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Original Article

Intra-aortic balloon pump-related thrombocytopenia: Its effects on in-hospital mortality in cardiogenic shock patients

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Abstract

Aim: The present study aimed to evaluate the potential role of intra-aortic balloon pump (IABP)-related thrombocytopenia in patients with cardiogenic shock (CS) due to ST elevation myocardial infarction (STEMI) dien in hospital.

Material and Methods: We retrospectively included 142 consecutive CS patients who were treated with IABP support from September 2013 to March 2017 in a tertiary heart center. IABP-related thrombocytopenia was defined as a platelet count of <150.000 mm3 or a 50% or greater reduction in the platelet count from the baseline following the IABP's insertion. In-hospital, all-cause mortality was the primary endpoint.

Results: The incidence rate of thrombocytopenia was 19% (n = 27 patients). In-hospital mortality was significantly higher in patients who experienced thrombocytopenia compared to those who did not [22 patients (81.5%) vs. 56 patients (48.7%), respectively; p=0.004]. In a multivariate analysis, a decline in platelet count (OR: 1.037, 95%; CI: 1.011–1.064; p = 0.005) was found to be independently associated with in-hospital mortality. In a receiver operating characteristic curve analysis, the optimal cut-off value of the decline in platelet count for the prediction of in-hospital mortality was ≥ 18.2%, with a sensitivity of 60% and a specificity of 77% [area under curve (AUC): 0.70, 95%; CI: 0.61–0.78; p <0.001].

Conclusion: In the present study, we observed that the development of thrombocytopenia during IABP support was independently associated with in-hospital mortality in CS patients.

Keywords: Intra-aortic balloon pump; thrombocytopenia; cardiogenic shock; in-hospital mortality.

INTRODUCTION

The intra-aortic balloon pump (IABP) is a mechanical circulatory support device that is commonly used for hemodynamically collapsed patients following cardiogenic shock (CS) due to ST elevation myocardial infarction (STEMI) (1). During the last two decades, there have been great advancements in the technology of the IABP to reduce complications and improve patients' hemodynamic status. However, IABP-related complications are still frequently observed in intensive care units (2,3). Previously published studies have reported that thrombocytopenia is the most common complication in patients with IABP support (4,5). IABP-related thrombocytopenia may range from 42% to as high as 87%, depending on the defined criteria (5). In the current literature, there is conflicting data on whether IABP-related thrombocytopenia is a predictor of in-hospital mortality. This conflict is likely due to the inclusion of heterogeneous groups of patients (5-7). These contrary results have led us to investigate the potential role of IABP-related thrombocytopenia regarding in-hospital mortality in patients who presented with CS due to STEMI and who underwent primary percutaneous coronary intervention (PCI).

MATERIAL and METHODS

Data collection

In the present study, we retrospectively included 142 consecutive CS patients who were treated with IABP support from September 2013 to March 2017 in a tertiary heart center. Patients who presented with CS due to reasons other than STEMI, underwent thrombolytic therapy, had acute liver failure, had acute infection(s), or had hematologic and autoimmune disorders that affect

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platelet count were excluded from the study. In addition, we excluded patients who had died within 12 h after the insertion of the IABP and had developed heparin-induced thrombocytopenia. Patients' baseline demographic characteristics and related clinical information were collected upon admission. The local ethics committee approved the study protocol, and it was conducted per the principles of the Declaration of Helsinki. Informed consent was not needed due the retrospective nature of the study.

PCI and IABP procedures

Before undergoing coronary angiography (CAG), all patients received the standard medical treatment, including 300 mg of acetylsalicylic acid and a loading dose of either 300–600 mg of clopidogrel or 180 mg of ticagrelor. In all patients, CAG and PCI were performed via the femoral artery with the standard techniques by an experienced interventionist. Anticoagulation was given during all procedures. The infusion of glycoprotein inhibitors IIb/IIIa was left to the operator's choice. All patients received standard medical therapy in their subsequent management.

In all patients, the IABP was inserted through the femoral artery by an experienced cardiologist in the catheterization laboratory under fluoroscopic guidance. Per hospital protocol, sheathless versus non-sheathless insertion was left to the operator's decision. The balloon catheter's size (30 cc or 40 cc) was selected per the patient's size.

Platelet count analysis

Basic hematologic parameters, including platelet counts, were analyzed using an automatic hematology analyzer (Coulter LH Series, Beckman Coulter, Inc.). In all patients, a daily platelet count was obtained during the IABP support, per the hospital's protocol. The baseline platelet count was accepted as the last sample that was obtained prior to insertion of the IABP. A trained study coordinator analyzed the platelet counts until either the patient died or the third day after removal of the IABP. A diagnosis of IABP-related thrombocytopenia was accepted as a platelet count of < 150.000 mm3 or a 50% or greater reduction in the platelet count from the baseline. Heparin-induced thrombocytopenia was defined by performing a solid phase enzyme-linked immunosorbent assay for the detection of platelet factor 4 heparin-dependent antibodies.

In-hospital follow-up and definitions

In-hospital all-cause mortality was accepted as a death from any cause(s). A trained study coordinator who evaluated all hospital electronic files determined in-hospital mortality. STEMI was defined as the universal definition of the myocardial infarction guideline of the European Society of Cardiology (8). CS was defined as either a systolic pressure of < 90 mm Hg or a systolic pressure drop of ≥ 40 mmHg for more than 15 minutes without a new-onset arrhythmia, hypovolemia, or sepsis (9).

Statistical analysis

SPSS version 22.0 (IBM, Chicago, Illinois) was used to perform the statistical analysis. The normality of the data was assessed using the Kolmogorov-Smirnov test. The analysis of variance test was used to compare the continuous variables with normal distribution, which are expressed as mean ± the standard deviation. The categorical variables were expressed as numbers (percentages) and were compared using Fisher's exact test or $\chi 2$-test. The independent predictors of in-hospital mortality were identified after performing a multivariate logistic regression analysis using variables that showed a statistical significance in a univariate analysis. To determine the best cut-off value of decline in platelet count in predicting in-hospital mortality, a receiver operating characteristic (ROC) curve analysis was performed. A 2-sided p value of < 0.05 was considered significant. The alpha level that was used for analysis was < 0.05. The in-hospital mortality incidences of the thrombocytopenia and no thrombocytopenia groups were 81% and 48%, respectively. The post-hoc power of the study was calculated as 91.4%.

RESULTS

The incidence rate of thrombocytopenia in the study was 19% (n = 27 patients). The study population was divided into two groups: patients who developed thrombocytopenia and those who did not. Table 1 presents the baseline demographic characteristics and angiographic findings of all patients. Patients who developed thrombocytopenia tend to be older (p<0.05). Baseline demographic characteristics, medications, and thrombolysis in myocardial infarction (TIMI) flow both before and after the intervention were not different between the groups (p> 0.05 for each). In terms of echocardiographic findings, both groups were similar (p>0.05 for each). The duration of the IABP support was also similar between the groups. We noted that the incidence rate of in-hospital mortality was significantly higher in patients who developed thrombocytopenia compared to those who did not [22 patients (81.5%) vs. 56 patients (48.7%), respectively; p=0.004]. The laboratory findings of all patients are depicted in Table 2. The minimum platelet count was significantly lower, and the decline in platelet count was significantly higher in patients with thrombocytopenia (p<0.05 for each). Other laboratory findings were not different between the groups (p>0.05 for each).

In the univariate analysis, age, chronic renal failure, TIMI flow ≤ 2 after intervention, left ventricle ejection fraction, left ventricle end-systolic diameter, blood urea nitrogen, and decline in platelet count were related to in-hospital mortality. These variables entered into the multivariate analysis, which resulted in the following: A TIMI flow ≤2 after intervention (OR: 6.440, 95%; CI: 2.882–15.362; p <0.001), left ventricle ejection fraction (OR: 0.944, 95%; CI:0.921–0.969; p = 0.004), and a decline in platelet count (OR: 1.037, 95%; CI: 1.011–1.064; p = 0.005) were found to be independently associated with in-hospital mortality in the study population (Table 3). In an ROC analysis, the optimal cut-off value of the decline in the platelet count for the prediction of in-hospital mortality was ≥ 18.2%, with a sensitivity of 60% and a specificity of 77% [AUC: 0.70, 95%; CI: 0.61–0.78; p < 0.001] (Figure 1).

Table 1. Comparison of demographic, echocardiographic, and angiographic characteristics of all patients according to the occurrence of thrombocytopenia

	Thrombocytopenia (n= 27)	No thrombocytopenia (n=115)	P value
Age, years	72 (64–77)	64.0 (56–70)	<0.001
Female/male, n (%)	10(37)/17(63)	38(33)/77(67)	0.866
Hypertension, n (%)	16 (59.3)	51 (44.3)	0.237
Diabetes mellitus, n (%)	17 (63)	56 (48.7)	0.262
Smoking, n (%)	18 (66.7)	69 (60)	0.674
Hyperlipidemia, n (%)	7 (25.9)	47 (40.9)	0.223
Previous MI, n (%)	4 (14.8)	23 (20)	0.730
Previous CVA, n (%)	1 (3.7)	6 (5.2)	1.000
Previous AVR, n (%)	0	1 (0.9)	1.000
Previous CABG, n (%)	5 (18.5)	14 (12.2)	0.278
Previous PCI, n (%)	4 (14.8)	26 (22.6)	0.528
CHF, n (%)	2 (7.4)	12 (10.4)	0.479
COPD, n (%)	1 (3.7)	16 (13.9)	0.122
CRF, n (%)	10 (37)	45 (39.1)	1.000
PAH, n (%)	4 (14.8)	7 (6.1)	0.132
Anterior MI, n (%)	14 (51.9)	65 (56.5)	0.823
AF, n (%)	3 (11.1)	4 (3.5)	0.126
TIMI flow in the culprit before the intervention	24 (88.9)	106 (92.2)	0.408
TIMI 0, n (%)	3 (11.1)	9 (7.8)	0.408
TIMI 1, n (%)			
TIMI flow in the culprit after the intervention			
TIMI ≤ 2, n (%)	11 (40.7)	42 (36.5)	0.852
TIMI 3, n (%)	16 (59.3)	73 (63.5)	0.852
Intervened vessel			
LAD, n (%)	15 (55.6)	65 (56.5)	1.000
CX, n (%)	3 (11.1)	6 (5.2)	0.231
RCA, n (%)	3 (11.1)	18 (15.7)	0.400
Multivessel, n (%)	5 (18.5)	26 (22.6)	0.838
Antiplatelet agent			
Clopidogrel, n (%)	16 (59.3)	53 (46.1)	0.308
Ticagrelor, n (%)	11 (40.7)	62 (53.9)	0.308
Tirofiban usage, n (%)	8 (29.6)	30 (26.1)	0.894
IABP usage, day	3 (2–4)	3 (1–5)	0.992
LVEF, %	30 (25–40)	30 (25–40)	0.792
LVEDD, cm	5.8 (5.4–6.4)	5.6 (5.2–6.1)	0.124
LVESD, cm	4.7 (4.2–5.4)	4.3 (3.6–5)	0.106
TAPSE, cm	1.7 (1.5–2.0)	1.9 (1.6–2.2)	0.323
PASP, mmHg	32(25– 38)	35 (25–40)	0.755
MR ≥+3, n (%)	14 (51.9)	42 (36.5)	0.212
In-hospital mortality, n (%)	22 (81.5)	56 (48.7)	0.004

Continuous variables are presented as mean ± SD or median, nominal variables presented as frequency (%)
Abbreviations: MI, myocardial infarction; HT, hypertension; DM, diabetes mellitus; CVA, cerebrovascular accident; AVR, aortic valve replacement; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; PAH, peripheral arterial disease; AF , atrial fibrillation; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; LAD, left anterior descending; CX, circumflex; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; TAPSE, tricuspid annular plane systolic excursion; PASP, pulmonary artery systolic pressure; MR, mitral regurgitation

Table 2. Comparison of laboratory parameters of all patients according to the occurrence of thrombocytopenia

	Thrombocytopenia (n= 27)	No thrombocytopenia (n=115)	P value
Hematocrit, %	34.9 (31.7–41.1)	36.5 (32.2–42.0)	0.298
Hemoglobin, g/dl	11.8 (11.0–13.7)	12.0 (11.1–13.9)	0.486
WBC, cells/μL	17.0 (10.6–19.8)	17.3 (13.8–23.2)	0.289
Admission platelet count, mm3	229 (192–272)	255 (212–283)	0.132
Minimum platelet count, mm3	94 (77–100)	208 (169–236)	<0.001
Decline in platelet count, %	58.8 (48.9–71.2)	16.3 (14.7–19.5)	<0.001
Creatinine, mg/dL	1.60 (1.07–2.50)	1.26 (0.91–1.90)	0.180
BUN, mg/dL	29.0 (21.0–38.0)	24.0 (16.0–34.0)	0.297
Potassium, mEq/L	4.30 (3.80–4.70)	4.30 (3.90–4.80)	0.426
Sodium, mEq/L	136 (133–140)	136 (133–140)	0.969
AST, U/L	111 (62–236)	102 (41–342)	0.886
ALT, U/L	52 (35–111)	58 (26–110)	0.884
LDH, U/L	569 (394–846)	515 (279–905)	0.449

Abbreviations: WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate amino transferase; ALT, alanine amino transferase; LDH, lactate dehydrogenase

Table 3. Univariate and multivariate analyses of in-hospital mortality

	Univariate analysis			Multivariate analysis		
	P value	OR	95% CI	P value	OR	95% CI
Age	<0.001	1.079	1.038–1.122	-	-	-
CRF	<0.001	3.882	1.887–7.987	-	-	-
TIMI ≤2 after intervention	<0.001	9.545	4.014–22.701	<0.001	6.440	2.882–15.362
LVEF	<0.001	0.962	0.931–0.995	0.004	0.944	0.921–0.969
LVESD	0.022	1.837	1.211–2.787	-	-	-
BUN	0.007	1.031	1.008–1.054	-	-	-
Decline in platelet count	0.003	1.035	1.012–1.059	0.005	1.037	1.011–1.064

OR, odds ratio; CI, confidence interval
Abbreviations: CRF, chronic renal failure; TIMI, thrombolysis in myocardial infarction; LVEF, left ventricle ejection fraction; LVESD, left ventricle end-systolic diameter; BUN, blood urea nitrogen

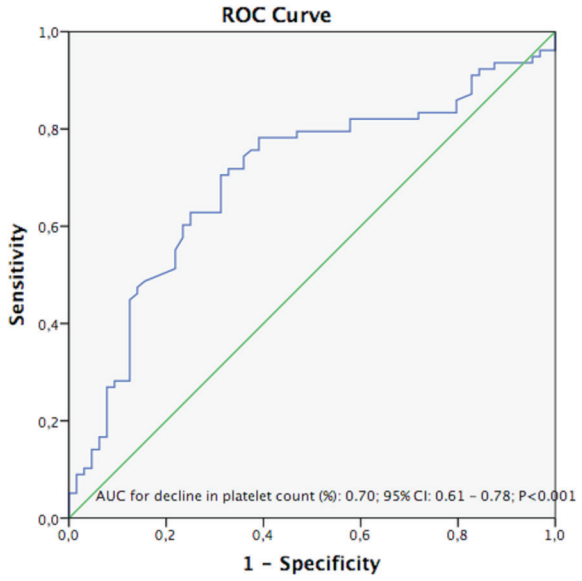

Figure 1. A receiver operating curve analysis of decline in platelet count for prediction of in-hospital mortality

DISCUSSION

In the present study, we observed that the development of thrombocytopenia during IABP support was independently associated with the in-hospital mortality of patients with CS. Notably; this finding may not be related to the anti-platelet and anticoagulation treatments that are extensively used in the current practice.

The IABP was introduced into clinical practice in 1968 (10). Since the development of a percutaneous technique by Bregman et al. in 1980 (11), it has become the most commonly used mechanical circulatory support device in hemodynamically unstable patients. However, IABP-related complications usually occur among these patients, which may limit the prolonged use of this support. Thrombocytopenia is the most commonly observed complication in patients who are undergoing IABP support, and it mainly occurs due to either the active destruction or consumption of platelets by the balloon pump (4–6). In a retrospective cohort study by Bream-Rouwenhorst et al., which included 107 patients,

IABP-related thrombocytopenia occurred in 57.9% of the patients (12). In addition, Vonderheide et al. reported that, in their study, thrombocytopenia developed in 47% of IABP patients compared with 12% of non-IABP patients (5). In our study, we observed that the incidence rate of thrombocytopenia was 19% (n = 27 patients), which was considerably lower than it was in the previously mentioned studies. We have considered that this finding might be due to either a shorter duration of IABP support or the use of a new generation IABP in our study compared to the previous studies.

As demonstrated in previous studies, thrombocytopenia is commonly seen in critical medical conditions, such as sepsis and CS (13,14). In addition, systemic anticoagulation is the standard medical treatment in patients with acute coronary syndrome (ACS) that is complicated with CS. It is well known that anticoagulation treatments, such as heparin or low molecular weight heparin, antiplatelet treatments, such as clopidogrel or ticagrelor, and glycoprotein IIb/IIIa inhibitors may induce thrombocytopenia (14). In our study, all patients were treated with the standard medical therapy in their subsequent management. However, no relation was found between thrombocytopenia and the use of antiplatelet and anticoagulation treatments in our study. Similarly, Roy et al., who demonstrated that systemic anticoagulation was not associated with IABP-related thrombocytopenia (4), might support our findings.

In the current literature, the association between IABP-related thrombocytopenia and in-hospital mortality has been reported with conflicting results. Per Vonderheide et al., IABP-related thrombocytopenia has not been related to elevated in-hospital mortality in heterogeneous groups of patients (5). By contrast, Sheng et al. and Gore et al. showed that IABP-related thrombocytopenia is a predictor of in-hospital mortality in patients with ACS (6,7). In our study, we also found that IABP-related thrombocytopenia might be an independent predictor of elevated in-hospital mortality in CS patients due to STEMI. Notably, our study only included patients with CS due to STEMI to create a more homogeneous group and to eliminate bias due to numerous confounding variables.

We could not evaluate whether IABP-related thrombocytopenia is associated with higher major bleeding events or thromboembolic complications; therefore, the contribution of IABP-related thrombocytopenia to in-hospital mortality was not elaborated. Our study findings thus require further investigation to understand the exact mechanisms of IABP-related thrombocytopenia on in-hospital mortality in patients with CS that is secondary to ACS.

Study limitations

Our study has the following limitations:

• It is retrospective in nature; therefore, major bleeding events and thromboembolic complications were not evaluated. However, our cohort was relatively large, and consecutive CS patients were enrolled.

• Our study was conducted in a one geographical area, which might single tertiary heart center, which might limit the generalizability of our results to other geographical areas.

• Although we performed a multivariate analysis to determine independent predictors of in-hospital mortality, some unmeasured confounding variables (including drugs given) might have affected the study's results.

• Our study only included patients with CS due to STEMI, meaning that the results might not be generalizable to all CS patients.

• Pseudo-thrombocytopenia may occur frequently secondary to samples taken in tubes with EDTA.

CONCLUSION

In the present study, we demonstrated that IABP-related thrombocytopenia is related to higher in-hospital mortality in CS patients. Based on our results, further research is needed to understand the potential role of IABP-related thrombocytopenia on in-hospital death in CS patients.

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