Duration of inotropic support after left ventricular assist device implantation: Risk factors and impact on outcome

Soren Schenk, MD,[a] Patrick M. McCarthy, MD,[a,b,c,d] Eugene H. Blackstone, MD,[b,d,e] Jingyuan Feng, MS,[d,e] Randall C. Starling, MD, MPH,[c,d,f] Jose L. Navia, MD,[b] Lingmei Zhou, MS,[d] Katherine J. Hoercher, RN,[b,c,d] Nicholas G. Smedira, MD,[b,c,d] and Kiyotaka Fukamachi, MD, PhD[a]

Objectives: Because duration of inotropic support after left ventricular assist device implantation has been recognized as a surrogate for right ventricular dysfunction, we sought to (1) identify its preimplantation risk factors, particularly its association with preimplantation right ventricular dysfunction, and (2) assess its impact on clinical outcomes.

Methods: Between 1991 and 2002, left ventricular assist devices were implanted in 207 patients, exclusive of those receiving preoperative mechanical circulatory support, which precluded measuring right ventricular stroke work. Duration of inotropic support was analyzed as a continuous variable, truncated by death or transplantation, and in turn as a risk factor for these 2 events.

Results: Inotropic support decreased from 100% on the day of implantation to 57%, 33%, and 22% by days 7, 14, and 21. Its duration was strongly associated with lower preimplantation right ventricular stroke work index, older age, and nonischemic cardiomyopathy and was associated ($P < .04$) with higher mortality before transplantation but not with transition to transplantation. We identified no preimplantation risk factors for right ventricular assist device use because of its relatively infrequent use in this population (18 patients, only 4 of whom survived to transplantation).

Conclusion: Duration of inotropic support after left ventricular assist device insertion is strongly correlated with low preimplantation right ventricular stroke work index. In turn, it was associated with reduced survival to transplantation. Thus, right ventricular stroke work measured before implantation might be useful in decision making for biventricular support, destination therapy, or total artificial heart.

From the Department of Biomedical Engineering, Lerner Research Institute,[a] the Department of Thoracic and Cardiovascular Surgery,[b] the George M. and Linda H. Kaufman Center for Heart Failure,[c] the Transplant Center,[d] the Department of Quantitative Health Sciences,[e] and the Department of Cardiovascular Medicine,[f] The Cleveland Clinic Foundation, Cleveland, Ohio.

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Address for reprints: Eugene H. Blackstone, MD, Department of Thoracic and Cardiovascular Surgery/JJ40, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195 (E-mail: blackse@ccf.org).

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Right ventricular dysfunction (RVD) limits the use and effectiveness of left ventricular assist devices (LVADs) as a bridge to transplantation or destination therapy. Identifying the factors anticipating its occurrence is therefore of clinical importance. However, RVD is a clinical diagnosis based on synthesizing a number of factors, rather than a single hemodynamic measurement. Therefore surrogates for RVD have been proposed, but these have limited utility for preimplantation decision making.

For example, right ventricular assist device (RVAD) support is a surrogate for severe RVD after LVAD implantation.[1-6] Not only is this not known before implantation, it identifies only the extreme of the RVD spectrum. Our clinical impression has been that RVD is an underappreciated problem with serious consequences that is more prevalent than reflected by contemporary use of RVAD support.

Prolonged inotropic support, arbitrarily defined as 14 days or longer, has been used as another surrogate for less severe forms of RVD.[5,6] It also is a postimplan-

Abbreviations and Acronyms
LVAD = left ventricular assist device
RV = right ventricular
RVAD = right ventricular assist device
RVD = right ventricular dysfunction
RVSWI = right ventricular stroke work index

tation variable; in addition, it has not been explicitly recognized that duration of support is a continuous variable that might be truncated by transplantation and death. Therefore, to better manage critically ill patients with clinically evident RVD and to assist in preimplantation decision making for biventricular support or cardiac replacement, we reexamined the duration of inotropic support as a surrogate for RVD by (1) identifying preimplantation factors associated with it, with particular emphasis on preinsertion right ventricular (RV) stroke work, and (2) assessing its impact on clinical outcomes.

Patients and Methods

Devices

The study was confined to implantable LVADs: the 1000 IP HeartMate (1991-1995, n = 56), VE HeartMate (1993-2002, n = 105), and Novacor N100 left ventricular assist system (1996-1998, n = 46). Patient selection criteria and management have been published previously.[7]

Patients

From December 1991 through July 2002, 259 patients underwent LVAD implantation at the Cleveland Clinic as a bridge to transplantation. Fifty-two patients on pre-LVAD extracorporeal membrane oxygenation or other temporary mechanical support devices (eg, Abiomed BVS 5000) were excluded because using these devices precludes accurately measuring hemodynamic components of RV stroke work. Thus, 207 patients were included in this analysis. During support, patients were maintained on the transplantation list. Demographic, medical history, hemodynamic, and laboratory values, and outcomes were extracted from our Unified Transplantation Database, which has been approved for use in research by the institutional review board (Table 1).

Inotropic Support and RVAD Use

Immediately after LVAD implantation, all patients received inotropes: milrinone, dobutamine, dopamine, or epinephrine, either alone or in combination. Inotropes were weaned off if LVAD flow was sufficient under optimal volume loading ($>2\ L \cdot min^{-1} \cdot m^{-2}$) and if stable hemodynamics were maintained without them. Patients were not considered to be on inotropic support if only renal dose dopamine ($\leq 3\ \mu g \cdot kg^{-1} \cdot min^{-1}$) was administered.

In 18 patients an RVAD was placed for severe clinically evident RVD with persistently low LVAD flow despite high-dose inotropic support.

TABLE 1. Characteristics of patients before left ventricular assist device implantation

Variable	n*	No.	%
Demography			
Female sex	207	30	14
Age, y (mean ± SD)	207		55 ± 11.1
Body mass index, $kg \cdot m^{-2}$ (mean ± SD)	197		27 ± 5.2
Medical history and comorbidity			
Ischemic cardiomyopathy	207	127	61
Pre-LVAD hospital stay, d (median [15th, 85th percentiles])	203		6 (2, 23)
Prior thoracic surgery	207	97	47
Acute myocardial infarction within 3 d before LVAD	207	38	18
Ventricular tachycardia or fibrillation within 3 d of implantation	207	74	36
ICD	207	35	17
Preoperative support (within 3 d of implantation)			
Inotropes	194	194	100
IABP	207	157	76
Mechanical ventilation	207	99	48
Hemodynamics			
Mean pulmonary artery pressure, mm Hg (mean ± SD)	204		37 ± 8.6
Central venous pressure, mm Hg (mean ± SD)	177		18 ± 6.0
Cardiac index, $L \cdot min^{-1} \cdot m^{-2}$ (mean ± SD)	201		1.85 ± 0.52
RVSWI, mm Hg · mL · m^{-2} (median [15th, 85th percentiles])†	187		390 (190-610)
Laboratory values			
Creatinine, $mg \cdot dL^{-1}$ (mean ± SD)	206		1.75 ± 0.90
Total bilirubin, $mg \cdot dL^{-1}$ (median [15th, 85th percentiles])	206		1.4 (0.8, 3.1)
AST, $U \cdot L^{-1}$ (median [15th, 85th percentiles])	174		45 (22, 200)

SD, Standard deviation; *LVAD,* left ventricular assist device; *ICD,* implantable cardioverter-defibrillator; *IABP,* intra-aortic balloon pump; *RVSWI,* right ventricular stroke work index; *AST,* aspartate transaminase. *Number of patients for whom data are available. †Derived from pulmonary artery catheter monitoring, according to the following RVSWI = $(\overline{PPA} - \overline{PCV}) \cdot SVI$, where SVI was derived from CI/HR ($\overline{PPA}$, mean pulmonary artery pressure; $\overline{PCV}$, mean central venous pressure; *SVI*, stroke volume index; *CI*, cardiac index; *HR*, heart rate).

Data Analysis

Data are summarized as percentages, means ± standard deviation, medians with 15th and 85th percentiles, or 68% confidence limits equivalent to ±1 standard deviation, as appropriate.

Duration of inotropic support. Because duration of inotropic support might be truncated (censored) by death or transplantation, it was analyzed from the time of LVAD implantation until the earliest occurrence of either of these competing events[8,9] by using nonparametric Kaplan-Meier and parametric hazard function methods.[10]

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