BRIEF REPORT

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Evaluation of Thrombocytopenia in Patients Receiving Percutaneous Mechanical Circulatory Support With an Impella Device

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OBJECTIVES: Evaluate the time course of thrombocytopenia in patients with Impella devices (Abiomed, Danvers, MA).

DESIGN: This was a retrospective, multicenter review of electronic medical records at a large hospital system from April 2018 to August 2020.

SETTING: Electronic medical records of patients at SSM Health hospitals were reviewed.

PATIENTS: Patients 18–89 years old admitted to an SSM Health hospital from April 2018 to August 2020 who received greater than or equal to 24 hours of percutaneous mechanical circulatory support (pMCS) with an Impella device were included. Exclusion criteria were use of other pMCS devices, history of heparin-induced thrombocytopenia (HIT), and presence of device upon transfer from an outside hospital.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Ninety-three patients were included. The median duration of pMCS was 63.5 hours. Thrombocytopenia occurred in 86% of patients and was evident 24 hours after device placement. The platelet nadir occurred 84 hours after device placement. Platelet recovery occurred 86.5 hours after device removal. The duration of thrombocytopenia was 156 hours. Signs of hemolysis were present in 44.09% of patients, were evident 12–24 hours after device placement, and resolved after device removal.

CONCLUSIONS: Thrombocytopenia occurred in the majority of patients and was evident 24 hours after device placement. The time course of thrombocytopenia mirrored that of hemolysis.

KEY WORDS: antithrombotic therapy; cardiogenic shock; heart-assist device; hemolysis; thrombocytopenia

Percutaneous mechanical circulatory support (pMCS) devices may be used to treat cardiogenic shock or facilitate high-risk coronary angioplasty by augmenting cardiac output and decreasing ventricular work (1–2). However, pMCS devices are accompanied by a number of complications, including thrombocytopenia, hemolysis, bleeding, and thrombosis.

Thrombocytopenia is a common complication of pMCS devices that may result from shear stress and platelet deposition on the device, critical illness, and antiplatelet and anticoagulant medications (e.g., heparin-induced thrombocytopenia [HIT]) (3–7). Thrombocytopenia may generate concern for HIT and result in a change from heparin to argatroban or bivalirudin, but HIT is uncommon during pMCS (5, 8). Evidence to guide such practices is limited and may increase the potential for bleeding and thrombotic events during pMCS.

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KEY POINTS

- **Question:** The purpose of our study was to evaluate the time course of thrombocytopenia and hemolysis in patients receiving pMCS with an Impella device.
- **Findings:** In this retrospective, multicenter review, thrombocytopenia occurred in 86% of patients and was evident 24 hours after device placement. Platelets recovered within 4 days of device removal. Signs of hemolysis were present in 44.09% of patients, were evident 12-24 hours after device placement, and resolved after device removal.
- **Meanings:** The time course of thrombocytopenia mirrors that of hemolysis during Impella support.

Up to 57.9% of patients receiving pMCS with intra-aortic balloon pumps (IABPs) have been found to develop thrombocytopenia (3–4). The onset of thrombocytopenia during IABP support usually occurs within 3 days of pump insertion, with platelet counts recovering after day 3 and returning to baseline by day 8 (3–4, 6). Data regarding the time course of thrombocytopenia in patients receiving pMCS with an Impella device (Abiomed, Danvers, MA) are deficient compared with data available for other devices. An observational study of 18 patients reported thrombocytopenia in 72% of patients with an onset less than 4 days after Impella placement and a mean platelet decline of 66% (5). This lack of data may lead to inaccurate assessments of the etiology of thrombocytopenia, and a more robust analysis of the time course of thrombocytopenia is necessary to inform clinical assessments and antithrombotic therapy management during pMCS.

The primary objective of our study was to evaluate the prevalence, onset, nadir, and duration of thrombocytopenia in patients receiving pMCS with an Impella device. Secondary objectives of our study included assessing the prevalence of hemolysis and HIT in patients receiving pMCS with an Impella device.

MATERIALS AND METHODS

This was a retrospective, multicenter review of electronic medical records at a large hospital system from April 2018 to August 2020. Patients 18–89 years old who received greater than or equal to 24 hours of pMCS with an Impella device were included in the study. Exclusion criteria were use of other pMCS devices, history of HIT, and presence of device upon transfer from a hospital outside of the hospital system.

A descriptive analysis of thrombocytopenia was performed to characterize the prevalence, onset, nadir, and duration of thrombocytopenia. Thrombocytopenia was defined as a reduction in platelets to less than 150,000/μL or greater than or equal to 50% decrease from baseline. Platelet nadir was defined as the lowest platelet count throughout the duration of pMCS. Platelet recovery was defined as median time to an increase in platelets to greater than or equal to 90% of baseline. Platelet counts were collected from baseline (prior to device placement) to 7 days following device removal. Additional data were collected to describe signs of hemolysis and prevalence of HIT. Signs of hemolysis included plasma-free hemoglobin (Hgb) greater than 40 mg/dL, lactate dehydrogenase (LDH) greater than 3× the upper limit of normal (ULN), haptoglobin less than 8 mg/dL, and total bilirubin greater than 1.2 mg/dL. 4T (magnitude of thrombocytopenia, timing of thrombocytopenia, thrombosis, other causes of thrombocytopenia) scores were calculated to estimate the probability of HIT. The 4T scoring system is described in **Supplemental Table 1** (http://links.lww.com/CCX/B71) (9). HIT was defined as a platelet factor-4 (PF4) antibody greater than 2 or a positive serotonin release assay (SRA) (10). The study protocol was approved by the Saint Louis University (approval number: 31558, approval date: November 18, 2020), SSM Health St. Louis (approval number: 20-11-1972, approval date: December 14, 2020), and University of Health Sciences and Pharmacy (UHSP) in St. Louis (approval number: 2021-07, approval date: March 9, 2021) Institutional Review Boards (IRBs). Informed consent was waived, and procedures were followed in accordance with the ethical standards of the Saint Louis University, SSM Health St. Louis, and UHSP in St. Louis IRBs and with the Helsinki Declaration of 1975.

Continuous variables were tested for normality with the Kolmogorov-Smirnov test. Data are presented as medians with interquartile ranges (IQRs), means with standard deviations (SDs), and numbers (percentages). The prespecified alpha was set at 0.05. Analyses were

TABLE 1.
Baseline Characteristics

Characteristic	All Patients (*N* = 93)
Demographics	
Age (year), mean (SD)	64.99 (11.17)
Height (inches), mean (SD)	67.52 (4.34)
Weight (kilograms), median (interquartile range)	81.6 (73–98.8)
Male, *n* (%)	60 (64.52)
Race, *n* (%)	
White	70 (75.27)
African American	21 (22.58)
Asian	1 (1.08)
Hispanic	1 (1.08)
Indication for Impella, *n* (%)	
Cardiogenic shock	67 (72.04)
High-risk coronary angioplasty	26 (27.96)
Type of Impella device, *n* (%)	
Impella CP	76 (81.72)
Impella 2.5	9 (9.68)
Impella RP	2 (2.15)
Impella 5 Left Direct (LD)	1 (1.08)
Medications, *n* (%)	
Antiplatelet medications	
Aspirin	86 (92.47)
Ticagrelor	42 (45.16)
Clopidogrel	24 (25.81)
Prasugrel	1 (1.08)
Anticoagulant medications	
Systemic heparin	72 (77.42)
Bivalirudin	7 (7.53)
Antibiotics	
Vancomycin	35 (37.63)
Piperacillin/tazobactam	22 (23.66)
Ampicillin	7 (7.53)
Sulfonamides	1 (1.08)
Other	
Acetaminophen	41 (44.09)
Purge solution	
Heparin 12.5 U/mL	9 (9.68)
Heparin 25 U/mL	59 (64.44)
Heparin 50 U/mL	32 (34.41)
No heparin	0 (0.00)
Comorbid conditions, *n* (%)	
Hypertension	70 (75.27)
Coronary artery disease	51 (54.84)
Hyperlipidemia	50 (53.76)
Obesity	41 (44.09)
Diabetes mellitus	41 (44.09)
Heart failure	28 (30.11)
Chronic kidney disease	20 (21.51)
Chronic obstructive pulmonary disease	16 (17.20)
Cancer	15 (16.13)
Chronic liver disease	4 (4.30)
Hepatitis C	3 (3.23)

performed using Microsoft Excel for Office 365 MSO (16.0.11328.20492) 64-bit (Microsoft Corp., Redmond, WA) and IBM SPSS Statistics for Windows Version 25 (IBM Corp., Armonk, NY).

RESULTS

One hundred fifty-five patients received pMCS with an Impella device. Ninety-three patients met criteria and were included in the analysis. Sixty-two patients were excluded from the analysis. Thirty-five patients were excluded for receiving pMCS less than 24 hours, 25 patients were excluded for use of other pMCS devices, and two patients were excluded for presence of device upon transfer from an outside hospital.

Baseline characteristics are summarized in **Table 1**. The most common indication for pMCS was cardiogenic shock (72.04%) followed by high-risk coronary angioplasty (27.96%). The Impella CP (86.36%) was most commonly used followed by the Impella 2.5 (10.23%), Impella RP (2.27%), and Impella 5 Left Direct (LD) (1.14%). The median duration of pMCS was 63.5 hours (IQR, 45–88.49 hr).

Most patients (63.44%) received a heparin 25 U/mL purge solution, and 72 patients (77.42%) received systemic heparin infusions. Neither bivalirudin nor argatroban was used in a purge solution. Other concomitant medications included aspirin (92.47%), ticagrelor (45.16%), clopidogrel (25.81%), and prasugrel (1.08%).

Thrombocytopenia occurred in 80 patients (86.00%). The median baseline platelet count was 220,000/μL (IQR, 178,000–279,500/μL). Platelets decreased immediately following device placement. Thrombocytopenia was present at 24 hours in 41 patients (44.09%). The median platelet count at 24 hours was 147,000/μL (IQR, 100,000–184,750/μL). The platelet nadir was 99,000/μL (IQR, 69,500–143,500/μL) and occurred 84 hours after device placement. The median duration of pMCS was 63.5 hours (IQR, 45–88.49 hr). Platelet recovery occurred 86.5 hours following device removal. The median duration of thrombocytopenia was 156 hours. Of the 80 patients who developed thrombocytopenia, 41 patients (51.25%) had already developed thrombocytopenia at 24 hours.

Platelet trends are summarized in **Figure 1**. The first 24 hours had the most data points (n = 85, n = 80, n = 64), with a decreasing sample size for time points past 24 hours. Hgb and hematocrit decreased immediately following device placement and remained lower than baseline for the duration of the study period (228 hr, or 7 d following device removal).

Signs of hemolysis were present in up to 44.09% of patients. Thirty-eight patients (40.86%) had an LDH greater than 3× ULN, 31 patients (33.33%) had a haptoglobin less than 8 mg/dL, and 41 patients (44.09%) had a total bilirubin greater than 1.2 mg/dL. LDH reached greater than 3× ULN 12 hours after device placement when the median LDH was 1,112 U/L (IQR 668.5–1,490 U/L) and fell below the ULN 104.5 hours after device removal when the median LDH was 228 U/L. LDH trends are summarized in **Figure 2**. The first 12 hours had the most data points (n = 52, n = 31), with a decreasing sample size for time points past 12 hours. Changes in haptoglobin were less uniform but followed a similar trend with a noticeable change at 12 hours and return to a normal value 56.5 hours following device removal. Total bilirubin reached greater than 1.2 mg/dL at 24 hours when the median total bilirubin was 1.3 mg/dL (IQR, 0.95–2.15 mg/dL). Unlike other hemolysis variables, total bilirubin remained elevated for the duration of the study period.

Based on the 4T score, the probability of HIT was low in 69 patients (74.19%), intermediate in 18 patients (19.36%), and high in six patients (6.45%). A PF4 antibody test and an SRA were ordered for 14 patients (15.05%) and three patients (3.23%), respectively. Nine patients (13.04%) with a low probability of HIT had a PF4 antibody and/or SRA ordered compared with three patients (16.67%) with an intermediate probability and two patients (33.33%) with a high probability of HIT. HIT was not confirmed for any patient. No patients had a PF4 antibody greater than 2 or a positive SRA.

DISCUSSION

Thrombocytopenia occurred in 86% of patients receiving pMCS with an Impella device. Platelets decreased rapidly following device placement, and thrombocytopenia was present at 24 hours. Hemolysis also occurred rapidly after device placement and recovered over a similar duration of time. Collectively, the time course of thrombocytopenia coincided with

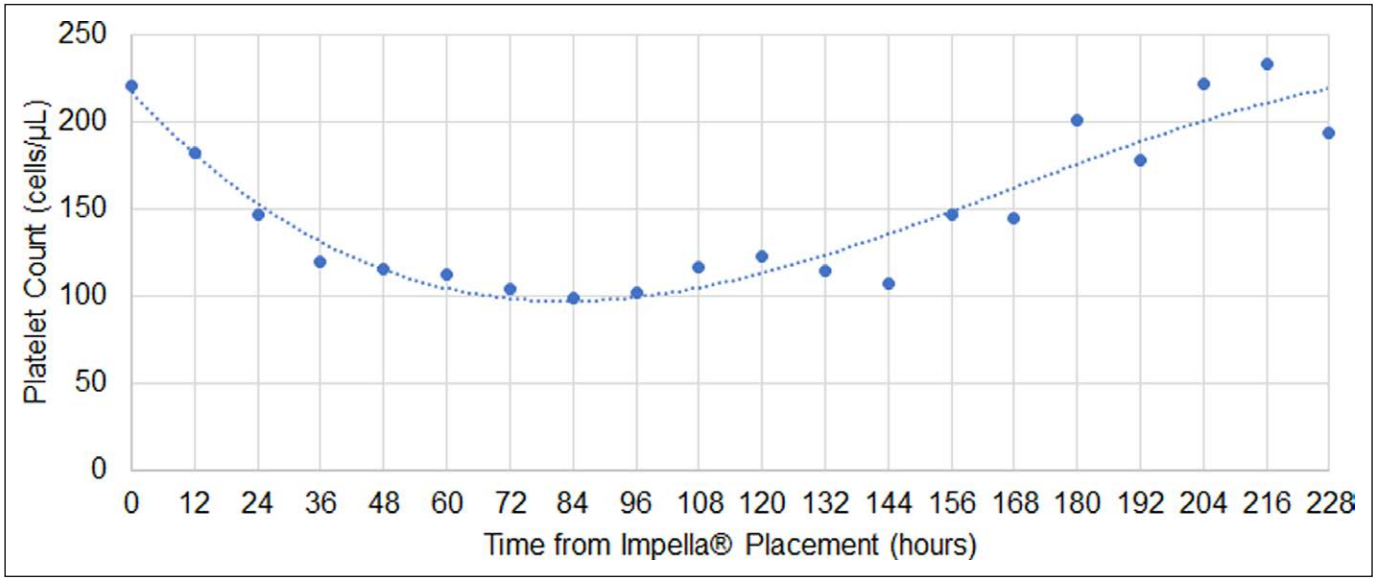

Figure 1. Platelet trends. Median platelets at baseline, during, and 7 d following Impella support.

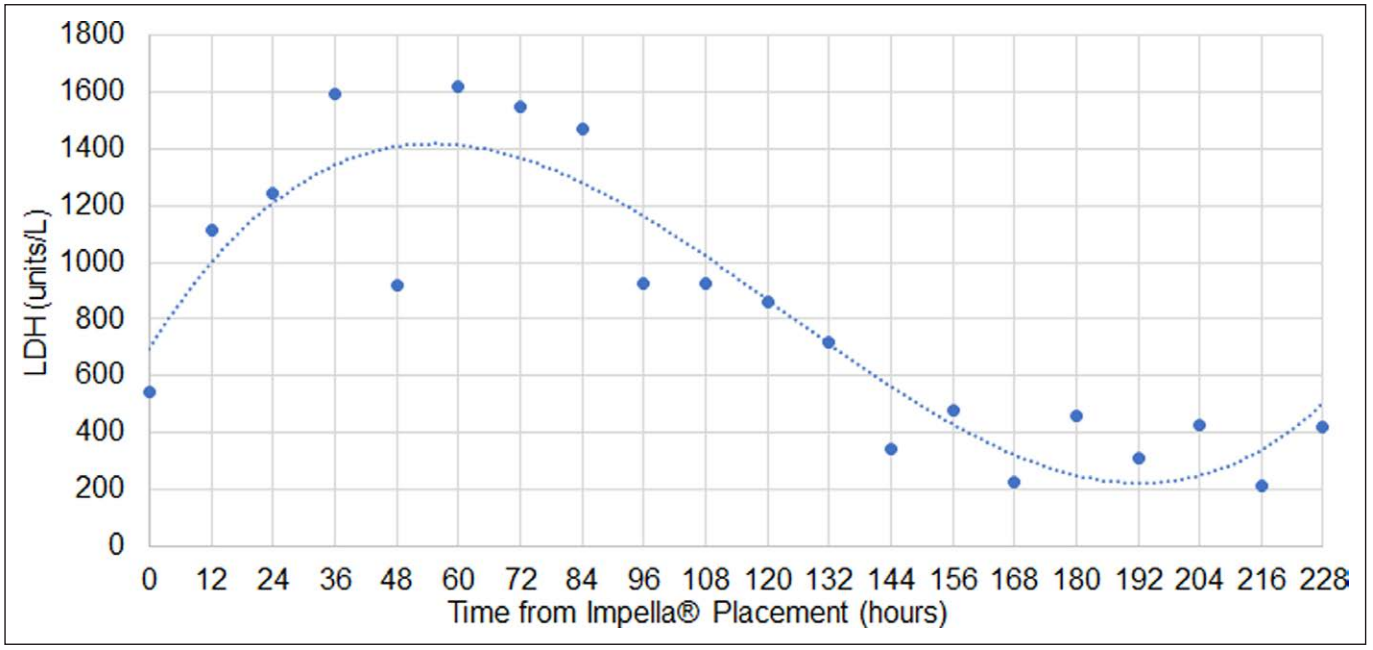

Figure 2. Lactate dehydrogenase (LDH) trends. Median LDH at baseline, during, and 7 d following Impella support.

changes in hemolysis laboratory variables and suggests thrombocytopenia is predominantly a consequence of the device rather than other etiologies.

Observations of thrombocytopenia and hemolysis in our study are mostly similar to other investigations. Newsome et al (5) observed a 72% prevalence of thrombocytopenia in a sample of 18 patients in a single-site, observational study. The onset of thrombocytopenia occurred within 4 days of device placement, and all patients showed decreasing platelet trends during device placement (5). Although the prevalence of 72% is lower than our study's prevalence of 86%, universal reductions in platelets were observed (5). Signs of hemolysis were present in 44.09% of patients in our study which corresponds to a similar observation of 62.5% in patients receiving greater than 6 hours of pMCS (11).

The time course of thrombocytopenia and hemolysis observed in our study implicates the device as the primary etiology. Microaxial support provided by the device increases shear stress on platelets and leads to platelet destruction. Platelets may also deposit on the device resulting in thrombocytopenia (3–7). Although data to describe heparin utilization during the 30 days prior to Impella insertion were not available in our sample, the rapid onset of thrombocytopenia after Impella insertion and prompt recovery after removal decrease the suspicion of alternative etiologies of thrombocytopenia.

Consistent with other studies, no patients developed HIT (5). Most patients had a calculated 4T score of less than or equal to 3 indicating a low probability of HIT. HIT tests were ordered for 13.04% of patients with low probability of HIT which may suggest poor risk stratification. Although the current sample is insufficient to estimate a true prevalence of HIT in patients receiving pMCS, the collective data indicate pMCS is associated with a low prevalence of HIT (5).

The high prevalence and early onset of thrombocytopenia observed with pMCS in this study should decrease providers' suspicion of HIT and encourage utilization of the 4T score to guide decisions to diagnose and presumptively initiate treatment for HIT. Use of bivalirudin or argatroban during Impella support is limited to case series, and substituting a direct thrombin inhibitor for heparin to prevent thromboembolic complications should be limited to patients classified as intermediate to high risk of HIT based on the 4T score (12–15).

To our knowledge, ours is the largest study characterizing thrombocytopenia with Impella devices. Detailed documentation of laboratory data throughout device support allowed a clear description of thrombocytopenia and hemolysis trends. Together, this information corroborates trends noted in smaller studies and adds to the body of literature describing thrombocytopenia in pMCS.

CONCLUSIONS

Thrombocytopenia occurred in 80 patients (86%) and was evident 24 hours after device placement. The time course of thrombocytopenia mirrors that of hemolysis.

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