Treating Heparin-Induced Thrombocytopenia in Patients Undergoing HeartMate 3 Left Ventricular Assist Device Implantation

Jonathan Eisenberger BSc[1], Shmuel Somer BSc[1], Eilon Ram MD[1,3], Eyal Nachum MD[1,3], Jonathan Frogal MD[2], Shany Levin MA[1,3], Jacob Lavee MD[1,3], Leonid Sternik MD[1,3], and Jeffrey Morgan MD[1,3]

[1]Department of Cardiac Surgery, Leviev Cardiothoracic and Vascular Center, Sheba Medical Center, Tel Hashomer, Israel
[2]Department of Anesthesiology, Sheba Medical Center, Tel Hashomer, Israel
[3]Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

ABSTRACT **Background:** Unfractionated heparin is the preferred anticoagulant used during open heart surgeries, including left ventricular assist device (LVAD) implantation. In cases in which patients are heparin-induced thrombocytopenia positive (HIT+), the accepted practice has been to substitute heparin with bivalirudin. This practice may be associated with significant bleeding and adverse outcomes.

Objectives: To review our experience with HIT+ patients who were heparin-induced thrombocytopenia with thrombosis negative (HITT-) and who underwent HeartMate 3 LVAD implantation using heparin intraoperatively rather than bivalirudin.

Methods: From 2016 to 2022, 144 adult patients were implanted with HeartMate 3 LVAD at our center. Among them, seven were detected as HIT+ but HITT- and therefore were prescribed intraoperatively with heparin and treated pre- and postoperatively with bivalirudin. We reviewed the preoperative, intraoperative, and postoperative characteristics as well as short-term mortality and the complication rates of these HIT+ patients.

Results: The median age of our cohort was 56 years (51–60), 71% were male (n=5), all were INTERMACS Level 1, and most were bridged to transplant (n=6, 86%). The 30-day mortality rate post-implantation was 0%. The average 24-hour chest drain postoperative output was 1502.86 ± 931.34 ml. There were no intraoperative pump thromboses, perioperative thromboses, cerebrovascular accidents, or gastrointestinal bleeding within the first 24 hours postoperative. One patient required a revision due to bleeding.

Conclusions: Intraoperative unfractionated heparin may be administered to patients who are HIT+ and HITT- while undergoing LVAD implantation. However, further investigation is required.

IMAJ 2023; 25: 757–759

KEY WORDS: cardiopulmonary bypass (CPB), heparin-induced thrombocytopenia (HIT), heparin-induced thrombocytopenia with thrombosis (HITT), left ventricular assist device (LVAD), platelet factor 4 (PF4)

Heparin-induced thrombocytopenia (HIT) is a severe complication that can occur when a patient is exposed to heparin [1-6]. There are several types of HIT; however, our research focused on HIT type 2 (HIT2). HIT2 differs from HIT type 1 (HIT1) in several ways. HIT2 is caused by an immune response of immunoglobulin G (IgG) antibodies, whereas HIT1 is mediated by a direct interaction between heparin and circulating platelets leading to platelet sequestration [7]. HIT1 tends to be clinically insignificant whereas HIT2 is clinically significant.

Under normal conditions, platelet factor 4 (PF4) is released from alpha granules when activated. Due to its positively charged nature, it binds to negatively charged heparin. This binding can produce the formation of PF4 IgG antibodies that are heparin-PF4 specific [8]. HIT2 occurs when IgG antibodies bind to the platelet FC receptor and activate the platelets, thus leading to further release of PF4. This reaction activates the platelets to release pro-thrombotic substances, such as thrombin, resulting in a vicious cycle causing hypercoagulation. This hypercoagulable state is very dangerous when performing cardiac surgery, especially when implanting an LVAD. Potential complications include cardiopulmonary bypass (CPB) circuit thrombosis and LVAD thromboses [9,10].

We describe our experience with seven HIT+ (heparin-induced thrombocytopenia with thrombosis negative (HITT-) patients who underwent seven LVAD implantations. Each of these patients was implanted with HeartMate 3 (HeartMate 3TM Abbott, Chicago, IL, USA) and was administered heparin intraoperatively.

PATIENTS AND METHODS

We conducted our research at the Sheba Medical Center, Israel. This single-center experience included seven HIT+

patients who underwent seven HeartMate 3 implantations administering unfractionated heparin as an anticoagulant intraoperatively and treated with bivalirudin preoperatively and bivalirudin and warfarin postoperatively. These seven patients were determined to be HIT+ using an ELISA assay. We followed these patients and collected data from October 2019 until April 2022. We collected and compared the preoperative, intraoperative, and postoperative characteristics as well as short-term mortality rates between these groups. All the data were collected from the Sheba Medical Center LVAD clinical database. This study was approved by our institutional review board. Due to the retrospective nature of the research, the review board waived the requirement to obtain patient consent.

Table 1. Patient demographics and preoperative characteristics

Characteristic	Value, n (%)
Age in years	56 ± 15.1
Male	5 (71%)
Female	2 (29%)
Body mass index, kg/m^2	26.87 ± 3.04
Implantable cardiac monitors	3 (43%)
Hypertensive heart disease	2 (29%)
Diabetes mellitus	2 (29%)
Smoking history	5 (57%)
Chronic obstructive pulmonary disease	0 (0%)
Previous cardiac surgery	2 (29%)
Extracorporeal membrane oxygenation	7 (100%)
Peripheral vascular disease	0 (9%)
Bridge to transplant	6 (86%)
INTERMACS level	7 (100%)

Table 2. Intraoperative characteristics

Characteristic	Value
Device type	HeartMate 3
Cardiopulmonary bypass time	
Mean	119.1 ± 62.2
Median	92
Interquartile range	81–165
Anticoagulant used	Heparin

PATIENT CHARACTERISTICS

We collected patient preoperative characteristics including age, sex, body mass index, previous cardiac surgery history, INTERMACS level, long-term treatment plan (bridge to transplant vs. destination therapy), and ischemic cardiomyopathy. Associated co-morbidities included diabetes mellitus, hypertension, chronic obstructive pulmonary disease, coronary heart disease, ischemic heart disease, chronic renal insufficiency, cerebrovascular accident, extracorporeal membrane oxygenation, smoking history, myocarditis, peripheral vascular disease, dyslipidemia, and hyperthyroidism [Table 1]. Average preoperative, intraoperative, and postoperative platelet counts included device type (HeartMate 3), CPB, and the anticoagulant used [Figure 1, Table 2]. Postoperative complications included re-operation for bleeding, gastrointestinal bleeding, and chest tube output at 24 hours postoperative [Table 3].

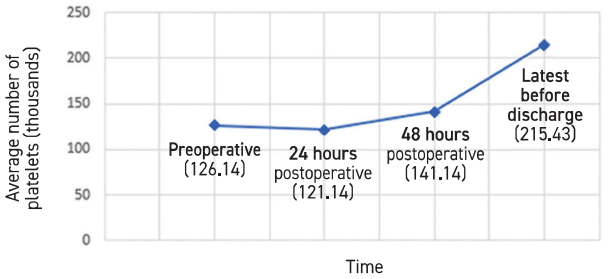
RESULTS

During our study, seven HIT+ patients underwent LVAD implantation (n=7). The median age was 56

Table 3. Chest tube output at 24 hours postoperative

Characteristic	Value, n (%)
Re-operation for bleeding	1 (14%)
Gastrointestinal bleeding	0 (0%)
Pump thrombosis	0 (0%)
Chest tube blood output (24 hours)	
Mean	1502.86 ± 931.34
Median	920
Interquartile range	855–590

Figure 1. Average platelet counts over time



years (interquartile range 51–60); five males (71%) and two female (29%). The patient demographics and operative characteristics are outlined in Table 1. The mean number of days the seven patients tested positive in an ELISA assay was 1 day preoperative. There were no observed intraoperative complications. In addition, the average platelet counts showed a minimal reduction at the 24-hour mark postoperative and showed an increase in platelets by the time of release from the hospital [Figure 1]. Postoperative gastrointestinal bleeding and pump thromboses were not observed, and there was an acceptable amount of blood drainage at the 24-hour mark post-surgery. One patient required reoperation due to bleeding [Table 3]. The short-term mortality rate was 0% as zero patients died in the 30-days postoperative.

DISCUSSION

The currently accepted practice to break the vicious cycle of hypercoagulation that HIT2 causes is to discontinue the use of heparin and to give bivalirudin as the attempted alternative. When performing cardiac surgery, specifically LVAD implantation, bivalirudin can lead to many complications, including life-threatening bleeding and hypercoagulation. However, heparin includes protamine as an antidote and can reverse the effects that heparin has on the blood. Bivalirudin lacks an antidote and requires waiting 25 minutes (bivalirudin's adult half-life). Alternatively, one can conduct hemodialysis, hemofiltration, and/or plasmapheresis to extract large amounts of bivalirudin from the blood and inactivate its effects [11]. However, when pressed for time, as is the case in LVAD implantation, this procedure can be a factor when deciding which anticoagulant to use. When blood is stagnant, bivalirudin is cleaved by thrombin causing hypercoagulation and thrombosis. This bivalirudin characteristic requires the surgeon and the perfusionist to constantly monitor proper blood flow. Constant awareness is required both at the surgical site and at the CPB machine thus leading to increased risk [12].

The main risk of HIT2+ patients receiving a dose of heparin during HeartMate 3 implantation is CPB circuit thrombosis and LVAD thromboses. In our study, we did not experience complications of this nature. In addition, when observing the chest tube output at the 24-hour mark postoperative, there was no significant difference in drainage compared with normal HeartMate 3 patient populations [Table 3]. We did not observe any mid-term postoperative complications such as gastrointestinal bleeds or stroke.

Our limited experience with seven HIT+ and HITT-suggested following a step-by-step treatment protocol of administering preoperative bivalirudin, intraoperative heparin, and postoperative bivalirudin with warfarin, which can be a safe alternative to the risk of severe bleeding when giving bivalirudin intraoperative.

CONCLUSIONS

When performing an LVAD implantation in HIT+ and HITT- patients, the complication and mortality rates of these patients can be decreased by administering a single dose of heparin intraoperatively.

Correspondence

Mr. J. Eisenberger
Dept. of Cardiac Surgery, Leviev Heart Center, Sheba Medical Center, Tel Hashomer 52621, Israel
Email: jonathaneisenberger1@gmail.com

References

1. Adatya S, Bennett MK. Anticoagulation management in mechanical circulatory support. *J Thorac Dis* 2015; 7 (12): 2129-38.
2. Naqvi SY, Jawaid A, Dao B, Falvey J, Vidula H, Gosev I, Thomas S. Management of heparin-induced thrombocytopenia using plasmapharesis in patients undergoing HeartMate 3 left ventricular assist device. *ASAIO J* 2022; 68 (9): e152-e155.
3. Shore-Lesserson L, Baker RA, Ferraris VA, et al. The Society of Thoracic Surgeons, The Society of Cardiovascular Anesthesiologists, and The American Society of ExtraCorporeal Technology: Clinical Practice Guidelines-Anticoagulation During Cardiopulmonary Bypass. *Ann Thorac Surg* 2018; 105 (2): 650-62.
4. Nuttall GA, Oliver Jr WC, Santrach PJ, et al. Patients with a history of type II heparin-induced thrombocytopenia with thrombosis requiring cardiac surgery with cardiopulmonary bypass: a prospective observational case series. *Anesth Analg* 2003; 96 (2): 344-50.
5. Nicolas D, Nicolas S, Hodgens A, Reed M. Heparin-Induced Thrombocytopenia. 2023 May 16. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. PMID: 29493955.
6. Zhou C-Z, Feng D-J, Fang Y, et al. Research on clinical characteristics and prognostic analysis of heparin-induced thrombocytopenia after surgery for acute type A aortic dissection. *J Cardiothorac Surg* 2021; 16 (1):96.
7. Ahmed I, Majeed A, Powell R. Heparin induced thrombocytopenia: diagnosis and management update. *Postgrad Med J* 2007; 83 (983): 575-82.
8. Levy JH, Winkler AM. Heparin-induced thrombocytopenia and cardiac surgery. *Curr Opin Anaesthesiol* 2010; 23 (1): 74-9.
9. Naqvi SY, Morris J, Falvey J, Gosev I, Barrus B, Vidula H. Management of type 2 heparin-induced thrombocytopenia prior to HeartMate 3 left ventricular assist device implantation: a case series. *J Am Coll Cardiol* 2019, 73 (9 Suppl 1) 2217.
10. Franchini M. Heparin-induced thrombocytopenia: an update. *Thromb J* 2005; 3: 14.
11. Goswami D, DiGiusto M, Wadia R, et al. The Use of bivalirudin in pediatric cardiac surgery and in the interventional cardiology suite. *J Cardiothorac Vasc Anesth* 2020; 34 (8): 2215-23.
12. Selleng S, Selleng K. Heparin-induced thrombocytopenia in cardiac surgery and critically ill patients. *Thromb Haemost* 2016; 116 (5): 843-51.