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The Prognostic Impact of the Platelet Dynamics and Subthreshold Thrombocytopenia in Intensive Care Patients: A Prospective Cohort Study

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Abstract

Background

Thrombocytopenia (TP) is common in intensive care unit (ICU) patients and has been associated with increased morbidity and mortality. However, the prognostic importance of platelet dynamics remains incompletely understood. We aimed to evaluate the prognostic impact of platelet dynamics and subthreshold/relative thrombocytopenia (< 200 ×10⁹/L) in ICU patients.

Methods

In this prospective observational cohort study, 280 adult patients admitted to the medical ICU were followed. TP was defined as PC < 150 $\times 10^9$/L and Subthreshold thrombocytopenia (STP) as PC < 200 $\times 10^9$/L. Patients were evaluated according to the presence, severity, duration (≥ 3 days vs < 3 days), and timing of TP (initial vs ICU-acquired). Clinical outcomes were analyzed. Multivariable logistic regression models was performed to determine independent predictors of ICU mortality.

Results

TP occurred in 42.1% of patients and was strongly associated with increased ICU, hospital, 28-day, and 90-day mortality (all p < 0.001). Mortality increased progressively with greater TP severity. Persistent TP (≥ 3 days) was independently associated with ICU mortality (aOR 2.75, 95% CI 1.50–5.02). Platelet count alone demonstrated limited discriminatory ability for predicting ICU mortality (AUC 0.58). Notably, a platelet threshold around 200 ×10⁹/L provided a more balanced sensitivity and specificity compared with the conventional 150 ×10⁹/L cut-off. Patients with STP showed greater disease severity and increased ICU mortality and need for organ support.

Conclusions

Beyond its presence alone, the severity and persistence of TP provide important prognostic information in critically ill patients. Our findings suggest that STP may represent an early marker of clinical deterioration, highlighting the potential role of STP as a dynamic biomarker for early risk stratification in ICU populations

Background

Platelets are short-lived, nucleated blood components that play an important role in haemostasis as well as in immune regulation, inflammation and endothelial interaction[1]. A decrease in platelet count (PC) is defined as thrombocytopenia (TP), and although previous publications have used different threshold

values (≤ 200 ×10^9/L, ≤ 80 ×10^9/L, ≤ 60 ×10^9/L) and rates of decrease (< 30%, 50%)[2], current literature defines TP as a PC below 150 ×10^9/L[3]. It is quite common in intensive care units (ICUs); reported prevalence rates vary considerably across studies (8–56%)[2–4]. Many causes of TP, such as sepsis, medications, trauma, and haemodilution, may coexist in critically ill patients[5,6]. Among these aetiologies, sepsis remains the most important cause of TP in the ICU and has led to the widespread use of the term "sepsis-associated thrombocytopenia" in the literature[7,8].

TP increases the risk of bleeding, length of stay (LOS) in the ICU/hospital, and the need for life support devices, vasopressors, and mortality [5,9,10]. A linear relationship has been found between the severity of TP and mortality and disease severity[11,12]. Moreover TP lasting longer than three days has been associated with poor prognosis and mortality[8]. Particularly in severe TP, fear of bleeding leads to delay in invasive procedures, postponement of prophylactic anticoagulation, and platelet transfusions[5,13,14]. Correcting one factor in the treatment of TP patients may not always lead to clinical improvement[11]. The most important aspect of treatment is to correct the underlying disease, if possible.

TP may be present at admission to the ICU or may develop during the course of treatment. The development of TP should be considered a consequence of the severity of the disease and the critical condition[15]. Therefore, monitoring the course of PC and the duration of TP is important in clinical follow-up.

Our primary objective was to evaluate the prognostic impact of platelet dynamics, including the presence, timing, and duration of TP in the ICU, on mortality and clinical outcomes, and to investigate whether there is a relationship between platelet counts below 200 x 10^9/L (subthreshold thrombocytopenia) and clinical outcomes.

Patients and methods

Study Population: This observational prospective cohort study was conducted in accordance with the STROBE Statement[16] for cohort studies. The study was conducted at Medical Intensive Care Unit-3 of Kayseri City Education and Research Hospital in Kayseri, Turkey. All consecutive patients aged 18 years and older admitted to the ICU and followed for more than 24 hours were eligible for inclusion in the study and had no missing critical information (death, organ failure, need for life support devices, need for blood product replacement) in their records. Patients with known terminal-stage solid or haematological malignancies, patients undergoing active chemotherapy, patients with end-stage (Child-pugh class C) liver cirrhosis, and patients with uncontrolled bleeding during hospitalisation were excluded from the study at the outset because they were associated with platelet abnormalities, regardless of their critical illness status. Inclusion of such patients could confound platelet kinetics and outcome analyses (Fig. 1). Of the 415 patients evaluated, 280 met the predefined inclusion criteria and were enrolled. Patients were followed until they were discharged from the hospital or for 90 days. The study was approved by the Institutional Ethics Committee (protocol number 2023–877). Patient enrollment began in September

2023 and ended in August 2024. All methods were performed in accordance with the relevant guidelines and regulations, in line with the principles of the Declaration of Helsinki. All patients provided written informed consent.

Due to its single-centre design and predefined exclusion criteria, selection bias cannot be entirely eliminated, and the findings may not be generalisable to all ICU populations, particularly surgical or haematology-focused cohorts.

Study Procedure: Patient eligibility was assessed upon admission to the ICU. Patients who met the inclusion criteria were informed about the study and enrolled on the same day. In line with the study objectives, standard ICU management protocols were applied without modification.

Sample Size

A pre-trial sample size calculation was performed using G*Power (version 3.1). Assuming a two-tailed alpha value of 0.05, statistical power of 80%, and a 20% difference in mortality rates between patients with and without thrombocytopenia (40% vs. 20%), a minimum of 104 patients were required. The final cohort comprised 280 patients, significantly exceeding the estimated requirement and thus enhancing the statistical precision of the analyses.

Study Data

Clinical data were obtained from patient medical records and the hospital's electronic medical record system (KEYDATA). The variables collected included demographic characteristics, comorbidities, reason for admission to the ICU, disease severity scores, therapeutic interventions, transfusion requirements, laboratory parameters, and clinical outcomes. The APACHE-II Score was calculated based on the worst values recorded within the first 24 hours of admission to the ICU. The SOFA score was calculated based on the values at the time of admission to the ICU. Recorded therapeutic interventions included anticoagulant and corticosteroid use, vasopressor support (VS), central venous catheter (CVC) placement, mechanical ventilation (MV), renal replacement therapy (RRT), and transfusion data. Laboratory variables included complete blood count (CBC) parameters, biochemical markers, inflammatory markers, coagulation parameters, and arterial blood gas measurements. Platelet counts (PC) were measured using impedance-based analysers and verified by optical methods when necessary. Peripheral blood smears were examined when clinically indicated. Routine laboratory assessments were performed at least once daily as part of standard ICU monitoring.

Definitions

Thrombocytopenia (TP) is defined as a PC < 150 $\times 10^9$/L. Relative Thrombocytopenia (RTP) or subthreshold thrombocytopenia (STP) is defined as PC < 200 $\times 10^9$/L. The RTP threshold was selected based on previous literature[2] and clinical observations indicating that relative platelet decline may have prognostic significance even above traditional TP thresholds.

TP severity is classified as mild (100–149 $\times 10^9$/L), moderate (50–99 $\times 10^9$/L), severe (20–49 $\times 10^9$/L) and very severe (< 20 $\times 10^9$/L)[17,18].

TP is also classified according to timing: “IT (Initial thrombocytopenia)” is defined as thrombocytopenia present upon admission to the ICU; “ICU-TP (ICU-acquired thrombocytopenia)” is defined as thrombocytopenia developing during the ICU stay; “AT (Any thrombocytopenia)” is defined as all thrombocytopenia present at admission and/or during ICU stay.

Duration-based TP is classified as Persistent (≥ 3 days) or Transient (< 3 days)[8]. Patients who died early may not have had sufficient time to develop persistent TP, which may have created survival bias in time-based analyses.

Bleeding events were graded according to World Health Organization criteria[19]. *Sepsis* was defined using Sepsis-3 criteria[12]. *Acute kidney injury (AKI)* was defined according to KDIGO guidelines[20]. *Acute liver injury (ALI) and Acute liver failure (ALF)* were defined as previously described[21,22]. *Disseminated Intravascular Coagulation (DIC)* was defined based on International Society of Thrombosis and Haemostasis Scientific and Standardization Committee criteria[23]. Blood and blood product *transfusions* followed current international guidelines[24–25]. *Heparin-induced thrombocytopenia (HIT)* was assessed using the 4T clinical probability score[26].

Outcomes: The primary outcome was the relationship between the presence, timing (at the time of admission or onset during the course), and duration (≥ 3 days or less) of TP and mortality in the ICU and the relationship between STP/RTP and ICU mortality. Secondary outcomes included the relationship between TP severity and ICU, hospital, 28, and 90 day mortality, and the relationship between TP and bleeding, thrombotic events and transfusion requirements.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Normality was assessed visually (histograms and Q–Q plots) and using the Shapiro–Wilk test. Continuous variables were expressed as mean±standard deviation or median (interquartile range), as appropriate. Student’s t-test or Mann–Whitney U test was used for group comparisons. Categorical variables were analyzed using Pearson’s chi-square or Fisher’s exact tests. Comparisons across TP severity groups were performed using the Kruskal–Wallis test. To evaluate whether thrombocytopenia was independently associated with ICU mortality, a series of prespecified multivariable logistic regression models were constructed. Variables with $p < 0.20$ in univariate analyses and those considered clinically relevant were entered into the multivariable models. To minimize collinearity and avoid circularity, the SOFA score was excluded from multivariable modeling because platelet count constitutes one of its components. Age was not included as a separate covariate, as it is embedded within the APACHE II score. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. Model discrimination was quantified using the area under the receiver operating

characteristic curve (AUC), whereas model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test. Optimal threshold values for TP in predicting ICU mortality were determined using the Youden index. A two-tailed p value < 0.05 was considered statistically significant. There were no missing data for the primary outcome.

Results

Study Population

A total of 280 patients were included in the study. The median age of the cohort was 72 years (IQR 61–82). At ICU admission, the median GCS score was 13 (IQR 10–15), APACHE-II score was 21 (IQR 15–29), and SOFA score was 5 (IQR 3–8). Sepsis was present in 165 patients (58.9%). The most common comorbidities were hypertension, diabetes mellitus, and chronic kidney disease. ICU mortality was 33.9%, while hospital, 28-day, and 90-day mortality rates were 38.9%, 31.8%, and 42.5%, respectively. The median ICU and hospital lengths of stay (LOS) were 5 (IQR 3–10) and 11 (IQR 7–26) days. Detailed baseline characteristics of the study population are presented in Table 1.

When evaluating the aetiologies of TP in the ICU, an average of 1.52 contributing causes per AT patient were identified. The most common cause was sepsis (73.7%), followed by DIC (28%), hemodilution (12.7%), bleeding (12.7%), drug-induced thrombocytopenia (7.6%), HIT (4.2%), other causes (trauma, malnutrition, vitamin deficiency) (10%), and unknown causes (3.3%).

Comparison According to the Presence of Thrombocytopenia

The baseline clinical characteristics, outcomes, and laboratory findings of the study population according to the presence of TP are presented in Table 2. Patients with TP were in a more severe clinical condition upon admission to the ICU and had significantly lower GCS scores and higher APACHE-II and SOFA scores compared to patients without TP (all p<0.001). Mortality outcomes in the TP group were higher: ICU mortality (53.4% vs. 19.8%), hospital mortality (59.3% vs. 24.1%), 28-day mortality (48.3% vs. 19.8%), and 90-day mortality (63.6% vs. 27.2%) (all p<0.001). Patients with TP also spent a longer time in ICU (p<0.001), but there was no significant difference in hospital stay between the groups. In terms of laboratory findings, lymphocyte counts, haemoglobin levels, and fibrinogen concentrations were significantly lower in thrombocytopenic patients, while AST, LDH, total bilirubin, creatinine, INR, D-dimer, lactate, and procalcitonin levels were significantly higher compared to non-thrombocytopenic patients. No significant differences were observed between the two groups in terms of age, gender distribution, neutrophil count, ALT levels, NLR, pH, or CRP levels.

ROC Curve Analysis of Platelet Count for Predicting ICU Mortality

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminatory ability of platelet count (PC) for predicting ICU mortality (Figure 2). The area under the curve (AUC) was 0.583 (95% CI, 0.508–0.657; p=0.023), indicating a limited discriminative performance. Using the Youden

index, the optimal PC cut-off value for predicting ICU mortality was identified as 205.5 ×10⁹/L, which provided a sensitivity of 50% and a specificity of 56%. In comparison, the conventional TP threshold of 150 ×10⁹/L demonstrated higher specificity (85%) but markedly lower sensitivity (34%). Similarly, the relative thrombocytopenia threshold of 200 ×10⁹/L showed a more balanced diagnostic performance, with a sensitivity of 47% and specificity of 59%, compared with the conventional thrombocytopenia threshold.

Relative Thrombocytopenia

Clinical features, outcomes, transfusion requirements, and complications according to the presence of RTP are presented in Table 3. Patients with RTP demonstrated significantly lower GCS scores and higher APACHE-II and SOFA scores compared to patients without RTP, indicating more severe disease at the time of admission to the ICU (p=0.043, p=0.002, and p<0.001, respectively). ICU mortality was significantly higher in the RTP group (38.3% vs. 23.8%, p=0.019), but hospital, 28-day and 90-day mortality rates did not differ significantly between groups. Patients with RTP required platelet transfusion and FFP/cryoprecipitate transfusion more frequently than those without RTP (p=0.002 and p=0.001, respectively), but red blood cell transfusion rates were similar between groups. Furthermore, the need for mechanical ventilation and vasopressor support was significantly higher in patients with RTP (p=0.006 and p<0.001, respectively). In terms of complications, DIC and AKI were significantly more prevalent in patients with RTP (p<0.001 and p=0.013, respectively)

Impact of Thrombocytopenia Duration on Mortality

The impact of TP/RTP duration on mortality outcomes is presented in Table 4. Patients with TP lasting ≥3 days had significantly higher ICU, hospital, and 90-day mortality rates compared with those with TP lasting <3 days. Specifically, prolonged TP was associated with increased ICU mortality (56% vs. 32.3%, OR 2.6, 95% CI 1.1–6.4, p=0.026), hospital mortality (64% vs. 35.5%, OR 3.2, 95% CI 1.3–7.7, p=0.007), and 90-day mortality (69.3% vs. 38.7%, OR 3.5, 95% CI 1.49–8.5, p=0.003). Although 28-day mortality was higher in patients with prolonged TP, the difference did not reach statistical significance (p=0.055). In contrast, the duration of RTP was not significantly associated with ICU, hospital, 28-day, or 90-day mortality.

Association Between Thrombocytopenia Severity and Mortality

The relationship between the severity of TP and mortality outcomes is presented in Table 5. Mortality rates increased progressively as the severity of TP increased. ICU mortality rose from 27.3% in patients with mild TP to 40.9% in patients with moderate TP and increased significantly in patients with severe and very severe TP (84% and 90.9%, respectively; p<0.001). A similar trend was observed in hospital mortality; the mortality rate, which was 33.3% in patients with mild TP, increased to 52.3% in patients with moderate TP and reached 84% and 90.9% in the severe and very severe TP groups (p<0.001). Likewise, 28-day and 90-day mortality rates also increased significantly with greater TP severity (p=0.006

and p<0.001, respectively), demonstrating a stepwise relationship between TP severity and adverse clinical outcomes.

Comparison Between Initial and ICU-Acquired Thrombocytopenia

A comparison of demographic, clinical, and laboratory characteristics between patients with thrombocytopenia at ICU admission (IT) and those who developed thrombocytopenia during ICU stay (ICU-TP) is presented in Table 6. There were no significant differences between the two groups regarding age, sex distribution, GCS score, APACHE-II score, or SOFA score. Similarly, ICU, hospital, 28-day, and 90-day mortality rates were comparable between the groups. However, TP lasting ≥3 days was significantly more common in the IT group compared with the ICU-TP group (87.5% vs. 52%, p<0.001). Patients with IT also had a longer hospital LOS than those with ICU-TP (p=0.049). Regarding laboratory parameters, patients who developed TP during ICU stay had significantly higher WBC and neutrophil counts, as well as higher lactate levels compared with patients with TP at admission. In contrast, lymphocyte counts and platelet counts were lower in the IT group. Other laboratory parameters, including haemoglobin, liver enzymes, bilirubin, creatinine, coagulation markers, and inflammatory markers, were similar between the two groups.

Transfusion Requirements, Complications and Clinical Interventions

The comparison of transfusion requirements, complications, and clinical interventions between patients with any thrombocytopenia (AT) and those who never developed thrombocytopenia (NT) is presented in Table 7. Patients with TP required significantly more platelet transfusions, RBC transfusions, and FFP/cryoprecipitate transfusions compared with patients without TP (all p<0.001). Regarding complications, sepsis, DIC, AKI, and acute liver injury were significantly more frequent in the TP group (all p<0.01). However, the rates of hemorrhage and thrombosis were similar between the groups. Patients with TP also required more intensive clinical support, including RRT, MV, and vasopressor therapy (all p<0.001). In addition, steroid therapy and CVC placement were significantly more common in patients with TP. In contrast, thromboprophylaxis practices and antibiotic therapy did not differ significantly between the groups.

Multivariable Analysis

Multivariable logistic regression analyses were performed to identify independent predictors of ICU mortality is presented in Table 8. In Model 1, TP was independently associated with increased ICU mortality (aOR 2.75, 95% CI 1.5–5, p=0.001). Higher APACHE-II scores (aOR 1.08, 95% CI 1.04–1.12, p<0.001) and the presence of sepsis (aOR 5.50, 95% CI 2.7–11.5, p<0.001) were also significant predictors. In Model 2, which additionally included clinical interventions, the requirement for mechanical ventilation emerged as the strongest predictor of ICU mortality (aOR 107.79, 95% CI 31.5–368.7, p<0.001), while sepsis remained independently associated with mortality. In this model, TP was not significantly associated with ICU mortality. In Model 3, DIC was strongly associated with ICU mortality (aOR 15, 95% CI 5.1–46.4, p<0.001). APACHE-II score and sepsis also remained independent predictors,

whereas TP showed a borderline association with ICU mortality. Overall, sepsis and disease severity consistently remained independent predictors of ICU mortality across all models.

Discussion

Main findings

In this single-centre prospective cohort study, we comprehensively evaluated the clinical significance of thrombocytopenia (TP) in critically ill patients by examining the presence, severity, duration, and temporal distribution of TP during the intensive care unit (ICU) stay. Below is a summary of the key findings of our study. Firstly, ICU, hospital, 28-day and 90-day mortality rates were significantly higher in critically ill patients with TP. Secondly, there was a stepwise correlation between the degree of TP and mortality; mortality progressively increased in patients with severe and very severe TP. Thirdly, significantly worse outcomes were associated with prolonged TP (≥ 3 days), suggesting that the persistence of TP may have important prognostic consequences. Finally, although the duration of Relative Thrombocytopenia (RTP) was associated with increased disease severity and increased need for organ support, it was not independently associated with mortality outcomes except in ICU.

Thrombocytopenia as a marker of disease severity

TP should be considered not only as a laboratory finding but also as an indicator of disease severity and organ dysfunction. This view is reinforced by the fact that patients with TP have lower GCS scores, higher SOFA and APACHE-II scores, increased use of organ support therapies such as vasopressors and RRT/MV, and significantly higher intensive care, hospital, 28-day and 90-day mortality rates. Large international cohorts also interpret the relationship between TP and mortality within the framework that, in most cases, TP is not a “cause” but a “reflection of disease burden and systemic inflammation”[18].

Coagulation disturbance and tissue hypoperfusion

Our findings indicate that markers reflecting coagulopathy and tissue hypoperfusion, including increased INR, decreased fibrinogen levels, elevated D-dimer, and elevated lactate, were more markedly altered in patients with TP. This pattern supports consumption-related mechanisms, which are frequently observed in critically ill patients, particularly in the context of sepsis and DIC. Recent evidence suggests that platelets play roles beyond haemostasis, contributing to immune regulation, inflammatory responses, and interactions between the endothelium and leukocytes. Therefore, TP in sepsis likely reflects not only platelet consumption but also the complex interplay between inflammation, coagulation, and endothelial dysfunction[2].

Inflammatory markers

In our study, commonly utilized inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) [28], exhibited no significant differences between patients with and without thrombocytopenia. While these indices are commonly employed as indicators of systemic inflammation

in critically ill patients, they may exhibit reduced sensitivity to the complex mechanisms driving platelet consumption and destruction in the ICU environment. Likewise, the AST/ALT ratio was moderately elevated in patients with TP. High AST/ALT ratios in very sick patients are often seen as signs of systemic stress, low blood flow, or extrahepatic AST release, not just liver cell damage[29]. These results indicate that standard inflammatory indices may inadequately reflect the intricate inflammatory and coagulopathic mechanisms linked to thrombocytopenia in critically ill patients.

Duration of thrombocytopenia

Our findings regarding the prognostic significance of TP duration are particularly valuable: an increase in mortality was observed in cases of TP lasting ≥ 3 days. This is consistent with recent multicohort analyses supporting the concept of “persistent/chronic sepsis-associated thrombocytopenia”; it has been shown that the risk of poor outcomes increases as the duration prolongs[8]. Clinically, this result suggests that in ICU monitoring, the trend and rate of recovery may be more meaningful than a single platelet count (PC). On the other hand, the fact that no significant difference in mortality was observed between the presence of TP at admission ICU and its development during the course of treatment emphasizes that “developing TP is at least as important as TP at admission” in clinical practice. This finding supports the interpretation that TP may be a dynamic marker that emerges as systemic inflammation and organ failure worsen during the course of ICU.

Platelet thresholds and relative thrombocytopenia

The definition of thrombocytopenia varies considerably across the literature, and no universally accepted diagnostic threshold exists. While most studies define TP using an absolute platelet count < 150×10^9/L, other thresholds and relative platelet decline criteria have also been proposed. When absolute PCs are used, a wide range of threshold values has been reported, including 200×10^9/L, 150×10^9/L, 80×10^9/L and 60×10^9/L. Similarly, studies based on platelet decline have applied reductions of > 30% or > 50% as diagnostic thresholds[2]. Nevertheless, in contemporary clinical practice and in the majority of published studies, TP is most commonly defined as an absolute PC < 150×10^9/L[11]. In our study, the modest discriminatory performance of PC in predicting ICU mortality (AUC = 0.58) indicates that PC alone is a weak prognostic marker. Although it is a weak independent predictor in organ failure modeling (due to the heavy dominance of the need for mechanical ventilation in model calibration), we also found that it is weakly associated with mortality when evaluated with DIC These findings indicate that TP may function both as a marker of critical illness severity and as a component of the complex inflammatory and coagulative cascade underlying mortality in ICU patients. Specifically, the higher optimal threshold value (< 200×10^9/L) determined using the Youden index suggests that clinically meaningful platelet decline may occur earlier and with relatively smaller decreases than those captured by the traditional < 150×10^9/L threshold. Although PC < 200×10^9/L does not meet the official definition of TP, it has been defined as “Relative Thrombocytopenia” [30] to facilitate the early diagnosis of high-risk patients. Although RTP is not associated with mortality (in our study, it was associated with ICU mortality), we propose the definition of “Subthreshold TP” for ICU patients as an early indicator of disease severity and recommend

further studies. However, these findings may be influenced by center-specific characteristics, patient case diversity, and timing of measurement, and therefore require external validation.

Steroid and antibiotic therapy

Corticosteroid use was more frequent among patients with TP. This finding likely reflects greater disease severity rather than a direct effect of corticosteroids on PCs. In critically ill patients, corticosteroids are commonly administered in the context of septic shock, refractory hypotension, or severe systemic inflammation[12] clinical scenarios that are themselves strongly associated with TP. Similarly, antibiotic use was highly prevalent in both groups and did not differ significantly between patients with and without TP. While certain antibiotics have been implicated in drug-induced thrombocytopenia, such effects are relatively uncommon and often difficult to distinguish from sepsis-related platelet consumption in critically ill patients[31]. In this context, the lack of a significant association between antibiotic therapy and TP supports the interpretation that TP in our cohort predominantly reflects underlying disease processes rather than antibiotic exposure per se.

Transfusion and complications

In terms of transfusion and complications, the higher use of blood and blood products in the TP group Patients with TP required significantly more blood and blood product transfusions. However, the absence of a significant difference in bleeding complications between groups may be related to our patient selection criteria and the restrictive transfusion strategies used in our centre. Current intensive care guidelines support a shift from “routine practices” to evidence-based, more restrictive strategies based on clinical context in transfusion decisions for critically ill patients without bleeding[24]. We believe that the real-world data from your study provides valuable insight into how TP affects transfusion decisions and invasive procedure planning in the clinical setting.

Strengths and Limitations of the Study

Several limitations of this study should be acknowledged. Its single-center design may limit the generalizability of the findings and the exclusion of certain patient groups, such as those with end stage cirrhosis or uncontrolled major bleeding, may have influenced the observed associations. As a single-center observational study, residual confounding and selection bias cannot be completely excluded, despite the prospective design and systematic data collection. in septic patients, sepsis was accepted as the primary etiology of TP and platelet consumption and increased destruction were simultaneously considered as underlying mechanisms. While this approach reflects routine clinical practice in the ICU, it may have led to overlapping etiological and mechanistic classifications and limited causal interpretation regarding specific pathways. Nevertheless, a comprehensive assessment of clinical and laboratory variables, along with detailed subgroup analyses based on thrombocytopenia severity, persistence, and timing, strongly emphasizes the clinical significance of TP and RTP (Subthreshold TP) in medical intensive care settings.

Conclusion

Thrombocytopenia is prevalent among critically ill patients and is strongly correlated with disease severity, organ dysfunction, and mortality. Our findings highlight that not only the presence but also the severity and persistence of thrombocytopenia carry important prognostic information. Additionally, a decrease in platelets beyond the standard thrombocytopenia threshold may indicate an early sign of clinical worsening. These observations support the interpretation of thrombocytopenia as a dynamic biomarker of critical illness rather than merely a laboratory abnormality. Future multicentre studies are needed to validate the concept of subthreshold thrombocytopenia and to clarify its potential role in early risk stratification in ICU patients.

Abbreviations

ALI	Acute Liver Injury
ALF	Acute Liver Failure
AKI	Acute Kidney Injury
APACHE-II	Acute Physiology and Chronic Health Evaluation II
AT	Any Thrombocytopenia
CBC	Complete Blood Count
CVC	Central Venous Catheter
DIC	Disseminated Intravascular Coagulation
FFP	Fresh Frozen Plasma
GCS	Glaskow Coma Scale
HIT	Heparin-induced thrombocytopenia
ICU	Intensive Care Unit
ICU-TP	ICU Acquired Thrombocytopenia
IT	Initial Thrombocytopenia
LMWH	Low Molecular Weight Heparin
MV	Mechanical Ventilation
NT	Never Thrombocytopenia

PC Platelet Counts (PC)

RBC Red Blood Cell

RRT Renal Replacement Therapy;

RTP Relative Thrombocytopenia

STP Subthreshold thrombocytopenia

TP Thrombocytopenia

VP Vasopressor

WBC White Blood Cell

Declarations

Ethical approval and consent to participate

The study is based on the ICU cohort of the Kayseri City Hospital which consists: A prospective cohort starting in September 2023 and August 2024. The Ethics Committee approval for the ICU cohort is dated July 25, 2023, and numbered 877. It was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent

Data availability statement:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author Contributions (CRediT Statement):

Kamil Deveci: Writing–review&editing, Writing–original draft, Data curation, Project administration, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Supervision. **Maruf Boran:** Writing–review&editing, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Kübra E. Bahar:** Writing–review&editing, Supervision, Resources, Methodology,

Formal analysis, Data curation, Conceptualization. **Fatma Sarıdağ:** Writing–review&editing, Supervision, Resources, Methodology, Formal analysis, Data curation, Conceptualization

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Tables

Tables 1 to 8 are available in the Supplementary Files section.

Figures

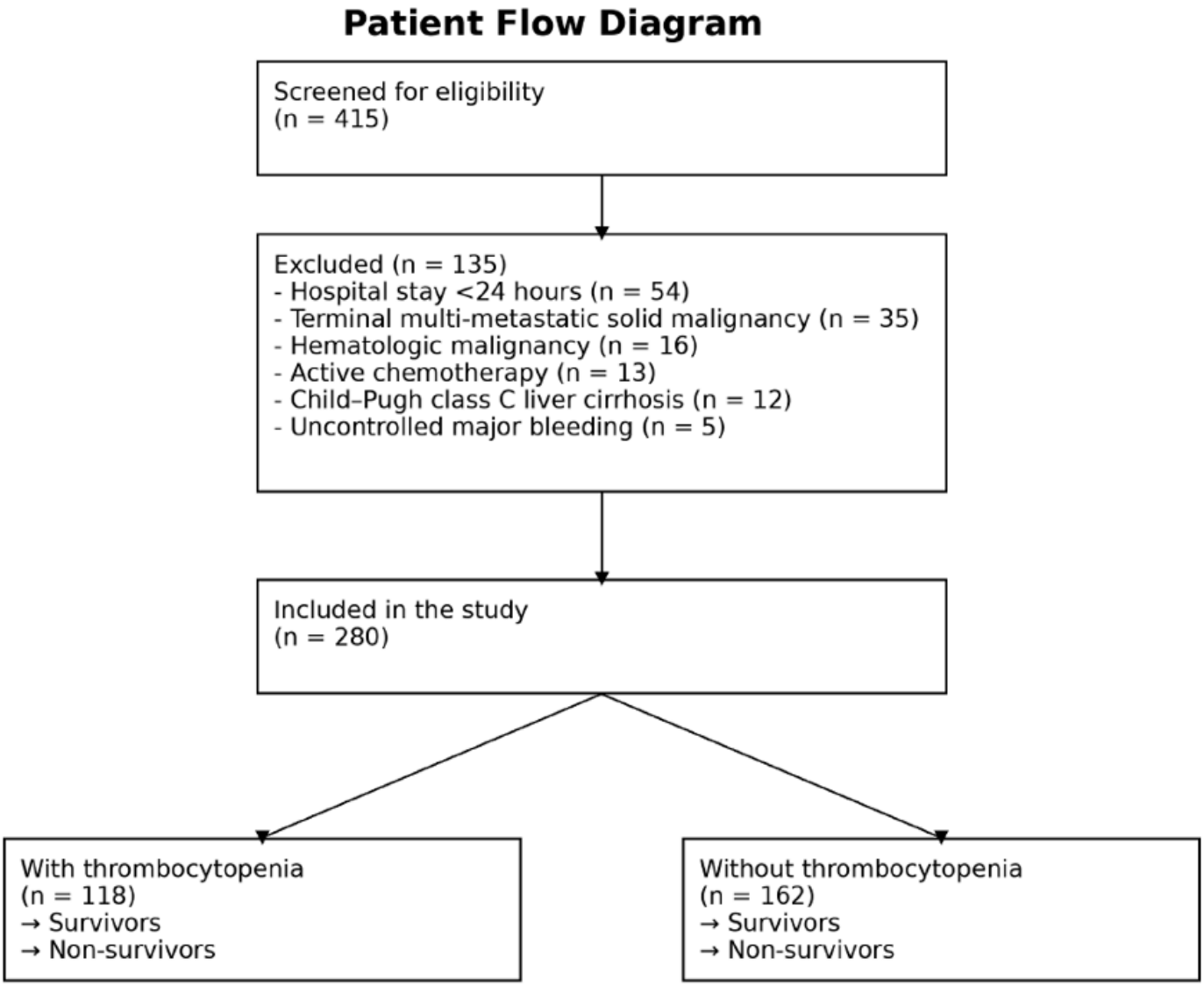


Figure 1

Patient Flow Diagram

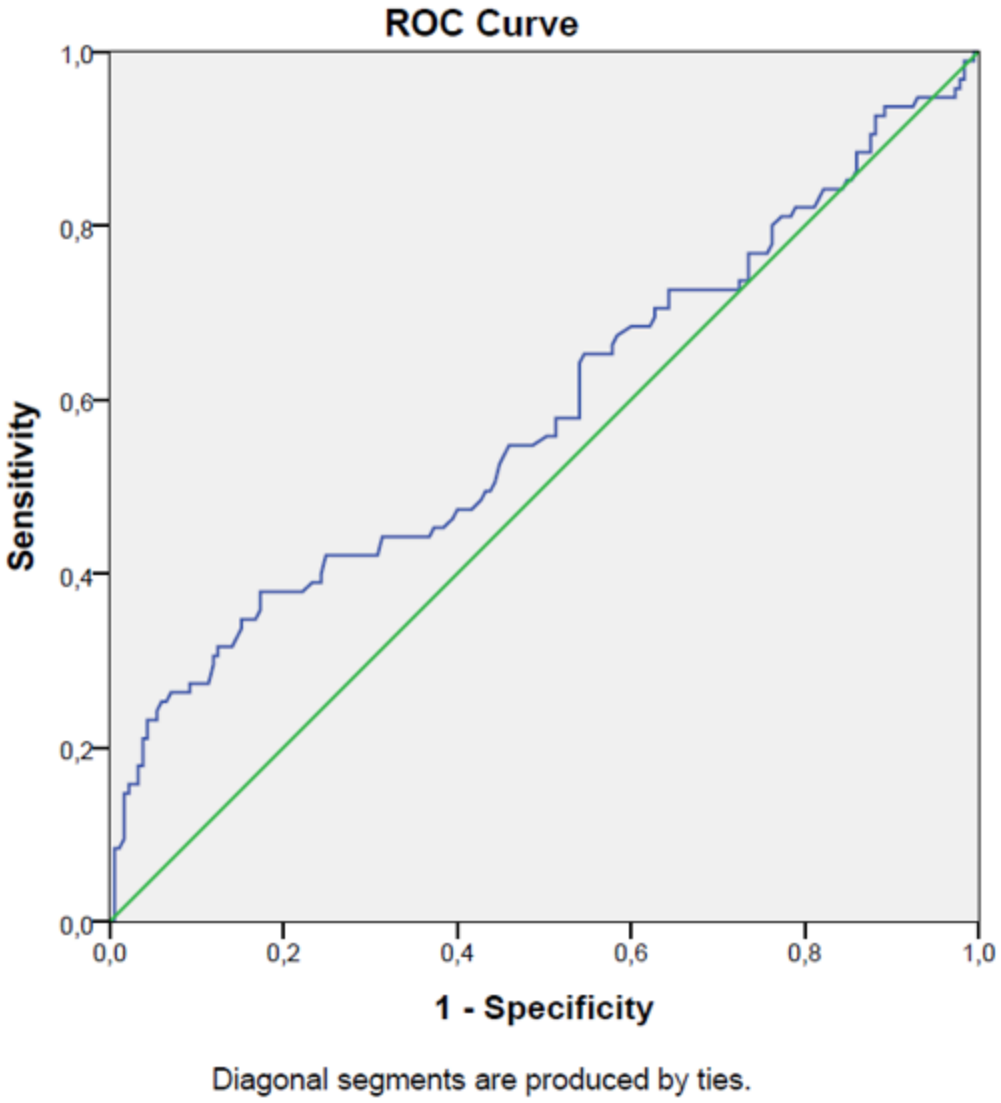


Figure 2

Predictive Performance of Platelet Count for ICU mortality assessed by ROC curve analysis

Supplementary Files

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- Tables.docx