Continuous-flow left ventricular assist device implantation as a bridge to transplantation or destination therapy: Racial disparities in outcomes

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**KEYWORDS:**
left ventricular assist device; race; African American; racial disparities; outcomes

**BACKGROUND:** There is a paucity of data assessing racial disparities in outcomes after left ventricular assist device (LVAD) implantation. This may be due to the relatively low percentage of African American (AA) patients at a given center. Given the high proportion of AAs in our patient population, we sought to evaluate outcomes of LVAD implantation in AAs vs Caucasians.

**METHODS:** We stratified 88 LVAD patients by AA or Caucasian race. Variables were compared using 2-sided t-tests, chi-square tests, Cox proportional hazards models, and log-rank tests to determine whether a difference existed between AAs and Caucasians and whether race was a significant independent predictor of outcome.

**RESULTS:** AAs represented 36.4% (32 of 88) of our LVAD patients. The two groups did not differ significantly in the incidence of hypertension, diabetes, or chronic renal insufficiency, reoperation rates, pre-operative body mass index, left ventricular ejection fraction, central venous pressure, pulmonary capillary wedge pressure, pulmonary artery pressure, or right ventricular function. Compared with Caucasians, AAs were significantly younger (48.6 vs 54.8 years, \( p = 0.019 \)), and had a significantly higher mean body surface area (\( p = 0.009 \)) and a higher rate of non-ischemic dilated cardiomyopathy (61% vs 39%, \( p = 0.008 \)). No significant difference was found in 30-day (\( p = 0.12 \)), 180-day (\( p = 0.166 \)), or 360-day (\( p = 0.18 \)) survival. Analysis by univariate Cox proportional hazard models (hazard ratio [95% confidence interval]) showed race was not an independent predictor of 30-day (4.5 [0.56–35.94], \( p = 0.157 \)), 180-day (3.9 [0.48–31.95], \( p = 0.2 \)), or 360-day survival (1.8 [0.6–5.71], \( p = 0.286 \)). Age and pre-operative renal failure were the only independent predictors of survival at 30 days (1.1 [1.02–1.19], \( p = 0.019 \); 4.99 [1.24–20], \( p = 0.023 \), respectively), 180 days (1.09 [1–1.18], \( p = 0.041 \); 4.14 [0.99–17.39], \( p = 0.05 \)), and 360 days (1.05 [1–1.1], \( p = 0.044 \); 2.52 [0.94–6.75], \( p = 0.05 \)). Analysis by a multivariate logistic regression model showed age and chronic renal failure were no longer statistically significant for survival at 30, 180, and 360 days.

**CONCLUSIONS:** Although multiple studies have demonstrated that AAs experience worse outcomes after coronary artery bypass grafting, heart transplantation, and valve surgery, we did not find similar results in our LVAD population. More rigorous pre-operative LVAD workup, including an evaluation by a multidisciplinary team, along with more intense post-operative follow-up, may explain improved outcomes in AAs after LVAD implantation compared with other cardiac surgical procedures, although additional analysis is required.

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Congestive heart failure is a major medical, social, and financial challenge worldwide. With an increasing incidence and prevalence of patients with heart failure, this disease has now reached epidemic proportions. Approximately 500,000 patients in the United States (U.S.) have end-stage heart failure refractory to optimal medical treatment,1 and of these, an estimated 150,000 patients would potentially be candidates for heart transplantation.2 With just over 2,000 heart transplants being performed annually in the U.S., the overall epidemiologic effect of cardiac transplantation on the treatment of congestive heart failure is minimal.

The landmark Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure (REMATCH) trial3 initiated a new era in the treatment of advanced heart failure. The superiority of mechanical circulatory support vs optimal medical therapy is now widely accepted. Favorable outcomes have been achieved with left ventricular assist devices (LVADs).4–6 However, whether all races benefit equally is unknown. Race-linked discrepancies, such as biologic, immunologic differences, and socioeconomic factors, may have important implications on surgical outcomes.

Previous studies have examined outcomes among different racial and ethnic groups after coronary artery bypass grafting (CABG), valve surgery, and heart transplantation.7–21 We initiated this study to explore whether race is a possible predictor of outcome for patients undergoing LVAD implantation. Worse outcomes in African Americans (AAs) compared with Caucasians have been demonstrated after CABG,7–13 heart transplantation,14–19 and isolated aortic or mitral valve replacement (AVR/MVR).20,21 Given the results of these studies, we hypothesized that the AA race would also be associated with increased morbidity and mortality after LVAD implantation.

Materials and methods

The Institutional Review Board of our health system approved this retrospective study. We reviewed our institution’s LVAD data set and analyzed patients who underwent continuous-flow LVAD implantation as a bridge to transplantation (BTT) or destination therapy (DT) from March 2006 until July 2011. We identified 90 patients and stratified them into groups by race. The analysis excluded 1 Asian and 1 Hispanic patient; thus, 88 patients formed the study cohort.

Patient data

Patient demographics and pre-operative characteristics included race, age, sex, body mass index, creatinine, left ventricular ejection fraction, etiology of heart failure, central venous pressure, pulmonary artery pressure, and pulmonary capillary wedge pressure. Operative characteristics included type of device (HeartMate II [Thoratec Corp, Pleasanton, CA] vs HeartWare [HeartWare International, Inc Framingham, MA]), implantation for BTT or DT, and cardiopulmonary bypass (CPB) time. Outcome variables were complications, post-operative mortality, survival at 30, 180, and 360 days, and causes of death. Complications assessed included pneumonia, driveline infections, right ventricular failure, ischemic stroke, transient ischemic attack, hemorrhagic stroke, gastrointestinal bleeding, and reoperation for bleeding.

Statistical analysis

Patients were grouped by AA and Caucasian race. Continuous variables are reported as mean, standard deviation, and minimum, median, and maximum, and were compared between racial groups using 2-sided 2-sample t-tests. Alternatively, a 2-sided Wilcoxon rank sum test was used if severe departures from normality were observed in the distributions. Categoric variables are reported as counts and percentages and compared between racial groups using chi-square tests. Alternatively, the Fisher’s exact test was used if expected counts were not sufficiently large. Similar tests were used to compare post-operative complications. Pre-operative and operative characteristics were evaluated using Cox proportional hazards models to test whether each individual characteristic was a significant predictor of post-operative 30-day, 180-day, and 360-day survival. Hazard ratios (HR) and their 95% confidence intervals (CIs) are reported. A conservative cutoff of $p < 0.10$ was used to place predictors in the univariate analysis, which were then placed in a multiple Cox proportional hazards model predicting post-operative 30-day, 180-day, and 360-day survival. Adjusted HRs and their 95% CIs are reported. Statistical tests were performed using SAS 9.2 software (SAS Institute, Cary, NC), and results were considered significant at $p < 0.05$.

Results

Demographic characteristics of AA and Caucasian LVAD recipients

During the study period, 88 patients underwent LVAD implantation as a BTT or DT at our center and were included in our study. Demographics and operative characteristics are summarized by race in Table 1. There were 32 AAs (36.4%), consisting of 20 men (62.5%) and 12 women (37.5%), and 56 Caucasians (63.6%), consisting of 43 men (76.7%; $p = 0.21$) and 13 women (23.2%; $p = 0.153$). AAs were significantly younger (48.6 vs 54.8 years; $p = 0.019$) and had a higher body surface area (BSA: 2.1 ± 0.2 vs 2.0 ± 0.3 m$^2$; $p = 0.009$) and a greater incidence of non-ischemic dilated cardiomyopathy (61% vs 39%; $p = 0.008$). The groups did not differ significantly in the incidence of hypertension, diabetes mellitus, chronic renal insufficiency, previous sternotomy, pre-operative left ventricular ejection fraction, central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, or right ventricular function.

BTT was the indication for the LVAD implant in 21 AAs (65.6%) and in 39 Caucasians (69.6%; $p = 0.54$). Among these, 6 of 21 AAs (28.6%) received a transplant vs 16 of 39 Caucasians (41%; odds ratio [OR], 1.75; 95% CI, 0.56–5.45; $p = 0.342$).

AA and Caucasian post-LVAD survival

Survival was similar for both groups, with 30-day, 6-month, and 1-year survivals of 96.9%, 96.9%, and 93.7%, respectively, for AA patients vs 87.5%, 85.7%, and 82.2%, respectively, for Caucasian patients ($p = 0.278$; Figure 1).
Post-operative complications, hospital length of stay, and readmission rates

Post-operative complication rates were similar for AAs and Caucasians, as summarized in Table 2, except for a higher risk of pneumonia in AA patients (22% vs 7%, $p = 0.044$). The post-operative hospital length of stay was 22.2 days for AAs and 21.4 days for Caucasians, which was not significantly different ($p = 0.559$). Readmission rates within 30 days of hospital discharge were also similar between races (16% in AAs and 13% in Caucasians, $p = 0.753$).

Causes of death

Causes of death among the 18 patients who died included septic shock in 4 (22.2%), right ventricular heart failure in 4 (22.2%), stroke in 3 (16.6%), bleeding in 2 (11.1%), bowel perforation in 1 (5.5%), and disconnection from power source in 1 (5.5%).
Effect of race on outcome by Cox proportional hazard models

Race was not a significant predictor of post-operative death, 180-day survival, or 1-year survival (Tables 3 and 4).

Discussion

This study was undertaken due to the relatively high percentage of AA patients in our institution. Overall, 36.4% of LVAD implantations, 20.7% of heart transplants, and 26.1% of all cardiac surgical procedures are performed at our center on AAs. The unanticipated finding in our analysis was that post-LVAD survival was similar between races.

Significant differences in patient and operative characteristics as a function of race were noted for age, BSA, ischemic cardiomyopathy, and CPB time. Average age was significantly lower in AAs, which suggests disparate access to preventive medical care and compliance issues. Unhealthy dietary behaviors, with associated higher BSA, are more prevalent in AAs. Polymorphisms of β1- and α2-adrenergic receptors have been reported as a risk factor for dilated cardiomyopathy in AAs, which explains the higher...

Table 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>African Americans (n = 32)</th>
<th>Caucasians (n = 56)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>7 (22)</td>
<td>4 (7)</td>
<td>0.044b</td>
</tr>
<tr>
<td>Driveline infection</td>
<td>2 (6)</td>
<td>1 (2)</td>
<td>0.551c</td>
</tr>
<tr>
<td>Right heart failure</td>
<td>6 (19)</td>
<td>9 (16)</td>
<td>0.748b</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>2 (6)</td>
<td>1 (2)</td>
<td>0.551c</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>3 (9)</td>
<td>3 (5)</td>
<td>0.664c</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>1 (3)</td>
<td>1 (2)</td>
<td>&gt;0.999c</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>7 (22)</td>
<td>7 (13)</td>
<td>0.247b</td>
</tr>
<tr>
<td>Restenotomy for bleeding</td>
<td>3 (9)</td>
<td>6 (11)</td>
<td>&gt;0.999c</td>
</tr>
<tr>
<td>Overall post-op stay, days</td>
<td>22.2 ± 20.0</td>
<td>21.4 ± 14.1</td>
<td>0.559d</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>7 (22)</td>
<td>15 (27)</td>
<td>0.609b</td>
</tr>
<tr>
<td>Dialysis</td>
<td>3 (9)</td>
<td>3 (5)</td>
<td>0.665c</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>2 (6)</td>
<td>3 (5)</td>
<td>&gt;0.999c</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>13 (43)</td>
<td>26 (47)</td>
<td>0.728b</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 (6)</td>
<td>2 (4)</td>
<td>0.617c</td>
</tr>
<tr>
<td>Severe post-op</td>
<td>0 (0)</td>
<td>3 (5)</td>
<td>0.550c</td>
</tr>
<tr>
<td>Readmitted within 30 days</td>
<td>5 (16)</td>
<td>7 (13)</td>
<td>0.753c</td>
</tr>
</tbody>
</table>

aCategoric variables shown as number (%). Continuous variables as mean ± standard deviation.
bProbabilities based on chi-square tests.
cProbabilities based on Fisher’s exact tests.
dProbabilities based on 2-sided Wilcoxon rank sum tests.
incidence of non-ischemic dilated cardiomyopathy in our AA cohort. Shorter CPB times may have contributed to improved outcomes in AAs. The longer CPB times in Caucasians correspond to the technical challenges associated with reoperative sternotomy: 35% (20 of 56) of Caucasians correspond to the technical challenges asso-
ciated with reoperative sternotomy: 35% (20 of 56) of Caucasians had undergone a previous cardiac 
procedure compared with 21.8% (7 of 32) of AAs.

Although no studies have focused on the influence of race on LVAD outcomes, racial disparities in morbidity and mortality after non-LVAD cardiac surgery have been studied:

- The Coronary Artery Surgery Study (CASS) study, reported by Maynard et al.24 compared 571 AAs and 22,754 Caucasians who underwent a previous cardiac surgical procedure compared with 21.8% (7 of 32) of AAs (p = 0.148).

Several underlying reasons account for the worse outcomes in AAs after cardiac surgery. Severe socioeconomic depression and poverty is more frequently seen in AAs. These factors are associated with unhealthy habits (diet, smoking), lower educational levels, unemployment, and stress. There is also a race-dependent distribution of comorbidities, such as hypertension, diabetes, chronic renal failure, chronic obstructive pulmonary disease, peripheral vascular disease; pre-ventricular assist device levels for aspartate transaminase, alanine aminotransferase, and albumin; days in the hospital, re-

erotomy, left ventricular ejection fraction, central venous pressure, pulmonary capillary wedge pressure, moderate–severe right ventricular failure, and pre-ventricular assist device systolic pulmonary artery pressure.

**Table 3** Univariate Analysis: Significant Predictors of Survival at 30, 180, and 360 Days

<table>
<thead>
<tr>
<th>Predictors of survival</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30-day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.10 (1.02–1.19)</td>
<td>0.019</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>4.99 (1.24–20.00)</td>
<td>0.023</td>
</tr>
<tr>
<td><strong>180-day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.09 (1.00–1.18)</td>
<td>0.041</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>4.14 (0.99–17.39)</td>
<td>0.050</td>
</tr>
<tr>
<td><strong>360-day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.05 (1.00–1.10)</td>
<td>0.044</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>2.52 (0.94–6.75)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

CI, confidence interval; HR, hazard ratio

- Variables analyzed in the model: African American race, body mass index, creatinine, bridge to transplant or destination therapy, ischemic cardiomyopathy, no ischemic cardiomyopathy, cardiopulmonary bypass time, age, body surface area, hypertension, diabetes, chronic renal failure, chronic obstructive pulmonary disease, peripheral vascular disease; pre-ventricular assist device levels for aspartate transaminase, alanine aminotransferase, and albumin; days in the hospital, rest-

erotomy, left ventricular ejection fraction, central venous pressure, pulmonary capillary wedge pressure, moderate–severe right ventricular failure, and pre-ventricular assist device systolic pulmonary artery pressure.

- Allen et al.27 reviewed the United Network of Organ Sharing data set for 20,185 adult heart transplants from 1997 to 2007 and reported an 11.4% decrease in 10-year survival in AAs. After risk adjustment, AAs continued to have a 46% increase in mortality compared with Caucasians (HR, 1.46; 95% CI, 1.24–1.72; p < 0.001).

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**Table 4** Multivariable Analysis: Predictors of Survival at 30, 180, and 360 Days

<table>
<thead>
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<th>Predictors of survival</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30-day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.07 (0.98–1.16)</td>
<td>0.127</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>2.87 (0.64–12.79)</td>
<td>0.168</td>
</tr>
<tr>
<td><strong>180-day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.07 (0.98–1.16)</td>
<td>0.119</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>2.75 (0.6–12.58)</td>
<td>0.193</td>
</tr>
<tr>
<td><strong>360-day survival</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.08 (0.98–1.16)</td>
<td>0.115</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>2.82 (0.63–12.65)</td>
<td>0.176</td>
</tr>
</tbody>
</table>

CI, confidence interval; HR, hazard ratio

- Variables analyzed in the model: African American race, body mass index, creatinine, bridge to transplant or destination therapy, ischemic cardiomyopathy, no ischemic cardiomyopathy, cardiopulmonary bypass time, age, body surface area, hypertension, diabetes, chronic renal failure, chronic obstructive pulmonary disease, peripheral vascular disease; pre-ventricular assist device levels for aspartate transaminase, alanine aminotransferase, and albumin; days in the hospital, rest-

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selection and pre-LVAD workup. As part of this process, a patient’s compliance is assessed, smoking cessation is conﬁrmed, and a patient’s access to post-operative care is solidiﬁed. A multidisciplinary approach to care before and after LVAD implant also contributes to improved outcomes. LVADs constitute most of the systemic output, and this artiﬁcial, complete maintenance of perfusion may be another potential reason for the reduction or neutralization of surgical risk factors associated with the AA race.

Our study has several limitations. First, our sample size was small, and the statistical tests were possibly insufﬁciently powered. Second, this was not a prospective randomized trial and subject to the limitations inherent to any retrospective study. Third, our study was not designed to delineate underlying mechanisms by which race affects outcomes. In addition, duration of follow-up in our study was relatively short. Long-term outcomes between races have yet to be deﬁned. Finally, this was a single-institution study, and selection bias may have been present.

In conclusion, this retrospective analysis compared outcomes between AAs and Caucasians after LVAD implantation. We found that although AAs are considered high-risk cardiac surgical candidates and are known to exhibit higher morbidity and mortality after CABG, valve surgery, and heart transplantation, our study suggests that peri-operative mortality, 180-day survival, and 1-year survival after LVAD implantation are comparable for both groups. Rigorous pre-LVAD workup, close post-operative follow-up, and dramatic improvement in systemic perfusion, albeit by an artiﬁcial mechanism, may explain improved outcomes in AAs after LVAD implantation compared with other non-LVAD cardiac surgical procedures. With the AA race generally being under-represented in most LVAD centers, multi-institutional studies would be beneﬁcial to corroborate these conclusions.

Disclosure statement

None of the authors has a ﬁnancial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conﬂicts of interest to disclose.

References


