Abciximab/Heparin Therapy for Left Ventricular Assist Device Implantation in Patients With Heparin-Induced Thrombocytopenia

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Background. **Optimal anticoagulation strategy remains uncertain in patients with heparin-induced thrombocytopenia (HIT) and undergoing left ventricular assist device (LVAD) implantation. We describe our protocol of abciximab and heparin in these patients.**

Methods. **Our protocol is to administer abciximab, 0.25 mg/kg loading dose, followed by continuous infusion of 0.125 μg · kg^{-1} · min^{-1} throughout cardiopulmonary bypass. Full-dose heparin is then given with subsequent additional doses to maintain an activated clotting time of 400 seconds or longer. The abciximab infusion is stopped 15 minutes after heparin reversal with protamine, and platelets are transfused.**

Results. **Six patients underwent LVAD implantation with this protocol in our program. HIT was confirmed in 4 patients was suspected in 2, which was negative after the operation. One patient received a HeartMate XVE (Thoratec Corp, Pleasanton, CA) and the others received HeartMate II (Thoratec Corp). There were no thromboembolic complications. One patient required chest reexploration for bleeding and temporary right VAD support. Postoperative anticoagulation with argatroban was restarted on median postoperative day 3 (range, days 1 to 6) and warfarin was started on day 5 (range, days 3 to 12). Median postoperative intensive care unit stay was 9 days (range, 5 to 76 days), and hospital stay was 22 days (range, 18 to 132 days). After the initial LVAD implantation, 1 patient required HeartMate XVE LVAD exchange to HeartMate II and subsequent heart transplant, both of which were performed with the abciximab/heparin protocol. A HeartMate II device was explanted in another patient after myocardial recovery. The remaining 4 patients are alive on device support.**

Conclusions. **This is the first report of a novel abciximab/heparin protocol for LVAD implantation in patients with HIT. The preliminary results suggest the feasibility and safety of this protocol.**

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End-stage heart failure patients are at risk of developing heparin-induced thrombocytopenia (HIT) because of their frequent exposure to heparin [1]. HIT is an immune-mediated disorder characterized by the production of platelet-activating antibodies to antigenic heparin-platelet factor 4 complexes that paradoxically cause thrombocytopenia and is frequently complicated by venous or arterial thrombosis [2]. HIT accounts for 5% of patients receiving heparin therapy, although the incidence may be less in patients with thrombocytopenia after cardiothoracic operations [3].

Postponing elective operations until the patient tests negative for HIT antibodies has been suggested [1]. However, in rare circumstances in which an emergency or urgent left ventricular assist device (LVAD) operation is necessary in patients with HIT, alternative anticoagulation strategies for cardiopulmonary bypass (CPB) are used [4–7]. LVAD implantation is associated with a higher risk of perioperative bleeding complications compared with non-LVAD cardiac operations [8] as well

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Abbreviations and Acronyms

4T	= Thrombocytopenia, Timing of platelet count fall, Thrombosis or other sequelae, other causes of Thrombocytopenia
Ab	= antibody
ACT	= activated clotting time
aPTT	= activated partial thromboplastin time
AVR	= aortic valve repair
CABG	= coronary artery bypass grafting
CM	= cardiomyopathy
CPB	= cardiopulmonary bypass
CV	= cardiovascular
DVT	= deep vein thrombosis
FFP	= fresh frozen plasma
GPI	= glycoprotein inhibitor
HIT	= heparin-induced thrombocytopenia
HM	= HeartMate
i.v.	= intravenous
IABP	= intraarterial balloon pump
ICU	= intensive care unit
IJV	= internal jugular vein
INTERMACS	= Interagency Registry for Mechanically Assisted Circulatory Support
LA	= left atrium
LAA	= left atrial appendage
LVAD	= left ventricular assist device
MVR	= mitral valve repair
OD	= optical density
OHT	= orthotopic heart transplant
PE	= pulmonary embolism
PF4	= platelet factor 4
PFO	= patent foramen ovale
POD	= postoperative day
PRBC	= packed red blood cells
RVAD	= right ventricular assist device
SRA	= serotonin release assay
TVR	= tricuspid valve replacement
UFH	= unfractionated heparin

as postoperative thromboembolic complications such as stroke and device thrombosis.

Optimal perioperative anticoagulation is essential for patients with HIT who need urgent LVAD implantation; however, the data on this topic are sparse, and there are no established standards to guide therapy in this critically ill population. Abciximab, a glycoprotein IIb/IIIa inhibitor that strongly inhibits platelet aggregation, has been widely used in percutaneous coronary intervention. In this report we describe our strategy and experience in the use of abciximab and heparin in patients with HIT who underwent LVAD implantation.

Patients and Methods

A retrospective review was conducted of all patients with confirmed HIT diagnosis who received LVAD implantation and concomitant abciximab administration from January 2008 to July 2016. The Columbia University Medical Center Institutional Review Board approved this study, and individual consent was waived.

Diagnosis of HIT

When HIT was clinically suspected, an enzyme-linked immunosorbent assay method to detect antibodies directed against platelet factor 4 (PF4) and polyvinyl sulfate complex (anti-PF4/heparin antibody) was first sent. Because the sensitivity of enzyme-linked immunosorbent assay testing for anti-PF4/heparin antibody exceeds 90% but specificity is 74% to 89% [8], the diagnosis was confirmed by serotonin release assay (SRA), which has a high sensitivity (88% to 100%) and specificity (89% to 100%) [9]. Before the HIT diagnostic guideline was published in 2012 [10], SRA tests were not routinely performed, and the diagnosis of the HIT was made with positive HIT antibodies and clinical 4Ts score by consultations with hematologists. The 4Ts score system, based on thrombocytopenia, timing of platelet count fall, thrombosis or other sequelae, and other cause for thrombocytopenia, is a validated clinical prediction of HIT [11]. Sensitivity and specificity for HIT diagnosis are increased when combined with enzyme-linked immunosorbent assay [12]. The interpretation of clinical condition, laboratory tests, and final diagnosis was made by our hematology consultants.

Perioperative Anticoagulation Protocol

The preoperative argatroban infusion was stopped 4 to 12 hours before the operation. After creation of the preperitoneal pocket and driveline tract, abciximab (0.25 mg/kg) was administrated and followed by continuous infusion of 0.125 $\mu g \cdot kg^{-1} \cdot min^{-1}$ throughout CPB. Heparin (300 U/kg) was given 3 minutes after abciximab administration before CPB was established. Anticoagulation was monitored by activated clotting time (ACT), with a goal of greater than 400 seconds. ACT was measured every 30 minutes, and additional heparin was given to maintain ACT of at least 400 seconds. At the end of CPB, heparin was completely reversed with protamine. The abciximab infusion was continued for an additional 15 minutes and then stopped. A transfusion of 3 to 4 single donor units (18 to 24 units) of platelets was used to reverse platelet dysfunction. Other blood products were also given as needed.

Postoperative anticoagulation with argatroban was restarted when output from the mediastinal tube became serosanguineous, and transition to warfarin was initiated when the platelet count exceeded 150×10^3 μL for at least 2 days. Clinical decisions in each patient were made at the discretion of the attending surgeons.

Results

Among 463 patients who received continuous-flow LVAD implantations between January 2008 and July 2016, 6 patients underwent LVAD implantation using the HIT abciximab/heparin protocol. HIT was confirmed in 4 patients; the other 2 patients had undergone LVAD