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EDITORIAL COMMENT

Managing VAD Complications

Our Growth Industry*

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The growing population of patients progressing to end-stage heart failure paradoxically represents our field's greatest success and failure. Individuals with previously mortal heart diseases now survive as a result of improved diagnostics, therapeutic innovation, and focused patient care efforts across an array of cardiovascular conditions, particularly ischemic heart disease. Unfortunately, myocardial injury with its attendant neurohormonal activation too commonly results in an insidious deterioration in cardiac function that is slowed (but not halted) by contemporary heart failure treatments. The result of our success is increasing pressure on heart failure teams to devise new and effective strategies that mimic the benefits of transplantation for the larger cohort with advanced heart failure. With little doubt, broader application of mechanical circulatory support has played an important role in filling this void and arguably has been the most epidemiologically impactful treatment in the history of advanced heart failure therapy (1).

Over the past decade, clinical trials of next-generation continuous-flow left ventricular assist devices (LVADs) demonstrated lower mortality, fewer adverse events, and better device durability relative to older pulsatile technology. European and US regulatory approval acknowledge an important role for these devices in the treatment of unstable patients awaiting transplantation or as permanent treatment for end-stage heart failure. However, we have neither engineered complications out of the devices nor developed sufficiently clever monitoring and therapeutic strategies to prevent serious adverse events, such as stroke, infection, right heart failure, and thrombosis. As a recent example, 3 high-volume LVAD centers reported an increase in the incidence of LVAD thrombosis (2). Although a smoking gun has yet to be found to explain this observation, the complex interplay between fundamental principles of hemocompatibility, platelet activation, sheer stress in the device, surgical implantation technique, and post-operative management are all potential contributory culprits, individually or in combination. Regardless of cause, the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) has demonstrated the negative effect of VAD thrombosis on patient survival (3).

LVAD thrombosis can manifest in many ways and requires a thoughtful diagnostic evaluation to distinguish it from other common complications. Pump thrombosis spans a spectrum from asymptomatic hemolysis with hemoglobinuria and elevated lactate dehydrogenase/plasma free hemoglobin to recurrent heart failure resulting from elevated left ventricular filling pressures and reduced device output or catastrophic device stoppage. Imaging studies including gated cardiac computerized tomography and static or dynamic transthoracic echocardiography in which LVAD speeds are altered to assess changes in ventricular diameter and aortic valve opening play pivotal roles in the diagnostic armamentarium of the VAD clinician. Additionally, information from LVAD interrogation is highly relevant in the differential diagnosis of hemolysis and device dysfunction. Thrombus can form along the entire LVAD system: the inflow cannula in the left ventricle, the interior housing of the device, and the outflow graft connecting the pump to the aorta. Thrombus in each of these components may produce differential changes in measurable parameters that provide clues regarding thrombus location. For example, contemporary LVADs are

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designed to consume whatever power necessary to spin the rotor at set speed. Thrombus on the rotor necessitates additional power consumption to maintain the speed and can be detected via device interrogation.

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In this issue of the *Journal*, Scandroglio et al. (4) present a large, single center study of patients implanted with a HeartWare LVAD (HeartWare Inc., Framingham, Massachusetts) who experienced device thrombosis and provide a diagnostic framework for detection and localization of the thrombus and outcomes following treatment. The authors retrospectively reviewed 524 LVAD-supported patients to find those with alarms demonstrating either high-power consumption or low device flow. Pump thrombosis was diagnosed by integrating laboratory studies of hemolysis, LVAD alarms, cardiac imaging, and interpretation of device power and flow waveforms. Serial measurement of the acoustic spectra (pump noise) was also used in the diagnostic algorithm. Thrombosis localized inside the device impacting free movement of the rotor was characterized by elevated power consumption. Obstruction at the inflow and outflow portion of the device was characterized by low-flow alarms and the acuity of flow reduction-inflow cannula obstruction was found to be more abrupt, whereas occlusion of the outflow graft occurred later in the course of LVAD support and progressed more slowly. Various approaches to treatment were used including intensified antiplatelet therapy, device exchange, or LVAD "washout" following insertion of carotid protection devices. Outflow graft thrombosis was treated with stenting.

Blood flow abnormalities occurred in 100 patients (0.143 events per patient-year of support) in this cohort and were associated with a 30-day mortality of 30%, a rate similar to the 2-year mortality of the entire INTERMACS Registry population (5). Of those with pre-pump thrombosis (n = 27), there was an equal distribution of treatment with thrombolysis, washout, and device exchange. The latter two approaches were uniformly successful with cases of peripheral embolization using the washout technique. The authors note multiple treatment attempts were required in some of their inflow cannula obstruction cohort. The most common thrombus location was in the device proper (n = 70). Nine of these patients were treated with thrombolysis (33% success), 53 had device exchange (94% success), and 3 had their device removed for recovery. Seven of these patients died and 2 spontaneously resolved. Post-device outflow graft obstruction was uncommon (n = 4) and was treated successfully with stenting in 2 cases.

Algorithms for the diagnosis and treatment of VAD thrombosis have been developed, but the threshold for treatment, timing of intervention, and specific therapies remain largely empirical and center-dependent driven by variability in the clinical manifestations and the potential for treatment-related harm (6). In this study, for example, the initial pharmacologic approach for clot lysis was the glycoprotein IIb/IIIa inhibitor tirofiban that was demonstrated to be successful in 44% of patients and was more likely to favorably impact inflow cannula obstruction. The fact that this approach was successful at all suggests acute thrombus and raises the possibility that thrombolytic therapy may have resulted in a greater success, particularly when coupled with the neuroprotection device used at this center to prevent embolic stroke. Second, the use of pump washout in which the device is transiently turned off and then turned back on with the intent of dislodging inflow cannula thrombus is interesting but requires additional, systematic study to establish safety and efficacy. The authors used carotid protection devices during this maneuver and report detectable thrombus in the peripheral arterial system. Another consideration is that a first LVAD thrombosis is predictive of recurrent thrombosis. The authors do not report the frequency of recurrent device thrombosis in this cohort. There are likely poorly characterized patient phenotypes whose risk of thrombosis/rethrombosis is sufficiently high that LVAD exchange should be questioned. Finally, despite an 85% success rate in restoration of normal blood flow through the device, only two-thirds of the patients who entered the hospital with VAD thrombosis survived and were discharged.

Although VAD therapy has undeniably altered the prognosis of end-stage heart failure and restored patients to more normal functionality, it is not without cost to the patient, their families, and the healthcare delivery system. INTERMACS has recently reported that 70% of patients with LVAD have an infection, bleeding, device malfunction, stroke, or death within 1 year following implantation (5). These patients are rehospitalized 2 to 3 times annually for adverse events. Mechanical circulatory support will not have achieved its ultimate potential and goal of delivering outcomes competitive to cardiac transplantation until refinements in device technology and management strategies mitigate adverse events.

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