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# Clinical Implications of Thrombocytopenia at Cardiogenic Shock Presentation: Data from a Multicenter Registry

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**Purpose:** Thrombocytopenia (platelet count <150×10$^3$/μL) is associated with poor outcomes in various critical illness settings. However, the prognostic value of platelet count in patients with cardiogenic shock (CS) remains unclear.

**Materials and Methods:** We enrolled 1202 patients between January 2014 and December 2018 from a multicenter retrospective–prospective cohort registry of CS. Clinical characteristics and treatment outcomes were compared between the patients with and without thrombocytopenia.

**Results:** At presentation with CS, 244 (20.3%) patients had thrombocytopenia. The patients with thrombocytopenia had lower blood pressure, hemoglobin level, and worse liver and renal functions compared to the patients without. During hospitalization, the patients with thrombocytopenia had more frequent gastrointestinal bleeding (10.5% vs. 3.8%, $p$=0.009), sepsis (8.3% vs. 2.6%, $p$=0.013), requirement of renal replacement therapy (36.5% vs. 18.9%, $p$<0.001), requirement of mechanical ventilation (65.2% vs. 54.4%, $p$=0.003), longer intensive care unit stay (8 days vs. 4 days, $p$<0.001), and thirty-day mortality (40.2% vs. 28.5%, $p$<0.001) compared to those without. In addition, the platelet count was an independent predictor of 30-day mortality (per 10$^3$/μL decrease; adjusted hazard ratio: 1.002, 95% confidence interval: 1.000–1.003, $p$=0.021).

**Conclusion:** Thrombocytopenia at CS presentation was associated with worse clinical findings, higher frequencies of complications, and longer stay at the intensive care unit. Also, thrombocytopenia was independently associated with increased 30-day mortality. (Clinical trial registration No. NCT02985008).

**Key Words:** Cardiogenic shock, thrombocytopenia, platelet, mortality, prognosis

## INTRODUCTION

Thrombocytopenia (platelet count <150×10$^3$/μL) is common in critically ill patients. Complement activation, extracellular histones, dilution, hemophagocytosis, and thrombin-mediated platelet activation are well-known key pathophysiologies underlying thrombocytopenia in these patients.[1] Since thrombocytopenia can contraindicate some invasive procedures or necessitate specific therapies, such as platelet transfusion,[2,3] its clinical implication is fairly evident in critically ill patients.[4-7]

In particular, thrombocytopenia is of great concern in pa-

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tients with severe cardiac diseases,[8] as anticoagulants, antiplatelet agents, or invasive procedures including percutaneous coronary intervention (PCI) and extracorporeal membrane oxygenation (ECMO) implantation are a vital part of treatment in these patients.[9-11] Actually, there have been several previous studies investigating the prognostic role of thrombocytopenia in patients with acute coronary syndromes.[12-14]

However, the prognostic value of thrombocytopenia has not been sufficiently evaluated in patients with cardiogenic shock (CS). Although there have been several biomarkers shown to be associated with prognosis in patients with CS, such as glucose, albumin, and lactate,[15-18] conflicting results have been reported regarding platelet count as a prognostic biomarker.[8,12,13] Consequently, well-known CS risk-scoring systems, including CardShock score or IABP-SHOCK II risk score, do not incorporate platelet counts or thrombocytopenia.[19,20]

Therefore, this study was conducted to identify the prevalence and prognostic significance of thrombocytopenia in patients with CS with the aim of providing a new perspective on the risk stratification of patients with CS.

## MATERIALS AND METHODS

### Study population

The SMart Angioplasty Research Team: A Multi-center, open, REtrospective and prospective observational Study to investigate Clinical oUtcomes and Efficacy of left ventricular-assist devices for Korean patients with cardiogenic shock (SMART RESCUE) study is a Korean retrospective and prospective, observational, multicenter registry for evaluating the clinical outcomes of patients aged ≥19 years with CS, recruited between January 2014 and December 2018 from 12 Korean tertiary care centers (ClinicalTrials.gov NCT02985008). The criteria for CS included systolic blood pressure <90 mm Hg for 30 minutes despite adequate fluid resuscitation or the need for inotropes or vasopressors to maintain systolic blood pressure ≥90 mm Hg, clinical signs of peripheral hypoperfusion (any of the following: altered mental status, cold extremities, urine output <0.5 mL/kg/h, serum lactate ≥2.0 mmol/L), and signs of acute pulmonary edema. Exclusion criteria included non-cardiac origin shock, shock accompanied by out-of-hospital cardiac arrest, patients allergic to heparin, or refusal to receive aggressive medical therapy.

Among 1247 CS patients in the registry, 20 patients with missing platelet counts and 25 patients with incomplete follow-up information were excluded. Consequently, a total of 1202 patients with CS were included in our analysis (Fig. 1). Written informed consent was obtained from the patient or the next of kin upon admission, and the Institutional Ethics Committees of each participating center approved this study (approval no. 4-2017-0880).

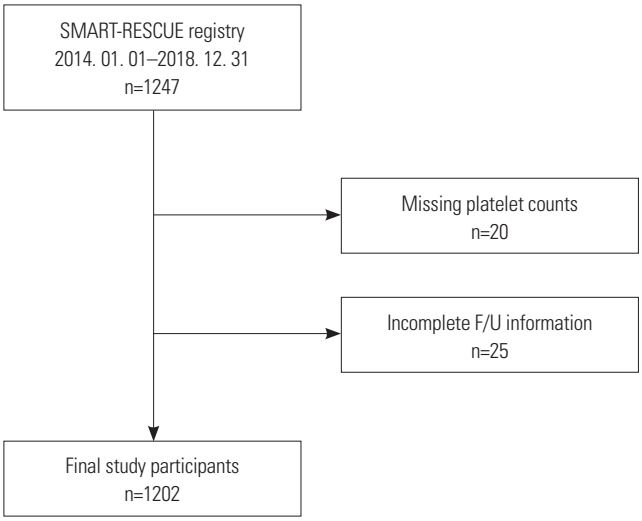


**Fig. 1.** Flowchart of the study. F/U, follow-up.

### Data collection and definition of clinical outcomes

Participants' data on the demographics, anthropometric indices, and underlying medical conditions were collected at baseline. Hemodynamic, laboratory, and echocardiographic parameters were measured at shock presentation to quantitatively assess the severity of patients' clinical status. In addition, the doses of required inotropes and/or vasopressors were measured and transformed into vasoactive inotropic scores to standardize the doses of different inotropes and vasopressors.[21] Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[22]

During the course of hospitalization, data were collected on survival and complications, such as gastrointestinal (GI) bleeding, sepsis, and stroke. Patient management strategies, including the decision for intra-aortic balloon pump and/or ECMO, were based on the clinical protocols of each center. All-cause 30-day mortality was assessed as a measure of clinical outcome, and the length of stay in the intensive care unit (ICU) and hospital were assessed among patients who survived to discharge.

### Statistical analysis

Continuous variables are expressed as mean±standard deviation for normally distributed variables or median [interquartile range] for variables with skewed distribution. The Student's t-test was used for between-group comparison of continuous variables. All categorical variables are expressed as number (proportion) and compared using either the chi-square test or Fisher's exact test.

The cumulative survival of participants according to the presence or absence of thrombocytopenia was estimated with the Kaplan-Meier method, and compared by the log-rank test. To identify and adjust for potential confounders, univariable Cox proportional hazards regression analyses were performed,


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followed by multivariable analysis. Covariates were selected based on their heterogeneity between groups, statistical significance on univariable analyses, or previously known relationship with major clinical outcomes in patients with CS.[15,17,19,20] Moreover, to examine any potential nonlinear relationship between platelet count and risk for 30-day mortality, restricted cubic spline plot was fitted with Cox proportional hazard model with the same covariates as above.

In addition, subgroup analysis was performed to identify any effect modification by demographic/clinical factors after stratifying participants according to age (<65 years, ≥65 years), sex, body mass index (<25 kg/m$^2$, ≥25 kg/m$^2$), history of coronary artery occlusive disease, systolic blood pressure (<60, 60–69, 70–79, and ≥80 mm Hg), left ventricular (LV) ejection fraction (≥40%, <40%), lactate level (≤5 mmol/L, >5 mmol/L), and cause of shock [acute myocardial infarction (AMI), non-

**Table 1.** Baseline Characteristics at Cardiogenic Shock Presentation

| | With thrombocytopenia (n=244) | Without thrombocytopenia (n=958) | *p*-value |
|---|---|---|---|
| Age (yr) | 66±14 | 66±14 | 0.732 |
| Men | 166 (68.0) | 660 (68.9) | 0.796 |
| Body mass index (kg/m$^2$) | 23.0±3.5 | 23.5±3.5 | 0.035 |
| Cardiovascular risk factors | | | |
| Current smoking | 57 (23.4) | 287 (30.0) | 0.042 |
| Hypertension | 127 (52.0) | 515 (53.8) | 0.633 |
| Diabetes | 89 (36.5) | 342 (35.7) | 0.821 |
| Dyslipidemia | 54 (22.1) | 271 (28.3) | 0.053 |
| History of CAOD | 49 (20.1) | 177 (18.5) | 0.630 |
| History of PAOD | 11 (4.5) | 39 (4.1) | 0.760 |
| History of CVA | 25 (10.2) | 89 (9.3) | 0.649 |
| History of CKD | 29 (11.9) | 89 (9.3) | 0.224 |
| Systolic BP (mm Hg) | 70 [60–80] | 77 [63–86] | 0.001 |
| Diastolic BP (mm Hg) | 45 [37–54] | 50 [40–59] | 0.001 |
| Mean BP (mm Hg) | 53 [44–62] | 58 [48–67] | <0.001 |
| Heart rate (beats per minute) | 88±31 | 86±31 | 0.289 |
| LV ejection fraction <40% | 107/177 (60.5) | 351/607 (57.8) | 0.591 |
| Platelet count (10$^3$/μL) | 106±32 | 238±68 | <0.001 |
| Hemoglobin (g/dL) | 11.6±3.0 | 12.9±2.4 | <0.001 |
| Total bilirubin (mg/dL) | 0.9 [0.5–1.9] | 0.6 [0.4–0.9] | <0.001 |
| Aspartate aminotransferase (IU/L) | 10.0 [3.9–31.0] | 4.6 [2.7–14.0] | 0.004 |
| Alanine aminotransferase (IU/L) | 5.2 [2.3–16.8] | 3.1 [1.8–6.7] | 0.001 |
| Estimated GFR (mL/min/1.73 m$^2$) | 54.1±28.3 | 61.3±27.3 | <0.001 |
| Glucose (mg/dL) | 182 [134–261] | 190 [141–278] | 0.503 |
| Creatine kinase-MB (μg/dL) | 5.3 [1.0–21.1] | 10.7 [2.0–28.3] | 0.345 |
| Troponin-I (ng/mL) | 5.3 [0.4–42.8] | 7.1 [0.6–50.0] | 0.027 |
| Lactate >5 mmol/L | 115/189 (60.8) | 328/687 (47.7) | 0.002 |
| Central venous oxygen saturation (%) | 64.6±23.1 | 64.8±21.2 | 0.961 |
| Vasoactive inotropic score* | 33.0 [7.0–100.0] | 22.2 [10.0–73.2] | 0.096 |
| Cause of shock | | | <0.001 |
| Acute myocardial infarction | 163 (66.8) | 809 (84.4) | |
| Dilated cardiomyopathy | 28 (11.5) | 46 (4.8) | |
| Myocarditis | 13 (5.3) | 24 (2.5) | |
| Valvular heart disease | 8 (3.3) | 10 (1.0) | |
| Refractory VT/Vf | 8 (3.3) | 22 (2.3) | |
| Pulmonary thromboembolism | 8 (3.3) | 15 (1.6) | |
| Others | 16 (6.6) | 32 (3.3) | |

BP, blood pressure; CAOD, coronary artery occlusive disease; CKD, chronic kidney disease; CVA, cerebrovascular accident; GFR, glomerular filtration rate; LV, left ventricular; PAOD, peripheral artery occlusive disease; Vf, ventricular fibrillation; VT, ventricular tachycardia.
Results are shown as mean±standard deviation or median [interquartile range] for continuous variables and n (%) or n/total n (%) for categorical variables.
*Vasoactive inotropic score was calculated as dopamine dose (ug/kg/min)+dobutamine dose (ug/kg/min)+100·epinephrine dose (ug/kg/min)+10·milrinone dose (ug/kg/min)+10000·vasopressin dose (U/kg/min)+100·norepinephrine dose (ug/kg/min).

AMI]. In addition, as the difference in revascularization could also be a potential confounder, the subgroup of patients with CS caused by AMI (AMI-CS) were further stratified according to the revascularization status, and an interaction analysis was performed. Proportional hazards assumption was tested with Schoenfeld residuals, and was found not to be violated. *P*-values <0.05 were considered statistically significant, and all statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

### Baseline characteristics

Among 1202 patients (mean age, 66 years; 69% men) with CS, 244 patients (20.3%) had thrombocytopenia at shock presentation, whereas 958 (79.7%) patients had normal platelet counts. Age and sex distribution did not differ significantly between groups, but patients with thrombocytopenia showed lower body mass index compared to those without. In addition, smoking rate, blood pressure, hemoglobin, eGFR, and troponin-I levels were lower, while total bilirubin, liver enzymes, and proportion of patients with lactate >5 mmol/L were higher in patients with thrombocytopenia. Regarding the cause of shock, AMI was less frequent in patients with thrombocytopenia compared to patients without (Table 1).

### In-hospital management and clinical outcomes

Among patients within the AMI-CS subgroup, revascularization was less frequently performed in thrombocytopenia group compared to normal platelet group (81.0% vs. 87.8%, $p$=0.001). However, mechanical circulatory support (intra-aortic balloon pump and/or ECMO), renal replacement therapy, and mechanical ventilation were more frequently required in patients with thrombocytopenia than in those without (all $p$ <0.05). Regarding clinical outcomes, the incidence of ischemic and hemorrhagic stroke did not differ significantly between groups, while GI bleeding and sepsis occurred more frequently in patients with thrombocytopenia compared to those without (10.5% vs. 3.8%, $p$=0.009 and 8.3% vs. 2.6%, $p$=0.013, respectively).

As a consequence, length of stay in ICU and hospital was longer in thrombocytopenia group (8 days vs. 4 days, $p$<0.001; 17 days vs. 10 days, $p$<0.001, respectively) among 801 (66.6%) patients who survived to discharge (Table 2). Overall, 30-day all-cause mortality was 30.9%, and it was significantly higher in patients with thrombocytopenia than in those without [40.2% vs. 28.5%, hazard ratio (HR) 1.51, 95% confidence interval (CI) 1.20–1.90, log-rank $p$<0.001) (Table 2 and Fig. 2).

In multivariable Cox model, every $10^3$/μL decrease of platelet count was associated with a 0.2% higher risk of all-cause mortality at 30 days (HR 1.002, 95% CI 1.000–1.003, $p$=0.021). Other independent predictors of 30-day mortality were age, LV ejection fraction <40%, eGFR, creatine kinase-MB levels, lactate >5 mmol/L, vasoactive inotropic score, the need for mechanical circulatory support, and the need for mechanical

**Table 2.** In-Hospital Management, Adverse Events, and Clinical Outcomes

| | With thrombocytopenia (n= 244) | Without thrombocytopenia (n=958) | *p*-value |
|---|---|---|---|
| In-hospital management | | | |
| Revascularization (among AMI patients) | | | 0.001 |
| PCI | 116/163 (71.2) | 678/809 (83.8) | |
| CABG | 11/163 (6.7) | 32/809 (4.0) | |
| No revascularization | 36/163 (22.1) | 99/809 (12.2) | |
| Mechanical circulatory support* | 161 (66.0) | 553 (57.7) | 0.023 |
| Renal replacement therapy | 89 (36.5) | 181 (18.9) | <0.001 |
| Mechanical ventilation | 159 (65.2) | 521 (54.4) | 0.003 |
| Adverse events during hospitalization | | | |
| Gastrointestinal bleeding | 14/133 (10.5) | 13/340 (3.8) | 0.009 |
| Hemorrhagic stroke | 3/133 (2.3) | 15/340 (4.4) | 0.404 |
| Ischemic stroke | 1/133 (0.8) | 10/340 (2.9) | 0.306 |
| Sepsis | 11/133 (8.3) | 9/340 (2.6) | 0.013 |
| Clinical outcomes | | | |
| Length of stay (days)† | | | |
| Intensive care unit | 8 [3–21] | 4 [2–10] | <0.001 |
| Hospital | 17 [8–40] | 10 [5–21] | <0.001 |
| 30-day mortality | 98 (40.2) | 273 (28.5) | <0.001 |

AMI, acute myocardial infarction; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.
Results are shown as mean±standard deviation or median [interquartile range] for continuous variables and n (%) or n/total n (%) for categorical variables.
*Mechanical circulatory support indicates implantation of intra-aortic balloon pump and/or extracorporeal membrane oxygenation, †Assessed in patients who survived to discharge.


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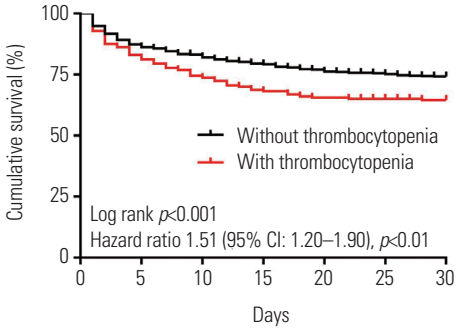
ventilation in our model (Table 3). In addition, restricted cubic spline plot showed that the platelet count is negatively associated with the risk of 30-day mortality, even when it is within its normal range (150–400·10$^3$/μL). The inflection point was 200·10$^3$/μL in our cubic spline model (Fig. 3).

Subgroup analysis showed that the risks of 30-day mortality for every 10$^3$/μL decrease of platelet count were consistent across all the subgroups (Fig. 4). Furthermore, when confined only to the patients within AMI-CS subgroup, platelet count was still independently associated with all-cause mortality at 30 days (HR 1.002, 95% CI 1.000–1.003, $p$=0.047; per 10$^3$/μL decrease), and the result did not differ by whether or not the patient had undergone revascularization ($p$ for interaction 0.709).




| Number at risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| With thrombocytopenia | 244 | 185 | 165 | 150 | 142 | 138 | 132 |
| Without thrombocytopenia | 958 | 787 | 733 | 685 | 640 | 607 | 582 |

**Fig. 2.** Cumulative survival of the participants according to the presence or absence of thrombocytopenia. Cumulative survival was estimated using the Kaplan-Meier method, and compared by the log-rank test.

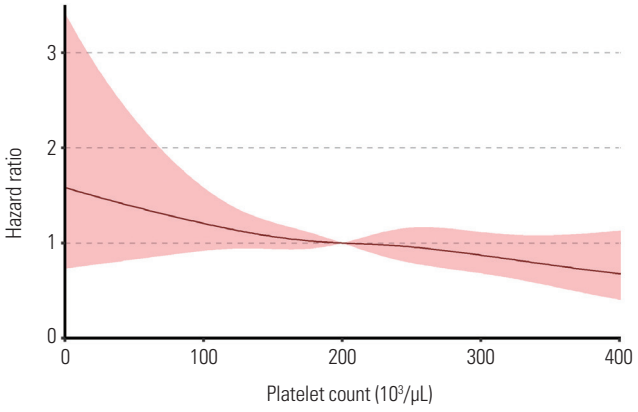



**Fig. 3.** Non-linear relationship between the platelet count and 30-day mortality. Restricted cubic spline plot shows hazard ratios with 95% confidence intervals for 30-day mortality according to the platelet count. The plot was fitted with Cox proportional hazards model, adjusting for age, sex, body mass index, current smoking, hypertension, diabetes, history of coronary artery occlusive disease, history of cerebrovascular accident, systolic blood pressure, left ventricular ejection fraction <40%, hemoglobin, total bilirubin, estimated glomerular filtration rate, glucose, creatine kinase-MB, lactate >5 mmol/L, vasoactive inotropic score, the need for mechanical circulatory support, and the need for mechanical ventilation.

**Table 3.** Predictors of 30-Day Mortality

| Variables | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | HR (95% CI) | $p$-value | HR (95% CI) | $p$-value |
| Platelet count (per 10$^3$/μL decrease) | 1.002 (1.001–1.003) | 0.003 | 1.002 (1.000–1.003) | 0.021 |
| Age (yr) | 1.022 (1.014–1.030) | <0.001 | 1.018 (1.007–1.030) | 0.001 |
| Men | 1.252 (1.011–1.549) | 0.039 | | 0.419 |
| Body mass index (kg/m$^2$) | 0.982 (0.953–1.011) | 0.222 | | 0.742 |
| Current smoking | 0.708 (0.556–0.902) | 0.005 | | 0.132 |
| Hypertension | 1.239 (1.008–1.523) | 0.041 | | 0.906 |
| Diabetes | 1.228 (0.998–1.511) | 0.053 | | 0.331 |
| History of CAOD | 1.109 (0.862–1.427) | 0.423 | | 0.862 |
| History of CVA | 1.255 (0.910–1.730) | 0.166 | | 0.753 |
| Systolic BP (mm Hg) | 0.989 (0.984–0.995) | <0.001 | | 0.076 |
| LV ejection fraction <40% | 2.537 (1.849–3.483) | <0.001 | 1.593 (1.116–2.274) | 0.010 |
| Hemoglobin (g/dL) | 0.929 (0.893–0.966) | <0.001 | | 0.374 |
| Total bilirubin (mg/dL) | 0.992 (0.932–1.055) | 0.797 | | 0.982 |
| eGFR (mL/min/1.73 m$^2$) | 0.985 (0.981–0.989) | <0.001 | 0.992 (0.987–0.997) | 0.002 |
| Glucose (mg/dL) | 1.002 (1.002–1.003) | <0.001 | | 0.076 |
| Creatine kinase-MB (μg/dL) | 1.004 (1.003–1.005) | <0.001 | 1.002 (1.001–1.004) | 0.003 |
| Lactate >5 mmol/L | 2.492 (1.952–3.181) | <0.001 | 1.578 (1.194–2.085) | 0.001 |
| Vasoactive inotropic score | 1.001 (1.001–1.002) | <0.001 | 1.001 (1.001–1.001) | <0.001 |
| The need for mechanical circulatory support | 2.913 (2.266–3.744) | <0.001 | 1.682 (1.249–2.265) | <0.001 |
| The need for mechanical ventilation | 6.094 (4.522–8.212) | <0.001 | 3.536 (2.493–5.016) | <0.001 |

BP, blood pressure; CAOD, coronary artery occlusive disease; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; LV, left ventricular.
Covariates were selected based on their heterogeneity between the study groups, statistical significance on univariable analyses, or previously known association with major clinical outcomes in patients with cardiogenic shock.

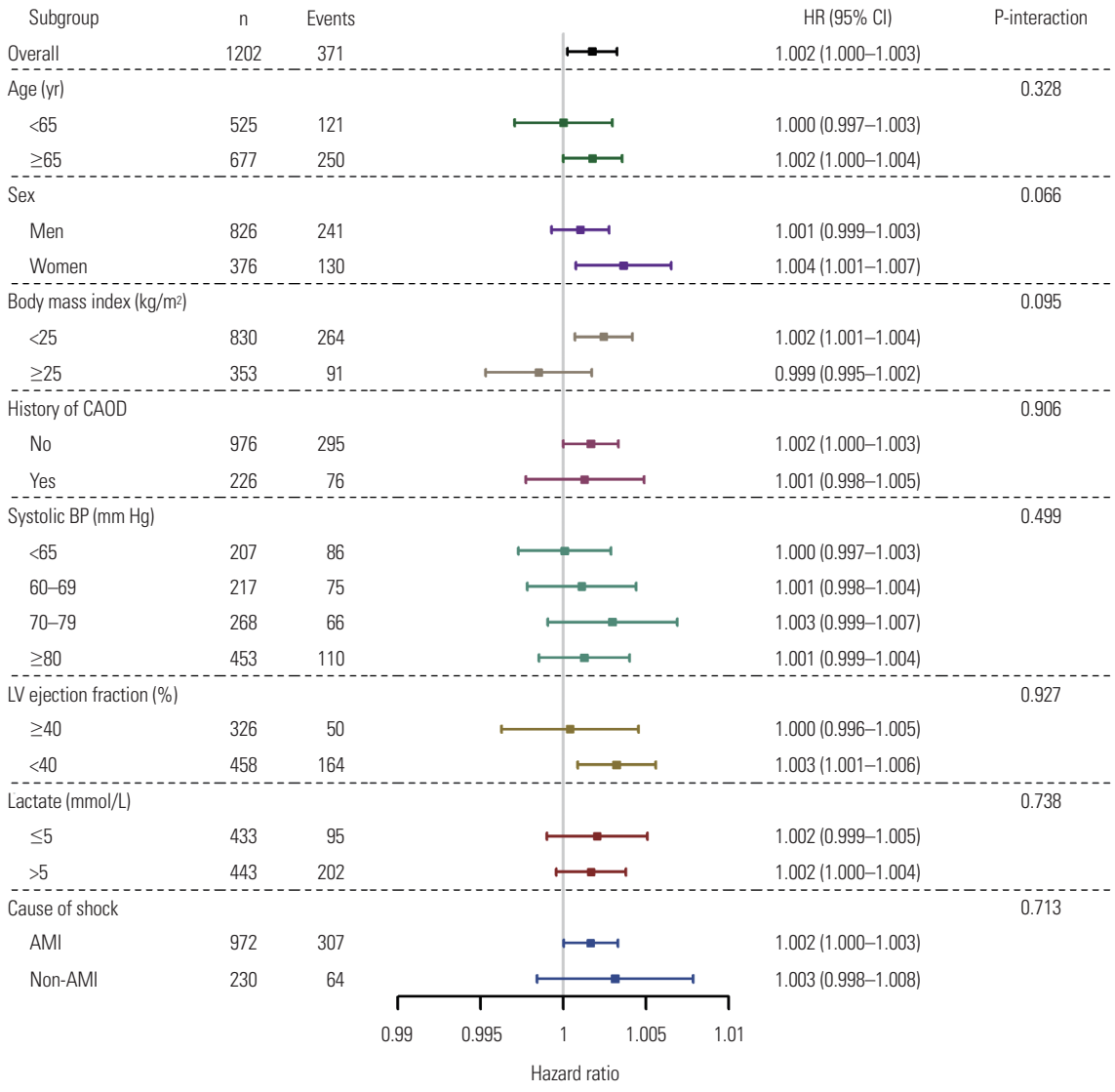



**Fig. 4.** Risk of all-cause mortality at 30 days for every $10^3$/μL decrease of platelet count in each subgroup. The results were adjusted for age, sex, body mass index, current smoking, hypertension, diabetes, history of coronary artery occlusive disease, history of cerebrovascular accident, systolic blood pressure, LV ejection fraction <40%, hemoglobin, total bilirubin, estimated glomerular filtration rate, glucose, creatine kinase-MB, lactate, vasoactive inotropic score, the need for mechanical circulatory support, and the need for mechanical ventilation, except for the variable stratified on. AMI, acute myocardial infarction; BP, blood pressure; CAOD, coronary artery occlusive disease; LV, left ventricular.

## DISCUSSION

The principal findings of the study were as follows: 1) one-fifth of the patients with CS had thrombocytopenia at shock presentation; 2) patients with thrombocytopenia at shock presentation showed lower blood pressure and hemoglobin level, worse hepatic and renal function, and higher lactate levels than patients without thrombocytopenia, suggesting worse clinical status; 3) patients with thrombocytopenia more frequently required mechanical circulatory support, renal replacement therapy, or mechanical ventilation and experienced adverse events, including GI bleeding and sepsis, compared to patients without thrombocytopenia; and 4) ICU and hospital stays were longer and 30-day mortality was higher in patients with thrombocytopenia than in those without. In addition, the platelet count remained an independent predictor of 30-day mortality after multivariable adjustment.

The proportion of patients with thrombocytopenia in our registry was 20%, which was relatively higher than that in previous studies.[12-14,23] This finding could be explained by the differences in baseline characteristics, as well as the higher severity of illness at shock presentation in our study's participants.

The detrimental effects of thrombocytopenia on clinical outcomes is probably attributed to increased bleeding complications, as demonstrated by more frequent GI bleeding among patients with thrombocytopenia in our study. This finding is consistent with those of previous studies, in which thrombocytopenia was associated with increased bleeding compli-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cation rates; however, these studies were not exclusively performed on patients with CS.[13,23] Although there are some contradictory results with regard to the association between thrombocytopenia and bleeding complications among patients with non-cardiac critical illnesses,[24,25] this discrepancy could be explained by the higher frequency of invasive procedures or more prevalent use of antithrombotic agents in patients with CS, all of which can potentiate the bleeding risk of thrombocytopenia.

In addition, the lower proportion of patients with AMI etiology, implicating less reversibility by timely interventions, and the higher proportion of patients who did not undergo revascularization of stenotic coronary arteries may also have contributed as key factors to the poorer prognosis of patients with thrombocytopenia. Moreover, the perceived high risk of bleeding in thrombocytopenia patients could have deterred interventionists from undertaking angioplasty and stent deployment for ambiguous coronary lesions. However, the association between platelet count and all-cause mortality at 30 days was consistent regardless of the revascularization status in AMI-CS patients in our analysis, implicating the possible presence of other additional mechanisms by which thrombocytopenia exerts negative effects on clinical outcomes in these patients.

Higher rate of sepsis among patients with thrombocytopenia might be one of those mechanisms.[7,26] As platelets are known to act as primary mediators of an immune system,[27,28] immune dysregulation due to thrombocytopenia may increase the risk of sepsis,[29,30] contributing to the higher risk of mortality in these patients. In addition, higher frequency of organ failure, including renal and respiratory, in our study might also have been caused in part by dysregulated inflammatory response in thrombocytopenia patients, as platelets frequently serve as inflammatory mediators and participate in neurohormonal and inflammatory responses that play a key role in the pathophysiology of CS.[31] However, the detailed mechanism by which platelets contribute to the development and progression of CS is not well-known, and warrants further investigation.

This study has several distinguishing points. First, to the best of our knowledge, this is the first study to demonstrate the effect of thrombocytopenia on clinical outcomes in patients with CS. Moreover, we identified a dose-response relationship between platelet count and all-cause mortality at 30 days, which further validates the results of our study. Finally, various outcome measures including 30-day mortality, length of stay in ICU and hospital, GI bleeding, stroke, and sepsis were analyzed, by which the reliability of the results could be enhanced.

However, our study also has some limitations. First, the causes of death were not identified, which made it difficult to analyze the association of thrombocytopenia with the direct causes of death in patients with CS. However, adverse events that might have significantly affected the hospital course were compared between groups, providing limited but meaningful information regarding the effect of thrombocytopenia on morbidity. Second, changes in platelet counts during the hospital course were not considered in our study. Moreover, the potential differences in medications, especially antithrombotic agents, between the study groups were not assessed in our analysis. As the differences in the use of antiplatelet agents or anticoagulants can influence the prognosis of patients with CS, further studies are required to identify whether thrombocytopenia is associated with poor outcome in CS regardless of antiplatelet or anticoagulant use. In addition, the time interval between symptom onset to hospital presentation or the door-to-balloon time among patients with AMI-CS were not considered in our analysis, which might also have influenced our results. Finally, only 30-day mortality was assessed in this study, and longer-term prognosis of CS patients with thrombocytopenia needs to be further investigated.

In conclusion, one-fifth of the patients with CS had thrombocytopenia at shock presentation in our study, and these patients showed lower blood pressure, worse renal and hepatic function, and poorer systemic tissue perfusion compared to patients without thrombocytopenia. Consequently, patients with thrombocytopenia experienced more frequent adverse events during hospitalization, and showed higher 30-day mortality than patients without thrombocytopenia. Moreover, low platelet count was an independent predictor of 30-day mortality in patients with CS in our study, along with age, LV ejection fraction <40%, eGFR, creatine kinase-MB, lactate >5 mmol/L, vasoactive inotropic score, the need for mechanical circulatory support, and the need for mechanical ventilation. Further, large-scale studies are required to investigate the consistency of the findings of our study in the long run, as well as the potential confounding effect of antiplatelet or anticoagulant use on the prognosis of patients with CS.

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