Predictors and Outcomes of Continuous Veno-venous Hemodialysis Use After Implantation of a Left Ventricular Assist Device

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Background: Post-operative renal failure is a common complication after left ventricular assist device (LVAD) implantation. This study was designed to evaluate predictors and outcomes of acute renal failure after LVAD insertion.

Methods: Two-hundred one patients undergoing LVAD implantation at a single institution from June 1996 through April 2004 were retrospectively analyzed. Patients were categorized into 2 groups: those who required post-operative continuous veno-venous hemodialysis (CVVHD) (Group 1, $n = 65$, 32.3%) and those who did not (Group 2, $n = 136$, 67.7%). Independent predictors of post-operative renal failure requiring CVVHD were determined using multivariate logistic regression techniques.

Results: Patients who had post-operative renal failure requiring CVVHD were older (53.7 ± 12.9 vs 48.2 ± 14.2 years, $p = 0.009$), had a higher incidence of intra-aortic balloon pump use (46.6% vs 26.2%, $p = 0.006$), and had a higher pre-operative mean LVAD score (5.8 ± 3.5 vs 3.8 ± 3.3, $p = 0.001$) than those without renal failure. LVAD score was the only independent predictor of post-operative renal failure requiring CVVHD (odds ratio = 1.226, $p = 0.006$). Sepsis rate was higher (33.3% vs 6.9%, $p < 0.001$) and bridge-to-transplantation rate was lower (52.4% vs 83.5%, $p < 0.001$) in Group 1 than in Group 2. Post-LVAD survival rates at 1, 3, 5 and 7 years for Group 1 and Group 2 were 43.2%, 39.1%, 34.7% and 34.7% vs 79.2%, 74.0%, 68.3% and 66.4%, respectively (log rank, $p < 0.001$).

Conclusions: Acute renal failure necessitating CVVHD remains a serious complication after LVAD and confers significant morbidity and mortality. Pre-operative evaluation of patient risk factors and optimization of peri-operative hemodynamics are of utmost importance to prevent this major complication. J Heart Lung Transplant 2006;25:404–8. Copyright © 2006 by the International Society for Heart and Lung Transplantation.

Left ventricular assist device (LVAD) implantation is an effective treatment option for patients with end-stage heart failure awaiting cardiac transplantation.[1–3] With the development of new devices, advances in technology, and greater experience, the complication profile of LVAD patients has improved compared with earlier reports.[4]

However, post-operative acute renal failure remains a common problem with incidences reported to be as high as 10% to 56%.[1,5,6] The presence of renal failure after implantation has previously been shown to independently predict mortality and lower bridge-to-transplantation rates.[5,7,8] This study was designed to determine predictors and outcomes of post-operative renal failure after LVAD implantation.

METHODS

Patient Population

From June 1996 to April 2004, 201 patients underwent implantation of a Thoratec HeartMate (Thoratec Corp., Pleasanton, CA) device at the Columbia–Presbyterian Medical Center (New York, NY). Patients were categorized into 2 groups: those requiring post-operative continuous veno-venous hemodialysis (CVVHD) (Group 1, $n = 65$, 32.3%), and those not requiring CVVHD (Group 2, $n = 136$, 67.7%). Groups were then compared with regard to demographics, co-morbidities and pre-implantation hepatic and renal serum profiles. Pre-operative LVAD scores for each patient were calculated using 5 clinical variables: post-cardiotomy shock; previous LVAD use; ventilatory status; central venous pressure >16 mm Hg; and prothrombin time >16 seconds.[9]

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Outcome measures included post-operative complications such as infection, bleeding requiring re-operation, stroke, intensive care unit (ICU) and hospital length of stay and bridge-to-transplantation rate. Long-term survival was calculated for both post-LVAD and post-transplantation intervals. Data were collected retrospectively by chart review.

Statistical Analysis

Continuous variables were represented as means with standard deviations, and categoric variables represented as proportions. Continuous variables were compared using independent-sample *t*-tests and categoric variables were compared by chi-square analysis. For all analyses, $p < 0.05$ was considered statistically significant. Significant predictors of post-operative renal failure requiring CVVHD were identified using logistic regression models.[10] Kaplan–Meier analysis was used to determine survival rates with a log-rank *p*-value calculation when comparing groups. All data were analyzed utilizing SPSS v11.5 software (SPSS, Chicago, IL).

RESULTS

Baseline Characteristics

Pre-operative patient characteristics are summarized in Table 1. Patients who had post-operative renal failure requiring CVVHD were older (53.7 ± 12.9 vs 48.2 ± 14.2 years, $p = 0.009$), had a higher incidence of intra-aortic balloon pump (IABP) use (46.6% vs 26.2%, $p = 0.006$), and had a higher pre-operative mean LVAD score (5.8 ± 3.5 vs 3.8 ± 3.3, $p = 0.001$) than those without renal failure. Groups were comparable with regard to race and gender. Although not statistically significant, higher rates of coronary artery disease and lower rates of idiopathic cardiomyopathy as the etiology of heart failure were observed in Group 1 compared with Group 2 (64.6% vs 52.2%, $p = 0.097$, and 24.6% vs 38.2%, $p = 0.056$, respectively). Pre-operative incidences of hypertension and diabetes were similar in both groups.

Table 1. Demographics and Pre-operative Characteristics

	CVVHD	No CVVHD	*p*-value
Number (%)	65 (32.3%)	136 (67.7%)	
Age	53.7 ± 12.9	48.2 ± 14.2	0.009
Female gender	23.1%	15.4%	0.187
Race			
White	66.2%	71.3%	0.456
Black	20.0%	16.2%	0.504
Other	13.8%	12.5%	0.790
Etiology of HF			
CAD	64.6%	52.2%	0.097
ICM	24.6%	38.2%	0.056
Other	10.8%	9.6%	0.789
Hypertension	30.5%	29.0%	0.834
Diabetes	26.2%	23.5%	0.685
IABP use	46.6%	26.2%	0.006
LVAD score	5.8 ± 3.5	3.8 ± 3.3	0.001

CVVHD, continuous veno-venous hemodialysis; HF, heart failure; CAD, coronary artery disease; ICM, idiopathic cardiomyopathy; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device.

Table 2. Pre-operative Renal and Hepatic Serum Profiles

	CVVHD	No CVVHD	*p*-value
BUN (mg/dl)	44.2 ± 26.7	39.9 ± 22.0	0.243
Creatinine (mg/dl)	1.9 ± 0.9	1.8 ± 0.8	0.147
Total protein (g/dl)	5.8 ± 1.4	6.4 ± 1.2	0.007
Albumin (g/dl)	3.3 ± 0.6	3.6 ± 0.6	0.009
Total bilirubin (mg/dl)	2.9 ± 2.9	2.5 ± 2.9	0.442
Direct bilirubin (mg/dl)	1.2 ± 1.7	1.0 ± 1.6	0.562
ALT (U/liter)	221.0 ± 446.3	133.3 ± 368.9	0.178
AST (U/liter)	258.3 ± 436.4	130.8 ± 288.7	0.021
ALP (U/liter)	99.7 ± 75.0	93.4 ± 50.6	0.505

BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

Pre-operative serum laboratory profiles of patients are listed in Table 2. Interestingly, mean pre-operative blood urea nitrogen (BUN) and creatinine levels were comparable in both groups. Both total protein and albumin levels were significantly lower in Group 1 compared with Group 2 (5.8 ± 1.4 vs 6.4 ± 1.2 g/dl, $p = 0.007$, and 3.3 ± 0.6 vs 3.6 ± 0.6 g/dl, $p = 0.009$, respectively). While the results of other liver function tests including alanine aminotransferase, total bilirubin, direct bilirubin and alkaline phosphatase levels were similar in both groups, mean aspartate aminotransferase level was significantly elevated in Group 1 compared to Group 2.

Post-operative Complications and Clinical Outcomes

Although overall device-related infections were comparable between groups, the incidence of post-operative sepsis was significantly higher in Group 1 compared with Group 2 (33.3% vs 6.9%, $p < 0.001$; Table 3).

Table 3. Post-operative Complications and Outcomes

	CVVHD	No CVVHD	*p*-value
Infection			
Driveline	3.5%	6.1%	0.466
Pocket	17.5%	13.7%	0.501
Pump	5.3%	5.3%	0.982
Wound	21.1%	16.0%	0.405
Sepsis	33.3%	6.9%	<0.001
Any	56.9%	41.2%	0.046
Re-operative bleeding	30.5%	18.9%	0.077
Stroke	7.7%	5.1%	0.476
ICU length of stay (days)	26.4 ± 27.1	11.9 ± 10.6	<0.001
Hospital length of stay (days)	40.1 ± 32.2	30.7 ± 23.9	0.028
Bridge to transplantation	52.4%	83.5%	<0.001

ICU, intensive care unit.

Table 4. Independent Predictors of Post-implantation Renal Failure: Multivariate Analysis

	B	SE	*p*-value	OR	95% CI
LVAD score[a]	0.204	0.074	0.006	1.226[b]	1.061–1.417

B, beta coefficient; SE, standard error; OR, odds ratio; CI, confidence interval.
[a]Out of 10 possible points.
[b]Odds ratio for every 1-point increase in LVAD score. Hosmer–Lemeshow goodness-of-fit test, *p*-value = 0.543.

There was a trend toward significance for a higher incidence of bleeding requiring re-operation in Group 1 (30.5% vs 18.9%, $p = 0.077$). Both ICU and hospital length of stay were longer in Group 1 compared with Group 2 (26.4 ± 27.1 vs 11.9 ± 10.6 days, $p < 0.001$, and 40.1 ± 32.2 vs 30.7 ± 23.9 days, $p = 0.028$, respectively). Bridge-to-transplantation rate was significantly lower in Group 1 compared with Group 2 (52.4% vs 83.5%, $p < 0.001$).

Predictors of Post-operative Renal Failure Requiring CVVHD

By multivariate logistic regression analysis, LVAD score was the only independent predictor of post-operative renal failure requiring CVHHD (odds ratio [OR] = 1.226, 95% confidence interval 1.061 to 1.417, $p = 0.006$; Table 4).

Post-LVAD Survival

Kaplan–Meier analysis for post-LVAD survival is depicted in Figure 1. Post-LVAD survival rates at 1, 3, 5 and 7 years for Groups 1 and 2 were 43.2%, 39.1%, 34.7% and 34.7% vs 79.2%, 74.0%, 68.3% and 66.4%, respectively (log rank, $p < 0.001$).

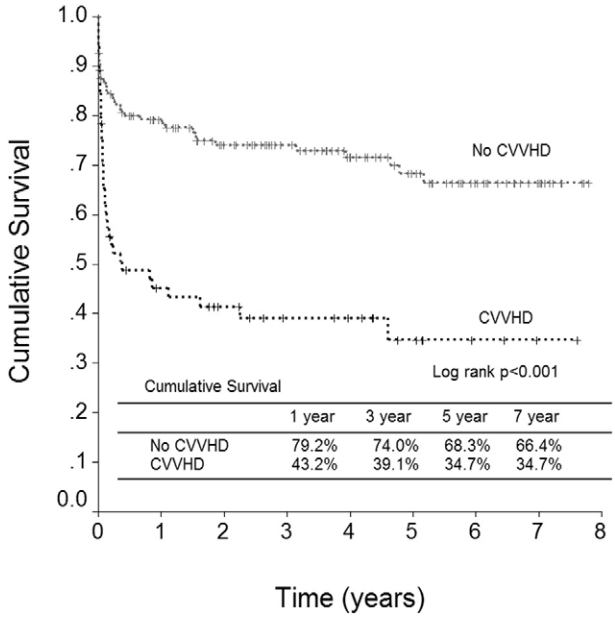

Figure 1. Post-LVAD survival: Kaplan–Meier analysis.

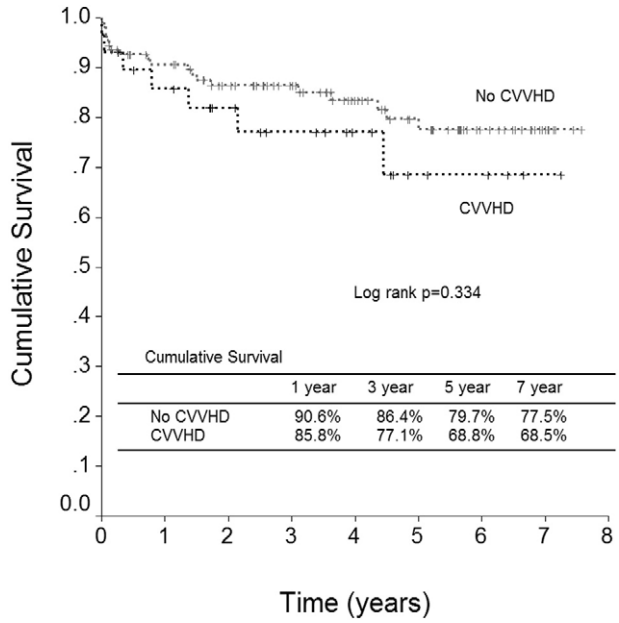

Figure 2. Post-transplantation survival: Kaplan–Meier analysis.

Post-transplantation Survival

Post-transplantation survival is depicted in Figure 2. Survival rates at 1, 3, 5 and 7 years for Groups 1 and 2 were 85.8%, 77.1%, 68.8% and 68.5% vs 90.6%, 86.4% 79.7% and 77.5%, respectively (log rank, $p = 0.334$).

DISCUSSION

Several reports have emphasized the clinical impact of pre-operative renal failure on patients undergoing implantation of a left ventricular assist device. In 1987, Kanter et al reported a 100% mortality rate in LVAD patients requiring dialysis in the peri-implantation period, and therefore pre-operative acute renal failure was considered a major risk factor for negative outcomes.[11] Later, in the original multicenter LVAD score model, pre-operative urine output <30 ml/hour was identified as a strong predictor of mortality (relative risk = 3.9) after LVAD implantation.[12] More recently, however, the presence of pre-operative renal dysfunction in LVAD patients has not been shown to be a risk factor for worse outcomes, an observation validated by the revised LVAD score model.[9] Khot et al reported similar bridge-to-transplantation rates and 1-year post-transplant survival rates in patients who developed pre-operative renal dysfunction compared with those who did not (61% vs 68%, $p = 0.549$, and 82% vs 88%, $p = 0.628$, respectively).[13] These changes may reflect improvement in the management of pre-operative acute renal failure (ARF), including a more aggressive approach upon manifestation of oliguria and an earlier institution of hemodialysis.

Despite improvements in device technology, surgical techniques, anesthetic management and peri-operative

care, post-operative ARF remains a challenging problem in LVAD recipients, with incidences reported up to 56%.[6] In a recent study, Kaltenmaier et al reported a 93% 6-month mortality rate in patients who developed ARF while on LVAD support.[5] Our institution's revised LVAD score model also determined post-operative ARF to be a significant predictor of mortality.[9] However, studies specifically looking at predictors and outcomes of post-LVAD ARF were still lacking in the literature.

The present study points out significant differences in the baseline characteristics of patients. The CVVHD ARF patients were significantly older. This observation parallels previous studies in which increased age was found to be a risk factor for the development of ARF.[14–16] The correlation between advanced age and ARF may relate to diminished renal function and reserve in the elderly, coupled with systemic and vascular pathologies.[15] The greater use of pre-operative IABP in patients requiring post-LVAD CVVHD suggests lower output states to begin with. Moreover, the presence of higher mean LVAD scores in this group of patients confirms their multi-system co-morbid conditions. Collectively, these findings suggest that patients who develop ARF after LVAD implantation are sicker at baseline.

A curious finding in the present analysis is the lack of a predictive effect of pre-implantation serum BUN and creatinine levels on post-LVAD ARF necessitating CVVHD. There were, in fact, no differences in mean BUN and creatinine levels between groups. Interestingly, mean total protein and albumin levels were significantly lower in patients who developed ARF requiring CVVHD. Low serum albumin is a marker of malnutrition, a major complication associated with heart failure, and an index of worse outcome.[17] Engelman et al showed that low pre-operative albumin (<2.5 g/dl) was an independent predictor of increased mortality, incidence of post-operative renal failure and hospital length of stay after cardiopulmonary bypass.[18] We therefore believe pre-operative nutritional evaluation should be considered part of the routine work-up in patients undergoing LVAD implantation.

In this study, the presence of post-operative ARF was associated with an increased incidence of other complications. Although the incidence of overall device-related infections was similar in both groups, the incidence of sepsis was notably higher in those requiring CVVHD. The exact reasons for this association are not known, but may relate to the use of hemodialysis catheters and their inherent risk of bacteremia.[19] Furthermore, post-operative renal failure in open-heart surgery patients is known generally to influence the frequency of serious infections.[20] ICU and hospital length of stay were longer in patients requiring post-operative CVVHD. This is likely attributable to both the use of CVVHD itself and the associated increased incidence of post-operative complications.

Post-LVAD CVVHD patients had significantly lower post-LVAD survival than their non-CVVHD counterparts, with a 1-year mortality rate of 56.8%. Overall bridge-to-transplantation rate in this group was 52.4%. Most of the deaths in the CVVHD group occurred within 1 year after LVAD implantation. Once patients recovered from ARF and survived to transplantation, survival was similar between groups.

Limitations of this study include those related to any retrospective analyses. Post-operative renal failure was defined as the requirement for CVVHD. This criterion alone therefore excluded patients who developed renal failure and did not require CVVHD. Moreover, pre-operative renal function was only evaluated using pre-implantation serum BUN and creatinine levels. Other renal parameters, such as urine output, kidney-specific proteins and pre-operative hemodialysis/CVVHD, use were not available for the analysis. Finally, the lack of a temporal relationship between post-operative renal failure and other complications is a major limitation in demonstrating causal effect.

In conclusion, post-LVAD renal failure necessitating CVVHD is a common and serious complication that carries high morbidity and mortality. Patients with multiple acute co-morbid conditions are at high risk for developing post-operative renal failure. Proper patient selection as well as optimizing peri-operative hemodynamics with an effective use of pressors, IABP and temporary assist devices would significantly decrease renal failure after LVAD implantation and improve outcomes among this population.

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