threshold for moderately severe to severe AP, persistent OF was significantly observed in 53.1 % in the group with MPV $<$11.8 fL and 93.4 % in the group with high MPV, $P < 0.0001$. ICU admission was required for 28 patients (87.5 %) in the group with MPV $<$11.8 fL. No deaths were observed in the group with MPV $<$11.8 fL, whereas 16 patients (21.1 %) died in the group with MPV $\geq$11.8 fL, $P = 0.005$. No significant difference was found between the groups with low MPV and high MPV with pancreatic necrosis, diagnosed by computed tomography. The median duration of hospital stay did not show a significant difference between the groups (21 (IQR 18.5–25) vs. 25 (IQR 20–28); $P = 0.226$). The need for ICU admission was required for 28 (87.5 %) patients in the group with MPV $<$11.8 fL, while all patients with high MPV had an episode of ICU stay, $P = 0.205$.

Table 2
Distribution of clinical outcomes according to RAC severity classification.

Outcomes	Moderately severe	Severe	P-value
	$n = 20$	$n = 88$	
Mortality, n (%)	0	16 (18.2)	0.039
Admission to ICU, n (%)	16 (80.0)	88 (100)	0.001
Need for intervention, n (%)	10 (50.0)	87 (98.9)	<0.0001
ICU length of stay, median days (IQR)	8 (4–11)	12 (8.7–15)	0.004
Hospital length of stay, median days (IQR)	21 (18–23)	25 (20–28)	0.008

ICU, intensive care unit; IQR, interquartile range; OF, organ failure.

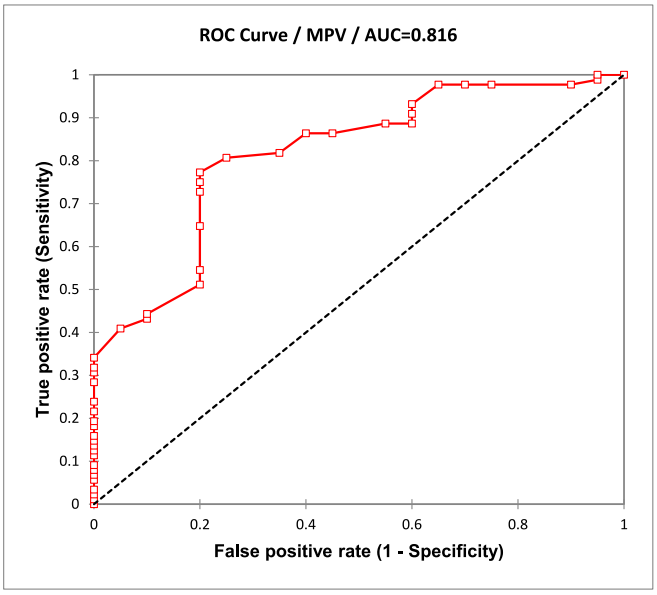

Fig. 1. ROC Curve for MPV in determining moderately severe and severe AP.

Table 3
Comparison of baseline clinical characteristics and outcomes between MPV categories in patients with acute pancreatitis.

Variables	Blood serum MPV (fL) within 24 h of hospitalization		
	Lower than 11.8(fL)	Greater or equal to 11.8(fL)	Trend
	N = 32	*N* = 76	
Demographic characteristics and comorbidities			
Mean age, years (IQR)	48 (37–57.5)	63 (51.5–73.0)	<0.0001
Male gender, N (%)	22 (68.8)	16 (64)	0.811
BMI ≥30, N (%)	8 (25.0)	45 (59.2)	0.001
Referred from other hospitals, N (%)	25 (78.1)	65 (85.5)	0.346
Diabetes mellitus at hospitalization, N (%)	4 (12.5)	39 (51.3)	0.0002
Ischemic heart disease at hospitalization, N (%)	9 (28.1)	51 (70.8)	<0.0001
Etiology			
Alcoholic, N (%)	23 (71.9)	40 (52.6)	0.064
Idiopathic, N (%)	6 (18.8)	27 (35.5)	0.084
Other, N (%)	3 (9.4)	9 (11.8)	0.710
Outcomes			
Early OF (within the first 7 days), N (%)	11 (34.4)	62 (81.6)	<0.0001
Persistent OF, N (%)	17 (53.1)	71 (93.4)	<0.0001
Multiple OF, N (%)	0 (0)	25 (32.9)	0.0002
Need for ICU admission, N (%)	28 (87.5)	76 (100)	0.002
Mean length of hospital stay (days) (IQR)	21 (18.5–25)	25 (20–28)	0.226
Mean length of ICU stay (days) (IQR)	10 (7–13)	12 (8.5–15)	0.205
Mortality, N (%)	0 (0)	16 (21.1)	0.005
Pancreatic necrosis, N (%)	22 (68.8)	61 (80.3)	0.195

BMI, body mass index; MPV, mean platelet volume; ICU, intensive care unit; IQR, interquartile range; OF, organ failure.

After identifying binary and multinomial clinical parameters significant for early OF, a multivariate logistic regression model was constructed, adjusted with correction for BMI ≥30 (95 % CI [OR] 0.16–1.67; $P = 0.258$), DM (95 % CI [OR] 0.54–6.16; $P = 0.334$), and MPV ≥11.8 fL (95 % CI [OR] 3.09–24.85; $P < 0.0001$), independently associated with early OF. Model characteristics are presented in Table 4.

The model based on BMI ≥30, DM and MPV ≥11.8 fL demonstrated a consistent association using the single indicator MPV ≥11.8 fL in predicting early OF. Preselection bias testing was not conducted, given the specified selection criteria that are known to inherently bias toward more severe cases of AP, as the study specifically focused on severe AP.

Discussion

In this study, we assessed the impact of blood serum MPV on the dynamics of the OF in patients with moderately severe and severe AP during the early phase in a prospective patient cohort. We comprehensively evaluated key characteristics, outcomes and complications, taking into account the distribution of patients based on the severity of AP. The sample predominantly consisted of patients with severe AP, as indicated by the presence of persistent OF lasting >48 h. Early OF, as the primary endpoint of the study, is one of the key adverse outcomes. A threshold MPV 11.8 fL was used for the sample, based on which two groups were identified. In these groups, we assessed clinical characteristics, medical history data, and clinical outcomes during the patients' hospital stay. There was a significant difference in age, BMI, as well as DM and ischemic heart disease at the time of admission between the groups. We also observed significant differences in the occurrence of early OF, persistent OF, multiple OF and the need for ICU admission. A multidimensional logistic regression model, including MPV, BMI and previously found DM, demonstrated a strong association with the early onset of the OF within 7 days from the onset of initial AP symptoms.

The MPV 11.8 fL was determined for group stratification based on the severity defined by persistent OF. Hence, it's not surprising that the MPV showed a high sensitivity specifically in assessing the dynamics of the OF. Various OF parameters, including duration, time of onset and a combination involving multiple organ systems, were evaluated accordingly. Among the above characteristics, MPV emerged as an independent factor that, at MPV ≥11.8 fL, indicates a high risk of early OF onset.

The demonstrated changes are associated with the active involvement of platelets in a variety of effects at the intersection of thrombosis and inflammation. New generations of platelets, activated by inflammation, correlate with increased MPV in response to systemic inflammatory factors [17]. Stress factors that induce cell death led to the release of damage-associated molecular patterns, including high mobility group box 1 (HMGB1), a substantial amount of which is found in platelets. HMGB1 activates pattern recognition receptors on the surface of other platelets, including Toll-like receptors (TLRs) such as TLR-4, as well as the receptor for advanced glycation end products. Thus, platelets participate in innate immunity and a range of non-specific immune processes in the body [10,18,19]. The inflammatory mediator IL-6, elevated in AP, leads to changes in the megakaryocyte-platelet axis, polyploidization and subsequent thrombopoiesis in the bone marrow, resulting in a shift toward high MPV [20].

Platelets play a direct role in the systemic inflammatory process, making MPV a valuable tool for rapid assessing disease activity in AP [6]. In AP, pancreatic lipase is released into the systemic circulation, increasing the production of inflammatory factors [21], leading to elevated production of young platelet forms accompanied by an increase

Table 4
Model characteristics of the relationship between proposed clinical parameters and early OF in acute pancreatitis.

Parameter	OR (95 % CI)	P-value
BMI ≥30	0.51 (0.16–1.67)	0.258
DM	1.82 (0.54–6.16)	0.334
[a]MPV ≥11.8 fL	8.77 (3.09–24.85)	<0.0001

AP, acute pancreatitis; BMI, body mass index; CI, confidence interval; OR, odds ratio; MPV, mean platelet volume.
[a] Peak level of MPV within 24 h after hospitalization with MPV (≥11.8 fL).

in MPV. Other potential mechanisms contributing to pancreatic damage include increased blood serum viscosity, leading to tissue hypoperfusion and ischemia [28].

There are various viewpoints on the role of platelets as acute-phase reactants. Chiba et al. [22] reported that patients with thrombocytopenia exhibited a greater frequency of systemic complications, renal dysfunction, cardiovascular dysfunction and mortality. Additionally, severe AP, respiratory dysfunction, acute necrotic collections, pancreatic necrosis, pancreas-related infections and paralytic ileus were more common among patients in the thrombocytosis and thrombocytopenia groups than among those with normal platelet counts. The MPV, C-reactive protein (CRP), and lactate dehydrogenase were also lower in the thrombocytosis and thrombocytopenia groups. Sun et al. [23] reported that a platelet count below 125 × 10^9/L or above 209 × 10^9/L was significantly associated with a higher risk of intra-abdominal infections, more frequent surgical interventions, and prolonged hospital stays. A linear relationship was observed between the number of platelets and the levels of specific inflammatory markers (CRP, white blood cell count, and procalcitonin). Research by Ranson et al. [24] revealed that an increased number of platelets was observed in patients with more severe forms of AP. However, validating these conclusions necessitates determining the severity of AP in the study's participants, in accordance with current severity classifications. Research conducted by Osada et al. [25] reported that the number of platelets was lower in patients with severe AP upon hospitalization than in those with mild AP. Fujimura et al. [26] reported that the absence or transient nature of thrombocytopenia generally indicates a favorable prognosis, while persistent thrombocytopenia typically signifies a higher mortality rate. Akbal et al. [27] found a negative correlation between the MPV and platelet count. The highlighted studies demonstrate the various methodologies applied to the measurement of platelet count and MPV. This emphasizes the need for further research that includes the standardization of methods for analyzing these indicators in patients with acute pancreatitis, particularly with regard to the severity of the condition.

Using multifactorial analysis combining APACHE-II with MPV, an increase in MPV was demonstrated with the severity of AP [28]. The study did not assess overall accuracy, sensitivity and specificity, so further multicenter randomized studies are needed to establish the relationship between elevated MPV and AP severity. Studies related to the development of respiratory failure and local complications have demonstrated that MPV >12 fL may serve as a risk factor for severe hypertriglyceridemic AP [29].

There are discrepancies in defining threshold levels of MPV for healthy individuals. This is associated with various factors, including a proven inverse correlation between MPV and platelet count [30–32]. The variation in platelet count in healthy individuals is strongly related to changes in MPV. The procedure for determining MPV is also associated with variations depending on the blood collection methodology, temperature conditions, time elapsed since blood sample collection for analysis, etc. The anticoagulant EDTA, widely used in blood sample preparation for analysis, has led to a 50 % change in MPV from the baseline level [33,34]. Further research is needed to determine threshold values for MPV in the normal range for healthy patients. Some studies report no significant differences in MPV, demonstrated between groups with moderately severe and severe courses of AP. In the study by Beyazit et al. [6], a decrease in MPV was demonstrated in the group with severe course of AP, but the lack of clearly defined time frames for the primary analysis of MPV and during remission, the use of the modified Glasgow scale as a criterion for determining the severity of AP and the grouping of patients with moderately severe and severe courses into one group limit the reliable interpretation of the findings of the study, considering current concepts of AP severity. The recent study that noted conflicting changes in MPV at the onset of AP and in remission did not provide a characterization of the investigated control group [9]. In this study, patients with high MPV were older and had a higher degree of metabolic disorders, including DM and obesity, compared to patients with MPV <11.8 fL. Type 2 DM, associated with the MPV, may partially reflect the state of insulin resistance. Insulin receptor binding leads to the activation of insulin receptor substrate 1 (IRS-1), which activates a cascade of mechanisms related to the inhibition of cyclic adenosine monophosphate. As a result, a decrease in platelet activity and their interaction with collagen has been demonstrated, weakening the effect of platelet aggregation agonists [35].

Given the significant difference in clinical outcomes among subjects with elevated MPV, clinicians should be aware of this high risk group. For patients with MPV ≥ 11.8 fL, the consideration of additional measures to support organ systems, including referral to the ICU, should be evaluated. However, no studies investigating such measures are currently found.

The current study has several strengths compared to previous reports, including its prospective design involving patient enrollment, the assessment of a range of factors correlating with MPV, considering the severity of AP. Key OF characteristics were considered, reflecting the severity of AP according to the RAC. The association between elevated blood serum MPV and early OF not only significantly depended on other relevant clinical factors but also corresponded to a discrete proportional trend. MPV measurement was performed for all patients within 24 h of hospitalization. Furthermore, all outpatient medical records were obtained and available MPV measurements were abstracted.

The present study did not demonstrate any significant association between elevated MPV and the etiology or local complications during the patient's hospital stay. The association with mortality should be interpreted cautiously due to the limited number of patients with moderately severe AP.

A potential limitation of the study is that more than half of the involved patients initially were admitted to other medical facilities before being referred to our tertiary-level center. Although the association of high MPV with early OF is striking in this study, this conclusion does not delineate the exact mechanistic role of MPV in the course of AP.

The MPV parameter demonstrated a proportionally dependent relationship with a tendency to increase with early OF. MPV >11.8 fL indicates a higher predicted risk of developing persistent or multiple OF. Patients with AP in the older age category, with obesity and comorbid DM or ischemic heart disease exhibit high MPV at the time of hospitalization. These findings need further evaluation in studies with larger datasets.

Abbreviations

AP	Acute pancreatitis
BMI	Body mass index
DM	Diabetes mellitus
ICU	Intensive care unit
MODS	Multiple Organ Dysfunction Score
MPV	Mean Platelet Volume
OF	Organ failure
PSMU	Poltava State Medical University
RAC	Revised Atlanta Classification
TLR	Toll-like receptors

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval

Approval for this study was obtained from the Ethics Committee (equivalent to an Institutional Review Board, IRB) of PSMU (formerly known as the Ukrainian Medical Stomatological Academy), as documented in the protocol No. 171 dated February 27, 2019.

CRediT authorship contribution statement

Heorhii Levytskyi: Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Volodymyr Sheiko:** Writing – review & editing, Validation, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

[1] Li CL, Jiang M, Pan CQ, Li J, Xu LG. The global, regional, and national burden of acute pancreatitis in 204 countries and territories, 1990-2019. BMC Gastroenterol 2021;21(1):332.

[2] Iannuzzi JP, King JA, Leong JH, Quan J, Windsor JW, Tanyingoh D, et al. Global incidence of acute pancreatitis is increasing over time: a systematic review and meta-analysis. Gastroenterology 2022;162(1):122–34.

[3] Skouras C, Hayes AJ, Williams L, Garden OJ, Parks RW, Mole DJ. Early organ dysfunction affects long-term survival in acute pancreatitis patients. HPB (Oxford) 2014;16(9):789–96.

[4] Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut 2004;53(9):1340–4.

[5] Akinsegun A, Akinola Olusola D, Sarah JO, Olajumoke O, Adewumi A, Majeed O, et al. Mean platelet volume and platelet counts in type 2 diabetes: mellitus on treatment and non-diabetic mellitus controls in Lagos, Nigeria. Pan Afr Med J 2014;18:42.

[6] Beyazit Y, Sayilir A, Torun S, Suvak B, Yesil Y, Purnak T, et al. Mean platelet volume as an indicator of disease severity in patients with acute pancreatitis. Clin Res Hepatol Gastroenterol 2012;36(2):162–8.

[7] Huang P, Zhang Y, Wu H. Mean platelet volume as an indicator of persistent organ failure in acute pancreatitis. Int J Clin Exp Pathol 2016;9(12):12883–9.

[8] Lei JIN, Shuping Z, Zijun CAO, Yadong Y. Correlation of platelet related parameters in predicting severity of acute pancreatitis. J Clin Emerg 2021;22(2):111–6.

[9] Kefeli A, Basyigit S, Ozgur Yeniova A, Kucukazman M, Nazligul Y, Aktas B. Platelet number and indexes during acute pancreatitis. Euroasian J Hepatogastroenterol 2014;4(2):67–9.

[10] Bakogiannis C, Sachse M, Stamatelopoulos K, Stellos K. Platelet-derived chemokines in inflammation and atherosclerosis. Cytokine 2019;122:154–7.

[11] Leppaniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg 2019;14:27.

[12] Alexiou A, Grundlingh J, Doe J. Acute pancreatitis. BMJ Best Practice [Internet] 2023. 15.08.2023 [cited 2023 15.08]. Available from: https://bestpractice.bmj.com/topics/en-gb/3000118.

[13] Nawaz H, Mounzer R, Yadav D, Yabes JG, Slivka A, Whitcomb DC, et al. Revised Atlanta and determinant-based classification: application in a prospective cohort of acute pancreatitis patients. Am J Gastroenterol 2013;108(12):1911–7.

[14] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62(1):102–11.

[15] Zaheer A, Singh VK, Qureshi RO, Fishman EK. The revised Atlanta classification for acute pancreatitis: updates in imaging terminology and guidelines. Abdom Imaging 2013;38(1):125–36.

[16] Addinsoft, editor. XLSTAT. 2021 ed. Addinsoft; 2021.

[17] Kerekes L, Arkossy P, Altorjay I, Huszka M, Kappelmayer J, Toth P, et al. Evaluation of hemostatic changes and blood antioxidant capacity in acute and chronic pancreatitis. Hepatogastroenterology 2001;48(42):1746–9.

[18] Pogorzelska K, Kretowska A, Krawczuk-Rybak M, Sawicka-Zukowska M. Characteristics of platelet indices and their prognostic significance in selected medical condition - a systematic review. Adv Med Sci 2020;65(2):310–5.

[19] Zusso M, Lunardi V, Franceschini D, Pagetta A, Lo R, Stifani S, et al. Ciprofloxacin and levofloxacin attenuate microglia inflammatory response via TLR4/NF-kB pathway. J Neuroinflammation 2019;16(1):148.

[20] Burstein SA, Peng J, Friese P, Wolf RF, Harrison P, Downs T, et al. Cytokine-induced alteration of platelet and hemostatic function. Stem Cells 1996;14(Suppl. 1):154–62.

[21] Slobodyanyk N, Neporada K. Pancreatic enzymes activity under the conditions of acute stress and melanin administration depending on the stress resistance. J Pharm Pharmacol 2015;3(5).

[22] Chiba N, Sugita A, Mizuochi M, Sato J, Saito T, Sakurai A, et al. Clinical significance of reactive thrombocytosis in the course of acute pancreatitis. BMC Gastroenterol 2023;23(1):206.

[23] Sun W, Huang J, Ni T, Wen Y, Menglu G, Yongguo W, et al. Moderate level platelet count might be a good prognostic indicator for intra-abdominal infection in acute pancreatitis: a retrospective cohort study of 1,363 patients. Front Med (Lausanne) 2022;9:1077076.

[24] Ranson JHC, Lackner H, Berman IR, Schinella R. The relationship of coagulation factors to clinical complications of acute pancreatitis. Surgery 1977;81(5):502–11.

[25] Osada J, Wereszczynska-Siemiatkowska U, Dabrowski A, Dabrowska MI. Platelet activation in acute pancreatitis. Pancreas 2012;41(8):1319–24.

[26] Fujimura Y, Hirota M, Ichihara A, Takamori H, Baba H. Platelet count as a sensitive and convenient parameter for assessing the prognosis in acute pancreatitis. Pancreas 2008;37(2):225–7.

[27] Akbal E, Demirci S, Kocak E, Koklu S, Basar O, Tuna Y. Alterations of platelet function and coagulation parameters during acute pancreatitis. Blood Coagul Fibrinolysis 2013;24(3):243–6.

[28] Mimidis K, Papadopoulos V, Kotsianidis J, Filippou D, Spanoudakis E, Bourikas G, et al. Alterations of platelet function, number and indexes during acute pancreatitis. Pancreatology 2004;4(1):22–7.

[29] Zeng L, Cai X, Chen J, Jin G, Zheng Y. Role of mean platelet volume in hypertriglyceridemia-induced acute pancreatitis during pregnancy. BMC Pregnancy Childbirth 2020;20(1):592.

[30] Klovaite J, Benn M, Yazdanyar S, Nordestgaard BG. High platelet volume and increased risk of myocardial infarction: 39,531 participants from the general population. J Thromb Haemost 2011;9(1):49–56.

[31] Panova-Noeva M, Schulz A, Hermanns MI, Grossmann V, Pefani E, Spronk HM, et al. Sex-specific differences in genetic and nongenetic determinants of mean platelet volume: results from the Gutenberg Health Study. Blood 2016;127(2):251–9.

[32] 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 epidemiologic study. Thromb Res 2011;128(4):358–60.

[33] Bowles KM, Cooke LJ, Richards EM, Baglin TP. Platelet size has diagnostic predictive value in patients with thrombocytopenia. Clin Lab Haematol 2005;27(6):370–3.

[34] Daves M, Zagler EM, Cemin R, Gnech F, Joos A, Platzgummer S, et al. Sample stability for complete blood cell count using the Sysmex XN haematological analyser. Blood Transfus 2015;13(4):576–82.

[35] Schuett K, Marx N. Diabetes, thrombosis, and cardiovascular risks. Platelets, haemostasis and inflammation. In: Cardiac and vascular biology. Springer International Publishing; 2017. p. 111–24.