

Henry Ford Health System

Henry Ford Health System Scholarly Commons

Pharmacy Articles

Pharmacy

8-1-2020

Safety and Efficacy of a Percutaneously Inserted Ventricular Support Device Purge Solution Heparin 25 U/mL

Christine Jiang

Misa M. Stuart

Charles T. Makowski

Douglas L. Jennings

Long To

Follow this and additional works at: https://scholarlycommons.henryford.com/pharmacy_articles

Safety and Efficacy of a Percutaneously Inserted Ventricular Support Device Purge Solution Heparin 25 U/mL

Annals of Pharmacotherapy

1–7

© The Author(s) 2020

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/1060028020944831

journals.sagepub.com/home/aop



Christine Jiang, PharmD, BCPS¹ , Misa Stuart, PharmD, BCPS¹,
Charles Makowski, PharmD, BCPS¹,
Douglas L. Jennings, PharmD, FACC, FAHA, FCCP, FHFSa, BCPS^{2,3}
and Long To, PharmD, BCPS¹

Abstract

Background: The Impella is a percutaneous ventricular assist device (pVAD) that provides temporary hemodynamic support to patients with cardiogenic shock or for protected percutaneous coronary intervention. The manufacturer recommends a 50-U/mL concentration of heparin purge solution (or 25 U/mL as an alternative), with systemic heparin to maintain therapeutic anticoagulation during device support. Concomitant use of systemic heparin with the purge solution may increase the risk of bleeding. **Objectives:** The primary objective of this study was to describe the prevalence of thrombosis and bleeding using a less-concentrated heparin purge solution (25 U/mL) in combination with systemic heparin therapy. **Methods:** This was a retrospective observational cohort study of patients who required at least 12 hours of pVAD support and received 25-U/mL concentration of heparin purge solution between January 1, 2014, and May 31, 2017. The primary end points were the rate of thrombotic and bleeding events. Secondary end points included the percentage of time within the therapeutic activated partial thromboplastin time (aPTT) range. Descriptive statistics were utilized for data analysis. **Results:** Of the 161 patients screened, 100 met inclusion criteria; 63% of patients experienced a bleeding event, with Bleeding Academic Research Consortium (BARC) type 3a being the most common. Median percentages of subtherapeutic and supratherapeutic aPTT values were similar between the bleeding and nonbleeding groups. Two patients experienced thrombotic events. **Conclusion and Relevance:** Based on our findings, the device thrombosis rate was 2% and the rate of major bleeding (BARC 3a and higher) was 35%. This study provides descriptive outcomes data of a lower-concentration heparin purge solution.

Keywords

percutaneous ventricular assist device, heparin, purge, ventricular support device

Introduction

The Impella device (Abiomed, Danvers, Europe) is a percutaneously inserted ventricular assist device (pVAD) indicated for hemodynamic support during high-risk percutaneous coronary interventions and cardiogenic shock in the setting of acute myocardial infarction (AMI) or severe heart failure. To maintain adequate purge pressure and prevent clot formation in the pVAD motor, a heparin-based purge solution that runs retrograde to the direction of blood flow is required. The manufacturer has historically recommended a purge solution using dextrose in water with heparin (50 U/mL) and systemic unfractionated heparin to provide optimal anticoagulation.¹ Recently, their recommendations were updated to include a heparin purge solution of 25 U/mL as an alternative option. However, no data exist describing the incidence of thrombosis or bleeding with the

lower heparin purge solution. Concomitant use with a heparin-based purge solution may pose a potential risk of excessive heparin exposure. Moreover, these patients are critically ill and likely carry other risk factors for bleeding, such as acute liver injury, recent myocardial infarction requiring stent placement and antiplatelet therapy, and chronic liver disease.^{2,3} Finally, the automatic rate adjustment of the heparin purge solution by the pVAD controller

¹Henry Ford Health System, Detroit, MI, USA

²NewYork-Presbyterian Hospital Columbia University Medical Center, New York, NY, USA

³Long Island University College of Pharmacy, New York, NY, USA

Corresponding Author:

Long To, Department of Pharmacy, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI 48201, USA.

Email: lto1@hfhs.org

may lead to unintended and unpredictable delivery of heparin, complicating management of systemic heparin therapy and potentially resulting in supratherapeutic exposure.

A previous case series conducted at our institution, which included 4 patients on a less-concentrated purge solution of heparin 25 U/mL in 5% dextrose, did not result in any bleeding episodes, thromboembolic events, or device thrombosis.⁴ We hypothesized that a less-concentrated heparin purge solution would reduce variability in the delivery of heparin, thereby decreasing the risk of supratherapeutic heparin exposure and iatrogenic bleeding.⁴ In another case series, 12 patients requiring pVAD support outside the catheterization laboratory were evaluated for supratherapeutic activated partial thromboplastin times (aPTTs) while receiving heparinized 50 U/mL purge solution without systemic heparin.⁵ Secondary outcomes included controller-mediated adjustments to the concentration of heparin purge solution, bleeding, and thrombotic events. Five patients had supratherapeutic aPTTs, 3 of whom required a decrease in the heparin purge solution concentration to 25 U/mL. Three patients experienced bleeding events. Because of the paucity of current data, this study was conducted in a larger population of patients who received a lower concentration of heparinized purge solution. The purpose of this study was to examine the safety and efficacy of a less-concentrated heparin purge solution (25 U/mL) in combination with systemic heparin therapy.

Methods

Study Population

This study was an institutional review board–approved, retrospective cohort analysis of patients at a large urban teaching hospital. Patients were included if they were at least 18 years of age, required at least 12 hours of pVAD support, and received a heparin-based purge solution. pVAD support devices included the following: Impella 2.5, Impella CP, Impella 5.0, and Impella RP. Exclusion criteria included history of heparin-induced thrombocytopenia, pregnancy, pVAD use limited to the catheterization laboratory, pVAD purge solution without heparin or with an alternative anticoagulant, or missing data points.

End Points

Primary end points were the proportion of patients who experienced thrombotic and bleeding events. The Bleeding Academic Research Consortium (BARC) definition was used to categorize bleeding events.⁴ The BARC definition is a 5-level categorical classification system based on the temporizing measures required for and the setting of the bleeding event. For this study, bleeding events were defined as BARC types 1 through 5. Thrombotic events were defined

by the following criteria: patients who underwent pump replacement, motor or pump thrombosis not requiring pump exchange, left-ventricular thrombosis, line clots, or receipt of tissue plasminogen activator for motor thrombosis. Secondary end points were percentage of patient time spent inside and outside of the protocol-specified therapeutic aPTT range. Events were recorded at the first occurrence.

Impella Protocol

At our institution, we implemented an anticoagulation protocol for patients with pVAD support. The standard purge solution for the pVAD device was heparin 12 500 U/500 mL (25 U/mL) in 5% dextrose. Dextrose concentration could be increased to 10% or 20% if necessary to achieve the manufacturer-recommended purge pressure of 300 to 700 mm Hg but was not adjusted in response to anticoagulation monitoring parameters. Systemic heparin was adjusted based on the institutional protocol for patients who require pVAD support, as described in the appendix. Our institution utilizes 2 heparin protocols: high intensity and low intensity. The high-intensity protocol has an aPTT target of 64 to 109 s, which correlates to an AntiXa range of 0.3 to 0.7 U/mL and is reserved for acute pulmonary embolism or deep vein thrombosis. Patients on an Impella device are initiated on the low-intensity heparin protocol, with a lower aPTT target of 55 to 75 s.

Data Collection

The electronic medical records of pVAD-supported patients who were hospitalized between January 1, 2014, and May 31, 2017, were reviewed for inclusion. Baseline demographics collected included sex, years of age, heparin dosing weight, days of Impella support, and hemoglobin value prior to initiating pVAD support. Relevant past medical history for factors that increased the risk of bleeding was collected: history of gastrointestinal bleed, intracranial hemorrhage, intraocular hemorrhage, recent surgery within the past 6 months, peptic ulcer disease, liver disease, international normalized ratio (INR) greater than 1.7 prior to initiation of pVAD support, or coagulopathies (factor V Leiden deficiency, platelet count less than 75 000/ μ L prior to pVAD initiation, hemophilia, or von Willebrand factor deficiency). Information about concomitant medications that increase bleeding risk was also collected: direct-acting oral anticoagulants, antiplatelet agents (aspirin, clopidogrel, prasugrel, ticlopidine, ticagrelor, cangrelor, cilostazol, or dipyridamole), or warfarin. Lactate dehydrogenase values during pVAD support were collected if available. Data on the indication for pVAD placement and the type of pVAD placed were collected. Evaluation of thrombotic and bleeding events were identified by a combination of structured keyword search (eg, thrombosis, clot, bleed, ooze) and

Table 1. Baseline Characteristics, Concomitant Medications, and Comorbidities That Increase Bleed Risk.

Characteristics	Bleeding events (n = 63)	No bleeding events (n = 37)	P value
Male, n (%)	41 (65)	27 (73)	0.51
Age, median (IQR), years	66 (57-76)	68 (59-75)	0.77
Weight, median (IQR), kg	83 (73.7-103.3)	89.2 (81.8-105.6)	0.09
Hemoglobin, median (IQR), g/dL	11.7 (10-13.1)	11.3 (9.8-12.9)	0.68
Documented history of major bleeding, n (%)	2 (3.2)	2 (5.4)	0.52
Indication for pVAD placement, n (%)			
Acute decompensated heart failure	21 (33.3)	15 (40.6)	0.48
Acute myocardial infarction	33 (52.4)	18 (48.6)	
Cardiac surgery: CABG	0 (0)	1 (2.7)	
Cardiac surgery: valve replacement	4 (6.4)	0 (0)	
Other	5 (7.9)	3 (8.1)	
Impella device, n (%)			
Impella 2.5	4 (6.3)	1 (2.7)	0.87
Impella CP	43 (68.3)	28 (75.7)	
Impella 5.0	10 (15.9)	6 (16.2)	
Impella RP	4 (6.3)	2 (5.4)	
Multiple Impella devices	2 (3.2)	0 (0)	
Concomitant medications that increase risk of bleeding, n (%)			
Aspirin monotherapy	17 (27)	9 (24)	0.82
P2Y12 inhibitor monotherapy	2 (3.2)	0 (0)	n/a
Dual antiplatelet therapy	33 (52.4)	18 (48.6)	0.84
Comorbidities that increase risk of bleeding, n (%)			
INR > 1.7 prior to initiation of pVAD	20 (32)	9 (24)	0.45
Active chronic liver disease	1 (1.6)	0 (0)	1
Peptic ulcer disease	0 (0)	0 (0)	1
Active coagulopathy	6 (9.5)	5 (13.5)	0.53

Abbreviations: CABG, coronary artery bypass grafting; INR, international normalized ratio; IQR, interquartile range; pVAD, percutaneous ventricular assist device.

manual review of each patient's progress notes and laboratory data.

aPTT values were considered evaluable if the laboratory specimens were obtained while the patient was receiving both systemic heparin and heparinized purge solution. Percentage of aPTT values within the therapeutic range (55-75 s) was determined by dividing the number of therapeutic aPTT values by the number of evaluable aPTT measurements for each patient. Analysis was conducted using descriptive statistics and completed using Microsoft Excel 2013.

Results

A total of 161 patients were screened for inclusion, 100 of whom were included in the study. The most common reason for exclusion was use of pVAD for less than 12 hours (n = 32), followed by patients transferred from an outside institution already on pVAD therapy (n = 19) and other exclusion criteria (use of purge without heparin, alternative anticoagulant in purge solution, missing data points; n = 10). In all, 68% of patients were male, and the median age

was 67 years; 51% of patients were placed on pVAD support secondary to an AMI (Table 1). Of the 100 patients, a majority were on antiplatelet therapy: 25% were on aspirin monotherapy, and 51% were on dual antiplatelet therapy with the following breakdown for the P2Y12 inhibitor—35 patients were on clopidogrel, 14 patients were on ticagrelor, and 2 patients were on prasugrel. Table 1 describes other concomitant disease states observed in these patients.

Patients were on pVAD for a median (IQR) of 59 hours (12-95). Most patients had an Impella CP (71%), followed by Impella 5.0 (16%), Impella RP (6%), and Impella 2.5 (5%). Two patients (2%) had 2 pVAD devices placed. The median (IQR) unfractionated heparin (UFH) purge and systemic infusion administration was 3.4 (2.6-4.6) and 5.1 (3.6-7.1) U/kg of total body weight per hour, respectively, with a net infusion rate (including both potential sources of heparin) of 8.8 (6.7-11.3) U/kg/h. The percentage of aPTT values within range per patient was 44.5% (17.5-60). In all, 63% of patients experienced a bleeding event, with BARC type 3a cases comprising the majority of bleeding events (26%), followed by type 1 and 2 (14% each), and type 3b (9%). No patient met criteria for BARC types 3c, 4, or 5

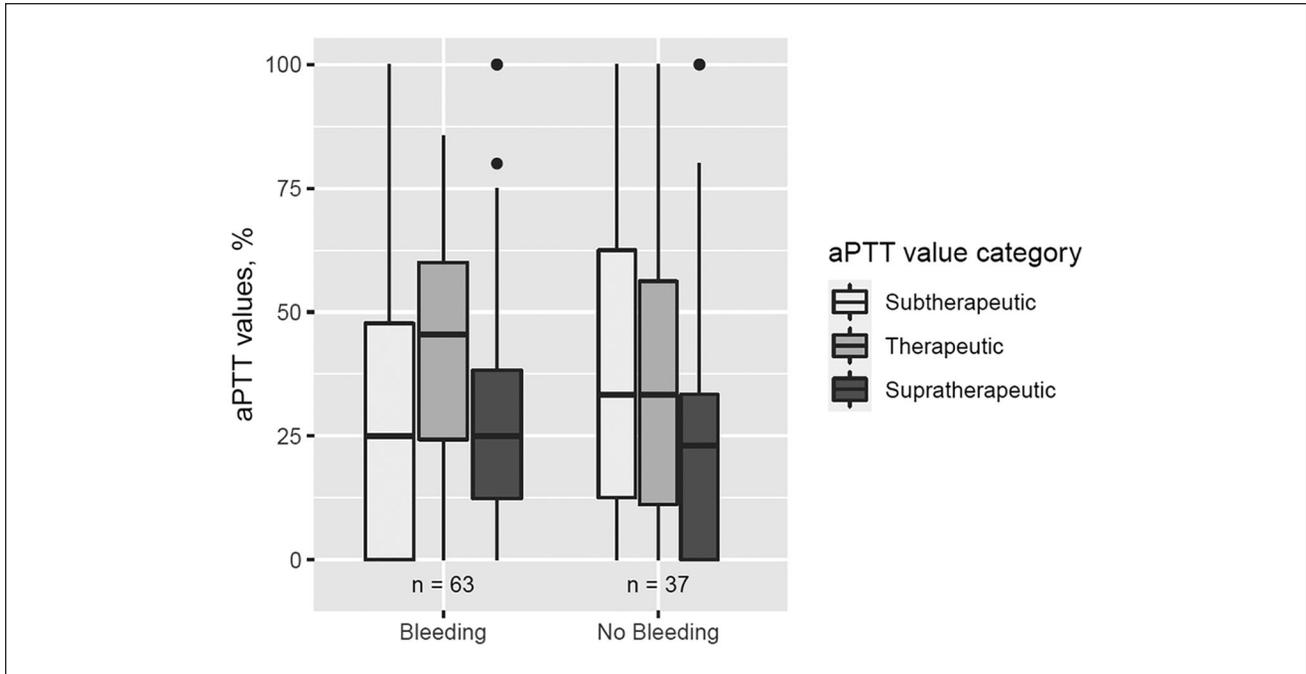


Figure 1. Median percentage of activated partial thromboplastin time (aPTT) values for patients with bleeding and without bleeding events (n, number of patients out of 100).

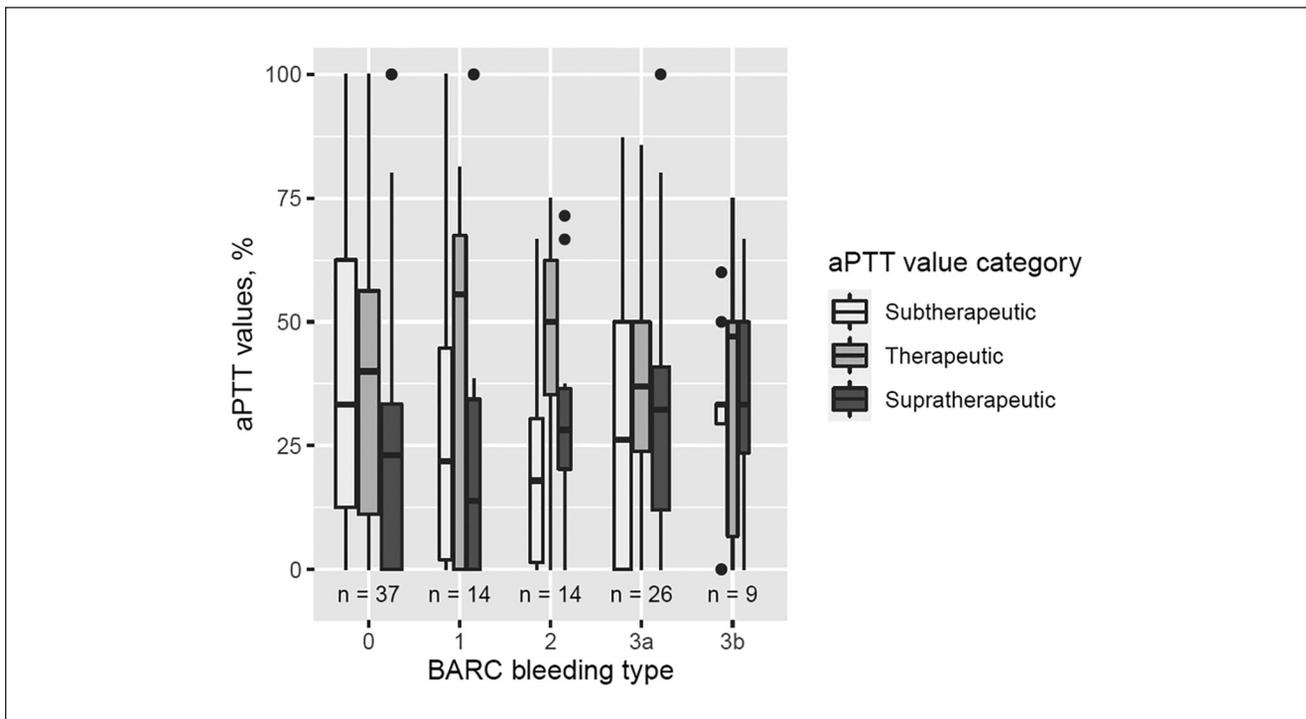


Figure 2. Median percentage of activated partial thromboplastin time (aPTT) values for patients based on Bleeding Academic Research Consortium (BARC) bleeding subtype (n, number of patients out of 100).

bleeding. Figure 1 illustrates the median percentage of aPTT values for patients with and without bleeding events, and Figure 2 illustrates the median percentage of aPTT

values for patients based on BARC bleeding subtypes that did not demonstrate a relationship between aPTTs and bleeding. At least 1 lactate dehydrogenase value was

Table 2. Heparin Dosages for Purge and Systemic Infusion Between Patients With and Without Bleeding Events.

Characteristic	Patients with bleeding event (n = 63)	Patients without bleeding event (n = 37)	P value
Purge solution heparin exposure, median (IQR), U/kg TBW/h	3.6 (2.8-4.6)	3.3 (2.1-4.5)	0.359
Systemic heparin exposure, median (IQR), U/kg TBW/h	4.7 (3.3-6.7)	6.2 (3.7-8.4)	0.119
Total heparin exposure, median (IQR), U/kg TBW/h	8.7 (6.7-10.2)	9.5 (6.9-12.8)	0.203
Purge solution heparin exposure, median (IQR), U/h	296.0 (243.7-356.1)	297.1 (205.5-402.4)	0.997
Systemic heparin exposure, median (IQR), U/h	407.5 (244.2-587.6)	530.5 (348.7-756.6)	0.080
Total heparin exposure, median (IQR), U/h	706.2 (542.9-947.1)	930.1 (598.6-1084.5)	0.109

Abbreviations: IQR, interquartile range; TBW, total body weight.

obtained for 48 patients and the highest value was recorded, with the median and interquartile range being 1140 IU/L (634-2224) for patients without bleeding events and 919 IU/L (613-2079) for patients with bleeding events. Two patients experienced a thrombotic event, both of which are described further in the Discussion section.

An analysis of patients with bleeding events versus those without bleeding revealed no significant differences in heparin dosages (Table 2). Of note, patients who did not experience a bleeding event had numerically higher systemic heparin exposure, resulting in a higher total heparin exposure overall. The median percentage of therapeutic aPTT values per patient was 40% for patients without bleeding events and 45% for patients with bleeding events. The percentages of aPTT values per patient that were supratherapeutic or subtherapeutic were similar between the bleeding and no bleeding subgroups.

A post hoc logistic regression was performed to establish known or potentially associated predictors of bleeding events (any severity and BARC 3a or worse) for the study population. Thrombotic events were not modeled, because of their low prevalence. Baseline or clinical characteristics preceding bleeding outcomes included in explanatory models were VAD indication, VAD type, baseline INR, presence of coagulopathy, duration of VAD support, percentage aPTT values in range, and concomitant antiplatelet or anticoagulant therapies. Candidate variables were incorporated in a hierarchical fashion based on data availability, biological plausibility, and established clinical knowledge; stepwise methods using covariate *P* value thresholds were not used. All constructed models of bleeding events, especially bleeding of any severity, demonstrated poor precision and unclear directionality and were not useful for descriptive purposes.

Discussion

The practice of anticoagulation for the Impella varies significantly in the United States. A recent survey by Reed et al⁶ reports that 52.4% of centers used the recommended manufacturer heparin purge concentration of 50 U/mL, and 41% of centers used lower heparin purge concentrations of

12.5 to 25 U/mL. To our knowledge, this is the first study to publish results on the incidence of bleeding and thrombosis of utilizing a lower-concentration heparin purge solution in patients requiring pVAD support. Based on the results of this study, a lower concentration of heparinized purge solution seems to confer low thrombotic events in these high-risk, critically ill patients. However, no definitive conclusions can be made because of the descriptive nature of this study. Of the 63 individuals who experienced a bleeding event, 35% experienced a major bleeding event (BARC type 3a/3b). Additionally, one-third of these individuals had concomitant comorbidities that increased the risk of bleeding (Table 1), 29% of patients had an INR >1.7 prior to initiation of pVAD, and the majority were on either dual antiplatelet therapy or aspirin monotherapy. Therefore, most of our patients had a higher baseline risk for bleeding prior to initiation of heparin therapy.

Interestingly, we found that patients in the bleeding group had numerically lower systemic heparin exposure than the nonbleeding group. We suspect that this is a result of conservative management because of known or suspected bleeding events. Our management of bleeding with the Impella is to decrease the rate of heparin infusion for supratherapeutic aPTT, hold systemic heparin for significant bleeding, or maintain lower dose to avoid worsening bleeding. Because of limitations with retrospective chart review, we are unable to provide an accurate assessment of the clinical decision made in regard to heparin adjustments in the bleeding group. However, the lower systemic heparin dose seems to align with clinical practice in patients with bleeding events. In addition, the bleeding group also had a higher percentage of patients with supratherapeutic aPTT (Figure 1). As a result, the heparin dosage would have to be decreased per protocol. With 63% of overall bleeding incidents and 35% with major bleeding, it would seem appropriate that the bleeding group has a slightly lower systemic heparin infusion dose.

A recent cohort study found significantly higher risk of in-hospital major bleeding with use of microaxial left VAD (LVAD) when compared with use of intra-aortic balloon pumps (31.3% vs 16.0%; *P* < 0.001), with both access site

and non-access site bleeding higher in the LVAD group. These results were consistent when a variable analysis was conducted among patients with cardiogenic shock secondary to AMI.⁷ There were similar rates of major bleeding comparing our current study with the recently published cohort study by Dhruva et al.⁷ When considering these critically ill patients who are already at a high risk of bleeding, initiation of a higher-concentration purge solution may potentially place them at even greater risk of bleeding events.

One of the patients who experienced a thrombotic event in our study was a 32-year-old man with past medical history significant for nonischemic cardiomyopathy, chronic systolic heart failure (ejection fraction 20%), and portal vein thrombosis who was transferred to our institution for evaluation of advanced heart failure therapies. He was placed on a pVAD secondary to cardiogenic shock because of his advanced heart failure. Of note, aPTTs measured while the patient was on the pVAD were all supratherapeutic. After 27 hours of pVAD use, the motor was clotted, and the patient was subsequently transitioned to a venoarterial extracorporeal membrane oxygenation device for hemodynamic support. The providers attributed the motor clot to an acute coagulopathy caused by multiorgan failure in addition to a hypercoagulable state at baseline, for which the workup was incomplete because the patient's clinical condition continued to decline despite maximal support. Because he was no longer a candidate for a permanent LVAD, the decision was made to withdraw support and initiate comfort measures only.

The second patient who experienced a thrombotic event in our study was a 62-year-old man who transferred to our facility with cardiogenic shock secondary to acute decompensated heart failure. A week after the pVAD was placed for support, the device appeared to be clotted. The patient was taken to the catheterization lab, where the device was noted to have flow obstruction and required an exchange. The aPTTs were within range prior to and during the time of the exchange. Unfortunately, the patient passed away later before a full workup could be completed to investigate the cause of the clot.

Strengths of this study include a fairly large sample size. However, it is important to note that this study was retrospective and descriptive in design and, therefore, is only hypothesis generating. Because this was a retrospective study, we were unable to determine the exact cause of the bleeding events that occurred. There may have been other confounders that could have increased the risk of bleeding, such as critical illness, liver dysfunction, or other concomitant medications (ie, glycoprotein IIb/IIIa inhibitors in post-MI patients). However, since the implementation of ticagrelor to our STEMI protocol, utilization of glycoprotein IIb/IIIa inhibitor is minimal. Any administration of glycoprotein IIb/IIIa inhibitor is from a single bolus and

unlikely to have a long-lasting effect for the duration of the Impella device.

Conclusion and Relevance

Within our study, 2% of patients experienced a thrombotic event involving the pump motor. Of the 63 bleeding events, 35 patients had clinically relevant bleeding (BARC 3a and 3b). Balancing the percentage of thrombosis versus that of bleeding events even with a lower-concentration purge solution suggests that additional bleeding avoidance measures should be investigated. Finally, our study provides descriptive outcomes data of a lower-concentration heparin purge solution.

Appendix

Impella Protocol

Manufacturer instructions for the pVAD recommend anticoagulation targets based on the activated clotting time; however, because of feasibility, systemic intravenous (IV) heparin is adjusted to achieve a goal aPTT of 55 to 75 s using a nurse-driven protocol. Bolus doses of IV heparin are not included in the protocol, to reduce the risk of bleeding. For protocol-based rate adjustments of the systemic IV heparin infusion, the heparin purge solution rate (in units per hour) is subtracted from the total IV heparin infusion rate. Any further adjustments is made to the systemic IV heparin infusion only. The aPTT is monitored every 6 hours for patients receiving both systemic and purge-based sources of heparin. For example,

A 75-kg female patient is admitted to the cardiovascular ICU (CVICU) with an Impella device in place. Her heparin purge solution is being delivered at 500 units (20 mL) per hour. Based on the heparin protocol, her net IV heparin infusion rate would be 900 units (12 U/kg body weight) per hour. The nurse would, therefore, administer the systemic IV heparin infusion at 400 U/h, for a final net rate of 900 U/h (heparin purge source of 500 U/h plus systemic IV heparin source of 400 U/h).

As previously noted, the pVAD controller automatically adjusts the purge solution to maintain adequate purge pressure for the device. The nurse will make hourly assessments of the purge solution rate and make necessary adjustments to systemic IV heparin infusion rate in order to maintain the intended net hourly dose of heparin. For example,

For the previous case, the patient's first aPTT value result after heparinization is 47 s. Based on the heparin protocol, the nurse will increase the systemic IV heparin infusion rate by 100 U/h, for a new final net infusion rate of 1000 U/h (heparin purge source of 400 U/h plus systemic IV heparin source of 600 U/h). Hourly adjustments will then be made to the systemic IV

heparin infusion until the next aPTT monitoring occurs 6 hours later.

For patients who require simultaneous left and right pVAD support, the nurse will have to account for the total amount of heparin the patient is receiving from both purge solutions. For example,

An 83-kg female patient is admitted to the CVICU with simultaneous biventricular support. Based on the heparin protocol, her net IV heparin infusion rate would be 1000 units (12 U/kg body weight) per hour. Her left heparin purge solution is being delivered at 400 units (16 mL) per hour and her right heparin purge solution is at 300 units (12 mL) per hour. The nurse would, therefore, administer the systemic IV heparin infusion at 300 U/h, for a final net rate of 1000 U/h (left and right heparin purge source of 400 and 300 U/h, respectively, plus systemic IV heparin source of 300 U/h).

If the total hourly heparin exposure were too high based on the patient's weight, the nurse would contact the physician to consider changing one of the purge solutions to a heparin-free dextrose product.

Authors' Note

This article has been presented in poster form at the American Society of Health-System Pharmacists (ASHP) Midyear Clinical Meeting in Orlando, FL (December 2017) and College of Clinical Pharmacy Annual (ACCP) Meeting Seattle, WA (October 2018).

Declaration of Conflicting Interests

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

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Christine Jiang  <https://orcid.org/0000-0003-3764-7572>

References

1. Abiomed. *Impella 2.5, 5.0, LD, and CP System Instructions for Use and Clinical Reference Manual*. Abiomed; 2020.
2. Eikelboom JW, Mehta SR, Anand SS, Xie C, Fox KAA, Yusuf S. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. *Circulation*. 2006;114:774-782. doi:10.1161/CIRCULATIONAHA.106.612812
3. Yang ZJ, Costa KA, Novelli EM, Smith RE. Venous thromboembolism in cirrhosis. *Clin Appl Thromb Hemost*. 2014;20:169-178. doi:10.1177/1076029612461846
4. Jennings DL, Nemerovski CW, Kalus JS. Effective anticoagulation for a percutaneous ventricular assist device using a heparin based purge solution. *Ann Pharmacother*. 2013;47:1364-1367. doi:10.1177/1060028013503623
5. Dietrich JN, Kazmi H. Bleeding risks in patients on percutaneous ventricular assist devices receiving two different dextrose concentrations of heparinized purge solution: a case series. *J Pharm Pract*. 2019;32:464-469. doi:10.1177/0897190018757148
6. Reed NB, DiDomenico JR, Allender EJ, et al. Survey of anticoagulation practices with the Impella percutaneous ventricular assist device at high-volume centers. *J Interv Cardiol*. 2019;2019:3791307.
7. Dhruva SS, Ross JS, Mortazavi BJ, et al. Association of use of an intravascular microaxial left ventricular assist device vs intra-aortic balloon pump with in-hospital mortality and major bleeding among patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA*. 2020;323:734-745. doi:10.1001/jama.2020.0254