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Incidence and clinical significance of late right heart failure during continuous-flow left ventricular assist device support

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right heart failure;
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Destination therapy

BACKGROUND: Right heart failure (RHF) is an unresolved issue during continuous-flow left ventricular assist device (LVAD) support. Little is known about the incidence and clinical significance of late RHF during LVAD support.

METHODS: Between May 2004 and December 2013, 336 patients underwent continuous-flow LVAD implantation. Of these, 293 patients (87%) discharged with isolated LVAD support were included in this study. Late RHF was defined as HF requiring re-admission and medical or surgical intervention after initial surgery.

RESULTS: Late RHF occurred in 33 patients (11%) at a median of 99 days after discharge (range 19 to 1,357 days). Freedom from late RHF rates were 87%, 84% and 79% at 1, 2 and 3 years, respectively. RHF recurred in 15 patients. Three patients required right ventricular assist device insertion. Univariable Cox proportional hazards regression model showed diabetes mellitus (HR 2.05, 95% CI 1.03 to 4.06, $p = 0.04$), body mass index >29 (HR 2.47, 95% CI 1.24 to 4.94, $p = 0.01$) and blood urea nitrogen level >41 mg/dl (HR 2.19; 95% CI 1.10 to 4.36; $p = 0.025$) as significant predictors for late RHF. Estimated on-device survival rates at 2 years were 73% in the RHF group and 82% in the non-RHF group ($p = 0.20$). However, overall survival at 2 years was significantly worse in patients who developed late RHF (60% vs 85%, $p = 0.016$). This reduction was mostly attributed to worse overall outcomes in the bridge-to-transplant (BTT) population.

CONCLUSIONS: Late RHF is common after continuous-flow LVAD implantation, but does not affect survival during LVAD support. However, it is associated with worse overall outcomes in the BTT population.

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Continuous-flow left ventricular assist device (LVAD) use has become standard care among patients with advanced heart failure.[1,2] Clinical outcomes continue to improve through better patient selection, surgical techniques and peri-operative management.[3,4] The data from the Inter-agency Registry for Mechanically Assisted Circulatory Support (INTERMACS) show that current 1- and 2-year survival rates reached 80% and 70%, respectively.[5] These favorable mid-term results have encouraged the increased use of continuous-flow LVADs.

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Despite these improvements, right heart failure (RHF) after LVAD implantation remains an unresolved issue. Approximately 20% of patients develop some form of RHF after contemporary continuous-flow LVAD placement.[6] Numerous studies have shown that RHF after LVAD insertion is a serious complication associated with poor outcomes and have identified risk factors for RHF development.[5–8] However, most published data focused on RHF occurring during the early phase after LVAD implantation.

In contrast to the continued improvement in survival with use of continuous-flow LVADs, there is an emerging issue about late adverse events and re-admissions during long-term LVAD support.[9,10] Despite decreasing rates of adverse events compared with pulsatile-flow LVADs,[1,2] re-admission because of device-related or unrelated complications is still frequently required. Although cardiac pathologies, including heart failure and arrhythmia, are leading causes of re-admission,[9,10] less certainty exists with regard to how many patients will develop clinically significant RHF late after LVAD implantation and how the RHF will impact outcomes. Thus, the aim of this study was to assess the incidence and clinical significance of late RHF during continuous-flow LVAD support.

Methods

Our institutional review board approved this study. We retrospectively reviewed our experiences with continuous-flow LVADs at the Columbia Presbyterian Medical Center between April 2004 and December 2013. During this period, 336 consecutive patients with advanced heart failure underwent continuous-flow LVAD insertion as either a bridge to transplant (BTT) or as destination therapy (DT). Patients who required long-term mechanical support with contraindications to heart transplantation, including elderly patients and those with non-reversible comorbidities, were placed on an LVAD as DT. Of these, 293 patients (87%) who were discharged with isolated LVAD support were included in this study.

Device used and concomitant valve procedures

Devices used as LVAD support included 252 HeartMate II (Thoratec Corp., Pleasanton, CA), 6 VentrAssist LVADs (Ventracor, Ltd., Chatswood, NSW, Australia), 7 DuraHeart LVASs (TerumoHeart, Ann Arbor, MI), 4 DeBakey VADs (MicroMed Technology, Inc., Houston, TX) and 24 HeartWare HVADs (HeartWare International, Inc., Framingham, MA).

In patients with mild or greater aortic insufficiency, either aortic valve repair or replacement with a tissue valve was performed. In most cases, aortic valve was repaired by approximating the raphe of each leaflet. Patients with a mechanical valve in the aortic position underwent the aortic valve oversewn with a patch. Mitral valve repair was performed in patients with severe functional mitral regurgitation according to discretion of the surgeon. The tricuspid valve was repaired in patients with moderate or greater tricuspid regurgitation. In cases with severe leaflet restriction or leaflet destruction by pacemaker leads, tricuspid valve replacement with a tissue valve was chosen.

Post-implant device management

After device implantation, all patients received a standardized heart failure medical regimen that included neurohormonal antagonists, diuretics and anti-arrhythmic agents, based on individual clinical pictures. Anti-coagulation therapy with aspirin and warfarin was implemented. The target international normalized ratio range varied according to device type. In HeartMate II patients, the target range was 2 ± 0.5. Before discharge, volume status was medically optimized in all patients. Furthermore, echocardiography was performed at our institution routinely for pump-speed optimization to ensure middle interventricular septum position and intermittent aortic valve opening while maintaining no more than mild mitral regurgitation.[11]

After discharge, nurse practitioners managed anti-coagulation with the repeat testing frequency dictated by the ease or difficulty of maintaining the patient within their target range. Anti-coagulation therapy was withheld in the event of bleeding and resumed once bleeding had stopped. Patients received follow-up at 1 week after the initial discharge and monthly thereafter unless an issue necessitated more frequent visits. Clinic visit frequency varied among patients depending on individual medical issues and travel distances.

Definition and management of late RHF

Late RHF was defined as right heart failure requiring rehospitalization after indexed hospital discharge and medical or surgical treatments, including strengthening of diuretics, inotropic support and right ventricular assist device (RVAD) implantation. Detection of RHF was based on clinical findings. Typical signs and symptoms of RHF included edema, weight gain, ascites and jugular venous distention. Clinical examination was performed on all of the patients by heart failure cardiologists. In this study, heart failure related to device failure or suspected device failure, such as device thrombosis, inflow and outflow obstruction or drive-line fracture, was not considered as late RHF. Each event was captured and assessed retrospectively by at least 2 reviewers (K.T. and S.H.). Patients were enrolled in the late RHF group if both reviewers agreed. Disagreements in "late RHF" interpretation were resolved by consensus.

Patients who were hospitalized due to symptoms of heart failure routinely underwent: (1) interrogation of the device and hemolysis work-up to rule out device failure and thrombosis; (2) implantable cardioverter-defibrillator/pacemaker interrogation to identify presence of arrhythmia that may have exacerbated RHF; and (3) echocardiography for optimization of pump speed. Initial medical management included intensification of diuretic therapy. Patients with severe RHF, as defined by the presence of end-organ dysfunction, underwent right heart catheterization, with inotropic therapy initiated if needed. In patients with medically refractory RHF, RVAD implantation was then considered.

Data collection and follow-up

All clinical data were collected through a review of electronic medical records. For each patient, pre-operative variables that could correlate with survival were retrospectively collected. These included baseline demographics, medical history, laboratory values and echocardiographic and hemodynamic parameters.

Intra-operative variables included concomitant procedures at the time of LVAD implantation, cardiopulmonary bypass time, aortic cross-clamp time, blood product use and nitric oxide use at