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FEATURED ARTICLES

Prior hematologic conditions carry a high morbidity and mortality in patients supported with continuous-flow left ventricular assist devices

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BACKGROUND: Mechanical support leads to an increased risk of both bleeding and thrombotic events, but little is known about the risk of device support in patients with a baseline predisposition to these events. The aim of this study was to examine outcomes among patients with baseline hematologic conditions who underwent continuous-flow LVAD implantation (CF-LVAD).

METHODS: We retrospectively reviewed records of 286 patients who underwent CF-LVAD implantation at the Columbia University Medical Center between April 2008 and December 2013. Patients diagnosed with the following hematologic conditions were enrolled: idiopathic thrombocytopenic purpura (ITP); Factor V Leiden; elevated Factor VIII; heparin-induced thrombocytopenia (HIT); or undefined hypercoagulable state.

RESULTS: Of the 286 CF-LVAD patients implanted during the study period, 12 were considered to have a significant hematologic condition predisposing them to either bleeding or thrombotic events. The study included 5 patients with ITP, 1 with Factor V Leiden, 1 with elevated Factor VIII, 2 with HIT and 3 patients with undefined hypercoagulable state. Patients were supported for a total of 168.46 months, with a median of 10.76 months (IQR 4.78 to 21.36 months). There was a high frequency of thrombotic (0.57 event per patient-year), neurologic (0.36 event per patient-year) and bleeding (0.64 event per patient-year). Actuarial survival rates at 6 and 12 months were 81.8%, but fell to 49% at 2 years.

CONCLUSIONS: Patients with a history of prior hematologic conditions are at high risk for bleeding, thrombotic and neurologic events during device support, leading to early mortality. This case series questions the benefit of CF-LVAD in these patients and the appropriate management with regard to anticoagulation. Further studies on the outcomes of these patients are warranted.

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Continuous-flow left ventricular assist devices (CF-LVADs) have demonstrated a clear survival benefit over both optimal medical therapy and first-generation LVADs in patients with end-stage heart failure.[1,2] However, a significant number of adverse events have been reported, in particular stroke, device thrombosis and bleeding, which

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may jeopardize the benefit achieved by this technology.[3–6] With the increased use of CF-LVADs, appropriate patient selection has become a major factor in reducing potentially life-threatening complications.

Placement of a CF-LVAD generates a unique physiologic interface with the human body, leading to major effects on the hematologic system.[7] CF-LVADs activate the coagulation system, resulting in device-related thrombus formation. These thrombi may occur within the device itself (motor, inflow and outflow cannula) or in the aortic root, and may embolize to the brain or coronary arteries, leading to stroke and myocardial infarction (MI), respectively.[7,8] Indeed, a number of studies have recently reported a worrisome increase in the frequency of device thrombosis.[3,6,9] Although aggressive anti-coagulation is required to prevent thrombosis, its use must be balanced with CF-LVAD patients' already heightened risk of bleeding, which is due in part to acquired von Willebrand's disease that develops as a consequence of high shear stress from the pump apparatus.[10,11] In fact, bleeding is the most common complication during device support.[12]

It has been shown that baseline laboratory hematologic and coagulation abnormalities correlate with increased hospital mortality[13]; however, little is known about the impact of baseline hematologic conditions on outcomes after device implantation. In this study we assessed the outcomes of CF-LVAD patients who were diagnosed preoperatively (at time of evaluation for CF-LVAD) with an inherited, acquired or undetermined hematologic condition, predisposing them to bleeding and/or thrombosis.

Methods

We conducted a retrospective review of 286 patients with CF-LVADs implanted at the Columbia University Medical Center between April 2008 and December 2013. The study was approved by the institutional review board of the Columbia University Medical Center. Our initial cohort consisted of all patients who had a prior hematologic diagnosis, as defined in the blood disorder section of the standardized LVAD initial consultation note. In addition, patients with a hematology consult prior to device implantation were included in the initial cohort. The final cohort was limited to those patients for whom a hematology attending physician determined the patient to have a hematologic condition, either defined or undefined, which predisposed them to either bleeding or thrombosis prior to device implantation. Conditions included: (1) idiopathic thrombocytopenic purpura (ITP); (2) undefined hematologic abnormality; (3) elevated Factor VIII; (4) Factor V Leiden; or (5) heparin-induced thrombocytopenia (HIT). The diagnosis of ITP was made clinically based on the recognition of an isolated true thrombocytopenia without another obvious cause of thrombocytopenia. Patients were considered to have an undefined hematologic condition if they had at least one unprovoked catastrophic bleeding or thrombotic event. Factor V Leiden and elevated Factor VIII levels were diagnosed on the basis of widely accepted genetic testing and Factor VIII:C activity assay, respectively. Diagnosis of HIT was based either on a combination of HIT antibody positivity and a high pre-test probability using the 4T score or serotonin release assay positivity in an appropriate clinical scenario.

Baseline characteristics were obtained for all patients and outcomes data were collected by electronic medical record review. Outcome measures were collected based on the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) definition for bleeding and neurologic events. To better assess the total thrombotic risk, thrombotic events included INTERMACS definitions of arterial non-central nervous system thromboembolism, venous thromboembolic event and MI, when the event was thought to be attributable to a thrombotic or thromboembolic event. For purposes of this study device thrombosis was also considered a thrombotic event.

Statistical methods

All statistical analyses were performed using MEDCALC software, version 12.7.3 (MedCalc Software, Ostend, Belgium). Categorical variables are reported as frequencies, and continuous variables are reported as mean ± standard deviation, or as median with interquartile range when applicable.

Results

A total of 286 patients underwent CF-LVAD implantation during the study period, 25 of whom required hematologic evaluation and clearance before device implantation. Of the 25 patients who had hematologic consults prior to device implantation, 13 were excluded from analysis for the following reasons: 7 had a history of malignancy (blood and solid tumors); 2 had anemia; and 3 had thrombocytopenia, considered unrelated to an underlying hematologic condition (i.e., drug-induced). Twelve patients were considered to have a significant hematologic condition, predisposing them either to bleeding or thrombotic events, and were included in our analysis (Figure 1). The average age of patients was 50.5 ± 16.8 years (53.8% male), with 66.6% indicated for bridge to transplant and 66.6% with baseline ischemic cardiomyopathy. Eleven patients received a HeartMate II device and 1 patient received a HeartWare HVAD.

Of the 12 patients included in the study, there were 5 patients with ITP, 3 with undefined hypercoagulable state, 1 with Factor V Leiden, 1 with elevated Factor VIII levels and 2 with HIT (Figure 1 and Table 1). Patients were supported for a total of 168.46 months, with a median of 10.76 months (interquartile range [IQR] 4.78 to 21.36 months). While on support, 8 thrombotic or thromboembolic events occurred in 5 patients. These events included 3 device thromboses, 3 aortic root thrombi and 2 MIs. Five neurologic events, all cerebrovascular accidents (CVAs), occurred in 4 patients. Nine major bleeding events occurred in 5 patients, which included 4 post-operative bleeds, 2 gastrointestinal bleeds and 3 other bleeding events. Of note, these events occurred in a total of 10 patients, with some patients having multiple types of events (Tables 2, 3 and 4). Overall, the mortality rate of this patient population at the time of analysis was 41.67% (5 of 12 patients). Six- and 12-month actuarial survival rates were both 81.8%, but fell to 49% at 2 years. Of the 5 deaths, 2 occurred during the initial hospitalization (at 36 and 44 days on support, respectively) and 2 patients died between