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Late-onset right ventricular dysfunction after mechanical support by a continuous-flow left ventricular assist device

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BACKGROUND: Right heart failure (RHF) is a serious post-operative complication of left ventricular assist device (LVAD) implantation, with significant morbidity and mortality. Many clinical, hemodynamic and laboratory variables have been shown to have prognostic value for appearance of RHF. We sought to investigate the incidence of new-onset right ventricular dysfunction (RVD) complicating the long-term use of LVADs.

METHODS: We retrospectively examined all patients supported with a continuous-flow LVAD for >1 year at our center.

RESULTS: Twenty patients (mean age 54 ± 10 years, 95% men, 60% with ischemic cardiomyopathy, left ventricular ejection fraction 22 ± 6%, pulmonary capillary wedge pressure 23.5 ± 7.5 mm Hg, brain natriuretic peptide [BNP] 1,566 ± 1,536 pg/ml, serum creatinine 1.6 ± 0.64 mg/dl, furosemide dose 643 ± 410 mg/day) underwent long-term mechanical support as destination therapy support with a continuous-flow LVAD (HeartMate II) at our center. During follow-up (1,219 ± 692 days), 9 patients (45%) manifested symptoms and signs of RVD (increase in right atrial pressure [RAP], BNP and daily furosemide dose compared with the early post-operative period). In these patients, RAP was increased by 6.6 ± 2.6 mm Hg and BNP by 526 ± 477 pg/ml, whereas furosemide dose increased by 145 ± 119 mg. The mean and median times of RVD onset were 2.3 ± 1.5 and 2.1 years, respectively, after LVAD implantation (range 0.4 to 4.8 years). Four of these patients (44.4%) demonstrated further deterioration of RV function and died 73 ± 106 days (median 25 days, range 9 to 231 days) after first manifestation of RVD. Comparisons of baseline variables regarding medical history and clinical status did not demonstrate significant differences between the patients with or without RVD, including parameters related to RV function at the time of implantation.

CONCLUSIONS: Late-onset RVD is a complication of LVAD support, which can manifest several months to years from device implantation. This complication has significant adverse implications with regard to patient outcome. Prognostic factors need to be identified to follow and treat high-risk patients more efficiently.

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Right ventricular failure (RVF) is a common complication of left ventricular assist device (LVAD) implantation.[1] It is usually reported in the early post-operative period and is accompanied by significantly increased peri-operative

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morbidity and mortality and a compromised survival to and after heart transplantation (HTx).[2–6] The pathophysiologic mechanisms underlying the development of RVF after LVAD implantation are complex. The improved cardiac output with LVAD assistance leads to a sudden increase in right ventricular (RV) pre-load. The leftward shift of the interventricular septum distorts RV geometry and diminishes the systolic capacity of the RV.[7] Moreover, during cardiopulmonary bypass, complement activation and blood transfusions also increase pulmonary vascular resistance and result in increased RV after load.[2] The RV cannot acutely increase its contractility in these conditions of increased pre- and after-load and RV failure ensues.

Timely identification of the patients who will postoperatively develop RVF represents a significant therapeutic target. These patients may be given a higher priority for HTx, and the implantation of a right ventricular assist device (RVAD) may be considered earlier. Nevertheless, the potential of late RV dysfunction (RVD) presentation after prolonged LV mechanical support has been neither recognized nor investigated until now.

Our study was designed to investigate the incidence of RVD after long-term mechanical support with a continuous-flow LVAD.

Methods

Devices

An implantable, second-generation, continuous-flow HeartMate II LVAD (Thoratec, Pleasanton, CA) was implanted in all patients.

Study sample

Over the 7.5-year period from February 2006 through November 2013, 30 patients underwent durable mechanical circulatory support with a HeartMate II LVAD at our tertiary-care university institute. All patients who were supported with an LVAD for a period of >1 year were identified from our database.

Study design

Medical history, clinical, laboratory, echocardiography and hemodynamic data at LVAD implantation from all patients were recorded. The study was approved by our institution's ethics review board and conformed to the principles outlined in the Declaration of Helsinki.

Medical history and clinical status

The parameters recorded and evaluated were: age; gender; body mass index; body surface area (using the Dubois formula)[8]; etiology of heart failure; time from first heart failure (HF) diagnosis; New York Heart Association functional class; pre-operative need for positive inotropic agents or intra-aortic balloon pump support; presence of diabetes mellitus; left bundle branch block and cardiac resynchronization therapy; pre-operative treatment with a β-blocker, an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker or a mineralocorticoid receptor blocker; pre-operative dosing of furosemide; and estimated 1-year probability of survival, according to the Seattle Heart Failure Model score.[9]

With regard to follow-up, the parameters recorded were treatment doses of β-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers or mineralocorticoid receptor blockers as well as the frequency of resynchronization therapy.

Laboratory data

Plasma hemoglobin, white cell blood count, liver function tests, blood urea, creatinine and uric acid, total serum bilirubin, sodium, cholesterol and brain natriuretic peptide (BNP) levels were recorded and included in the analysis.

Echocardiography measurements

The parameters recorded and evaluated were LV end-diastolic and end-systolic diameters, RV mid-regional end-diastolic diameter, severity of mitral and tricuspid valve regurgitation and LV ejection fraction (Simpson's method).

Hemodynamic measurements

A pulmonary artery catheter was used to measure capillary wedge pressure, RV pressure, pulmonary artery pressure (PAP), right atrial pressure (RAP) and cardiac index (CI). Systemic vascular resistance (in dynes/s/cm^5) and pulmonary vascular resistance (Wood units) were calculated. RV stroke work index (RVSWI) was calculated using the following formula: RVSWI = (mean PAP – mean RAP) × SVI × 1,000, where SVI (stroke volume index) equals CI divided by heart rate.

RVF and RVD definitions

RVF is defined and classified according to the International Mechanically Assisted Circulatory Support Registry (available online at http://www.ishlt.org/registries/protocol.asp/) as follows:

- Severe right heart failure (RHF): Need for RV assist device implantation.
- Moderate RHF: Inotrope or intravenous or inhaled pulmonary vasodilator (e.g., prostaglandin E or inhaled nitric oxide) for a duration of >1 week at any time after LVAD implantation.
- Mild RHF: Meeting 2 of the 4 following clinical criteria:
  CVP > 18 mm Hg or mean RAP > 18 mm Hg.
  CI < 2.3 liters/min/m^2 (according to Swan).
  Ascites or evidence of moderate to worse peripheral edema.
  Evidence of elevated central venous pressure (CVP) by echocardiography (dilated vena cava, inferior vena cava with collapse), physical examination (signs of increased jugular venous pressure).

RVD in our study was defined as the appearance of persistent symptoms and signs of peripheral vascular congestion (elevated CVP, hepatomegaly or congestion-related pain of the right upper quadrant, peripheral edema, ascites, increase in BNP values) necessitating the significant up-titration of diuretics dose (increase of >80 mg or 3-fold the intial dose) or use of positive inotropic agents.