# Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: Incidence, risk factors, and effect on outcomes

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**Objective:** The aim of this study was to evaluate the incidence, risk factors, and effect on outcomes of right ventricular failure in a large population of patients implanted with continuous-flow left ventricular assist devices.

**Methods:** Patients (n = 484) enrolled in the HeartMate II left ventricular assist device (Thoratec, Pleasanton, Calif) bridge-to-transplantation clinical trial were examined for the occurrence of right ventricular failure. Right ventricular failure was defined as requiring a right ventricular assist device, 14 or more days of inotropic support after implantation, and/or inotropic support starting more than 14 days after implantation. Demographics, along with clinical, laboratory, and hemodynamic data, were compared between patients with and without right ventricular failure, and risk factors were identified.

**Results:** Overall, 30 (6%) patients receiving left ventricular assist devices required a right ventricular assist device, 35 (7%) required extended inotropes, and 33 (7%) required late inotropes. A significantly greater percentage of patients without right ventricular failure survived to transplantation, recovery, or ongoing device support at 180 days compared with patients with right ventricular failure (89% vs 71%, $P < .001$). Multivariate analysis revealed that a central venous pressure/pulmonary capillary wedge pressure ratio of greater than 0.63 (odds ratio, 2.3; 95% confidence interval, 1.2–4.3; $P = .009$), need for preoperative ventilator support (odds ratio, 5.5; 95% confidence interval, 2.3–13.2; $P < .001$), and blood urea nitrogen level of greater than 39 mg/dL (odds ratio, 2.1; 95% confidence interval, 1.1–4.1; $P = .02$) were independent predictors of right ventricular failure after left ventricular assist device implantation.

**Conclusions:** The incidence of right ventricular failure in patients with a HeartMate II ventricular assist device is comparable or less than that of patients with pulsatile-flow devices. Its occurrence is associated with worse outcomes than seen in patients without right ventricular failure. Patients at risk for right ventricular failure might benefit from preoperative optimization of right heart function or planned biventricular support. (J Thorac Cardiovasc Surg 2010;139:1316-24)



An estimated 200,000 Americans over the age of 45 years have advanced heart failure for which medical therapy is insufficient.[1] Although cardiac transplantation remains an attractive therapeutic option for select patients, only 2000 heart transplantations are performed each year in the United States, largely as a result of donor shortages.[2] This continued limitation underscores the need for alternative avenues of treatment for this patient cohort.

Mechanical circulatory support, and more specifically left ventricular assist devices (LVADs), can be used in this setting as a bridge to transplantation (BTT), as destination therapy for patients who are not suitable for transplantation, and as temporary support for patients whose cardiac function is expected to recover. However, outcomes of patients are critically dependent on right ventricular (RV) function, which must provide sufficient flow through the pulmonary vasculature to fill the LVAD and ensure optimal performance. The physiology of right ventricular failure (RVF) in patients with LVADs has been evaluated previously, and the role of septal position and movement secondary to LVAD assistance was demonstrated as a potential mechanism for RVF, which is

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**Abbreviations and Acronyms**

BiVAD = biventricular assist device
BTT = bridge to transplantation
BUN = blood urea nitrogen
CI = confidence interval
CVP = central venous pressure
IABP = intra-aortic balloon pump
LVAD = left ventricular assist device
MRVFRS = University of Michigan right ventricular failure risk score
OR = odds ratio
PCWP = pulmonary capillary wedge pressure
RV = right ventricular
RVAD = right ventricular assist device
RVF = right ventricular failure
RVSWI = right ventricular stroke work index
VAD = ventricular assist device
WBC = white blood cell count

counterbalanced by significant reductions in RV afterload and pulmonary pressures.[3,4] However, these mechanisms were derived mostly from the study of pulsatile LVADs, and there is a question about whether these precepts are still applicable for continuous-flow pumps.

The development of RVF in patients with an LVAD has a direct effect on mortality and is associated with prolonged length of intensive care unit and hospital stay.[5-10] Patients with severe RVF requiring biventricular assist devices (BiVADs) have been shown to be more severely ill, with significantly higher preoperative creatinine levels, total bilirubin levels, and need for intra-aortic balloon pump (IABP) support than patients who were adequately supported with isolated LVADs.[11] Furthermore, RVF in patients with LVADs leads to increased morbidity, including end-organ dysfunction,[8,11] which can deteriorate further after LVAD implantation, resulting in poor outcomes after cardiac transplantation.[12] With proper identification of patients at high risk for RVF, planned use of paracorporeal BiVADs might be appropriate in such patients.[13,14] Temporary right ventricular assist devices (RVADs) can also be used in conjunction with chronic LVADs for patients who are identified as only needing a few days or weeks of RV support. Consequently, recent studies have attempted to ascertain univariate,[8,15] as well as multivariate,[16] predictors of RVF to identify patients at risk for RVF after LVAD implantation. Preoperative identification of such patients might help in pre-emptive placement of RVADs, which could improve overall VAD outcomes.[13]

Most of the current studies describing RVF in patients with LVADs are either limited by a small sample size or a single-center experience or were done on earlier-generation pulsatile devices.[8,9,15,17] The incidence of the need for RVADs and extended inotropic support have been published for the initial HeartMate II (Thoratec, Pleasanton, Calif) trial results.[18,19] However, a detailed analysis of multicenter data for the risks of RVF with the continuous-flow devices has not been established for a large group of patients. The aim of this study was to evaluate the incidence, risk factors, and effect on outcomes of RVF in patients implanted with the HeartMate II continuous-flow LVAD.

## MATERIALS AND METHODS

### Study Design

Data were analyzed from the multicenter HeartMate II pivotal clinical trial for BTT. Details of the study design and trial results have been previously published for the initial 133 patients,[18] and updated results have been published for 281 patients.[19] Between March 2005 and April 2008, the total enrollment reached 484 patients at 36 centers, and these patients were included in this analysis. Patients listed as status 1A or 1B on the heart transplant list were implanted with the HeartMate II LVAD, and survival to transplantation, actuarial survival, functional status, quality of life, and adverse events were determined. All adverse events, including RVF, were adjudicated by an independent clinical events committee.

RVF was defined in the HeartMate II clinical trial as either the need for an RVAD in addition to the LVAD (group 1), continuous inotropic support for at least 14 days after implantation (group 2), or late inotropic support starting 14 days after implantation (group 3). Data from groups 1 and 2 were combined to form an early RVF group, whereas group 3 patients were examined separately (late RVF group). The rationale for differentiating early and late occurrences of RVF is that the cause of the RVF is likely triggered by different mechanisms. Baseline preoperative demographic, clinical, hemodynamic, and laboratory data were compared between patients with early RVF (groups 1 and 2) and patients without RVF to identify potential predisposing risk factors. The effect of RVF on survival to transplantation, recovery, or continuing support at 180 days after implantation and on Kaplan–Meier actuarial survival was also determined.

Data analyzed included patients' characteristics and demographics (age, sex, cause of heart failure, and body surface area), baseline hemodynamics (cardiac index, pulmonary capillary wedge pressure [PCWP], mean pulmonary artery pressure, systolic pulmonary artery pressure, diastolic pulmonary artery pressure, central venous pressure [CVP], CVP/PCWP ratio,[20] right ventricular stroke work index [RVSWI], systolic blood pressure, left ventricular ejection fraction, and left ventricular end-diastolic volume), use of an IABP or ventilator support, laboratory data (blood urea nitrogen [BUN], creatinine, alanine aminotransferase, total bilirubin, hematocrit, white blood cell count [WBC], platelet count, and international normalized ratio), and postoperative bleeding and transfusion requirements. The University of Michigan RVF risk score (MRVFRS) was calculated based on the formula provided by Matthews and colleagues.[16]

### Statistical Analysis

Differences between measures of continuous variables with and without RVF were analyzed by using the independent-samples $t$ test for normal data and the Mann–Whitney $U$ test for nonnormal data. For multiple groups (no RVF vs RVF–RVAD [group 1] vs RVF–continuous inotropic support for $\geq$14 days after implantation [group 2] vs RVF–late inotropic support starting 14 days after implantation [group 3]), single-factor analysis of variance was performed. When the residuals were not normally distributed, the Kruskal–Wallis multiple-comparisons test was performed instead. For categoric variables, Fisher's exact test was used for comparing 2 groups, and Pearson's $\chi^2$ test was used for more than 2 groups. All statistical comparisons were 2-sided. Univariate logistic regression was performed on all variables to identify the potential risk factors for early RVF, followed by stepwise forward multivariate logistic regression on the univariate predictors, with an entry criterion