ORIGINAL RESEARCH

Metabolic Dysfunction in Continuous-Flow Left Ventricular Assist Devices Patients and Outcomes

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***Background*—**Metabolic impairment is common in heart failure patients. Continuous-flow left ventricular assist devices (CF-LVADs) improve hemodynamics and outcomes in patients with advanced heart failure; however, the effect of CF-LVADs on metabolic status is unknown. This study aims to evaluate the changes in metabolic status following CF-LVAD implantation and measure the correlation of metabolic status with outcomes.

***Methods and Results*—**Prospective data on CF-LVAD patients were obtained. Metabolic evaluation, including hemoglobin A1C, free and total testosterone, thyroid-stimulating hormone (TSH), and free T4, was obtained before and at multiple time points following implantation. Patients with nonelevated thyroid-stimulating hormone and normal hemoglobin A1C and testosterone levels were defined as having normal metabolic status. Baseline characteristics, hemodynamics, and outcomes were collected. One hundred six patients were studied, of which 56 had paired data at baseline and 1- to 3-month follow-up. Before implantation, 75% of patients had insulin resistance, 86% of men and 39% of women had low free testosterone, and 44% of patients had abnormal thyroid function. There was a significant improvement in hemoglobin A1C, free testosterone, and thyroid-stimulating hormone following implantation ($P<0.001$ for all). Patients with normal hemoglobin A1C (<5.7%) following implantation had higher 1-year survival free of heart failure readmissions (78% versus 23%; $P<0.001$). Patients with normal metabolic status following implantation also had higher 1-year survival free of heart failure readmissions (92% versus 54%; $P=0.04$).

***Conclusions*—**Metabolic dysfunction is highly prevalent in advanced heart failure patients and improves after CF-LVAD implantation. Normal metabolic status is associated with a significantly higher rate of 1-year survival free of heart failure readmissions. **(*J Am Heart Assoc*. 2019;8:e013278. DOI: 10.1161/JAHA.119.013278.)**

Key Words: diabetes mellitus • heart failure • left ventricular assist device • testosterone • thyroid hormones

Heart failure (HF) remains a leading cause of hospitalizations and death in the United States.[1,2] Currently, neurohormonal blockade with guideline-directed medical therapy remains the cornerstone of HF therapy.[3] Data increasingly highlight the prevalence and impact of metabolic impairment in HF patients.[4–8] Metabolic dysfunction may represent a novel therapeutic target to slow disease progression and impact the outcomes of patients with HF.[9]

Continuous-flow left ventricular assist devices (CF-LVADs) have improved the quality of life and survival for advanced HF patients.[10] It is unknown whether CF-LVADs alter the metabolic dysfunction that exists in HF patients and whether changes in metabolic status are associated with better outcomes. In this study, we investigated the metabolic impairment of patients before and after CF-LVAD implantation and assessed whether metabolic status after implantation is associated with clinical outcomes.

Methods

Patient Selection

The data, analytical methods, and study materials will be made available by the corresponding author to any researchers upon reasonable request. This prospective

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Accompanying Data S1, Table S1, and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013278

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Clinical Perspective

What Is New?

- Metabolic dysfunction is common in advanced heart failure patients and improves after continuous-flow left ventricular assist device implantation.
- Patients who attain normal metabolic status at 3 months after implantation have a higher 1-year survival free of heart failure readmission.

What Are the Clinical Implications?

- Understanding the metabolic status of a patient after continuous-flow left ventricular assist device implantation may help to identity patients at risk for worse outcomes.
- Large, prospective, randomized, controlled trials need to be performed to determine whether treating metabolic abnormalities in advanced heart failure patients improves outcomes.

cohort study was conducted at our institution between August 2016 and December 2018, and consecutive patients who underwent CF-LVAD implantation were included in the analysis. Metabolic labs, including free and total testosterone, thyroid-stimulating hormone (TSH) and free T4, and hemoglobin A1C (HbA1C) were obtained at several time points: (1) before LVAD implantation; (2) within 1 month after LVAD implantation; (3) 1 to 3 months after LVAD implantation; (4) 3 to 6 months after LVAD implantation; and (5) >6 months after LVAD implantation. All patients received guideline-directed medical therapy, including antiplatelet therapy and warfarin, per our institutional protocol. Metabolic abnormalities were treated at the discretion of attending physicians and after consultation with an endocrinologist. The institutional review board of the University of Chicago approved this study, and all subjects gave informed consent.

Metabolic Parameters

Patients were grouped according to metabolic status in a categorical manner. For testosterone, patients were grouped by low free testosterone (<90 pg/mL for men or <3 pg/mL for women) or normal free testosterone (>90 pg/mL for men or >3 pg/mL for women). For thyroid function, patients were grouped based on elevated TSH (>4.0 μU/mL) or nonelevated TSH (<4.0 μU/mL). Insulin resistance was stratified based on abnormal HbA1C (>5.7%) or normal HbA1C (<5.7%). Additionally, a composite category of metabolic status was created. Normal metabolic status (NMS) was defined as HbA1C <5.7%, TSH <4.0 μU/mL, and free testosterone >90 pg/mL in men or >3 pg/mL in women.

Variables Evaluated and End Points

All clinical variables were obtained from electronic medical records. Baseline characteristics, metabolic labs, hospital readmissions, and survival data were collected. Our primary end point was the percent of patients with paired data at baseline and 1- to 3-month follow-up who achieved normal values of each of the metabolic markers (HbA1C, TSH, and free testosterone), as well as the percent of these patients who achieved NMS. Secondary end points included correlation of metabolic status at 1 to 3 months after CF-LVAD implantation with hemocompatibility-related adverse events, hemodynamic values, and survival free of HF readmissions. A HF readmission was defined as left- or right-sided HF requiring admission with intravenous diuretics. Finally, we collected medication data on neurohormonal blockade, thyroid hormone replacement, and diabetes mellitus treatment at these 2 time points for comparison. Metabolic status 1 to 3 months after CF-LVAD implantation was chosen because it allowed for sufficient recovery from the postoperative metabolic disarray.

Statistical Analysis

Statistics were performed using SPSS (version 22; SPSS, Inc, Chicago, IL) and STATA MP software (Version 15; StataCorp LP, College Station, TX). For baseline clinical characteristics, continuous variables are expressed as means±SDs or medians with interquartile ranges depending upon normality, whereas categorical variables are expressed as relative counts and percentages. Wilcoxon signed-rank tests were utilized to compare parameters at different time points,[11] whereas the Cuzick nptrend (a nonparametric test for trend across ordered groups) test was used to analyze the trend across the 5 time periods.[12] The Bonferroni correction was used to control for false discovery rate possibly caused by multiple testing. A multivariate logistic regression was conducted to determine which baseline clinical characteristics were associated with achieving NMS, whereby the model included ischemic etiology and body mass index and was adjusted for age, sex, and race. Independent parameters were checked for multicollinearity using Spearman rank correlations, whereby there were no multicollinearity issues between the independent parameters. The relationships between metabolic and hemodynamic variables were assessed by Spearman rank-correlation coefficients. Kaplan–Meier curves were generated to describe time to survival free from HF readmission and then compared using log-rank tests. For Kaplan–Meier curves which cross over each other, the proportional hazards assumption was violated, and thus the log-rank test was unable to be used. The Cox proportional hazards model was used to calculate relative risk of NMS and was adjusted for age and ischemic etiology.[13] Patients were

Table 1. Baseline Characteristics

Baseline Characteristics	Entire Cohort (N=106)	Secondary Analysis Cohort (N=56)
Age, y	58 (45, 64)	59 (48, 66)
Male	64 (60%)	31 (55%)
Black race	62 (59%)	35 (63%)
Diabetes mellitus	42 (40%)	21 (38%)
Ischemic cardiomyopathy	19 (34%)	19 (34%)
Body mass index, kg/m^2	28.4 (24.6, 34.0)	26.7 (24.5, 32.9)
Axial flow pump	19 (18%)	11 (20%)
Inotropes before implantation	87 (82%)	48 (86%)
Mechanical support before implantation	43 (41%)	27 (48%)

right-censored if they had their first event, died, or were lost to follow-up. Tests were 2-tailed and considered statistically significant with $P<0.05$.

Results

Baseline Characteristics

One hundred six patients were included in the analysis of the primary end point. Patients were 58 (45, 64) years old, 60% were men, 59% were blacks, and the body mass index was 28.4 (24.6, 34.0) kg/m^2 (Table 1). Fifty-six patients were included in the analysis of the secondary end points. Baseline characteristics of these 56 patients showed no significant differences from the entire cohort: age 59 (48, 66) years, 55% men, 63% black, and body mass index of 26.7 (24.5, 32.9). Pre-LVAD hemodynamics and metabolic labs for the secondary end point cohort are presented in Table 2. Additional information regarding patient data and follow-up at each time point can be found in Data S1.

Table 2. Baseline Hemodynamics and Metabolic Parameters of Secondary Analysis Cohort

Hemodynamics and Metabolic Labs	Secondary Analysis Cohort (N=56)
Pre-LVAD hemodynamics	
CVP, mm Hg	13.9±7.1
PCWP, mm Hg	25.2±8.8
Cardiac Index, L/min per m^2	1.98±0.51
Pre-LVAD metabolic labs	
HbA1C, %	6.4±1.2
TSH, μU/mL	3.8±3.1
Free testosterone (M), pg/mL	55.4±38.2
Free testosterone (F), pg/mL	2.7±2.3

CVP indicates central venous pressure; HbA1C, hemoglobin A1C; LVAD, left ventricular assist device; PCWP, pulmonary capillary wedge pressure; TSH, thyroid-stimulating hormone.

Baseline Metabolic Status

Before CF-LVAD implantation, 75% of patients had insulin resistance and 25% did not (n=106; Figure 1A). In men, 86% had low free testosterone and (Figure 1B), and in women, 39% had low free testosterone (Figure 1C). Finally, 44% of patients had abnormal thyroid function and 56% had normal thyroid function (n=106; Figure 1D).

Trend in Metabolic Labs

HbA1C was significantly lower at each time point compared with baseline ($P<0.05$ for all). The overall trend of HbA1C also decreased significantly ($P<0.001$; Figure 2A). In men, free testosterone decreased significantly at 1 month and, at all subsequent time points, was elevated compared with baseline ($P<0.05$ for all). There was an increase in free testosterone overall by trend analysis ($P<0.001$; Figure 2B). In women, there was no significant change in free testosterone at any time point compared with baseline (Figure 2C). TSH increased from baseline to 1 month and was then significantly lower than baseline at all other time points ($P<0.05$ for all). The overall trend of TSH decreased significantly over time ($P<0.001$; Figure 2D). Because of multiple testing of 5 time points, these results were adjusted using a Bonferroni correction, whereby the P values were compared to an alpha of 0.01.

Prevalence of Metabolic Dysfunction

Figure 3A shows the prevalence of normal metabolic parameters at baseline and at the 1- to 3-month time point in the 56 patients with complete paired data. Prevalence of normal HbA1C increased from 26.8% (15 of 56) to 71.4% (40 of 56; $P<0.001$). Prevalence of nonelevated TSH increased from 58.9% (33 of 56) to 82.1% (46 of 56; $P<0.001$). In men, prevalence of normal free testosterone increased from 19.3% (6 of 31) to 35.5% (11 of 31; $P<0.001$). In women, there was no change in prevalence of normal free testosterone. Finally, prevalence of NMS increased from 1.8% (1 of 56) at baseline to 21.4% (12 of 56) at 1 to 3 months ($P<0.001$; Figure 3B). In univariate analysis, there were no factors associated with achieving NMS (Table 3). When the cohort was stratified by the presence of diabetes mellitus, there were significant increases in normalization of HbA1C in both diabetic and nondiabetic patients (Figure S1). There were also

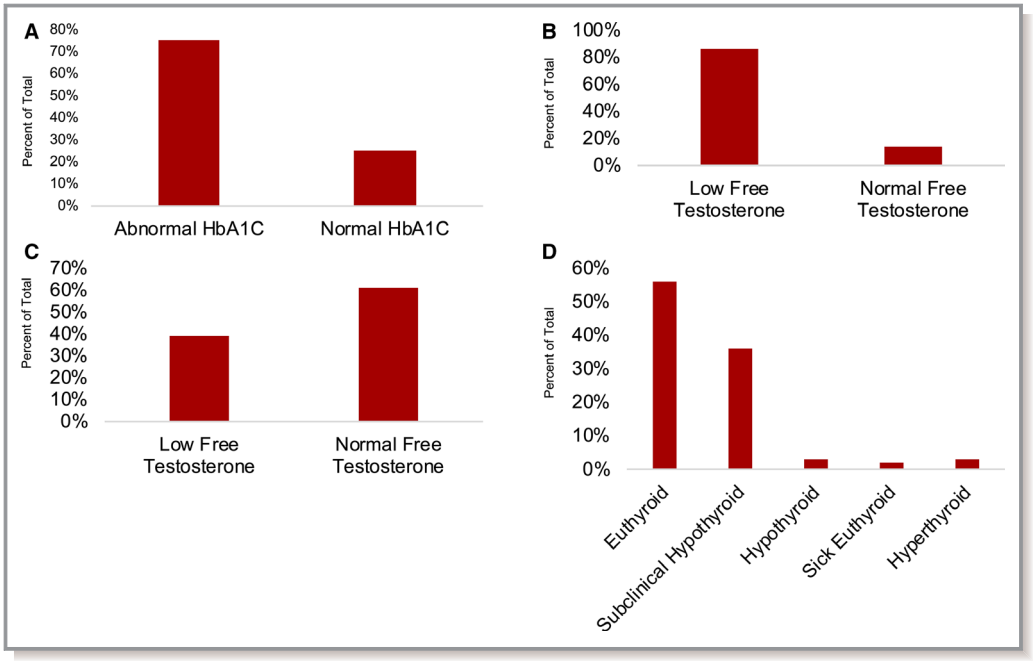

Figure 1. Baseline metabolic status before CF-LVAD implantation. **A**, Baseline insulin resistance (n=106). **B**, Baseline testosterone status in men (n=59). **C**, Baseline testosterone status in women (n=33). **D**, Baseline thyroid status (n=106). CF-LVAD indicates continuous-flow left ventricular assist device; HbA1C, hemoglobin A1C.

improvements in the proportion of patients with normal TSH in both groups, although this only reached significance in the nondiabetics (likely attributed to the small number of patients in the diabetes mellitus group).

Comparison of Medication Usage

In the 56 patients with paired data at baseline and 1 to 3 months after CF-LVAD implantation, we collected medication data on neurohormonal blockade, thyroid hormone replacement, and treatment of diabetes mellitus. Beta-blocker use increased from 38% to 56%, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker use increased from 25% to 63%, mineralocorticoid receptor antagonist use remained the same from 54% to 57%, hydralazine use decreased from 21% to 13%, levothyroxine remained the same from 13% to 18%, and, finally, treatment of diabetes mellitus (with insulin or oral medications) remained the same from 38% to 32%. No patients were on supplemental testosterone before or after CF-LVAD implantation.

Achievement of NMS and Outcomes

Of the 56 patients analyzed for the secondary end point, 12 patients achieved NMS and 44 did not at 1 to 3 months after CF-LVAD implantation (Figure 4). There was no difference in the incidence of hemocompatibility-related adverse events (gastrointestinal bleeding, pump thrombosis, pump thrombosis, or stroke) between the group with NMS and the group without NMS. Additionally, central venous pressure, pulmonary capillary wedge pressure, and cardiac index were not correlated with metabolic parameters at 1 to 3 months (Table S1). Death or HF readmissions were observed in 3 of 12 in the NMS group and 12 of 44 in the group without NMS. The NMS group had a significantly higher survival free of HF readmissions than the group without NMS (92% versus 54%; P=0.04; Figure 5A). Death or HF readmissions were observed in 2 of 16 in the normal HbA1C group and in 13 of 40 in the abnormal HbA1C group. Patients with a normal HbA1C at 1 to 3 months had a 78% survival free of HF readmissions as compared with a 23% survival free of HF readmissions in those with an abnormal HbA1C (P<0.001; Figure 5B). There was no difference in survival free of HF readmissions when patients were stratified by testosterone or TSH (Figure 5C through 5E).

Discussion

In this study, we assessed changes in prevalence of metabolic dysfunction after CF-LVAD implantation and whether metabolic dysfunction postimplantation is associated with adverse outcomes. First, we found that metabolic dysfunction is highly prevalent in advanced HF patients: Most patients had insulin resistance, the majority of men had testosterone deficiency, and half of all patients had thyroid dysfunction. Second, after

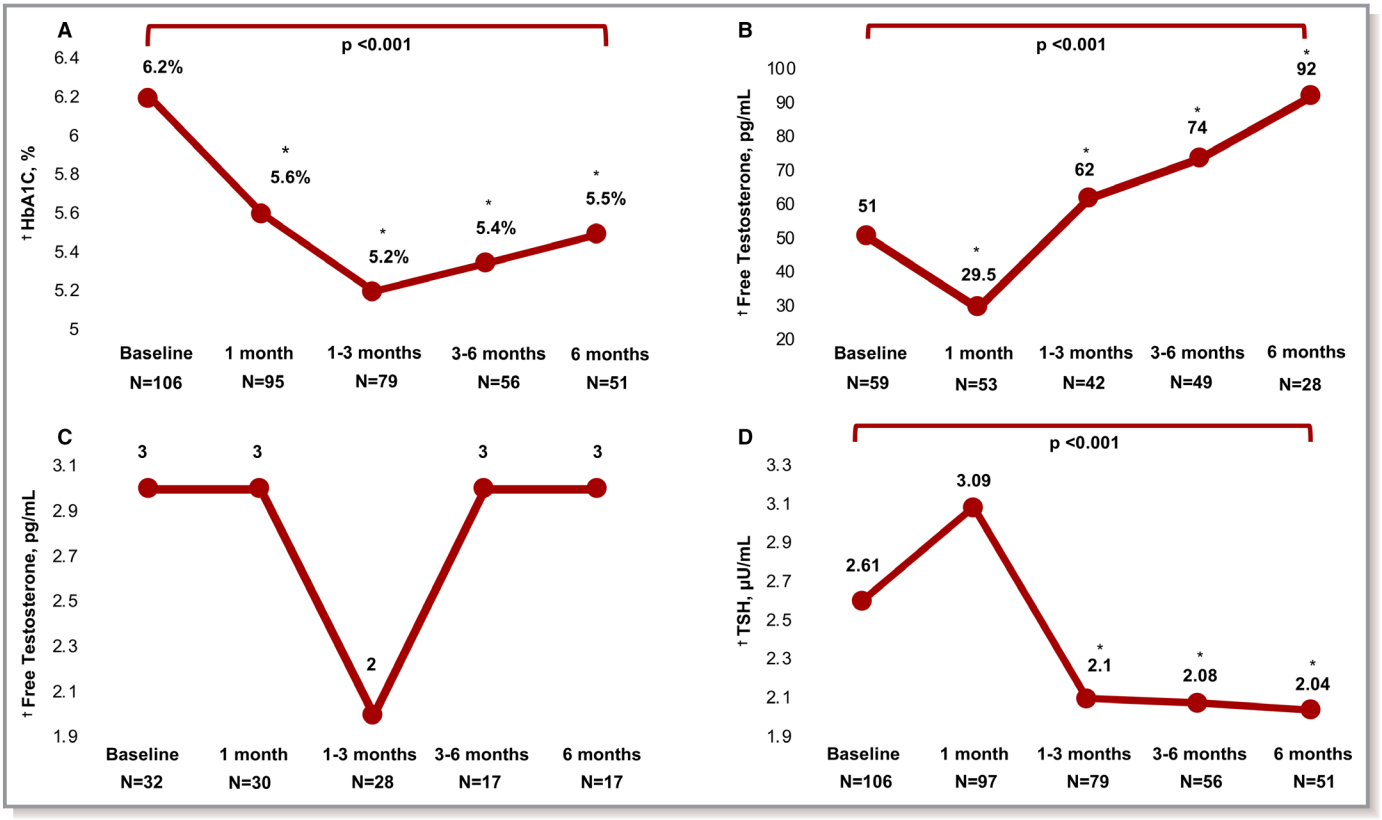

Figure 2. Longitudinal trend of metabolic parameters. **A**, HbA1C. **B**, Free testosterone in men. **C**, Free testosterone in women. **D**, Thyroid-stimulating hormone. HbA1C indicates hemoglobin A1C; TSH, thyroid-stimulating hormone. †Median value; **P*<0.05 compared with baseline.

CF-LVAD implantation, levels of HbA1C, free testosterone in men, and TSH improved significantly. Last, achieving NMS and normal HbA1C at 1 to 3 months after implantation were associated with improved HF-free survival at 1 year.

HF is a state of metabolic incompetence,[4–8] and we have demonstrated in this study that a large number of advanced HF patients have some degree of metabolic derangement. The underlying reasons for the presence of metabolic abnormalities in HF is not fully elucidated, and it is unknown whether the metabolic dysfunction is a consequence of HF or a cause of myocardial dysfunction.

Insulin Resistance

In a previous study, we demonstrated that diabetic patients undergoing CF-LVAD implantation have improved insulin

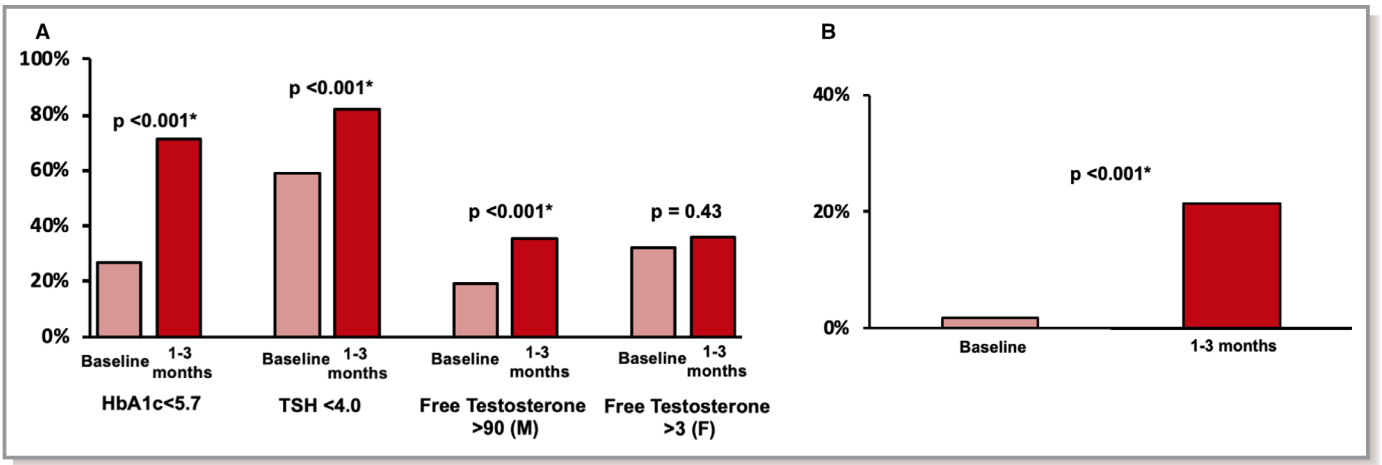

Figure 3. **A**, Change in metabolic status from baseline to 1 to 3 months. **B**, Change in normal metabolic status from baseline to 1 to 3 months. HbA1c indicates hemoglobin A1C; TSH, thyroid-stimulating hormone.

Table 3. Factors Associated With Achieving Normal Metabolic Status

Characteristics	Odds Ratio (95% CI)	*P* Value
Age, y	0.99 (0.94–1.03)	0.49
Female	1.32 (0.37–4.73)	0.67
White race	0.80 (0.19–3.42)	0.76
Ischemic etiology	0.58 (0.14–2.47)	0.46
Body mass index	1.05 (0.95–1.16)	0.39

resistance as demonstrated by a reduction in HbA1C and insulin use postimplantation.[14] Hereby, we demonstrated again an improvement in insulin resistance following CF-LVAD support. Advanced HF is associated with an upregulated catecholamine drive, which suppresses glucose transport by glucose transporter type 4 and causes insulin resistance.[15] Furthermore, increases in inflammatory cytokines, oxidative stress, and tissue hypoperfusion can all lead to insulin resistance.[4] Insulin resistance further limits the ability of the cells, including cardiomyocytes, to transport glucose into the cells and use it as energy. As such, the proinflammatory environment further deteriorates cardiomyocyte activity and accelerates the HF syndrome. The question that should be asked is whether reversal of insulin resistance will lead to improvement in cardiac function, and whether we should focus on improvement of insulin resistance as part of HF management. Preliminary data to help answer this question were provided by the EMPA-REG OUTCOME (BI 10773 [Empagliflozin] Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients) trial. In this study, diabetic patients treated with empagliflozin had significant lower HF admission.[9] This finding has been primarily attributed to the diuresis induced by inhibition of sodium-glucose cotransporter-2. However, the effect of this medication class on HF is probably more complex and may be associated with reduced cardiac oxidative stress and inflammation, improved ion homeostasis, and decreased myocardial fibrosis, all leading to enhanced myocardial function.[16]

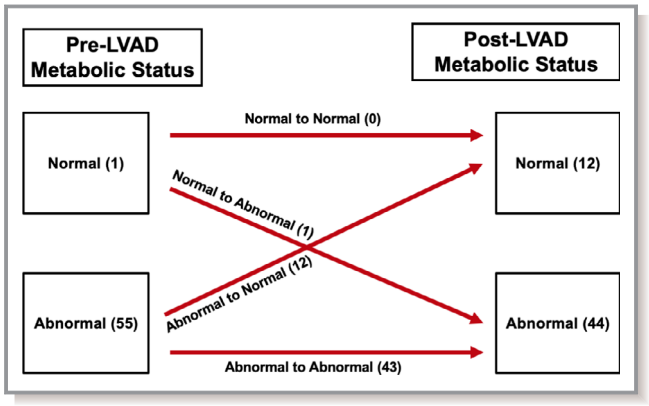

Figure 4. Prevalence of metabolic status from baseline to 1 to 3 months. LVAD indicates left ventricular assist device.

Anabolic/Catabolic Imbalance

Insulin resistance is only 1 part of the metabolic derangement we observe in advanced HF patients, given that thyroid dysfunction and testosterone deficiency are common as well. In general, the metabolic shift in HF is toward catabolism and away from anabolic pathways mainly attributed to an impairment of the growth hormone/insulin-like growth factor-1 axis.[17–20] The result is excessive lipolysis and skeletal muscle proteolysis, with an increase in circulating free fatty acids and an overall imbalance of the skeletal muscle protein pool.[5] Deficiencies in anabolic steroids, including dehydroepiandrosterone sulfate, testosterone, and insulin-like growth factor-1, are common in men with HF and independently predict a poor prognosis, with an additive effect if >1 of these hormones are deficient.[21] Testosterone deficiency specifically has been observed in as many as 26% to 37% of men with chronic HF.[22–24] The deficiency is associated with impaired exercise capacity and increased HF symptoms.[25] In our study, 86% of the men were testosterone deficient at baseline, and this improved in some, but not all, patients following CF-LVAD implantation. This is in striking contrast to the above-cited studies and could be a reflection of the end-stage HF in the patients evaluated in this study. The next step of interest will be to evaluate whether testosterone supplementation in CF-LVAD patients with persistently abnormal testosterone levels will improve outcomes.

Thyroid Dysfunction

The most challenging hormonal abnormality lies in the thyroid. Altered thyroid hormone function is a known cause of HF. Bioactive T3 has direct effects on myocardial activity, and hyper- or hypothyroidism can lead to cardiovascular injury resulting in HF.[26] Similarly, subclinical hypothyroidism can lead to cardiac myocyte dysfunction. Higher TSH levels have been shown to increase hospitalizations and are independently associated with HF progression.[27,28] Furthermore, several studies have shown that a low T3 state is associated with worse prognosis in HF patients and is linked to poor exercise capacity and oxygen consumption.[29,30] In our cohort, 44% of patients had a thyroid abnormality and most of them improved following CF-LVAD implantation. Whether thyroid supplementation during the initial shock thyroid period will improve patient outcomes has not been demonstrated in the CF-LVAD population. Furthermore, our findings are also

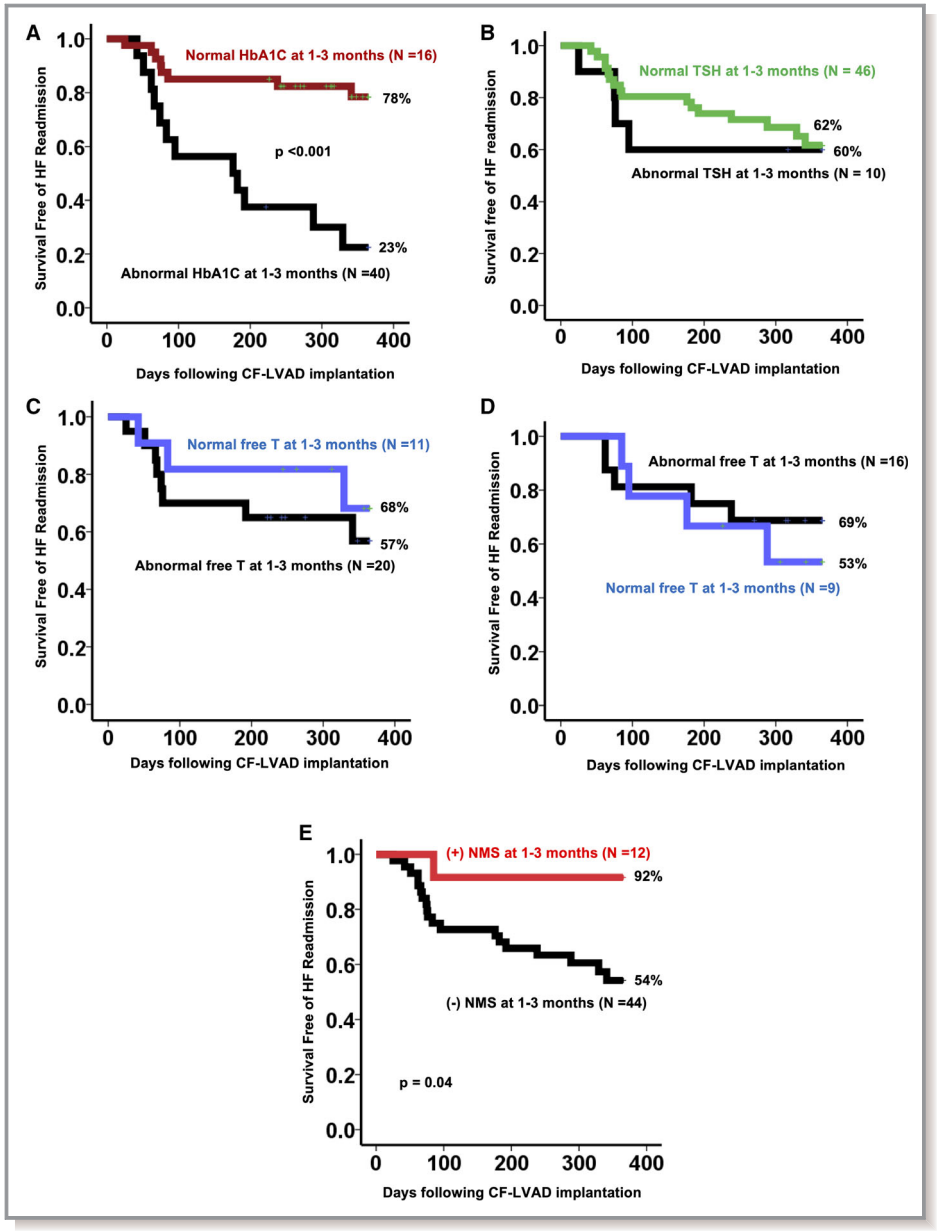

Figure 5. One-year survival free of heart failure–free readmission. **A**, By hemoglobin A1C. **B**, By thyroid-stimulating hormone. **C**, By free testosterone in men. **D**, By free testosterone in women. **E**, By normal metabolic status. CF-LVAD indicates continuous-flow left ventricular assist device; HF, heart failure; LVAD, left ventricular assist device; NMS, normal metabolic status; T, testosterone; TSH, thyroid-stimulating hormone.

relevant for the general HF population, raising the question of whether thyroid status should be a target of HF.[31]

Reversal of Metabolic Dysfunction After CF-LVAD Implantation

Our study showed a significant improvement in HbA1C, TSH, and free testosterone in men at 1 to 3 months after CF-LVAD implantation. This was not explained by more-aggressive direct treatment of these individual metabolic imbalances, given that we found that the rate of treatment with thyroid hormone replacement and diabetes mellitus medications did not change after implantation. However, we did find an increase in the use of neurohormonal blockade with beta-blockers and angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker. It is impossible to say whether the CF-LVAD or neurohormonal blockade improved the metabolic dysfunction after implantation. Ultimately, both treat HF, and this supports the notion that treating HF is associated with reversal of metabolic dysfunction.

The significance of metabolic normalization after CF-LVAD implantation is not clear. Theoretically, with optimal unloading and improved tissue perfusion, there should be an improvement of most, if not all, metabolic labs. However, in our study, only 21.4% of patients achieved NMS at 1 to 3 months after CF-LVAD implantation. This percentage might increase with more time on CF-LVAD support, but these data show that only a small number of patients can quickly reverse a dysfunctional metabolic state. One explanation for this is that despite having improved cardiac output, CF-LVAD patients continue to exhibit an HF phenotype, which speaks to the fact that a CF-LVAD does not cure HF, but simply treats HF by unloading the left ventricle. It is noteworthy that achieving NMS led to significant improvements in clinical outcomes. Whether these patients represent a healthier subset of CF-LVAD patients, or whether normalizing metabolic status improves the HF syndrome, is unknown. These results support a focus on optimizing metabolic status in a prospective study to determine whether this intervention can improve functional status and survival in CF-LVAD patients.

Limitations

Despite prospective data collection, the missing data points during follow-up create a selection bias. However, reasons for missing data are clearly outlined, and patients with matched data points analyzed for the secondary end point of outcomes had similar baseline characteristics to the entire cohort. Additionally, our study did not analyze the treatment of metabolic abnormalities and whether or not this had an impact on outcomes. Finally, we recognize that CF-LVAD patients are more closely followed after implantation, and that any improvement in metabolic status could be explained by this more-aggressive follow-up, rather than by improvement in HF from the CF-LVAD. This study is purely observational and is meant to show that no matter how NMS is achieved after CF-LVAD implantation, NMS is associated with improved survival free of HF readmission. The findings of our study call for a multicenter, prospective registry to assess overall prevalence of metabolic abnormalities in CF-LVAD patients and a randomized control trial to evaluate whether treatment of metabolic dysfunction leads to improved survival. Further research could also evaluate the role of metabolic status in myocardial recovery during CF-LVAD support.

Conclusions

In conclusion, metabolic dysfunction is highly prevalent in advanced HF patients undergoing CF-LVAD implantation. Failure to normalize metabolic dysfunction after CF-LVAD implantation was associated with worse survival free of HF readmissions. Surveillance of metabolic dysfunction after CF-LVAD implantation should be considered to identify patients at high risk for poor outcomes.

Acknowledgments

All listed authors have contributed to and seen the manuscript and have approved mention of their names in the article.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Data S1.

Baseline Characteristics

At 1 month after CF-LVAD implantation, 97 patients were included in the analysis (2 out of study range, 4 deaths, and 3 non-compliance). At 1-3 months after CF-LVAD implantation, 79 patients were included in the analysis (12 out of study range, 5 deaths, 8 non-compliance, 2 lost to follow-up). At 3-6 months after CF-LVAD implantation, 56 patients were included in the analysis (25 out of study range, 7 deaths, 13 non-compliance, 5 lost to follow-up). At >6 months after CF-LVAD implantation, 51 patients were included in the analysis (33 out of study range, 8 deaths, 6 non-compliance, 6 lost to follow-up, 2 decommissions). Of the patients with data, 19 had incomplete data at baseline, 5 had incomplete data at 1 month, 4 had incomplete data at 1-3 months, 2 had incomplete data at 3-6 months, and no patients had incomplete data at >6 months. Between the 106 patients with baseline data and the 79 patients with 1-3-month data, there were 56 patients with complete paired data sets who were used for analysis of the secondary endpoints.

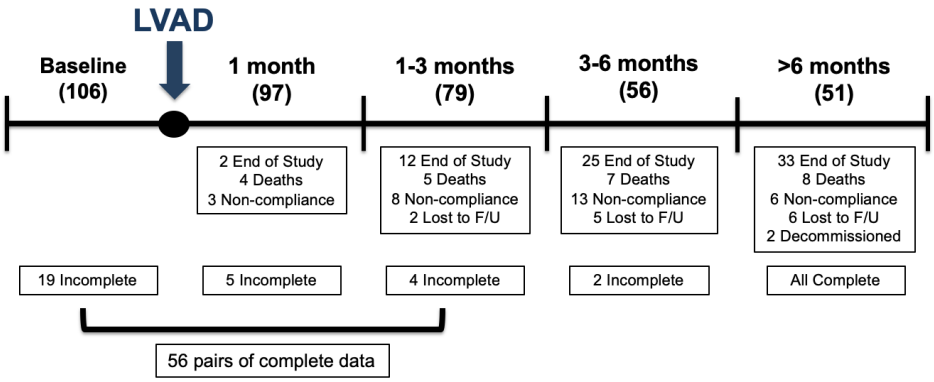
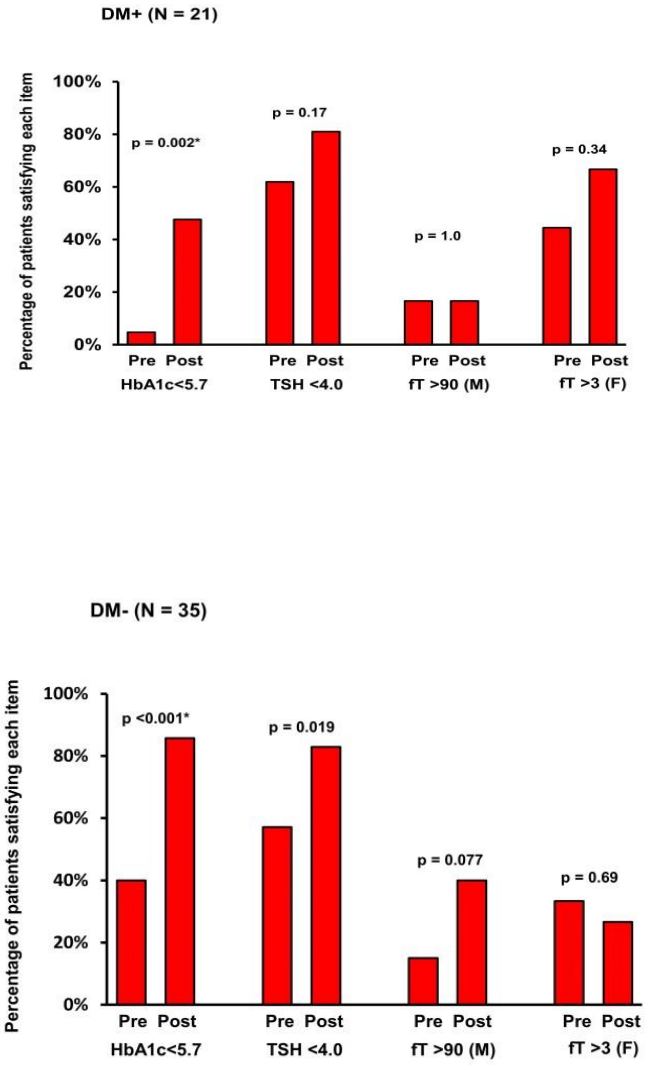


Table S1. Correlation between Hemodynamic Values and Metabolic Parameters at 1-3 Months.

	Correlation Coefficient	P Value
HgbA1C		
CVP	0.21	0.31
PCWP	0.23	0.25
Cardiac Index	0.14	0.51
Free Testosterone (Men)		
CVP	0.47	0.04
PCWP	0.17	0.46
Cardiac Index	-0.29	0.21
Free Testosterone (Women)		
CVP	0.51	0.08
PCWP	0.55	0.05
Cardiac Index	-0.25	0.42
TSH		
CVP	-0.07	0.74
PCWP	0.16	0.43
Cardiac Index	0.27	0.18

CVP = central venous pressure; PCWP = pulmonary capillary wedge pressure; TSH = thyroid stimulating hormone; HgbA1C = hemoglobin A1C

Figure S1. Prevalence of metabolic status before and 3 months after continuous-flow left ventricular assist device implantation stratified by presence of diabetes.



HbA1c indicates hemoglobin A1C; TSH, thyroid stimulating hormone; fT, free testosterone; DM, diabetes mellitus.