Journal of the American College of Cardiology
© 2012 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 59, No. 1, 2012
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2011.09.038

Changes in Renal Function After Implantation of Continuous-Flow Left Ventricular Assist Devices

Tal Hasin, MD,* Yan Topilsky, MD,* John A. Schirger, MD,* Zhuo Li, MS,† Yanjun Zhao, RPH,† Barry A. Boilson, MD,* Alfredo L. Clavell, MD,* Richard J. Rodeheffer, MD,* Robert P. Frantz, MD,* Brooks S. Edwards, MD,* Naveen L. Pereira, MD,* Lyle Joyce, MD,† Richard Daly, MD,† Soon J. Park, MD,† Sudhir S. Kushwaha, MD*

Rochester, Minnesota

Objectives The aim of this study was to determine renal outcomes after left ventricular assist device (LVAD) implantation.

Background Renal dysfunction before LVAD placement is frequent, and it is unclear whether it is due to primary renal disease or to poor perfusion.

Methods A retrospective single-center analysis was conducted in 83 consecutive patients implanted with HeartMate II continuous-flow LVADs (Thoratec Corp., Pleasanton, California). Calculated glomerular filtration rate (GFR) was assessed on admission and 1, 3, and 6 months after implantation. To define predictors for improvement in GFR, clinical variables were examined in patients with decreased renal function (GFR <60 ml/min/1.73 m^2) before LVAD, surviving and dialysis-free at 1 month ($n = 44$).

Results GFR significantly increased from admission (53.2 ± 21.4 ml/min/1.73 m^2) to 1 month after LVAD implantation (87.4 ± 27.9 ml/min/1.73 m^2) ($p < 0.0001$). Subsequently, at 3 and 6 months, GFR remained significantly ($p < 0.0001$) above pre-LVAD values. Of the 51 patients with GFRs <60 ml/min/1.73 m^2 before LVAD surviving at 1 month, 34 (67%) improved to GFRs >60 ml/min/1.73 m^2. Univariate pre-operative predictors for improvement in renal function at 1 month included younger age ($p = 0.049$), GFR improvement with optimal medical therapy ($p < 0.001$), intra-aortic balloon pump use ($p = 0.004$), kidney length above 10 cm ($p = 0.023$), no treatment with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers ($p = 0.029$), higher bilirubin ($p = 0.002$), higher Lietz-Miller score ($p = 0.019$), and atrial fibrillation ($p = 0.007$). Multivariate analysis indicated pre-operative improved GFR (slope = 0.5 U per unit improved; 95% confidence interval: 0.2 to 0.8; $p = 0.003$), atrial fibrillation (slope = 27; 95% confidence interval: 8 to 46; $p = 0.006$), and intra-aortic balloon pump use (slope = 14; 95% confidence interval: 2 to 26; $p = 0.02$) as independent predictors.

Conclusions In most patients with end-stage heart failure considered for LVAD implantation, renal dysfunction is reversible and likely related to poor renal perfusion. (J Am Coll Cardiol 2012;59:26–36) © 2012 by the American College of Cardiology Foundation

Renal dysfunction (RD) is frequent in patients with chronic congestive heart failure (1). Moderate to severe RD, defined by a glomerular filtration rate (GFR) <60 ml/min/1.73 m^2, has been documented in up to 45% of patients with ambulatory heart failure (2) and in 64% of patients hospitalized for decompensated heart failure (3). Compared with patients with heart failure without RD, these patients experience higher morbidity and mortality (4). The optimal management of these patients is unclear, because they have been generally excluded from the major trials of congestive heart failure (5–7).

The question of renal function is especially important in those patients with end-stage heart failure who are considered for advanced therapy such as left ventricular assist device (LVAD) placement or heart transplantation. Cardiac transplant recipients have an increased risk for renal impairment after transplantation (8), which is higher than for other forms of cardiac surgery (9). Subsequently, there is continuous risk related to calcineurin-inhibitor immunosuppressive medication, which also results in a progressive decline in renal function. Indeed, the preferred strategy at

From the *Department of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota; and the †Department of Cardiovascular Surgery, Mayo Clinic, Rochester, Minnesota. Drs. Hasin, Park, and Kushwaha received an unrestricted grant from Thoratec Corporation for a different unrelated project. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received May 17, 2011; revised manuscript received August 29, 2011, accepted September 20, 2011.

many cardiac transplantation centers for the treatment of heart transplantation candidates with significant RD is to consider heart-kidney transplantation.

LVADs are increasingly implanted in patients with end-stage heart failure as a bridge to transplantation (BTT) or as destination treatment (DT) and have dramatically improved both survival and morbidity (10,11). The newer axial-flow and centrifugal-flow devices have the advantage of better durability and smaller size and, therefore, have largely replaced older pulsatile devices for both BTT and DT. Therefore, many patients with heart failure with RD are considered for LVAD implantation. However, whether LVAD implantation improves or worsens renal function is unclear and has not been specifically addressed by the major multicenter LVAD trials (12–14).

The presence of pre-existing RD increases the risk after general cardiac surgery (15) as well as after LVAD implantation (16). Renal function may also deteriorate acutely after cardiac surgery, and post-surgical acute RD has been identified in up to 45% of LVAD recipients. Surgical risk factors including prolonged bypass time, increased intra-operative blood loss, post-operative need for venovenous hemodialysis, and reoperation were identified as negative predictors of poor outcomes (17,18). Acute renal failure (ARF) after LVAD implantation has been identified as a negative predictor of outcomes (10,18,19). Another consideration is whether the presence of a low pulsatility circulation, a result of a continuous-flow device, might cause chronic deterioration of renal function. Therefore, severe RD (need for hemodialysis or serum creatinine >2.5 to 3 mg/dl deemed irreversible) is considered a significant comorbidity and a relative contraindication for LVAD implantation (20,21).

However, it is also possible that improved cardiac output and hemodynamic status with reduction in venous pressure may improve renal function. A recent study demonstrated that 65.3% of patients with RD (GFR <60 ml/min/1.73 m^2) actually had improved renal function by 1 month after LVAD implantation, to GFR >60 ml/min/1.73 m^2. This improvement was associated with improved survival. The absence of diabetes was the only significant predictor identified for renal recovery (16).

Therefore, the aim of this study was to evaluate the effects of LVAD support on renal function in our cohort of BTT and DT patients implanted with continuous-flow HeartMate II devices (Thoratec Corporation, Pleasanton, California) and to identify pre-operative predictors for improved renal function within this population.

Methods

Patients. A retrospective analysis of data was performed for our single-center experience of LVAD implantation for 103 patients from February 2007 to June 2010. Only HeartMate II continuous-flow devices were followed (n = 83, 80% of adult LVAD implantations), and both BTT and DT patients were included. Twenty patients with other devices (8 with Jarvik 2000 [Jarvik Heart, Inc., New York, New York], 6 with VentrAssist [Ventracor, Sydney, Australia] and 6 with HeartMate XVE [Thoratec Corporation] were excluded from analysis. This study was approved by the institutional review board.

Abbreviations and Acronyms

ARF = acute renal failure
BTT = bridge to transplantation
CI = confidence interval
DT = destination treatment
GFR = glomerular filtration rate
IABP = intra-aortic balloon pump
LVAD = left ventricular assist device
RD = renal dysfunction

Renal function. Renal function was assessed by calculating the GFR using the abbreviated Modification of Diet in Renal Disease equation: GFR = $186 \times (\text{serum creatinine [mg/dl]})^{-1.154} \times (\text{age [years]})^{-0.203} \times 0.742$ (if female) (22). The equation has previously been validated in the general, heart failure, (23,24) and heart transplantation (8) populations. Previous studies in the LVAD population have used both the Cockcroft-Gault (25) and the Modification of Diet in Renal Disease equations (16).

Renal function was assessed at admission for LVAD implantation (determined as baseline renal function), the morning before LVAD implantation, and 1 month (range 14 to 46 days), 3 months (range 56 to 120 days), and 6 months (range 150 to 240 days) after implantation during routine follow-up visits. Stages of RD were determined according to calculated GFR in accordance with established guidelines. A GFR cutoff of >60 ml/min/1.73 m^2 was used to differentiate mild or normal renal function from more severe RD (26). Data were considered missing if a patient died or underwent transplantation (for GFR after death date or transplantation date) and if no creatinine measurement was available. Patients requiring hemodialysis were considered in stage 5 (GFR <15 ml/min/1.73 m^2). Because the actual GFRs in these patients were undetermined, they were considered missing for analysis requiring numerical GFR measurement.

Predictors of RD improvement. Possible pre-operative predictors affecting renal function after LVAD implantation for patients with available GFRs at 1 month (n = 72) were derived from patient files and electronic data. Special attention was given to patients with baseline GFRs <60 ml/min/1.73 m^2 for whom GFRs were available at 1 month (n = 44), because there is often uncertainty regarding the recoverability of renal function in these patients going into LVAD implantation. Therefore, it would be helpful to know which factors predict whether renal function is likely to recover.

Statistical analysis. Data were collected into a JMP file and analyzed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina) for association with renal function independently by a coauthor of this report (Z.L.). Descriptive statistics for categorical variables are reported as frequencies and percentages, while continuous variables are

reported as mean ± SD or as median (range) as appropriate. Change of GFR from 1 time point to another was tested using paired *t* tests or Wilcoxon signed rank tests. The Bonferroni method was used to assess the significance of multiple comparisons. Linear regression models were used to find the univariate and multivariate predictors of change in GFR at 1 month. GFR was evaluated as a continuous variable, as previously described (27). The multivariate model considered pre-operative univariately significant variables ($p < 0.05$), excluding variables with more than 20% missing values. We used model selection using the stepwise backward and forward selection. All statistical tests were 2-sided, with the alpha level set at 0.05 for statistical significance.

Results

Patient characteristics. Baseline characteristics for the 83 LVAD patients are shown in Table 1. The mean age was 63 ± 12 years, and the majority of patients were men (82%). The majority of LVADs (70%) were implanted as DT, and about half of the patients had ischemic etiology. The main reason for DT in these patients was older age (median 70 vs. 55 years for patients bridged to transplantation, $p < 0.0001$) as well as the presence of other comorbidities. About one-half of the patients had chronic RD. Table 1 also shows the baseline characteristics for the subset of 54 LVAD patients with GFRs on admission <60 ml/min/1.73 m^2 in whom predictors of improvement in renal function were subsequently evaluated. This cohort had a mean admission GFR of 40 ± 12 ml/min/1.73 m^2. Compared with patients with preserved renal function (GFR ≥60 ml/min/1.73 m^2), those with low baseline GFRs were significantly older, with more chronic kidney disease and longer pre-operative hospital stays. These patients also had more right ventricular dysfunction and higher wedge pressures.

Renal function after LVAD implantation. GFR over the follow-up time period is shown in Figure 1A. GFR measurements at 1 month were available for 72 patients (87%) and at 6 months were available for 57 patients (69%). At 6 months, 12 patients had died, 6 patients had undergone transplantation, 5 patients had no follow-up creatinine measurements, and 3 patients were alive on chronic dialysis. Overall GFR significantly improved 1 month after LVAD implantation (from 53.2 ± 21.4 to 87.4 ± 27.9 ml/min/1.73 m^2, $p < 0.0001$). Thereafter, GFR partially declined at 3 months in 41 of 66 patients with GFR estimates at both time points (77.6 ± 22.8 ml/min/1.73 m^2, $p = 0.0001$, compared to 1 month). Between 3 and 6 months, GFR further declined in 36 of 55 patients with available GFR estimates (71.2 ± 21.0 ml/min/1.73 m^2, $p = 0.0032$, compared to 3 months). Only 6 patients had continuous GFR improvements without any decline over the study period (67 had some decline or no recovery of RD, and data were missing for 10 patients). Overall, GFR remained significantly higher at 6 months compared to pre-operative GFR ($p < 0.0001$). Figure 1B shows the changes in GFR over time for the subsets of patients with pre-operative RD (GFR <60 ml/min/1.73 m^2) and preserved renal function (GFR ≥60 ml/min/1.73 m^2). Overall, both subsets followed the same pattern of change in GFR as the entire cohort. The subset with pre-operative RD had a significant increase at 1 month ($p < 0.0001$), a partial decline (1 to 3 months, $p = 0.0059$; 3 to 6 months, $p = 0.0258$), and overall improvement over 6 months ($p < 0.0001$). The distribution of the stages of RD before and during follow-up after LVAD implantation is illustrated in Figure 2A. Consistent with the findings in Figure 1, an improved stage distribution was noted after LVAD implantation. Similar trends were noted for the large subset of patients in stage 3 before implantation, as illustrated in Figure 2B. Indeed, for patients with available renal staging at 1 month, 57 patients (72%) improved their RD stages or remained at stage 1. Fourteen patients (18%) remained in their pre-operative renal stages (10 in stage 2, 4 in stage 3), and 8 (10%) deteriorated (2 from stage 4 to 5, 5 from stage 3 to 5, and 1 from stage 2 to 3).

Renal failure after LVAD implantation. Eight patients (10%) developed ARF after LVAD implantation necessitating acute hemodialysis. Of these, 2 died in the early post-operative period, and 2 recovered renal function. Four patients (5%) continued with chronic hemodialysis. The clinical characteristics and post-operative courses of these patients are summarized in Tables 2 to 4. Predisposing comorbidities included severe RD necessitating acute dialysis before transplantation (Patients #1, #5, and #7), prior renal transplantation with severe RD for Fabry disease (Patient #2), multiple comorbidities (Patients #3 and #6), and insulin-dependent diabetes mellitus (Patients #4 and #8). Most patients (except Patient #8) had low GFRs before LVAD implantation. Patient #3 underwent emergent implantation for previous device (HeartMate XVE) failure. All patients had significant post-operative complications, including right ventricular dysfunction, infections, bleeding, and need for prolonged inotropic support. Renal function recovered in 2 patients. Four patients (Patients #2, #5, #6, and #8) died during the initial hospital stay after prolonged complicated courses. The 2 other patients survived longer (1.5 and 2.5 years) and died of nonrenal causes.

Predictors of improved GFR 1 month after LVAD implantation. We used a univariate model for predicting an increase in GFR (as a continuous variable) for the 72 patients with available GFR measurements at 1 month. Significant positive predictors associated with GFR improvement were the use of an intra-aortic balloon pump (IABP) before surgery (slope = 17, $p = 0.003$), higher bilirubin (slope = 12.1, $p = 0.002$) alanine transaminase (slope = 0.03, $p = 0.041$), Lietz-Miller score (slope = 1.5, $p = 0.003$), and higher right atrial pressure (slope = 0.97, $p = 0.048$). An increase in GFR with optimal medical treatment before surgery was associated with further improvement 1 month after surgery (slope = 0.6 per ml/min/1.73 m^2,

Table 1 Patient Characteristics

Characteristic	All Patients (n = 83)	GFR <60 ml/min/1.73 m^2 (n = 54)	GFR ≥60 ml/min/1.73 m^2 (n = 29)	p Value
Demographic				
Age (yrs)	63.0 ± 12.3	65.9 ± 8.8	57.7 ± 15.8	0.020
Men	68/83 (81%)	41/54 (76%)	27/29 (93%)	0.053
Hypertension	31/83 (37%)	20/54 (37%)	11/29 (38%)	0.936
Diabetes	24/83 (29%)	19/54 (35%)	5/29 (17%)	0.086
Chronic kidney disease	45/83 (54%)	41/54 (76%)	4/29 (14%)	<0.001
Ischemic etiology	46/83 (55%)	30/54 (56%)	16/29 (55%)	0.973
BTT	27/83 (32%)	15/54 (28%)	12/29 (41%)	0.207
Clinical				
GFR (ml/min/1.73 m^2)	53.2 ± 21.4	40.5 ± 12.3	76.8 ± 12.7	<0.001
GFR pre-operative	64.5 ± 22.5	55.4 ± 18.2	81.3 ± 20.2	<0.001
Admission to operation time (days)	9.4 ± 9.3 (n = 83)	10.8 ± 10.2 (n = 54)	6.8 ± 6.6 (n = 29)	0.039
BMI (kg/m^2)	28.9 ± 5.6	28.8 ± 5.8	29.2 ± 5.3	0.782
NYHA class IV	50/81 (62%)	31/52 (60%)	19/29 (66%)	0.577
Prior sternotomy	42/83 (51%)	28/54 (52%)	14/29 (48%)	0.756
Atrial fibrillation	14/83 (17%)	8/54 (15%)	16/29(21%)	0.500
Kidney length (cm)				
Left	11.7 ± 1.2	11.5 ± 1.2	11.9 ± 1.3	0.287
Right	11.5 ± 1.1	11.5 ± 1.1	11.5 ± 1.3	0.868
Preoperative IABP use	28/83 (37%)	20/54 (37%)	8/29 (28%)	0.385
Need for inotropes	59/83 (71%)	41/54 (76%)	18/29 (62%)	0.184
ACE inhibitors or ARBs	54/78 (69%)	34/51 (67%)	20/29 (69%)	0.585
Spironolactone	43/81 (53%)	29/53 (55%)	14/28 (50%)	0.686
Beta-blockers	68/81 (84%)	44/53 (83%)	24/28 (86%)	0.753
Loop diuretic agents	69/75(92%)	44/48 (92%)	25/27 (93%)	0.887
Digoxin	43/75 (57%)	28/48 (58%)	15/27 (56%)	0.815
Urine protein (mg/dl)	7 (4–23) (n = 71)	7 (4–30) (n = 45)	7 (4–18) (n = 26)	0.756
Hemoglobin (g/dl)	11.9 ± 1.9	11.7 ± 2.0	12.4 ± 1.7	0.100
Platelet count (×1,000)	175.6 ± 70.0	167.1 ± 61.0	191.0 ± 83.0	0.286
Bilirubin (mg/dl)	1.2 ± 0.7	1.2 ± 0.7	1.4 ± 0.8	0.171
NT-proBNP (pg/ml)	6,004 ± 5,812 (n = 47)	7,521 ± 6,578 (n = 29)	3,559 ± 3,143 (n = 18)	0.014
Albumin (g/dl)	3.8 ± 0.6	3.7 ± 0.5	3.8 ± 0.7	0.486
BUN (mg/dl)	31.6 ± 16.8	35.2 ± 17.6	25.0 ± 12.9	0.005
Creatinine (mg/dl)	1.6 ± 0.7	1.9 ± 0.7	1.1 ± 0.2	<0.001
Lietz-Miller score	9.6 ± 6.0	10.3 ± 6.0	8.6 ± 5.7	0.156
Vo_2max (% predicted)	39.4 ± 11.3 (n = 42)	39.6 ± 8.5 (n = 25)	39.1 ± 11.8 (n = 17)	0.885
Pre-operative echocardiography				
Left ventricular diastolic diameter (mm)	67.2 ± 9.5 (n = 82)	67.9 ± 9.4 (n = 53)	66.0 ± 9.6	0.379
Ejection fraction (%)	19.8 ± 8.6 (n = 83)	19.2 ± 6.3 (n = 54)	20.9 ± 11.7 (n = 29)	0.908
RIMP	0.6 ± 0.2 (n = 75)	0.6 ± 0.2 (n = 48)	0.5 ± 0.3 (n = 27)	0.440
RV dysfunction more than moderate	54/81 (67%)	40/52 (77%)	14/29 (48%)	0.009
Pre-operative catheterization				
Mean right atrial pressure (mm Hg)	15.4 ± 6.7 (n = 80)	15.9 ± 6.5 (n = 52)	14.5 ± 7.2 (n = 28)	0.388
Mean pulmonary pressure (mm Hg)	36.1 ± 9.3 (n = 80)	36.8 ± 9.0 (n = 52)	34.8 ± 9.9 (n = 28)	0.350
RVSWI (g/m^2/beat)	7.1 ± 3.9 (n = 74)	7.0 ± 3.7 (n = 49)	7.3 ± 4.3 (n = 27)	0.776
Mean wedge pressure (mm Hg)	23.5 ± 6.9 (n = 77)	24.6 ± 6.6 (n = 50)	21.4 ± 7.1 (n = 27)	0.049
Cardiac index (l/min/m^2)	1.9 ± 0.5 (n = 78)	1.9 ± 0.6 (n = 50)	2.1 ± 0.5 (n = 28)	0.073
Operation				
Bypass time (min)	103.6 ± 33.7 (n = 82)	105.6 ± 32.9 (n = 54)	99.8 ± 35.5 (n = 28)	0.350
Duration of hospitalization (days)	21.4 ± 13.3 (n = 75)	22.2 ± 14.2 (n = 47)	20.1 ± 11.8 (n = 28)	0.576

Values are mean ± SD or n/N (%). The table depicts baseline characteristics of 83 patients implanted with HeartMate II LVADs and of the subgroups of patients with baseline GFRs <60 or >60 ml/min/1.73 m^2. All comparisons are between patients with baseline GFR <60 and >60 ml/min/1.73 m^2.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BMI = body mass index; BTT = bridge to transplantation; BUN = blood urea nitrogen; GFR = glomerular filtration rate; IABP = intra-aortic balloon pump; LVAD = left ventricular assist device; NT-proBNP = N-terminal pro–B-type natriuretic peptide; NYHA = New York Heart Association; RIMP = right index of myocardial performance; RV = right ventricular; RVSWI = right ventricular stroke work index; Vo_2max = peak oxygen uptake.

JACC Vol. 59, No. 1, 2012
December 27, 2011/January 3, 2012:26–36

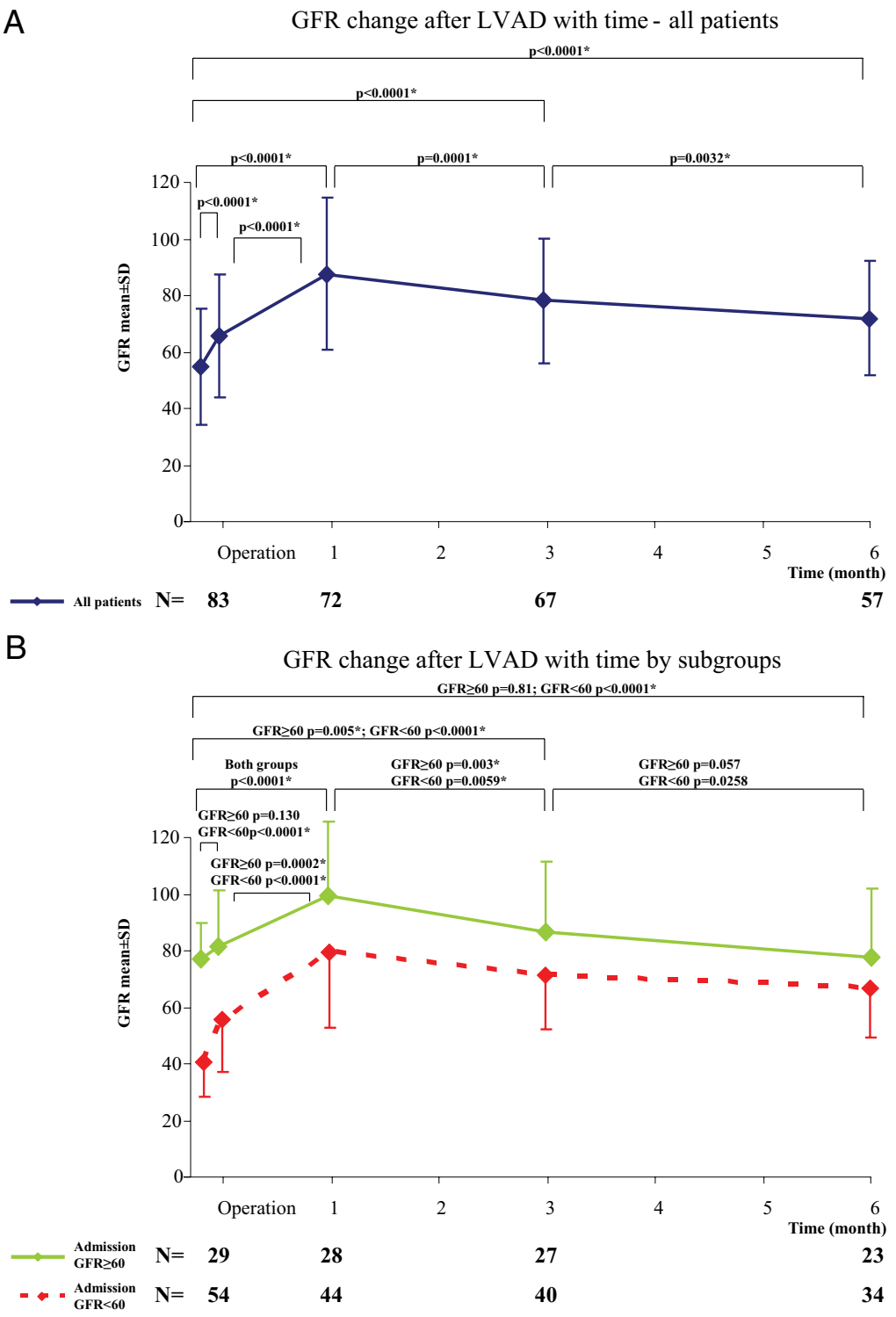
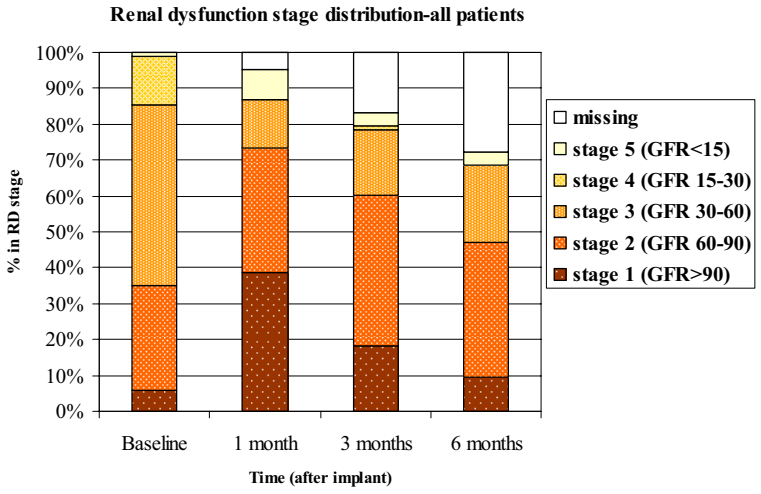


Figure 1 GFR Change After LVAD Implantation With Time

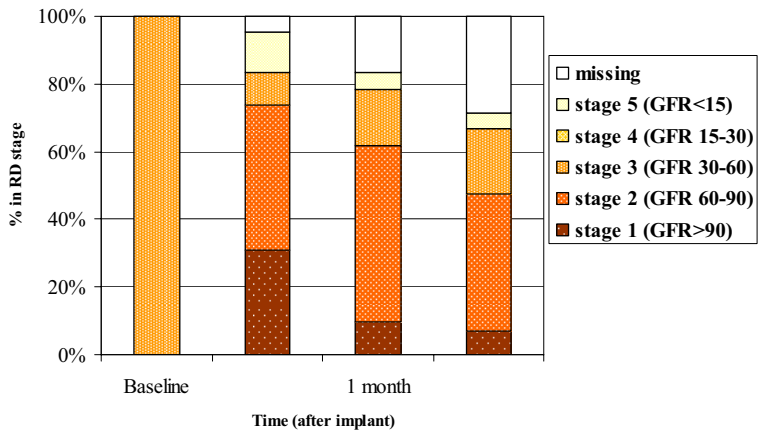
Glomerular filtration rate (GFR) is shown **(A)** for the whole group and **(B)** for the subgroup with admission GFRs ≥60 ml/min/1.73 m^2 **(full line, upper error bars)** and the subgroup with admission GFRs <60 ml/min/1.73 m^2 **(dashed line, lower error bars)**. GFR was calculated using the Modification of Diet in Renal Disease equation according to creatinine levels at admission for left ventricular assist device (LVAD) surgery, on the day of operation, and at the 1-, 3-, and 6-month scheduled visits for available patients (see text). Change of GFR between 2 time points was tested using paired *t* tests by using patients whose GFR data were available at both time points compared. *p < 0.007 represent significant differences between measurements by Bonferroni correction for multiple comparisons.

A



Renal dysfunction Stage (GFR range)	Baseline		1 month		3 months		6 months	
	n	%	n	%	n	%	n	%
Stage 1 (>90)	5	6	32	38	15	18	8	10
Stage 2 (60-90)	24	29	29	35	35	42	31	37
Stage 3 (30-60)	42	51	11	13	15	18	18	22
Stage 4 (15-30)	11	13	0	0	1	1	0	0
Stage 5 (<15)	1	1	7	8	3	4	3	4
missing	0	0	4	5	14	17	23	28

B



Renal dysfunction Stage (GFR range)	Baseline		1 month		3 months		6 months	
	n	%	n	%	n	%	n	%
Stage 1 (>90)	0	0	13	31	4	10	3	7
Stage 2 (60-90)	0	0	18	43	22	52	17	40
Stage 3 (30-60)	42	100	4	10	7	17	8	19
Stage 4 (15-30)	0	0	0	0	0	0	0	0
Stage 5 (<15)	0	0	5	12	2	5	2	5
missing	0	0	2	5	7	17	12	29

Figure 2 **RD Stage Distribution Before and After LVAD Implantation**

The figures and corresponding tables illustrate the distribution of glomerular filtration rate (GFR) by the various stages of renal dysfunction (RD) before left ventricular assist device (LVAD) implantation (baseline) and during follow-up (1, 3, and 6 months). Data for all patients **(A)** and for those with stage 3 RD **(B)** are shown. Missing data include patients in whom creatinine was not measured as well as those who died or underwent transplantation during follow-up.

JACC Vol. 59, No. 1, 2012
December 27, 2011/January 3, 2012:26–36

Table 2 Demographic Characteristics of Patients Needing Chronic Dialysis After LVAD Implantation

Patient #	Age (yrs)	Sex	Medical History	Transplantation Candidacy	Small Kidney (<10 cm)	NYHA Functional Class	Rhythm	LM Score
1	59	Female	HTN, CKD (CVVHD), severe lung disease	BTT	Yes	IV	AF	13
2	62	Male	CKD s/p transplantation, (Fabry), lung disease, s/p TVR	BTT	NA	IIIb	AF	21
3	74	Male	HTN, CKD, IHD	DT	No	IIIb	AF	22
4	61	Male	HTN, DM	DT	No	IV	Sinus	6
5	67	Male	Complex congenital heart disease, recurrent VT, CKD (CVVHD)	BTT	No	IV	Sinus	24
6	73	Male	s/p B-cell lymphoma, s/p CABG, DM, CKD, on continuous milrinone infusion (4 yrs)	DT	NA	IV	AF	4
7	45	Female	Recent mitral repair + Maze procedure, shock, acute renal failure (CVVHD)	BTT	No	IV	AF	20
8	48	Male	Radiation cardiomyopathy, s/p NHL, DM, CVVHD	BTT	No	III	Paced	10

Demographic characteristics of patients who succumbed to chronic need for hemodialysis are summarized, including the LM score for post-LVAD prognosis and the dimension of the kidney as determined by ultrasound before implantation.

AF = atrial fibrillation; CABG = coronary artery bypass grafting; CKD = chronic kidney disease; CVVHD = continuous venovenous hemodialysis; DM = diabetes mellitus; DT = destination therapy; HTN = hypertension; IHD = ischemic heart disease; LM = Lietz-Miller; NA = not available; NHL = non-Hodgkin lymphoma; s/p = status post; TVR = tricuspid valve replacement; VT = ventricular tachycardia; other abbreviations as in Table 1.

$p < 0.001$). Higher pump speed at discharge (slope = 5.9 per 200-rpm increase, $p = 0.01$) was also associated with improved GFR. Negative predictors were having at least 1 kidney smaller than 10 cm on ultrasound (slope = −23.7, $p = 0.01$) and treatment with an angiotensin pathway inhibitor (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker) before surgery (slope = −15.7, $p = 0.006$). The multivariate model suggested that having at least 1 kidney smaller than 10 cm (slope = −21; 95% confidence interval [CI]: −37.7 to −4.6; $p = 0.012$), use of an IABP (slope = 11.8; 95% CI: 0.8 to 22.8; $p = 0.035$) and Lietz-Miller score (slope = 1.2 per unit increase; 95% CI: 0.25 to 2.11; $p = 0.013$) were independent predictors.

To determine the predictors of improved GFR after LVAD implantation in patients with significant pre-operative RD, we focused our analysis on patients with baseline GFRs <60 ml/min/1.73 m^2 (stages 3 to 5). For this subset of 54 patients, data were available at 1 month for 44 patients, as 3 died and 7 were on hemodialysis. Overall, GFR improved from 40 ± 12 to 80 ± 27 ml/min/1.73 m^2, as shown in Figure 1B. For patients with available staging, 34 (67%) had improved GFRs (to >60 ml/min/1.73 m^2) at 1 month, and 17 (33%) did not. A univariate model for prediction of increase in GFR (as a continuous variable) is shown in Table 5. Positive predictors associated with GFR improvement included atrial fibrillation at baseline, higher bilirubin and Lietz-Miller score, an increase in GFR (from 40 ± 12 to 55 ± 18 ml/min/1.73 m^2) with optimal medical treatment before surgery, the use of an IABP before surgery, higher LVAD pulsatility index at discharge, and pump speed setting in the higher range (>9,200 rpm). Negative predictors included older age, having at least 1 kidney smaller than 10 cm (on ultrasound before operation), and treatment with an angiotensin pathway inhibitor (angiotensin-converting enzyme inhibitor or angiotensin receptor blocker) before surgery. The multivariate model suggested that the increase in GFR with optimal treatment before surgery (slope = 0.5 U per unit increase; 95% CI: 0.2 to 0.8; $p = 0.0028$), atrial fibrillation at baseline (slope = 27; 95% CI: 7.7 to 46.4; $p = 0.0062$), and the use of an IABP (slope = 13.9; 95% CI: 1.8 to 26.1; $p = 0.0244$) were independent predictors.

Discussion

The issue of RD after LVAD implantation is important for a number of reasons. First, the possible need for chronic dialysis after LVAD implantation may influence the decision about whether to proceed. Second, the question of reversibility of RD is important regarding the need for

Table 3 Pre-Operative Clinical Characteristics of Patients Needing Chronic Dialysis After LVAD Implantation

Patient #	GFR (ml/min/1.73 m^2)	Pre-Operative GFR Improvement	Hb (mg%)	Albumin (g%)	IABP	TR	MR	RVSWI	RAP (mm Hg)	Wedge Pressure (mm Hg)
1	24	+24	9.2	3.1	No	Severe	Moderate to severe	5	25	21
2	20	+10	11.2	2.8	Yes	Severe	Moderate	1.3	12	22
3	39	+17	10.2	3.3	No	Moderate	None	11.7	11	19
4	38	+0	9.8	3.8	Yes	Moderate	None	1.9	34	32
5	32	−13	11.1	3.3	Yes	None	None	NA	NA	NA
6	40	+18	12.4	3.5	Yes	Moderate	Mild	5.1	23	27
7	41	+43	9.8	3.3	Yes	Severe	None	2.4	20	25
8	76	+0	10.9	NA	Yes	Moderate	Mild	1.4	35	35

Pre-operative clinical characteristics of patients who succumbed to chronic need for hemodialysis are summarized, including laboratory results (GFR, albumin, and Hb), use of IABP, echocardiographic parameters (TR and MR), and catheterization parameters (RVSWI, RAP, and wedge pressure).

Hb = hemoglobin; MR = mitral regurgitation; RAP = right atrial pressure; RVSWI = right ventricular stroke work index; TR = tricuspid regurgitation; other abbreviations as in Tables 1 and 2.

Table 4 Post-Operative Characteristics of Patients Needing Chronic Dialysis After LVAD Implantation

Patient #	Complications	Duration of Inotropic Support (h)	Hospital Stay	Late Outcome
1	GI bleeding, pneumonia, prolonged intubation, RV dysfunction, MR (moderate), continued need for dialysis	160	65 days	Died (sepsis) 2.5 yrs after implantation
2	Early RV failure, sepsis, prolonged intubation, VT	1,032	Death 76 days	In-hospital death
3	Early HeartMate XVE failure, emergent HeartMate II implantation, mediastinitis, RV dysfunction	446	28 days	Withdrew support 1.5 yrs after implantation
4	Early RV failure, prolonged intubation, sepsis, RV dysfunction	504	52 days	Recovered renal function 6 months after implantation
5	Early RV failure, prolonged intubation, recurrent VT encephalopathy, sepsis, ileus, hyperbilirubinemia	1,488	Death 37 days	In-hospital death
6	Delayed chest closure, prolonged intubation, encephalopathy, biliary sepsis	1,056	Death 44 days	In-hospital death
7	Early RV failure, delayed chest closure, prolonged ventilation	1,320	61 days	Recovered renal function 45 days after implantation
8	Chest reopening for severe bleeding, shock	168	Death 7 days	In-hospital death

Post-operative characteristics of patients who succumbed to chronic need for hemodialysis are summarized.
GI = gastrointestinal; other abbreviations as in Tables 1 to 3.

additional renal transplantation in addition to cardiac transplantation in BTT candidates. Therefore, it would be helpful to be able to predict whether renal function is likely to improve or worsen after axial-flow LVAD implantation.

Our study cohort reflects the current trends in LVAD implantation as recently documented in the third Interagency Registry for Mechanically Assisted Circulatory Support report, with increasing proportions of DT implantations and continuous-flow devices (28). In some respects, however, our cohort may represent a more chronically ill population, as it includes older patients and fewer BTT candidates (30% vs. 40%). Given that continuous-flow pumps currently account for more than 98% of adult primary LVAD implantations in the United States, our choice of pump is in keeping with national trends. The HeartMate II pump is currently the only device approved by the U.S. Food and Drug Administration for the rapidly expanding DT population, and therefore we felt that restricting our analysis to HeartMate II implantations was reasonable.

The major finding of this study is the dramatic improvement in renal function with LVAD support. The small but significant improvement in renal function before operative intervention can be attributed to improved hemodynamic management and consequent better renal perfusion. However, despite this initial improvement, we observed continued improvement after LVAD implantation, suggesting that medical and IABP intervention was not sufficient to restore optimal renal perfusion. Previous studies have focused on the occurrence of ARF early after LVAD implantation, with incidence as high as 32% or 45% (17,18) and 16% in the Thoratec HeartMate II LVAS (Left Ventricular Assist System) for Destination Therapy study (14). In the present study, the development of ARF was less frequent (10%). We agree with previous reports that the development of ARF may result from an unfavorable early post-operative course and early hemodynamic instability (17). The majority of patients in our cohort actually had improved renal function with LVAD support. GFR significantly increased from 53.2 ± 21.4 ml/min/1.73 m^2 at baseline to 87.4 ± 27.9 ml/min/1.73 m^2 at 1 month and to 71.2 ± 21.0 ml/min/1.73 m^2 at 6 months. Among patients with pre-operative RD, 34 (67%) had improved GFRs to above 60 ml/min/1.73 m^2 at 1 month. These results are in agreement with previous reports for the pulsatile pump (25) as well as continuous-flow implants in the BTT population (16). Our findings therefore validate previous observations showing improved renal function in the current population of patients with LVAD implants with continuous-flow pumps.

The reversibility of RD in the cardiorenal syndrome is a major issue in patients being considered for heart transplantation. RD is the most common modifiable contraindication to heart transplantation in LVAD patients (28). Indeed, in the face of progressive RD, heart transplantation may be deferred, or heart-kidney instead of heart transplantation alone may be considered. In a recent analysis, a cutoff GFR <33 ml/min/1.73 m^2 was suggested for this strategy, with 1-year results better than for heart transplantation alone (29). Another report identified less post-transplantation RD in a small group of patients supported with LVADs as BTT compared with inotropic support (30). Our findings suggest that LVAD support before heart transplantation may help differentiate between reversible and nonreversible kidney disease.

Another interesting observation is that although GFR generally improves with LVAD support, a gradual partial but significant decline was observed at 3 and at 6 months compared with 1 month after the operation. These findings are also consistent with previous reports (16), and 1 explanation may be that the very low muscle mass after surgery may decrease creatinine levels and result in overestimation of GFR at 1 month. In our analysis, low pre-operative albumin as a marker for cachexia showed a trend for predicting higher GFR (lower creatinine). The progressive expected increase in muscle mass at 3 and 6 months may correct for that bias. Resuming treatment with angiotensin pathway inhibitors could influence the late decline in renal function. However, this did not come up as a significant predictor in our analysis (data not shown). Another explanation is that lack of pulsatile flow may

JACC Vol. 59, No. 1, 2012
December 27, 2011/January 3, 2012:26–36

Table 5 Univariate Linear Regression Model Predicting Increase in GFR 1 Month After LVAD Implantation for Patients With Admission GFRs <60 ml/min/1.73 m^2

	n	Parameter Estimate	95% CI	p Value
General				
Age	44	−0.8	−1.6 to 0.0	0.049
Male*	44	4.2	−12.8 to 21.1	0.630
HTN*	44	−0.4	−15.1 to 14.2	0.954
DM*	44	−0.6	−15.4 to 14.2	0.936
CKD*	44	−11.5	−27.1 to 4.1	0.151
BTT*	44	9.1	−6.6 to 24.9	0.256
Ischemic etiology*	44	4.5	−10.1 to 19.0	0.549
Weight	44	−0.2	−0.6 to 0.2	0.300
Body surface area	44	−18.1	−46.0 to 9.8	0.204
Diastolic blood pressure	44	−0.2	−1.2 to 0.5	0.474
Systolic blood pressure	44	−0.2	−0.7 to 0.3	0.413
Heart rate	44	0.0	−0.5 to 0.5	0.974
AF*	44	31.8	8.8 to 54.7	0.007
NYHA class IV*	44	10.0	−4.1 to 24.1	0.163
Small kidney (<10 cm)*	40	−24.7	−46.0 to −3.5	0.023
Vo_2max (% predicted)	20	0.6	−0.5 to 1.7	0.294
GFR increase, admission to pre-operative	44	0.6	0.3 to 0.9	<0.001
Scores				
Lietz-Miller score	44	1.6	0.2 to 2.9	0.019
Matthews score	44	2.4	−0.4 to 5.2	0.091
Kormos score	41	3.5	−1.2 to 8.2	0.149
Treatment before surgery				
IABP used*	44	20.5	6.7 to 34.2	0.004
Inotropes*	43	−2.8	−20.1 to 14.4	0.745
ACE inhibitors or ARBs*	44	−15.5	−29.4 to −1.6	0.029
Beta-blockers*	44	−5.4	−23.9 to 13.0	0.562
Aldosterone inhibitors*	44	5.6	−8.5 to 19.8	0.435
Diuretic agents*	40	−14.4	−39.4 to 10.6	0.258
Amiodarone*	40	−6.9	−22.8 to 8.9	0.390
ICD/CRT*	40	−4.7	−20.0 to 10.7	0.550
Digoxin*	40	−8.1	−23.6 to 7.4	0.307
Statins*	40	7.0	−9.5 to 23.5	0.404
Laboratory results				
Urine protein	36	0.1	−0.1 to 0.3	0.466
GFR on admission	44	−0.1	−0.7 to 0.4	0.626
Hemoglobin	44	−0.5	−4.0 to 3.0	0.779
Bilirubin	44	14.6	5.6 to 23.7	0.002
AST	44	0.0	0.0 to 0.1	0.193
ALT	41	0.0	0.0 to 0.0	0.157
LDH	37	0.0	0.0 to 0.0	0.210
BNP	25	0.0	0.0 to 0.0	0.768
Platelets	44	0.0	−0.1 to 0.1	0.943
BUN	44	0.0	−0.4 to 0.4	0.975
Albumin	43	−13.2	−28.1 to 1.7	0.082
Echocardiography				
RIMP	39	−3.2	−38.5 to 32.2	0.861
TR time (corrected)	42	−0.1	−0.2 to 0.0	0.174
LVEDD	44	−0.4	−1.3 to 0.4	0.320
Mitral E-wave	39	5.3	−17.7 to 28.2	0.653
LA volume index	43	−0.1	−0.5 to 0.4	0.794
EF	44	−0.2	−1.4 to 0.9	0.684
LV mass	34	0.0	−0.1 to 0.0	0.130
TR (more than moderate)	44	−0.5	−14.8 to 13.7	0.941
AR (more than moderate)	44	−7.1	−35.3 to 21.1	0.623
MR (more than moderate)	44	3.5	−10.9 to 17.8	0.633
Catheterization				
Stroke volume index	42	−0.2	−0.9 to 0.6	0.682
RVSWI	42	−0.7	−2.8 to 1.5	0.537
Cardiac index	42	−2.7	−16.7 to 11.3	0.704
SVR	31	−0.6	−1.5 to 0.4	0.242
PVR	42	−0.4	−2.7 to 2.0	0.757
RA pressure (mean)	43	0.7	−0.5 to 2.0	0.262
Wedge pressure (mean)	41	−0.4	−1.5 to 0.7	0.452
PA pressure (mean)	43	0.1	−0.7 to 0.9	0.821
Surgery and pump settings				
Bypass time	44	0.0	−0.2 to 0.2	0.928
Discharge pump flow	43	0.5	−9.5 to 10.5	0.920
Discharge LVAD pulsatility index	42	12.6	0.5 to 24.8	0.042
Discharge pump speed (200 rpm)	42	7.4	1.8 to 13.0	0.009
Discharge pump speed >9,200 rmp*	42	22.0	6.9 to 37.2	0.004

The table shows the results of a univariate linear regression analysis for prediction of increase in GFR 1 month after LVAD implantation. GFR was evaluated as a continuous variable. We estimated the associations of various pre-operative variables with increased GFR (operative time and LVAD settings were also included). Estimates were calculated depicting the change in mean GFR associated with the variable measured before and 1 month after operation. Estimates for continuous variables are for change in mean per unit increase in the evaluated variable. p values <0.05 were considered significant. TR time was corrected for pulse; RIMP = (TR time − RV ejection time)/RV ejection time; RVSWI = [0.0136 × (MPAP − RAP) × stroke volume index]; kidney size was assessed by pre-operative abdominal ultrasound. Scores for prediction of outcomes (Lietz-Miller, Matthews, Kormos) were calculated as previously published. *Categorical predictors were assessed using 1-way analysis of variance.

ALT = alanine transaminase; AR = aortic regurgitation; AST = aspartate transaminase; BNP = B-type natriuretic peptide; CI = confidence interval; CRT = cardiac resynchronization therapy; EF = ejection fraction; ICD = implantable cardioverter-defibrillator; LA = left atrial; LDH = lactate dehydrogenase; LVEDD = left ventricular end-diastolic dimension; PA = pulmonary artery; PVR = pulmonary vascular resistance; RA = right atrial; SVR = systemic vascular resistance. Other abbreviations as in Tables 1 to 4.

result in gradual renal deterioration over time. Previous studies comparing non-pulsatile-flow and pulsatile-flow LVADs were not supportive of this suggestion (31). In the present study, higher pump speed settings were associated with improved 1-month renal function. In contrast, a higher pump pulsatility index was also associated with improved GFR. Further study is needed to evaluate for long-term effects of axial-flow LVAD support on renal function as well as ways to facilitate optimal cardiac output, venous pressures, and arterial pulsatility with a continuous-flow pump.

One of our major goals was to ascertain pre-operative predictors for improved renal function in patients with LVAD support. We focused our analysis on patients with pre-operative RD (grade 3 and below) who had the potential for improved renal function. Interestingly, our univariate analysis identified high bilirubin, atrial fibrillation, and partial reversibility of RD with optimal treatment before operation as well as the use of an IABP as positive predictors

of improved GFR. Not surprisingly, older age and small kidney size were negative predictors. We found the negative association of angiotensin inhibitors surprising, although previous reports of kidney dysfunction after heart transplantation suggested similar results (8). The predictors that were significant in the multivariate model were RD partial reversibility, the use of an IABP, and atrial fibrillation. Previous studies have identified only diabetes mellitus as a significant predictor (16). Despite a similar proportion of patients with diabetes in the present study, we did not find this to be a significant predictor. Recently, a new nomenclature for the cardiorenal syndromes was developed, differentiating between primarily cardiac or renal etiology (7). The positive predictors found in our analysis (atrial fibrillation, high right atrial pressure) may represent stronger cardiac-derived cardiorenal syndrome (type 2), while the negative predictors (small kidney, older age) represent less primary renal (type 4) cardiorenal syndrome.

The use of LVADs has improved our ability to understand the physiology of complex multiple-organ syndromes involving the heart, because they acutely improve cardiac output and hemodynamic status. We observed that in our population of patients with advanced heart failure, prompt assistance of left ventricular function resulted in reversibility of established cardiorenal syndrome. Therefore, our results suggest that although long-standing renal hypoperfusion may cause RD, irreversible pathological tissue damage is limited and restoration of perfusion is likely to improve function.

Study limitations. Our study had the limitations of a retrospective analysis. A further limitation was the declining number of patients in whom renal function was evaluated during follow-up (because of patient death, transplantation, missing measurements, and renal deterioration leading to hemodialysis). Therefore, the GFR estimates later in the post-implantation course might be biased to healthier patients. We therefore examined GFR at various time points, used paired analysis for trends in GFR, and selected the 1-month GFR (with less patient dropout) for our analysis of predictors. Because of the limited data points, only 3 parameters could be fitted into the multivariate model. This potentially could result in the underestimation of other potential independent predictors beyond the ones evaluated. Baseline comparison between the 72 patients with GFR results at 1 month and the 11 patients missing indicates that missing patients were sicker (more chronic kidney disease, lower GFRs on admission, lower hemoglobin, higher aspartate transaminase, higher international normalized ratios). They also had shorter tricuspid regurgitation times and smaller left ventricles. Operations were longer, with more need for blood products, and their hospital stays were longer as well. Detailed investigation of the duration, course, and contributing factors of pre-operative RD was not available in our analysis and might have added predictive variables to our predictive model.

Conclusions

In most patients with end-stage heart failure considered for LVAD, renal dysfunction is reversible. Acute renal failure after LVAD is less common than previously reported and is associated with a complicated post-operative course. Prediction of post-operative improvement in renal dysfunction should take into account the likely contribution of renal hypoperfusion and congestion, irreversible renal injury and response to medical treatment pre-implant.

Reprint requests and correspondence: Dr. Sudhir S. Kushwaha, Mayo Clinic, Department of Cardiovascular Diseases, 200 First Street, SW, Rochester, Minnesota 55905. E-mail: kushwaha.sudhir@mayo.edu.

REFERENCES

1. Heywood JT. The cardiorenal syndrome: lessons from the ADHERE database and treatment options. Heart Fail Rev 2004;9:195–201.
2. Ahmed A, Rich MW, Sanders PW, et al. Chronic kidney disease associated mortality in diastolic versus systolic heart failure: a propensity matched study. Am J Cardiol 2007;99:393–8.
3. Heywood JT, Fonarow GC, Costanzo MR, Mathur VS, Wigneswaran JR, Wynne J. High prevalence of renal dysfunction and its impact on outcome in 118,465 patients hospitalized with acute decompensated heart failure: a report from the ADHERE database. J Card Fail 2007;13:422–30.
4. Nohria A, Hasselblad V, Stebbins A, et al. Cardiorenal interactions: insights from the ESCAPE trial. J Am Coll Cardiol 2008;51:1268–74.
5. Coca SG, Krumholz HM, Garg AX, Parikh CR. Underrepresentation of renal disease in randomized controlled trials of cardiovascular disease. JAMA 2006;296:1377–84.
6. Kaisar MO, Isbel NM, Johnson DW. Recent clinical trials of pharmacologic cardiovascular interventions in patients with chronic kidney disease. Rev Recent Clin Trials 2008;3:79–88.
7. Ronco C, McCullough P, Anker SD, et al. Cardio-renal syndromes: report from the consensus conference of the acute dialysis quality initiative. Eur Heart J 2010;31:703–11.
8. Jokinen JJ, Tikkanen J, Kukkonen S, et al. Natural course and risk factors for impaired renal function during the first year after heart transplantation. J Heart Lung Transplant 2010;29:633–40.
9. Martinelli SM, Patel UD, Phillips-Bute BG, et al. Trends in cardiac surgery-associated acute renal failure in the United States: a disproportionate increase after heart transplantation. Ren Fail 2009;31:633–40.
10. Daneshmand MA, Rajagopal K, Lima B, et al. Left ventricular assist device destination therapy versus extended criteria cardiac transplant. Ann Thorac Surg 2010;89:1205–9.
11. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 2001;345:1435–43.
12. Miller LW, Pagani FD, Russell SD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med 2007;357:885–96.
13. Pagani FD, Miller LW, Russell SD, et al. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol 2009;54:312–21.
14. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 2009;361:2241–51.
15. Filsoufi F, Rahmanian PB, Castillo JG, Chikwe J, Carpentier A, Adams DH. Early and late outcomes of cardiac surgery in patients with moderate to severe preoperative renal dysfunction without dialysis. Interact Cardiovasc Thorac Surg 2008;7:90–5.
16. Sandner SE, Zimpfer D, Zrunek P, et al. Renal function and outcome after continuous flow left ventricular assist device implantation. Ann Thorac Surg 2009;87:1072–8.

17. Alba AC, Rao V, Ivanov J, Ross HJ, Delgado DH. Predictors of acute renal dysfunction after ventricular assist device placement. J Card Fail 2009;15:874–81.
18. Topkara VK, Dang NC, Barili F, et al. Predictors and outcomes of continuous veno-venous hemodialysis use after implantation of a left ventricular assist device. J Heart Lung Transplant 2006;25:404–8.
19. Kaltenmaier B, Pommer W, Kaufmann F, Hennig E, Molzahn M, Hetzer R. Outcome of patients with ventricular assist devices and acute renal failure requiring renal replacement therapy. ASAIO J 2000;46:330–3.
20. Lietz K, Miller LW. Patient selection for left-ventricular assist devices. Curr Opin Cardiol 2009;24:246–51.
21. Lund LH, Matthews J, Aaronson K. Patient selection for left ventricular assist devices. Eur J Heart Fail 2010;12:434–43.
22. McBride LR, Naunheim KS, Fiore AC, et al. Risk analysis in patients bridged to transplantation. Ann Thorac Surg 2001;71:1839–44.
23. O'Meara E, Chong KS, Gardner RS, Jardine AG, Neilly JB, McDonagh TA. The Modification of Diet in Renal Disease (MDRD) equations provide valid estimations of glomerular filtration rates in patients with advanced heart failure. Eur J Heart Fail 2006;8:63–7.
24. Smilde TD, van Veldhuisen DJ, Navis G, Voors AA, Hillege HL. Drawbacks and prognostic value of formulas estimating renal function in patients with chronic heart failure and systolic dysfunction. Circulation 2006;114:1572–80.
25. Butler J, Geisberg C, Howser R, et al. Relationship between renal function and left ventricular assist device use. Ann Thorac Surg 2006;81:1745–51.
26. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139:137–47.
27. Smith GL, Vaccarino V, Kosiborod M, et al. Worsening renal function: what is a clinically meaningful change in creatinine during hospitalization with heart failure? J Card Fail 2003;9:13–25.
28. Kirklin JK, Naftel DC, Kormos RL, et al. Third INTERMACS annual report: the evolution of destination therapy in the United States. J Heart Lung Transplant 2011;30:115–23.
29. Russo MJ, Rana A, Chen JM, et al. Pretransplantation patient characteristics and survival following combined heart and kidney transplantation: an analysis of the United Network for Organ Sharing Database. Arch Surg 2009;144:241–6.
30. Bank AJ, Mir SH, Nguyen DQ, et al. Effects of left ventricular assist devices on outcomes in patients undergoing heart transplantation. Ann Thorac Surg 2000;69:1369–74.
31. Sandner SE, Zimpfer D, Zrunek P, et al. Renal function after implantation of continuous versus pulsatile flow left ventricular assist devices. J Heart Lung Transplant 2008;27:469–73.

Key Words: assist device ■ heart failure ■ outcome ■ predictors ■ renal dysfunction.