Mechanical circulatory support by a left ventricular assist device (LVAD) is used to bridge patients with advanced heart failure to transplant or as a definitive treatment. We retrospectively sought predictors of long-term outcome in a cohort of 83 patients who had undergone LVAD treatment. We subjected perioperative clinical data of patients to statistical analysis to establish parameters associated with all-cause mortality, and the cutoff values, sensitivity, and specificity of those that had a statistically significant relation with survival. Mean follow-up was 717 days (standard deviation, 334 days; range, 17–1,392 days). Fourteen patients (16.8%) died, but nine (10.8%) were weaned from support. Serum brain natriuretic peptide (BNP) concentration measured 60 days after implantation was significantly associated with all-cause mortality. The optimal BNP cutoff value to predict death during LVAD support was 322 pg/ml, with a sensitivity of 71.4% and specificity of 79.8%. Two-year survival was 92.0% in those with 60 days serum BNP concentration <322 pg/ml compared with 70.5% in those in whom it was ≥322 pg/ml (p = 0.003). The relation between BNP and survival likely reflects recovery of native myocardial function and improvements in global health and should assist clinicians in the on-going management of long-term LVAD therapy. ASAIO Journal 2015; 61:373–378.

Key Words: natriuretic peptide, left ventricular assist device, heart failure, cardiac recovery, long-term prognosis

Heart transplantation (HTx) is reserved for patients with advanced heart failure refractory to conventional medical therapies; however, the shortage of donor organs coupled with ever-growing waiting lists for HTx means that only a limited number of patients become HTx recipients. Against this background, the left ventricular assist device (LVAD) can be used to achieve sufficient hemodynamic stability and recovery of secondary organ function to act as a bridge to transplantation (BTT) in patients with advanced heart failure. The survival of patients undergoing LVAD treatment has significantly improved with advances in technology and greater clinical expertise; consequently, LVAD therapy has become a more routine part of clinical practice. These developments have been accompanied by a recognition that mechanical circulatory support can be used not only as a BTT but also as a destination therapy (DT) as the incidence of adverse events declines and the quality of life of patients with an implanted LVAD improves.

Despite continuous improvements and refinements in LVAD technology and clinical outcomes, the life expectancy of patients with an LVAD remains impaired. Findings reported from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) clearly show that early postoperative outcome in advanced heart failure patients undergoing LVAD implantation is strongly influenced by their preoperative condition, and several studies have identified preoperative risk factors that predict early death after implantation. Although the postoperative survival of patients enrolled in the INTERMACS register shows that the risk of very early death after implantation is greatest in those with the least favorable preoperative profile, their mortality rate is broadly comparable with patients with more favorable preoperative profiles 2–3 months after implantation. Furthermore, studies designed to have stratified preoperative risk aimed to detect factors predicting early complications rather than long-term prognosis after LVAD implantation. As implantation of an LVAD is an increasingly common treatment for bridging and DT, it is important to identify predictors of long-term prognosis if possible. The aim of this study was to identify clinical predictors of long-term survival in patients receiving LVAD support regardless of preoperative factors.

Materials and Methods

Study Design

We retrospectively analyzed the records of 108 patients (82 men and 26 women) with advanced heart failure who had undergone LVAD implantation between May 2001 and July 2012 at the National Cerebral and Cardiovascular Center, Osaka, Japan. To elucidate the predictive factors for mid- to long-term prognosis more than 90 days after LVAD implantation, patients who died within 90 days of implantation (n = 5,
4.6%) were excluded from the analysis. Patients with biventricular support (n = 2, 1.8%), and those with incomplete data (n = 18, 16.7%), which mainly consist of patients receiving HTx at foreign country, were also excluded from the analysis. Ultimately, the data of 83 patients implanted with an LVAD were analyzed. All patients had undergone a detailed clinical evaluation before implantation, including clinical history, physical examination and evaluation of laboratory investigations, echocardiography, and cardiac catheterization. The study end-point was all-cause mortality after LVAD implantation. The institutional review board of the National Cerebral and Cardiovascular Center approved data collection, analysis and reporting.

Data Collection and Patient Follow-up

Baseline demographic data were collected retrospectively from the medical records, including age, sex, height, weight, underlying heart disease, duration of mechanical circulatory support, INTERMACS profile, and the manufacturer and model of the LVAD implanted. Baseline clinical data and laboratory evaluations had all been performed within 24 hours of surgery. Echocardiography was performed in all patients in the week before implantation. Conventional echocardiograms and laboratory investigations were subsequently undertaken 30, 60, and 90 days after implantation.

Laboratory Investigations

Laboratory investigations, including white blood cell count, hemoglobin, platelet count, and the serum concentrations of bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, blood urea nitrogen, uric acid (UA), sodium, potassium, chloride, C-reactive protein (CRP), total protein, albumin, total cholesterol, triglyceride, low-density lipoprotein, high-density lipoprotein, cholesterinesterase, lymphocytes, and brain natriuretic peptide (BNP) were recorded.

Echocardiography

A standard two-dimensional transthoracic echocardiogram was recorded, and left ventricular ejection fraction (LVEF) calculated by using Simpson’s method. The Teichholz M-method or visual estimates of LVEF were made when left ventricular (LV) tracing was not possible. Measurements of left ventricular end-diastolic diameter (LVDd) and left ventricular end-systolic diameter (LVDs) were obtained from the parasternal long-axis view and measured as the largest or smallest ventricular diameter, which did not necessarily coincide with electrocardiographic (ECG) diastole owing to the asynchronous relation between the cardiac and LVAD cycles. The severity of aortic valve regurgitation was semiquantitatively graded by using color-flow Doppler and characterized as none or trivial (0), mild (1), moderate (2), moderate to severe (3), or severe (4). Pulmonary artery systolic pressure was estimated from Doppler measurements of the tricuspid regurgitant jet, described by the tricuspid regurgitation pressure gradient (TRPG). All post-operative echocardiograms were performed under LVAD support.

Statistical Analysis

Patients were divided into two groups based on whether they survived or died during LVAD support. Data are presented as mean ± standard deviation. The clinical characteristics, laboratory data, and echocardiographic data of the groups before LVAD implantation were compared using the unpaired Student’s t-test or by the nonparametric Mann–Whitney test as appropriate. Univariate Cox proportional hazard analyses were performed with continuous variables, and a p value <0.15 was used as the threshold for inclusion in multivariate models to identify the risk of death during LVAD support. Receiver operating characteristic curves were plotted, and the areas under the curves calculated to assess the optimal cutoff values for factors that predicted all-cause mortality during LVAD support. The sensitivity, specificity, positive predictive value, and negative predictive value also were calculated. Patients were allocated into groups on the basis of the cutoff value of each parameter. Kaplan–Meier analysis was undertaken to estimate the overall survival rate, and the survival of different groups was compared using log-rank analysis. Patients were censored for HTx or if they were weaned from LVAD. Because BNP concentrations were markedly skewed, we assessed the logarithmic transformation (log10) of BNP concentration. All p values were two sided, and values <0.05 were considered be statistically significant. All data were analyzed using JMP version 10.0 (SAS Institute Inc., Cary, NC).

Results

Baseline Characteristics

Of the 83 patients included in the analysis implanted with LVADs between May 2001 and July 2012 in our

| Etiology                | Total (n = 83) |
|-------------------------|---------------|
| DCM                     | 62 (74.7)     |
| dHCM                    | 12 (6.1)      |
| ICM                     | 3 (3.6)       |
| Others                  | 6 (7.2)       |
| IABP, n (%)             | 50 (60.2)     |
| IABP support duration, days | 6.9 ± 9.2 |
| ECMO, n (%)             | 17 (20.5)     |
| ECMO support duration, days | 4.6 ± 6.6 |
| Mechanical ventilation, n (%) | 18 (19.3) |
| Mechanical ventilation duration, days | 3.9 ± 6.3 |
| INTERMACS profile, n (%) | 30 (36)       |
| Profile 1               | 27 (31)       |
| Profile 2               | 26 (31)       |
| Profile 3               | 27 (31)       |
| Device, n (%)           | 63 (75.6)     |
| NIPRO TOYODO            | 12 (14.6)     |
| DuraHeart               | 4 (4.8)       |
| HeartMate II            | 1 (1.2)       |
| Jarvik2000              | 1 (1.2)       |
| HeartMate              | 1 (1.2)       |
| Novacor                |               |

Table 1.  Patients’ Baseline Characteristics

Data given as mean ± SD or the number (%).

DCM, idiopathic dilated cardiomyopathy; dHCM, dilated phase hypertrophic cardiomyopathy; IABP, intraaortic balloon pumping; ICM, ischemic cardiomyopathy; INTERMACS, interagency registry for mechanically assisted circulatory support; LVAD, left ventricular assist device.
institution, 63 patients received pulsatile extracorporeal pumps (Toyobo-VAS; NIPRO, Tokyo, Japan), 2 received pulsatile implantable pumps (HeartMate XVE [Thoratec, Pleasanton, CA] or Novacor [WorldHeart, Oakland, CA]), and 18 received continuous-flow implantable pumps (EVAHEART [Sun Medical, Nagano, Japan]; DuraHeart [Terumo Heart, Ann Arbor, MI]; HeartMate II [Thoratec]; or Jarvik 2000 [Jarvik Heart, New York, NY]). The baseline clinical characteristics of all patients are summarized in Table 1. Their mean age was 39.3 ± 12.4 years, and 75.9% were men. The most common cause of heart failure was idiopathic dilated cardiomyopathy (74.7%). All patients had New York Heart Association class IV symptoms of congestive heart failure and had required inotropic support. All patients underwent LVAD implantation for BTT. Patients were followed for a mean 717 ± 334 days (range, 17–1,592 days). Thirty-eight patients (45.7%) underwent HTx after a mean 891 ± 329 days of LVAD support (range, 99–1,592 days). Forty-five patients (52.3%) underwent HTx after a mean 717 ± 334 days (range, 17–1,592 days). Twenty-two (26.5%) were awaiting HTx on LVAD support at the time of LVAD implantation. Patients (10.8%) were successfully weaned from LVAD therapy, and five (5.8%) died due to complications. The most common cause of death was sepsis (three cases), followed by right heart failure (two cases) and cerebrovascular events (two cases). Nine patients required inotropic support and were eventually weaned from LVAD therapy, and two (2.5%) were awaiting HTx at the end of the study period.

Table 2. Univariate Cox Proportional Hazard Analysis of pre-LVAD and Postoperative Variables

| Variables               | Pre-LVAD          | 30 Days           | 60 Days           | 90 Days           |
|-------------------------|-------------------|-------------------|-------------------|-------------------|
| White blood cell count  | 0.99 (0.99–1.00)  | 0.99 (0.99–1.00)  | 0.99 (0.99–1.00)  | 0.99 (0.99–1.00)  |
| Hemoglobin              | 0.84 (0.63–1.09)  | 0.72 (0.45–1.09)  | 0.96 (0.64–1.42)  | 0.70 (0.48–1.04)  |
| Platelets               | 0.99 (0.95–1.01)  | 0.98 (0.94–1.01)  | 0.99 (0.94–1.00)  | 1.00 (0.99–1.01)  |
| Serum total bilirubin   | 0.75 (0.42–1.11)  | 0.95 (0.47–1.17)  | 1.12 (0.54–1.74)  | 0.95 (0.15–3.90)  |
| Serum AST               | 1.00 (0.99–1.00)  | 0.97 (0.92–1.01)  | 1.02 (0.99–1.04)  | 0.92 (0.85–0.98)  |
| Serum ALT               | 1.00 (0.99–1.00)  | 0.96 (0.97–1.01)  | 1.00 (0.99–1.01)  | 0.96 (0.89–1.00)  |
| Serum creatinine        | 1.25 (0.77–1.82)  | 1.80 (0.21–15.1)  | 0.89 (0.11–4.89)  | 0.44 (0.04–3.61)  |
| Serum blood urea nitrogen | 1.00 (0.97–1.02) | 0.98 (0.90–1.05)  | 0.73 (0.95–1.06)  | 0.42 (0.09–1.04)  |
| Serum uric acid         | 1.02 (0.89–1.15)  | 0.89 (0.68–1.14)  | 0.94 (0.73–1.21)  | 0.56 (0.35–0.84)  |
| Serum sodium            | 0.97 (0.89–1.06)  | 1.00 (0.86–1.15)  | 0.98 (0.85–1.16)  | 0.82 (0.82–1.06)  |
| Serum potassium         | 1.38 (0.56–3.15)  | 1.06 (0.37–2.86)  | 0.89 (0.64–1.23)  | 0.43 (0.08–1.72)  |
| Serum chloride          | 0.94 (0.88–1.01)  | 1.00 (0.97–1.06)  | 0.97 (0.89–1.08)  | 0.89 (0.80–1.00)  |
| Serum C-reactive protein| 0.92 (0.80–0.97)  | 0.98 (0.80–0.97)  | 1.05 (0.85–1.21)  | 0.78 (0.67–1.29)  |
| Serum creatinine        | 1.03 (0.61–3.03)  | 1.32 (0.56–2.99)  | 1.43 (0.63–3.39)  | 0.86 (0.47–2.82)  |
| Serum albumin           | 2.39 (0.55–10.6)  | 0.51 (0.13–1.97)  | 0.33 (0.08–1.29)  | 0.10 (0.01–0.67)  |
| Serum total cholesterol | 1.00 (0.98–1.01)  | 0.84 (0.80–1.10)  | 0.86 (0.80–1.02)  | 0.50 (0.09–1.02)  |
| Serum triglyceride      | 1.00 (0.98–1.00)  | 0.99 (0.99–1.01)  | 0.49 (0.99–1.01)  | 0.50 (0.98–1.00)  |
| Serum LDL               | 1.01 (0.99–1.02)  | 1.00 (0.96–1.02)  | 0.93 (0.98–1.01)  | 0.43 (0.08–1.72)  |
| Serum HDL               | 0.98 (0.93–1.03)  | 1.01 (0.94–1.11)  | 0.97 (0.95–1.07)  | 1.01 (0.95–1.06)  |
| Serum ChE               | 1.00 (0.99–1.00)  | 0.99 (0.97–1.00)  | 0.99 (0.99–1.00)  | 0.48 (0.98–1.00)  |
| Lymphocytes             | 0.99 (0.90–1.06)  | 0.99 (0.90–1.06)  | 0.98 (0.96–1.08)  | 0.43 (0.09–1.03)  |
| Log BNP                 | 1.00 (1.00–0.99)  | 0.93 (0.80–1.21)  | 0.47 (1.53–15.4)  | 0.06 (1.89–21.8)  |

*p value based on univariate Cox proportional hazard analysis; values of p < 0.05 are significant.

ALT, alanine aminotransferase; Ar, aortic regurgitation; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; ChE, cholinesterase; CI, confidence interval; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein; LVAD, left ventricular assist device; LVDd, left ventricular end-diastolic diameter; LVds, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; TRPG, tricuspid regurgitation pressure gradient.

The results of univariate Cox proportional hazard analysis of clinical variables measured during treatment pathways of patients are shown in Table 2: preoperative CRP and TRPG showed statistical significance in the univariate analysis, but neither remained significant on multivariate analysis. None of the variables measured 30 days after implantation achieved statistical significance. At 60 days, serum AST, ALT, and albumin concentrations and log_{10} BNP concentration were significantly associated with all-cause mortality during LVAD support on univariate analysis, but only log_{10} BNP concentration remained significant on multivariate analysis (Table 3). Hemoglobin, serum AST, UA, chloride, CRP, and albumin concentrations and log_{10} BNP concentration at 90 days also showed significance in the univariate analysis, and hemoglobin, serum AST, UA, and albumin concentrations were found to be significant factors on multivariate analysis. Notably, echocardiographic measurements were not associated with overall mortality on univariate analysis at any time and thus were not included on multivariate analysis.
Quantitative Analysis of BNP Concentration

We further examined the relation between serum BNP concentration and prognosis after LVAD implantation. Serum log BNP concentration showed a continuous decrease from a mean of 3.00 ± 0.34 just before LVAD implantation to 2.46 ± 0.43 at 30 days, 2.21 ± 0.46 at 60 days, and 2.15 ± 0.51 at 90 days. The difference between preoperative and postoperative concentration became statistically significant at 60 days before a steady state was achieved. There was no statistically significant difference between BNP concentrations measured at 60 and 90 days.

Survival After LVAD Implantation

Receiver operating characteristic curve analysis revealed that the optimal BNP cutoff value 60 days after implantation to predict all-cause mortality during LVAD support was 322 pg/ml, and the area under the curve was 0.779; this cutoff value had a sensitivity of 71.4% and specificity of 79.8%.

Comparison of the Kaplan–Meier curves of patients with an LVAD with BNP concentration <322 pg/ml and those with a BNP concentration ≥322 pg/ml 60 days after implantation showed that a significantly greater proportion of the group with the lower BNP concentration were alive 2 years after surgery. At 6 months, survival was 100% in both groups. At 1 year, survival was 98.5% and 96% in the low and high BNP groups, respectively. By 2 years, however, survival was 92.0% in the BNP <322 pg/ml group compared with 70.5% in the BNP ≥322 pg/ml group (p = 0.003).

Discussion

The outcomes of patients receiving mechanical circulatory support have gradually improved over time owing to improvements in device technology, appropriate patient selection, and refinements in postoperative patient care. In a clinical context, after technological advances, judicious patient selection is thought to have had the next greatest impact on outcome. To date, multiple organ dysfunction caused by cardiogenic shock and severe right heart failure manifested by increased serum bilirubin concentration have been reported to predict postoperative prognosis, informing the selection of suitable candidates for LVAD implantation. However, risk indices based on these preoperative factors have only been shown to predict outcome in the first 30–90 postoperative days.

The technology underpinning LVAD therapy is evolving steadily. Until recently, the primary indication for LVAD implantation was as a BTT, and LVADs were expected to be needed for at most a couple of months until HTx could be undertaken. Therefore, previous studies that aimed to stratify the risks of LVAD implantation focused on very short-term outcomes. Since 2010, when the implantable continuous-flow
strongs in response to the stress and stretching of cardiac myocytes. Serum BNP concentration correlates with dilatation of the left ventricle, decreased left ventricular contractility, and ventricular stiffness; consequently, it is used as a valuable diagnostic tool in patients with heart disease. The outlook for patients with advanced heart failure has been drastically improved by LVAD therapy: implantation of an LVAD immediately improves the heart function as a result of the mechanical circulatory support provided. This in turn will likely improve prognosis by reducing the incidence of post-LVAD complications such as right heart failure, pump thrombosis, and de novo aortic insufficiency and the adverse events most likely to be fatal later in the postoperative period. It should be noted that BNP may also be influenced by confounding factors such as central nervous system disease and sepsis, which suggest that other mechanisms may also contribute to an elevated serum BNP concentration. Serum BNP concentration measured at 60 days may be a systemic biomarker of a patient’s more general health, with cardiac and noncardiac influences. In our study, such influential factors as administration of NH blockade, right heart function estimated by right heart catheter, serum creatinine, serum CRP, serum albumin, and serum total bilirubin did not show substantially different between the two groups (BNP concentration: $\leq 322$ pg/ml and $\geq 322$ pg/ml). Although other factors may play less influential roles, this does not diminish the clinical use of BNP concentration as an independent long-term prognostic indicator—and indeed may help to explain it.

**Conclusions**

Serum BNP concentration 60 days after LVAD implantation independently predicted long-term survival of patients receiving LVAD support. As the need for long-term BTT and DT will likely grow further, the ability to predict long-term prognosis during LVAD support will have substantial clinical benefit. More data from larger cohorts are needed to substantiate our findings.

**Limitations**

Our study had several limitations. First, it was retrospective and conducted in a single center and, consequently, included a relatively small number of patients. Second, the etiology of heart failure in our patient cohort varied widely. Third, only 18 patients with a continuous-flow LVAD were included in the analysis, and only one patient had died during this study period; as these devices were not available in Japan before April 2011, we were unable to draw any firm conclusions about the influence of different devices on outcomes. As there appears to be a worldwide trend to implant continuous-flow LVADS, there is an urgent need to study patients who have been implanted with these devices.

**References**

1. Stehlik J, Edwards LB, Kucheryavaya AY, et al; International Society of Heart and Lung Transplantation: The Registry of the International Society for Heart and Lung Transplantation: 29th official adult heart transplant report—2012. J Heart Lung Transplant 31: 1052–1064, 2012.

2. Dang NC, Topkara VK, Kim BT, Mercando ML, Kay J, Naka Y: Clinical outcomes in patients with chronic congestive heart failure who undergo left ventricular assist device implantation. J Thorac Cardiovasc Surg 130: 1302–1309, 2005.

3. Hiestand BC: Circulatory assist devices in heart failure patients. Heart Fail Clin 5: 55–62, vi, 2009.

4. Rogers JG, Aaronson KD, Boyle AJ, et al; HeartMate II Investigators: Continuous flow left ventricular assist device improves functional capacity and quality of life of advanced heart failure patients. J Am Coll Cardiol 55: 1826–1834, 2010.

**Table 3. Multivariate Cox Proportional Hazard Analysis of Parameters Measured 60 Days After Implantation**

| Parameter               | HR (95% CI)   | p Value* |
|-------------------------|---------------|----------|
| Serum AST               | 1.00 (0.95–1.05) | 0.7499   |
| Serum ALT               | 1.00 (0.98–1.02) | 0.5312   |
| Serum albumin           | 0.60 (0.11–3.41) | 0.4429   |
| Log BNP                 | 1.00 (1.00–1.00) | 0.0243   |

*p value based on univariate Cox proportional hazard analysis; values of p < 0.05 are significant.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; CI, confidence interval; HR, hazard ratio.
5. Kirklin JK, Nafte DC, Kormos RL, et al: The Fourth INTERMACS Annual Report: 4,000 implants and counting. J Heart Lung Transplant 31: 117–126, 2012.

6. Starling RC, Naka Y, Boyle AJ, et al: Results of the post-U.S. Food and Drug Administration-approval study with a continuous flow left ventricular assist device as a bridge to heart transplantation: A prospective study using the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) J Am Coll Cardiol 57: 1890–1898, 2011.

7. Kirklin JK, Nafte DC, Kormos RL, et al: Fifth INTERMACS annual report: Risk factor analysis from more than 6,000 mechanical circulatory support patients. J Heart Lung Transplant 32: 141–156, 2013.

8. Rose EA, Gelijns AC, Moskowitz AJ, et al: Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group: Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 345: 1435–1443, 2001.

9. Kirklin JK, Nafte DC, Kormos RL, et al: Third INTERMACS Annual Report: The evolution of destination therapy in the United States. J Heart Lung Transplant 30: 115–123, 2011.

10. Lietz K, Long JW, Kfouri AG, et al: Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: Implications for patient selection. Circulation 116: 497–505, 2007.

11. Sabashnikov A, Mohite PN, Zych B, et al: Outcomes and predictors of early mortality after continuous-flow left ventricular assist device implantation as a bridge to transplantation. ASAIO J 60: 162–169, 2014.

12. Boyle AJ, Ascheim DD, Russo MJ, et al: Clinical outcomes for continuous-flow left ventricular assist device patients stratified by pre-operative INTERMACS classification. J Heart Lung Transplant 30: 402–407, 2011.

13. Cowger J, Sundaeswaran K, Rogers JG, et al: Predicting survival in patients receiving continuous flow left ventricular assist devices: The HeartMate II risk score. J Am Coll Cardiol 61: 313–321, 2013.

14. Klotz S, Vahlhaus C, Riehl C, Reitz C, Sindermann JR, Scheld HH: Pre-operative prediction of post-VAD implant mortality using easily accessible clinical parameters. J Heart Lung Transplant 29: 45–52, 2010.

15. Lund LH, Matthews J, Aaronson K: Patient selection for left ventricular assist devices. Eur J Heart Fail 12: 434–443, 2010.

16. Miller LW, Guglin M: Patient selection for ventricular assist devices: A moving target. J Am Coll Cardiol 61: 1209–1221, 2013.

17. Stevenson LW, Pagani FD, Young JB, et al: INTERMACS profiles of advanced heart failure: The current picture. J Heart Lung Transplant 28: 535–541, 2009.

18. Maisel AS, Krishnaswamy P, Nowak RM, et al: Breathing Not Properly Multinational Study Investigators: Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med 347: 161–167, 2002.

19. Madigan JD, Barbone FK, Choudhri AF, et al: Time course of reverse remodeling of the left ventricle during support with a left ventricular assist device. J Thorac Cardiovasc Surg 121: 902–908, 2001.

20. Milting H, EL Banayossy A, Kassner A, et al: The time course of natriuretic hormones as plasma markers of myocardial recovery in heart transplant candidates during ventricular assist device support reveals differences among device types. J Heart Lung Transplant 20: 949–955, 2001.

21. Sodian R, Loebe M, Schmitt C, et al: Decreased plasma concentration of brain natriuretic peptide as a potential indicator of cardiac recovery in patients supported by mechanical circulatory assist systems. J Am Coll Cardiol 38: 1942–1949, 2001.

22. Xydas S, Rosen RS, Ng C, et al: Mechanical unloading leads to echocardiographic, electrocardiographic, neurohormonal, and histologic recovery. J Heart Lung Transplant 25: 7–15, 2006.

23. Dang NC, Topkara VK, Mercando M, et al: Right heart failure after left ventricular assist device implantation in patients with chronic congestive heart failure. J Heart Lung Transplant 25: 1–6, 2006.

24. Trivedi JR, Sobieski MA, Schwartz S, Williams ML, Slaughter MS: Novel thrombosis risk index as predictor of left ventricular assist device thrombosis. ASAIO J 59: 380–383, 2013.

25. Pizarro R, Bassino OO, Oberti PF, et al: Prospective validation of the prognostic usefulness of B-type natriuretic peptide in asymptomatic patients with chronic severe aortic regurgitation. J Am Coll Cardiol 58: 1705–1714, 2011.

26. Toda K, Fujita T, Domae K, Shimahara Y, Kobayashi J, Nakatani T: Late aortic insufficiency related to poor prognosis during left ventricular assist device support. Ann Thorac Surg 92: 929–934, 2011.

27. Tomita H, Metoki N, Saitoh G, et al: Elevated plasma brain natriuretic peptide levels independent of heart disease in acute ischemic stroke: Correlation with stroke severity. Hypertens Res 31: 1695–1702, 2008.

28. Mäkikallio AM, Mäkikallio TH, Korpelainen JT, et al: Natriuretic peptides and mortality after stroke. Stroke 36: 1016–1020, 2005.

29. McLean AS, Huang SJ, Hyams S, et al: Prognostic values of B-type natriuretic peptide in severe sepsis and septic shock. Crit Care Med 35: 1019–1026, 2007.