

**Preoperative Echocardiographic Predictors of
Right Ventricular Performance After Left
Ventricular Mechanical Support**

James Peacock

STUDY PURPOSE AND RATIONAL

Nearly 5 million Americans suffer from heart failure. An estimated 250-500,000 people in the US and 2 million people worldwide are in the terminal phase of heart failure with an annual mortality reaching 50% despite optimal medical management (1). For this population, heart transplantation is the only therapeutic option, but limited donor availability limits transplants to only 2400 transplants per year in the US with 4000 patients awaiting transplant at any given time (2). Because of the shortage of donor hearts, left ventricular assist devices (LVADs) have emerged as life-saving therapy, either as a bridge to transplantation, bridge to recovery or as destination therapy.

Right ventricular failure is a serious complication of LVAD support that manifests as post-operative cardiogenic shock, liver congestion, bleeding and often renal failure. Frequently these patients require placement of a temporary right ventricle support device. For patients who are awaiting transplant, right ventricle support device confines them to the hospital until transplantation. For destination therapy patients, there is no FDA-approved biventricular device so if their right ventricle fails they often have a long hospitalization ending in the withdrawal of care. It is estimated that 20-40% of patients develop peri-operative RV failure (3,4,5,6) after LVAD surgery which was associated with greater incidence of blood transfusion requirement, end-organ failure, increased length of stay in the intensive care unit and hospital overall, and a high risk mortality rate as compared to patients who did not develop RV dysfunction.

The mechanisms of right ventricular failure after LVAD insertion are not well understood and therefore largely unpredictable. In a retrospective analysis of 69 patients at Columbia University Medical Center who received LVAD, RVSWI had a trend toward being lower in right ventricle dysfunction (4.1 ± 3.2 versus 6.1 ± 3.7 , $p = 0.06$) (7). In another retrospective study looking at 245 patients, low mean pulmonary pressure (mean PAP 33 ± 7 vs 37 ± 9 mmHg, $p < 0.04$) as well as low RVSWI (2.85 ± 1.96 vs 4.00 ± 2.21 mmHg \cdot m 2 \cdot L $^{-1}$) were associated with RV failure (8). While RVSWI and low mean PAP measurements provide some method of predicting which patient will likely suffer from post-operative RV failure, in clinical practice they have proven inadequate to predict RV failure, and therefore these measurements have not truly altered patient selection practices.

More recently, a group at the University of Pennsylvania published an algorithm that can predict which LVAD patients will require RVAD with 83% sensitivity and 80% specificity by applying multivariate logistic regression to various characteristics, laboratory values and hemodynamic data from 266 LVAD recipients (9). This study, however, did not look at echocardiographic parameters to assess right ventricular function. In recent years, echocardiography has made tremendous progress in providing detailed quantitative information about the RV and the interaction between the RV and LV, in both load and load-independent states. In addition, multiple doppler echocardiographic measures of right heart pressures and hemodynamics have been described and validated. We propose that pre-operative echocardiographic measures using the most up-to-date imaging techniques along with routine laboratory data and hemodynamic measures will more accurately predict which patients with advanced heart failure who require surgery to implant a LVAD will go on to develop peri-operative right heart failure.

STUDY DESIGN AND PROCEDURES

This is a physician-initiated, observational study of all patients with advanced heart failure who require LVAD surgery from February 2009 until February 2011 at Columbia University

Medical Center (CUMC) and Mount Sinai. Each institution performs 50-70 LVADs per year with a greater than 30% right sided heart failure rate. The study will be conducted for 48 months with an anticipated total cohort of 200 patients. The screening data listed below will not cost anything to the patient, as all of it is considered standard of care in the management of this patient population. This includes pre-operative non-invasive echocardiogram. The research measurement will take an additional 30 minutes. There will be no additional billing for the research portion of the echo. As part of usual medical care prior to going to the operating room, all patient will have the following evaluation:

Recording of age, gender, body mass index (BMI), etiology of heart failure, NYHA class, duration of heart failure, co-morbidities such as pulmonary disease, liver disease

Physical exam

Complete standard pre-operative blood work including beta natriuretic peptide (BNP)

Estimated creatinine clearance by the Cockcroft-gault equation

Right heart catheterization

Transthoracic echocardiogram with 30 minutes of additional research images

STATISTICS:

This is an observational study of approximately 200 patient undergoing LVAD surgery for advanced heart failure at Columbia University and Mount Sinai. The incidence of right heart failure in this setting is greater than 30%. 33 echocardiographic parameters along with clinical, lab and hemodynamic variables will be analyzed. Significant variables by univariate analysis ($P < 0.001$) will undergo multivariate logistic regression to develop a risk score equation. Previous risk scores using similar clinical and hemodynamic parameters yielded a sensitivity and specificity of approximately 80%. With the addition of echocardiographic parameters we are expecting an improvement in the risk score accuracy. Assuming an accuracy of 90%, 150 patients will be required for a power of 90% to detect an accuracy greater than 80% with a $P < 0.05$.

STUDY DRUGS: none

STUDY QUESTIONNAIRES: none

STUDY SUBJECTS, INCLUSION AND EXCLUSION CRITERIA: Patients must be 18 years of age or older and have advanced heart failure requiring LVAD surgery, as determined by the Columbia University or Mount Sinai Heart Failure and Transplant Team. Patients will be excluded from the study if they emergently require LVAD surgery and are too ill to tolerate a detailed pre-operative echocardiogram.

RECRUITMENT: All patients who are scheduled for LVAD surgery will be asked to participate in the study. Subjects will only be approached if their primary Cardiologist has agreed to permit the patient to be approached to participate in this study. Subjects will be approached only by an Attending Cardiologist. Written informed consent will be obtained by all patient prior to the study.

CONFIDENTIALITY OF STUDY DATA: Each investigator has completed HIPAA training. HIPAA guidelines will be explained to potential subjects and a HIPAA form will be signed by each subject. All patient data will be de-coded so that patient identity cannot be determined.

POTENTIAL RISKS: There are no risks to this study other than possible discomfort in an extra 30 minutes of echocardiographic imaging

BENEFITS: There is no immediate or personal benefit to the subjects. The benefit may be for future patients who require LVAD surgery.

ALTERNATIVES: Subjects may refuse to participate in the extra 30 minutes of echo imaging and receive the standard care for pre-operative evaluation for LVAD surgery.

REFERENCES:

(1)www.americanheart.org

(2)www.unos.org

(3)Farrar DJ, Compton PG, Hershon JJ et al. Right heart interaction with the mechanically assisted left heart. *World J Surg.* 1985;9:89-102.

(4)Sun BC, Catanese KA, Spanier TB et al. 100 long-term implantable left ventricular assist devices: The Columbia Presbyterian interim experience. *Ann Thorac Surg.* 1999;68:688-694.

(5)Fukamachi K, McCarthy PM, Smedira NG et al. Preoperative risk factors for right ventricular failure after implantable left ventricular assist device insertion. *Ann Thorac Surg.* 1999;68:2181-2184.

(6)Kavarana MN, Pessin-Minsley MS, Urtecho J et al. Right ventricular dysfunction and organ failure in left ventricular assist device recipients: a continuing problem. *Ann Thorac Surg.* 2002;73:745-750.

(7) Kavarana, Minoo N., Pessin-Minsley, Melissa S., Urtecho, Jacqueline, Catanese, Katharine A., Flannery, Margaret, Oz, Mehmet C., Naka, Yoshifumi; Right ventricular dysfunction and organ failure in left ventricular assist device recipients: a continuing problem. *Ann Thorac Surg* 2002 73: 745-750

(8) Yoshie Ochiai, Patrick M. McCarthy, Nicholas G. Smedira, Michael K. Banbury, Jose L. Navia, Jingyuan Feng, Amy P. Hsu, Michael L. Yeager, Tiffany Buda, Katherine J. Hoercher, Michael W. Howard, Masami Takagaki, Kazuyoshi Doi, and Kiyotaka Fukamachi. Predictors of Severe Right Ventricular Failure After Implantable Left Ventricular Assist Device Insertion: Analysis of 245 Patients. *Circulation* 106: I-198-2021-, doi:10.1161/01.cir.0000032906.33237.1c

(9) J. Raymond Fitzpatrick III et al. Risk Score Derived from Pre-operative Data Analysis Predicts the Need for Biventricular Mechanical Circulatory Support