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Renal Function and Outcomes With Use of Left Ventricular Assist Device Implantation and Inotropes in End-Stage Heart Failure: A Retrospective Single Center Study

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Abstract

Background: Left ventricular assist device (LVAD) and inotrope therapy serve as a bridge to transplant (BTT) or as destination therapy in patients who are not heart transplant candidates. End-stage heart failure patients often have impaired renal function, and renal outcomes after LVAD therapy versus inotrope therapy have not been evaluated.

Methods: In this study, 169 patients with continuous flow LVAD therapy and 20 patients with continuous intravenous inotrope therapy were analyzed. The two groups were evaluated at baseline and at 3 and 6 months after LVAD or inotrope therapy was started. The incidence of acute kidney injury (AKI), need for renal replacement therapy (RRT), BTT rate, and mortality for 6 months following LVAD or inotrope therapy were studied. Results between the groups were compared using Mann-Whitney U test and Chi-square with continuity correction or Fischer's exact at the significance level of 0.05.

Results: Mean glomerular filtration rate (GFR) was not statistically different between the two groups, with P = 0.471, 0.429, and 0.847 at baseline, 3 and 6 months, respectively. The incidence of AKI, RRT, and BTT was not statistically different. Mortality was less in the inotrope group (P < 0.001).

Conclusion: Intravenous inotrope therapy in end-stage heart failure patients is non-inferior for mortality, incidence of AKI, need for RRT, and renal function for 6-month follow-up when compared to LVAD therapy. Further studies are needed to compare the effectiveness of inotropes versus LVAD implantation on renal function and outcomes over a longer time period.

Keywords: Left ventricular assist device; Inotrope; Renal function; Acute kidney injury; Cardiovascular disease; Congestive heart failure

Introduction

End-stage heart failure is a growing public health concern, with an estimated 5.7 million people in the United States suffering from heart failure [1], many of which have concurrent renal failure. The only cure for end-stage heart failure is heart transplantation, which has the largest survival benefit. Heart transplantation is available for a minority of patients, with less than 3,000 donor organs available yearly [2]. In patients who are on maximum medical therapy, mechanical circulatory support is superior for outcomes and mortality [2]. Left ventricular assist device (LVAD) therapy is a viable and effective option as a bridge to transplant (BTT) or for destination therapy (DT) for patients who are unable to receive heart transplant. It has improved morbidity and survival [3]. LVAD therapy improves functional status as well as quality of life in patients [4, 5]. However, little is known about long term renal function in patients after beginning LVAD therapy.

The relationship between renal disease (RD) and heart failure has considerable overlap with up to 45% of heart failure patients having a glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 in the outpatient setting [6]. Another study estimates the presence of chronic kidney disease (CKD) to be close to two-thirds of patients hospitalized with heart failure, with 44% with CKD stage 3, 14% stage 4, and 7% stage 5 [7]. A few studies compared renal function following LVAD therapy and with inconsistent results [8-10]. Studies typically follow patients for up to 6 months after LVAD therapy [11, 12]. In this study, the authors evaluate mortality, renal outcomes (need for replacement therapy (RRT), incidence of acute kidney injury (AKI), and BTT) and other laboratory outcomes which may be affected by enhanced renal perfusion (albumin, hemoglobin, blood urea nitrogen (BUN), and brain natriuretic peptide (BNP)) after LVAD therapy for 24 months.

Mortality, renal function, and laboratory values that may be affected by increased renal perfusion in patients with base-

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line preexisting RD (GFR < 60 mL/min/1.73 m^2) versus those with normal renal function (GFR ≥ 60 mL/min/1.73 m^2) for follow-up of 24 months post-LVAD therapy were further evaluated. The presence of preexisting RD increases the risk of mortality in the short term [12, 13], but studies have not compared patients with preexisting RD to those without for an extended time period.

Renal function and outcomes in patients after LVAD therapy versus intravenous inotrope therapy with milrinone or dobutamine for 6 months follow-up were also evaluated. Both inotrope therapy and LVAD therapy provide hemodynamic support in end-stage heart failure patients by increasing cardiac output and renal perfusion [14]. Inotrope versus LVAD therapy has not been directly compared for renal function and outcomes.

Methods

Design and study sample

This retrospective study analyzed 169 patients with New York Heart Association (NYHA) class IV symptoms and end-stage heart failure who underwent continuous flow LVAD therapy from 2010 to 2013 as a BTT or as DT (LVAD group). Renal function was assessed by calculating the GFR using the modification of diet in renal disease (MDRD) equation: GFR $=189 \times (\text{serum creatinine (mg/dL)})^{-1.154} \times (\text{age})^{-0.203} \times 0.742$ (if female) [15]. Renal function was measured at baseline prior to LVAD implantation and then at 3-month intervals. All patients in the LVAD group were followed until 24 months after LVAD therapy, death, or cardiac transplant. Other laboratory values that were compared prior to LVAD and at 3-month intervals post-LVAD included: BUN, albumin, BNP, and hemoglobin. Other outcome measures included: the incidence of AKI, defined as an increase in creatinine of 0.3 mg/dL in 48 h or 1.5 times the baseline in the last 7 days after LVAD therapy, need for RRT, BTT rate, and mortality within 24 months following LVAD.

The LVAD group was then divided into two subgroups based on baseline GFR prior to LVAD, and defined as having normal renal function if GFR was ≥ 60 mL/min/1.73 m^2 (n = 79), and as having RD if GFR was < 60 mL/min/1.73 m^2 (n = 84) at baseline prior to LVAD therapy. Baseline creatinine was not available for six out of the 169 patients because they had their LVAD placed at an outside center and therefore they were not included in subgroup analysis of the LVAD group. Just as in the LVAD group, the incidence of AKI, BTT rate, need for RRT, mortality, BUN, albumin, BNP, and hemoglobin for 24 months after LVAD therapy were compared at 3-month intervals between subgroups.

In this study, 20 end-stage heart failure patients with NYHA class IV symptoms, who declined LVAD therapy, and began continuous intravenous inotrope therapy with milrinone or dobutamine (inotrope group) were compared to the LVAD group. Renal function, incidence of AKI, BTT rate, need for RRT, mortality, BUN, albumin, BNP, and hemoglobin for 6 months follow-up were compared in the LVAD and inotrope groups.

Statistical analysis

The comparison of categorical variables (e.g. gender, hypertension, etc.) between patients receiving LVAD versus inotrope was conducted using Chi-square with continuity correction or Fischer's exact at the significance level of 0.05. The baseline characteristic and results for 6 months follow-up in the LVAD versus inotrope groups following LVAD or inotrope therapy were investigated using Mann-Whitney U test.

The comparison of categorical variables (e.g. need for RRT, BTT rate, etc.) between patients with GFR < 60 mL/min/1.73 m^2 versus GFR ≥ 60 mL/min/1.73 m^2 was conducted using Chi-square test with continuity correction or Fischer's exact at the significance level of 0.05. The results from baseline characteristic to 24 months of follow-up in the patients with GFR < 60 mL/min/1.73 m^2 versus GFR ≥ 60 mL/min/1.73 m^2 were investigated using Mann-Whitney U test. The results from baseline characteristic to 24 months follow-up in the patients with LVAD therapy were investigated using the pairwise *t* test. All statistical analyses were conducted using the SPSS v 22.0 software.

Results

Patient demographic and baseline characteristics

Baseline characteristics for the LVAD group are as follows: mean age 57.8 ± 1.1 years; males 76.3%; Caucasians 76.9%, African American 13.6%, Hispanic 5.9%, and other ethnicities 3.6%; 43.8% CKD; 45% type 2 diabetes mellitus; and 60.9% hypertension. In the LVAD group, 24.3% received cardiac transplant during the 24-month follow-up and 40.2% died during this time. Baseline characteristics in the inotrope group are similar to the LVAD group (Table 1). Baseline characteristics are similar in the subgroup with baseline GFR ≥ 60 mL/min/1.73 m^2, and the RD subgroup with baseline GFR < 60 mL/min/1.73 m^2 (Table 2).

Renal function and outcomes after LVAD therapy

Paired sample analysis in the LVAD group for GFR prior to LVAD therapy and follow-up showed the following changes in mL/min/1.73 m^2: baseline to 3 months, 53.1 ± 15.4 to 56.9 ± 18.5 (P = 0.013); baseline to 6 months 53.3 ± 15.1 to 56.3 ± 17.8 (P = 0.049). Full paired sample analyses for 24 months follow-up after LVAD are in Table 3.

In the LVAD group, 47.3% had an AKI in the immediate postoperative period following LVAD. Only 3.6% required RRT after LVAD, with most cases of AKI post procedure being transient and not severe enough to necessitate RRT. Similarly, paired sample analysis for BUN showed significant improvement from baseline to 3 months after LVAD and baseline to 6 months. Full paired sample analysis until 24 months follow-

Table 1. LVAD Group Versus Inotrope Group

Characteristic	Follow-up time (months)	LVAD group values, mean ± SD or n/N (%)	Inotrope group values, mean ± SD or n/N (%)	P value
Age (years)		57.8 ± 14.0	56.9 ± 13.4	0.624
Men		129/169 (76.3%)	14/20 (70%)	0.352
Hypertension		103/169 (60.9%)	15/20 (75%)	0.220
Diabetes mellitus type 2		76/169 (45%)	5/20 (25 %)	0.088
CKD		74/169 (43.8%)	9/20 (45%)	0.918
Tobacco use		81/169 (47.9%)	9/20 (45%)	0.804
BMI (kg/m^2)		29.2 ± 6.2	27.5 ± 5.4	0.293
Albumin (mg/dL)	Baseline	3.1 ± 0.6	3.5 ± 0.6	0.013
	3	3.4 ± 0.5	3.6 ± 0.4	0.235
	6	3.6 ± 0.5	3.8 ± 0.5	0.082
BNP (pg/dL)	Baseline	1,206.2 ± 1,214.6	1,199.6 ± 1,005.1	0.674
	3	326.7 ± 302.0	686.6 ± 854.2	0.090
	6	312.1 ± 382.0	583.0 ± 401.1	0.05
Hemoglobin (mg/dL)	Baseline	12.3 ± 1.8	11.3 ± 2.0	0.03
	3	12.1 ± 1.7	11.2 ± 2.1	0.533
	6	11.9 ± 1.7	11.9 ± 1.7	0.621

Values are mean ± standard deviation or number of patients positive for the characteristic (n) divided by the total number of patients in the group (N). The table depicts baseline characteristic and results for 6 months of follow-up in the LVAD and inotrope groups following LVAD placement or inotrope initiation. CKD: chronic kidney disease; BMI: body mass index; BNP: brain natriuretic peptide.

up is in Table 3. Other laboratory values measured prior and after LVAD therapy include albumin, BNP, and hemoglobin. Results are included in Table 3.

Renal function and outcomes in GFR ≥ 60 mL/min/1.73 m^2 versus GFR < 60 mL/min/1.73 m^2 subgroups

The LVAD group was further divided into two subgroups, those with RD and GFR < 60 mL/min/1.73 m^2 (n = 84) versus those with normal renal function and GFR ≥ 60 mL/min/1.73 m^2 (n = 79) and compared for renal function and outcomes. Six patients had missing values precluding them from being further subgrouped by GFR and were not included in subgroup analysis. Mean GFR in the RD subgroup was 39.6 ± 13.9 and 63.6 ± 7.7 mL/min/1.73 m^2 in the normal renal function subgroup at baseline prior to LVAD (P < 0.001). Mean GFR up to 24 months is in Table 2. The incidence of AKI, need for RRT, and BTT are not statistically different for 24-month follow-up between the two subgroups (Table 2). Mean BUN between the RD subgroup and normal renal function subgroup in mg/dL is as follows: 32.9 versus 19.2 prior to LVAD (P < 0.001); 25.1 versus 19.7 at 3 months post-LVAD (P = 0.001); 19.6 versus 24.4 at 6 months follow-up (P = 0.005). The BUN throughout follow-up in the baseline normal renal function subgroup was less (Table 2).

Just as for the entire cohort of 169 patients who received LVAD, other laboratory studies possibly thought to be affected by enhanced renal perfusion are compared within the two subgroups. There are no statistical differences at baseline or at follow-up after LVAD therapy at 3, 6, 9, 12, 15, 18, 21, and 24 months for albumin, BNP, or hemoglobin (Table 2).

Renal function and outcomes in LVAD versus inotrope groups

The LVAD and inotrope groups were compared for renal function and outcomes at 3-month intervals for 6 months. Mean GFR in mL/min/1.73 m^2 between the LVAD group and inotrope group was as follows: 51.1 ±1.3 versus 51.1 ± 4.6 prior to LVAD or inotrope therapy (P = 0.471); 56.9 ± 1.6 versus 53.3 ± 5.1 at 3-month follow-up (P = 0.429); 56.1 ± 1.6 versus 58.1 ± 5.4 at 6-month follow-up (P = 0.847). BUN between the LVAD and inotrope group was as follows: 26.1 ± 15.1 versus 28.7 ± 15.0 prior to LVAD or inotrope therapy (P = 0.280); 22.3 ±13.2 versus 29.5 ± 14.5 at 3-month follow-up (P = 0.016); 21.9 ± 9.8 versus 29.4 ± 14.5 at 6-month follow-up (P = 0.056).

AKI in the immediate postoperative time occurred in 47.3% in the LVAD group and 30% in the inotrope group (P = 0.141). In this study, six patients in the LVAD group and one patient in the inotrope group needed RRT (P = 0.549) during 6-month follow-up. Also, four patients in the LVAD group and one patient in the inotrope group underwent transplant within 6 months after LVAD or inotrope therapy (P = 0.119). A total of 41 patients underwent transplant in the LVAD group but 37 of these patients received transplant greater than 6 months after their LVAD therapy. During 6-month follow-up zero patients in the inotrope group and 34 patients in the LVAD group died (P < 0.001). Mean albumin, mean BNP, and mean hemoglobin

Table 2. LVAD Subgroup Analysis, GFR ≥ 60 mL/min/1.73 m^2 Versus GFR < 60 mL/min/1.73 m^2

Characteristic	Follow-up time, (months)	GFR ≥ 60 mL/min/1.73 m^2 values, mean ± SD or n/N (%)	GFR < 60 mL/min/1.73 m^2 values, mean ± SD or n/N (%)	P value
Age (years)		55.4 ± 15.2	59.9 ± 12.2	0.930
Men		60/79 (75.9%)	66/84 (78.6%)	0.690
Hypertension		42/79 (53.1%)	58/84 (69%)	0.037
Diabetes mellitus type 2		33/79 (41.8%)	41/84 (48.8%)	0.367
Tobacco use		39/79 (49.4%)	40/84 (47.6%)	0.823
AKI postoperative		40/79 (50.6%)	39/84 (46.4%)	0.591
BTT rate		22/79 (27.8%)	18/84 (21.4%)	0.341
Need for RRT		2/79 (2.5%)	4/89 (4.8%)	0.450
Mortality over 24 months		26/79 (32.9%)	38/84 (45.2%)	0.107
BMI (kg/m^2)		29.5 ± 6.0	29.1 ± 6.5	0.521
GFR (mL/min/1.73 m^2)	Baseline	63.6 ± 7.7	39.6 ± 13.9	< 0.001
	3	62.8 ± 16.9	50.8 ± 18.3	< 0.001
	6	62.2 ± 17	50.1 ± 15.8	< 0.001
	9	63.3 ± 18.7	49.1 ± 19.1	< 0.001
	12	59.9 ± 14.1	47.0 ± 15.2	< 0.001
	15	62.3 ± 16.3	48.7 ± 14.9	< 0.001
	18	61.2 ± 17.2	50.9 ± 13.5	< 0.001
	21	60.8 ± 17	48.9 ± 14.6	< 0.001
	24	54.6 ± 16.9	47.6 ± 15.3	< 0.001
BUN (mg/dL)	Baseline	19.2 ± 8.5	32.9 ± 17.6	< 0.001
	3	19.7 ± 13.2	25.1 ± 12.8	0.001
	6	19.6 ± 8.7	24.4 ± 10.6	0.005
	9	20.3 ± 8.2	26.2 ± 12.2	0.004
	12	22.5 ± 10.2	26.5 ± 13.8	0.122
	15	22.9 ± 11.5	24.4 ± 10.7	0.390
	18	21 ± 11.8	23.9 ± 11.0	0.093
	21	22.6 ± 11.8	23.8 ± 13.8	0.827
	24	19.5 ± 8.0	25.3 ± 11.3	0.036
Albumin (mg/dL)	Baseline	3.1 ± 0.6	3.2 ± 0.6	0.498
	3	3.5 ± 0.5	3.4 ± 0.6	0.294
	6	3.6 ± 0.5	3.6 ± 0.5	0.550
	9	3.6 ± 0.5	3.6 ± 0.5	0.520
	12	3.5 ± 0.6	3.5 ± 0.6	0.946
	15	3.5 ± 0.6	3.6 ± 0.5	0.878
	18	3.6 ± 0.6	3.6 ± 0.5	0.896
	21	3.6 ± 0.5	3.5 ± 0.5	0.325
	24	4.0 ± 1.7	3.6 ± 0.5	0.191
BNP (mg/dL)	Baseline	1,035 ± 975.1	1,329.1 ± 1,384.1	0.311
	3	282.3 ± 169.5	372.5 ± 388.4	0.737
	6	305.9 ± 474.1	310.6 ± 284.7	0.619
	9	281.5 ± 301.2	328.8 ± 295.2	0.396
	12	306.7 ± 280.3	363.5 ± 438.3	0.842

Table 2. LVAD Subgroup Analysis, GFR ≥ 60 mL/min/1.73 m^2 Versus GFR < 60 mL/min/1.73 m^2 - *(continued)*

Characteristic	Follow-up time, (months)	GFR ≥ 60 mL/min/1.73 m^2 values, mean ± SD or n/N (%)	GFR < 60 mL/min/1.73 m^2 values, mean ± SD or n/N (%)	P value
	15	395.9 ± 382.6	411.1 ± 603.1	0.807
	18	224.1 ± 173.8	308.9 ± 412.1	0.592
	21	338.5 ± 301.5	329.7 ± 270.2	0.940
	24	269.8 ± 267.7	259.2 ± 181.8	0.670
Hemoglobin (mg/dL)	Baseline	11.4 ± 2	11.2 ± 1.8	0.436
	3	11.5 ± 1.9	11.1 ± 2.0	0.247
	6	11.4 ± 1.8	11.4 ± 1.9	0.889
	9	11.7 ± 2.4	11.5 ± 1.9	0.670
	12	11.7 ± 2.5	11.5 ± 2.2	0.792
	15	11.7 ± 2.3	11.7 ± 1.9	0.930
	18	11.7 ± 2.3	11.5 ± 1.9	0.520
	21	11.9 ± 2.3	11.6 ± 1.6	0.277
	24	11.8 ± 2.1	11.6 ± 2.1	0.683

Values are mean ± standard deviation or number of patients positive for the characteristic (n) divided by the total number of patients in the group (N). The table depicts baseline characteristic and results for 24 months of follow up in the group with GFR ≥ 60 mL/min/1.73 m^2 versus GFR < 60 mL/min/1.73 m^2. AKI: acute kidney injury; BTT: bridge to transplant; RRT: renal replacement therapy; BMI: body mass index; GFR: glomerular filtration rate; BUN: blood urea nitrogen; BNP: brain natriuretic peptide.

are compared between the LVAD group and inotrope group for 6 months follow-up (Table 1).

Discussion

LVAD implantation as a BTT and DT is gaining popularity as a feasible alternative for both patient and physicians. Statistically significant improvement was seen in GFR in the LVAD group at 3 and 6 months, similar to other studies with a total of 6 months follow-up [11, 12]. Unlike many previous studies, renal outcomes at 3-month intervals following LVAD for 24 months were measured. Previous studies measured renal function 1 month after LVAD noting a significant improvement in GFR but also noting a decline in improvement in GFR from 1 to 6 months follow-up [11, 12]. For this reason, we did not measure 1-month follow-up GFR as it is likely not an accurate indicator of renal function long term after LVAD. In this cohort improvement in GFR down trended or seemed to plateau with longer follow-up. The reasons for why GFR may initially improve significantly and gradually decline and plateau are likely multifactorial. A possible explanation includes decreased creatinine due to the decreased muscle mass in the months following recovery from LVAD surgery which may falsely elevate GFR in the initial month of follow-up. Lower preoperative albumin, as a marker for nutritional status, correlated with higher GFR presumably due to decreased muscle mass, lower creatinine, and elevated GFR [11]. Overall, GFR improved following LVAD therapy over 24-month follow-up.

Other laboratory values thought to be possibly affected with LVAD and improved cardiac output and enhanced renal perfusion include BNP, albumin, and hemoglobin. BNP significant improvement from baseline to follow-up at all months of follow-up ($P < 0.024$) except at measurement at 21 months ($P = 0.071$). The significant improvement in BNP following LVAD is best explained by improved cardiac output and decreased fluid overload causing decreased heart ventricle stretch and less BNP release. The exact importance of BNP measurement in heart failure as a prognostic tool is unclear but the majority of patients show decreased mortality and morbidity with lower BNP [16]. Following LVAD, neurohormonal activity decreases, improving heart failure symptoms. Renin, atrial natriuretic peptide, aldosterone, and arginine vasopressin, decrease after LVAD [17]. Hemoglobin and albumin improve overall in 24-month follow-up as well. This is important as anemia is associated with poor outcomes following LVAD surgery [18]. Pre-operative hypoalbuminemia is associated with poorer outcomes following LVAD. Postoperative improvement in albumin is associated with better survival following LVAD [19]. Albumin may be used as a measure of nutritional status, inflammation as it is a negative acute phase reactant, catabolic state, and hepatic function [20, 21]. Albumin improvement following LVAD is likely most notably due to increased hepatic perfusion, decrease in neurohormonal activation leading to decreased inflammatory/catabolic state, and improved volume status.

The mortality over 24-month follow-up in the LVAD group was 40.2%. In the REMATCH study, 48% and 75% of LVAD recipients died at 1 and 2 years, respectively [2]. More recent studies have shown 27% and 15% mortality respectively at 1-year follow-up after LVAD therapy [22, 23]. Mortality after LVAD is most commonly due to sepsis, ischemic stroke, and hemorrhagic stroke, with the most common complications being right-sided hearted failure, bleeding, reoperation and arrhythmias [24].

Not all patients are able to receive LVAD therapy given

Table 3. LVAD Group Results

Characteristic	Follow-up time (months)	Baseline values, mean ± SD	Follow-up values, mean ± SD	P value
GFR (mL/min/1.73 m^2)	3	53.1 ± 15.4	56.9 ± 18.5	0.013
	6	53.3 ± 15.1	56.3 ± 17.8	0.049
	9	54.2 ± 14.7	56.7 ± 20.1	0.133
	12	53.9 ± 14.5	53.7 ± 15.9	0.860
	15	54.1 ± 14.9	55.6 ± 16.9	0.399
	18	53.9 ± 15.2	55.8 ± 16.1	0.280
	21	53.9 ± 15.0	54.5 ± 16.9	0.758
	24	54.8 ± 13.8	54.6 ± 16.9	0.950
BUN (mg/dL)	3	25.2 ± 13.7	22.3 ± 13.2	0.024
	6	24.9 ± 13.1	21.8 ± 9.8	0.006
	9	24.6 ± 13.2	23.3 ± 10.9	0.255
	12	24.8 ± 13.2	24.5 ± 12.3	0.826
	15	24.4 ± 12.5	23.5 ± 10.9	0.587
	18	24.8 ± 12.9	22.4 ± 11.2	0.119
	21	24.9 ± 13.6	23.9 ± 13.8	0.600
	24	24.1 ± 12.4	23.0 ± 10.9	0.465
Albumin (mg/dL)	3	3.2 ± 0.5	3.4 ± 0.5	0.001
	6	3.2 ± 0.6	3.6 ± 0.5	< 0.001
	9	3.2 ± 0.5	3.6 ± 0.5	< 0.001
	12	3.2 ± 0.5	3.5 ± 0.6	0.001
	15	3.3 ± 0.5	3.6 ± 0.6	0.002
	18	3.3 ± 0.5	3.6 ± 0.6	0.001
	21	3.3 ± 0.5	3.5 ± 0.6	0.011
	24	3.2 ± 0.5	3.7 ± 0.6	< 0.001
BNP (pg/mL)	3	1,010.1 ± 1,112.9	333.8 ± 303.7	< 0.001
	6	1,009.4 ± 1,154.2	303.4 ± 377.2	< 0.001
	9	894.8 ± 995.4	315.0 ± 303.4	< 0.001
	12	917.5 ± 1,105.1	345.6 ± 384.5	< 0.001
	15	830.4 ± 1,199.6	401.5 ± 528.0	0.024
	18	830.4 ± 1,117.4	277 ± 335.0	0.007
	21	738.8 ± 1,162.4	333.4 ± 282.2	0.071
	24	781.9 ± 1,157.5	268.0 ± 223.5	0.015
Hemoglobin (mg/dL)	3	10.9 ± 1.9	11.2 ± 2.1	0.181
	6	10.9 ± 2.0	11.4 ± 2.0	0.067
	9	10.8 ± 2.0	11.5 ± 2.4	0.017
	12	10.8 ± 1.9	11.5 ± 2.5	0.015
	15	10.9 ± 1.8	11.7 ± 2.1	0.020
	18	10.8 ± 1.7	11.6 ± 2.0	0.015
	21	0.9 ± 1.7	11.8 ± 1.9	0.009
	24	11.0 ± 1.9	11.8 ± 1.9	0.044

their significant comorbidities and others desire a less invasive means for treatment. Alternatively, some patients do not want to undergo surgical procedures such as LVAD or cardiac transplant and choose continuous inotrope treatment as a BTT or a bridge to end of life [25]. Limited data on renal function and outcomes are available when comparing these alternate means to increase cardiac output and increase renal perfusion. In this study, inotropes improve renal function and were non-inferior in outcomes including incidence of AKI, RRT, BTT, and actually superior for mortality for 6 months follow-up. There is no statistical significance seen between GFR between the LVAD and inotrope groups for 6-month follow-up.

Inotrope therapy is a controversial topic in the management of heart failure and inotrope use is often associated with the notion of increased mortality with prolonged use. However, there are a few randomized controlled trials and much of the data are anticipated and based on registry data which suggest high mortality in this population of patents who are inotrope dependent [25-28]. Much of the data are on inotropes no longer used in clinical practice, on patients without correct indication of inotropes, or before automatic cardio-defibrillators were placed for primary prevention [26]. It is to be expected that this population has high mortality given that the patients that require continuous inotrope typically have decompensated end-stage heart failure along with multiple underlying comorbidities. A meta-analysis of multiple placebo trials failed to show increased mortality with inotropes [29]. While results of much of the data remain conflicting, there have been multiple studies showing improved renal and hepatic function with use of inotropes [30, 31]. Numerous studies show improvement in re-hospitalization rate, NYHA class, reduction in cost of care, and overall symptomatic improvement following continuous inotrope therapy [30, 32-35]. Inotropes may have their place in select end-stage heart failure patients as a BTT or to end of life care while preserving other end organ function, most notably renal function. It is also important to understand predictors of poor outcomes in patients undergoing LVAD therapy. Preexisting RD as a predictor for poor outcomes and renal function following LVAD is a controversial topic with mixed results [9, 13, 36]. In this cohort, there is no statistical difference in mortality, incidence of AKI, need for RRT, and BTT for 24-month follow-up between the preexisting RD or normal renal function subgroups. In previous study, GFR is not an independent predictor of post-LVAD mortality in multivariate analysis though baseline RD is associated with significantly higher mortality rate and less BTT rate [12]. Another study which used the Cockcroft-Gault formula to estimate renal function also showed increased mortality in patients with baseline RD following LVAD therapy [13]. However, in patients with baseline RD there appears to be significant amount of recovery in renal function following LVAD and similar survival for 6-month follow-up after LVAD [37]. In this study of 169 patients there was similar survival even up to 24 months of follow-up in the subgroups. The MDRD formula is superior to the Cockcroft-Gault formula in estimating the GFR in heart failure patients which is why it is used in this study [38].

Incidence of AKI and BTT is not statistically different in the two subgroups as well. AKI is associated with increased mortality following LVAD [12]. AKI is associated with decrease BTT after LVAD. Therefore, it is important to predict which type of patients may have AKI after LVAD. Previous studies show inconsistent results with RD as a predictor for AKI after LVAD [12, 37, 39]. In this cohort of 169 LVAD patients baseline RD is not associated with higher incidence of AKI. This is important as some transplant centers use baseline RD as an exclusion criterion or criterion necessitating a kidney-heart transplant and not just heart transplant alone. These centers believe those patients may have higher incidence of AKI, morbidity and mortality following LVAD, but this was not the case in this cohort.

This study has limitations. First, it is retrospective; second, the number of patients declined during follow-up from death, or were transplanted; and third there was 169 patients who received LVAD while 20 patents had continuous inotrope therapy without LVAD support.

Conclusion

Overall, there is not a significant difference in renal function measured by GFR and renal outcomes, including incidence of AKI, need for RRT, and BTT between patients who receive continuous inotrope versus LVAD therapy. Mortality was significantly better in the inotrope group for up to 6 months follow-up. This study suggests that continuous inotrope therapy may be just as effective for renal function and outcomes as LVAD therapy for up to at least 6 months. Further studies to compare the effectiveness of inotrope versus LVAD therapy on renal function and renal outcomes over a longer time period are needed.

Disclosure

None of the authors declare a competing interest. All work was performed at Tampa General Hospital Tampa, FL.

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