Physiological and Psychological Stress among Left Ventricular Assist Device Patients

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by
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Abstract

Background: Advanced heart failure patients who face end-of-life may require a left ventricular assist device (LVAD) and emotional distress and psychological sequelae have been noted following device insertion. The purpose of this study was to describe physiological and psychological stress and to examine relationships between physiological and psychological stress response and outcomes among LVAD patients.

Design: A descriptive observational design was used to describe physiological and psychological stress response among LVAD patients.

Methods: Data was collected for patients more than 3 months post-LVAD implantation. Surveys, a Six Minute Walk Test and salivary specimens were collected. Relationships among indicators of stress and outcomes were examined using descriptive statistics and regression models.

Results: The overall sample ($N = 62$) was male (78%), black (47%), and married (66%) with mean age 56.5± 13 years. Normal cortisol awakening response ($n = 44$) was seen in most participants (62%). There were no differences in cortisol, sleep, psychological stress or outcomes between bridge to transplant and destination therapy patients. However, when comparing the sample by perceived stress level, those with moderate to high perceived stress had worse depression, fatigue and more mal-adaptive coping. Poor sleep quality was correlated with increased psychological stress and QOL ($p< 0.01$). Regression analysis demonstrated perceived stress and fatigue were significant correlates of overall HRQOL (adj. $R^2=0.41$, $p < 0.0001$). High social support moderated the relationship between perceived stress and QOL when controlling for fatigue ($R^2 = 0.49$, $p< 0.0001$).

Conclusions:

This study reveals important links between physiological and psychological stress response among LVAD patients. The overall sample seemed to have a moderate stress profile: moderate perceived stress, low depressive symptoms and moderate fatigue, with a lot of social support. We did not find differences by implant strategy. In addition, higher perceived stress was related to worse sleep quality, depression, fatigue and mal-adaptive coping. Further, the influence of high levels of social support to improve QOL despite fatigue is confirmation of the need to continually assess the social support available to LVAD patients. Future research should investigate how interventions may be tailored to meet the psychosocial needs of this vulnerable population.

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In Memoriam

Christopher S. Abshire
&
John Earl Boyle, III

There are no events in my life that have had a more profound impact
than the loss of these two men.

"…knowing that suffering produces endurance,
[4] and endurance produces character,
and character produces hope,[5]
and hope does not disappoint us…"
Romans 5: 3-5

It is in their memory and in gratitude of their love that I choose to hope.

Preface

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Chapter 1: Introduction

LVAD therapy is complex and costly

Heart failure affects over 5.7 million people in the US and 50% of those with HF will die within five years of diagnosis.[23] Due to effective medical management and advances in HF treatment, people are living longer with more advanced disease. Still, 55,000 deaths per year are the primary result of HF.[24] With increasing numbers of patients with end-stage HF and rapid advances in LVAD technology, it is expected that numbers of patients receiving LVADs and the number of LVAD centers will increase.[25] LVAD implantations cost an average of $193,812 with 5-year patient costs estimated to be $360,407.[26] Patients living with an LVAD live nearly four times longer than end-stage HF patients who are medically managed; quality-adjusted life years are almost 6 times higher for patients living with an LVAD.[27] Still, LVAD outcomes fall short of those found with heart transplant, the only curative treatment for HF.[4,28,29] Stress is known to negatively impact cardiovascular outcomes and may be an important mediator of LVAD-related patient outcomes.[30–33]

Outcomes in patients living with an LVAD: Quality of Life, Functional Status and Hospitalizations

Recent studies have confirmed improvements in QOL for patients with continuous flow devices and related them to functional outcomes.[11,28,34–37] FS continued to improve after LVAD implantation over the first six months and remained stable for the duration of therapy, while QOL seemed to improve over the first three months and remained stable.[11] While improved QOL has been demonstrated, there is still significant room for improvement in our understanding of factors that contribute to QOL in patients living with an LVAD. There are many similarities between heart transplant patients and patients living with an LVAD, but consistent findings that QOL and FS outcomes are worse among patients living with an LVAD.[4,38] This is particularly important for patients who receive an LVAD as destination therapy. Both QOL and FS approached normative data for heart transplant patients (controlling for gender, age and BMI), however for patients living with an LVAD QOL approached only 50% of these adjusted norms.[28] Further influencing QOL, patients living with an LVAD were often hospitalized for long periods of time (two weeks on average) and more than 75% of long-term patients living with an LVAD required re-operations.[11] This high level of hospitalization and related impact on the experience of stress among patients living with an LVAD has not been well-examined in the literature. Greater understanding of LVAD-related physiological and psychological stress may lead to the development of improved LVAD management strategies, including interventions that reduce stress and further improve QOL, FS and hospitalization outcomes in this costly therapy for a high-risk, end-of-life population.

Options for end-stage heart failure (HF) patients include palliative medical management, left ventricular assistive device (LVAD) therapy or heart transplant. LVADs, pumps surgically inserted into the failing heart, are powered through a driveline that extends through the abdomen and attaches externally to batteries or alternating current power. LVAD technology is advancing rapidly and it is estimated that between 40,000 - 200,000 HF patients may benefit from the support of an LVAD.[1] Despite positive effects of LVAD on mortality, Quality of Life (QOL), and functional status (FS) when compared to medical management, these outcomes remain suboptimal for most patients living with an LVAD.[2–4]

Individuals living with an LVAD require complex, multi-disciplinary team management and a dedicated caregiver throughout treatment. The complexity of lifestyle adjustment and device manipulation likely contributes to the stress of having an LVAD. Emotional distress, areas of disability and adjustment disorders have been identified after device implant.[5] Moreover, qualitative research has suggested unique aspects of having an LVAD that may be stressful, including: alterations in body image while becoming accustomed to new scars and a driveline extending out of the body, managing the device and batteries, limitations of bathing and swimming, driving restrictions and effects on intimacy.[6–10] In comparison to age-adjusted norms and even post-heart transplant patients, patients living with an LVAD consistently were found to have worse QOL and functional status.[4,11]

Physiological and psychological stresses have been demonstrated to affect cardiovascular health outcomes such as hypertension and myocardial infarction as well as affect QOL and mortality among HF and heart transplant patients.[12–14] Several factors, which may be related to stress and stress response, have been associated with outcomes among patients living with an LVAD. For example, emergent implantation leads to higher risk of early mortality and worse outcomes.[5] Additionally, healthcare utilization is extremely high among these patients, a factor that may affect QOL and FS, which may be an indication of poor physiological response to the device. More than 75% of individuals with an LVAD will require reoperation within the first year with a mean of 13% of that year spent in the hospital.[11] Implant strategy is a term used to explain the plan for LVAD support; patients who are likely to qualify for heart transplant are classified "bridge to transplant" and those who are not expected to qualify are "destination therapy". Little is known about the differences in stress response between implant strategy classes.

A better understanding of stress appraisal and coping strategies, which are positively associated with improved QOL in the general HF population, may improve understanding of the treatment and care needs for this at-risk population.[15–17] Additionally, social support may help moderate LVAD outcomes as it does for HF patients.[18,19] Finally, stress, which may be an important mediator of outcomes among patients living with an LVAD, has not been examined in this population. The purpose of this cross-sectional study was to characterize physiological and psychological stress response and the association of stress response with QOL, FS and hospitalization among patients living with an LVAD.

Specific Aims:

1. Examine the relationships among individual characteristics of patients living with an LVAD, implant strategy (i.e, bridge to transplant vs. destination therapy), time with LVAD, emergent implantation, and number of stressful life events with physiological (cortisol and C-reactive protein (CRP)) and psychological (perceived stress, depression and coping) stress response measures when controlling for potential co-variates.

H_{1a}: Patients living with an LVAD with emergently-inserted devices will demonstrate higher levels of stress response (physiological and psychological) than those with non-emergent placement.

H_{1b}: Stress response levels (physiological and psychological) will be higher for destination therapy versus bridge to transplant patients when controlling for time since LVAD implantation.

2. Examine the relationships among physiological (cortisol and CRP) and psychological (perceived stress, depression and coping) stress response to LVAD with QOL, FS and hospitalization outcomes when controlling for potential co-variates.

H_{2a}: High levels of cortisol, a physiologic biomarker of stress response, will be associated with low QOL, low FS and high hospitalization rates.

H_{2b}: High psychological stress response measures will be associated with low QOL, low FS and high hospitalization rates.

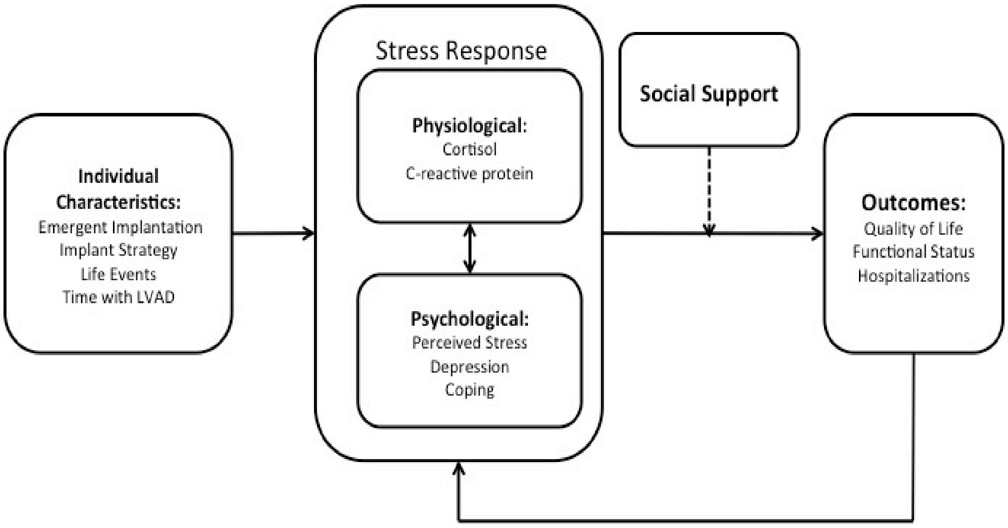
Exploratory Aim: Test social support as a moderator of the effect of physiological and psychological stress response on outcomes (QOL, FS and hospitalization).

This study will provide important data to guide the development and testing of interventions to improve outcomes among patients living with an LVAD.

Conceptual Framework: The Stress Response to LVAD

The conceptual framework for this study is an adaptation of the principles from the Lazarus and Folkman Stress Model and the Allostatic Load Model (see figure 1).[13,40] A stressor is a stimulus that requires a physiological, psychological and/or behavioral (i.e, coping) response.[13,41] The experience of HF requiring LVAD therapy is conceptualized as the stressor in this study. In this conceptual framework, individual characteristics are expected to influence stress response, which encompasses physiological stress response (i.e, cortisol and CRP levels) and psychological stress response (i.e, perceived stress, affective symptoms of depression and coping). Coping is defined as the cognitive and behavioral efforts to manage stress.[42] Social support may moderate the relationship between stress response variables and outcomes. This comprehensive view of the stress is consistent with the Allostatic Load model, including the response of the stress hormone system to maintain allostasis, which is homeostasis achieved through biological or behavioral compensatory mechanisms.[13] The conceptual framework in Figure 1 guided selection of variables of interest and the aims are organized according to the framework.

Figure 1: The Stress Response of LVAD Conceptual Framework



Key Conceptual and Variable Explanations

Individual characteristics including psychosocial factors may be related to LVAD outcomes. However, thus far, few independent predictors of LVAD outcomes have been identified. However, **emergent** implantation has had significant impact on outcomes. The International Registry of Mechanical Circulatory Support established profiles of acuity prior to device implantation and demonstrated worse outcomes for emergently placed, decompensated patients.[5] Another key individual characteristic of patients living with an LVAD is the **implant strategy**. Whether the device will be used as a bridge to transplant or destination therapy may have an impact on how they perceive and react to stress.[43] As destination therapy is increasing in use, it is appropriate to consider this important characteristic, but thus far there has been very little difference demonstrated by implant strategy in QOL and FS outcomes.[34] Also, the accumulation of **stressful life events** may impact illness outcomes in certain populations.[44] However, a study of HF patients found perceived stress to be a stronger predictor of outcomes than a stressful life event tally.[45,46] This work has not been done in patients living with an LVAD. It is expected that the LVAD implantation is the most significant event for most patients, but that there may be some for whom life event stress has a significant effect on their response to the stressful experience of living with an LVAD. Finally, **time with LVAD** is included as a variable because this characteristic influences FS and QOL outcomes and also helps to address the cross-sectional nature of this study.

Stress Response:

When the brain perceives a stressful event, it will stimulate both physiological and psychological response.[41] Actual or interpreted threats to an individual's homeostatic balance initiate the sympathetic–adrenal–medullary (SAM) axis release of catecholamines. Also, the hypothalamic–pituitary–adrenal (HPA) axis secretion of glucocorticoids then mobilizes fight-or-flight responses through release of energy.[47] Chronic exposure to HPA axis stimulation leads to cardiovascular ischemic disease, the most common cause of HF.[47,48] LVAD therapy likely subjects patients to additional SAM and HPA axis stimulation. The LVAD is an unusual situation in that many common measures of stress (i.e. blood pressure and heart rate) may be less relevant because of the continuous flow of the device.

Psychological stress and cortisol, a stress biomarker, have a well-established association in the literature.[49,50] Psychological stress can result in increased cortisol and has been associated with increased cardiac troponins even among healthy older participants.[51] In addition, increased cortisol is an independent predictor of mortality and cardiac events in HF patients.[12] Although few LVAD studies have examined cortisol, one small study (n=6) found cortisol to be elevated pre-LVAD, resolved to normal wakening levels by 14 days post-implantation and remained stable over 90 days.[52] C-reactive protein is a stable biomarker of chronic, cumulative inflammation. It is less responsive to daily physiological and psychosocial stimuli in contrast to cortisol which is more susceptible to change in response to these stimuli.[13,53] C-reactive protein has been recommended as a biomarker to examine during the selection process for LVAD placement (with higher levels indicating a potentially higher risk patient) as well as a marker of decompensation during LVAD therapy.[25,54] Examining cortisol and CRP in patients living with an LVAD who have recovered from implant surgery has not been done previously and will contribute to our understanding of the inflammatory response to LVAD.

As patients respond to the stress of the LVAD experience, a range of psychological responses may include perception of and coping with stress as well as mal-adaptive responses such as depression. Psychological stress response characterized by high levels of perceived stress and depression has been associated with poor health outcomes among cardiac patients.[30,55] Increased perceived stress has also been related to decreased physical activity, a prevalent limitation for patients living with an LVAD.[56] Similarly, depression in HF negatively impacts FS, social isolation, self-care and is associated with impaired cognition. HF patients who are depressed and have low social support have increased co-morbidity, readmission rates, healthcare costs and non-adherence to medication regimen.[57–62] Affective symptoms of depression significantly impact HF outcomes regardless of chronic depression diagnosis, suggesting the need for affective symptom assessment.[63,64]

This study will evaluate perceptions of stress and affective symptoms of depression to give insight into how patients living with an LVAD experience and process living with the demands of advanced HF supported by this cutting-edge technology.

Coping strategies among individuals living with an LVAD have been examined using qualitative methods only. Studies have explored problem-focused strategies and found that some coping mechanisms involved intentionally keeping a positive attitude, having a sense of humor and keeping busy with social activities.[31,33,40,42] However, emotion-based strategies, such as disclaiming or escape-avoidance, have not been well explored in patients living with an LVAD and are associated with worse outcomes in HF patients.[65] Describing the coping strategies of patients living with an LVAD, establishing associations between important predictors that may influence coping and examining the impact of coping on relevant outcome variables will help inform future research and interventions.

Higher levels of **social support** have led to better cardiac health outcomes in HF and LVAD studies.[14,19,66] Each LVAD patient has a caregiver, identified prior to implantation that is fully involved in all aspects of day-to-day care. Additionally, the strain of a difficult caregiver-patient relationship is demonstrated in qualitative studies among patients living with an LVAD.[8,10,67] Therefore, it is believed that while all patients living with an LVAD experience some degree of social support, there may be a moderating relationship between stress, and selected outcomes at a certain level of social support.

Dissertation Organization

This dissertation consists of six chapters. Chapter one provides an overview of the study, with a description of the purpose and aims of the dissertation, the conceptual framework, and important concepts.

Chapter two is a literature review that was published in the Journal of Cardiac Failure in 2014. It analyzes the findings from studies of functional outcomes among LVAD patients. It is a critical review of the articles and provides recommendations for balancing functional outcomes with QOL and psychosocial outcomes.

Chapter three is a meta-synthesis of the qualitative literature regarding LVAD patient adaptation and coping throughout LVAD support. It was published in Heart & Lung: the Journal of Acute and Critical Care in 2016. It depicts the LVAD transactional conceptual model for stress and coping and highlights the need to assess stress and coping among LVAD patients.

Chapter four (data-based manuscript one) reports the findings from examining psychological stress, coping and the moderation effect of social support.

Chapter five (data-based manuscript two) reports the findings from comparing physiological markers of stress with psychological stress and their relationships to outcomes.

Chapter six presents: (1) a concise summary of the dissertation findings reported in Chapters four and five; (2) study strengths and limitations; (3) and study implications.

Chapter 2: Functional Status in Left Ventricular Assist Device Supported Patients: A Literature Review

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Abstract

The prevalence of advanced heart failure (HF) is increasing due to the aging population and improvements in HF management strategies. Left Ventricular Assist Device (LVAD) technology and management continue to advance rapidly and it is anticipated that the number of LVAD implants will increase. LVADs have been demonstrated to extend life and improve outcomes in patients with advanced HF. The purpose of this article is to review and synthesize the evidence on impact of LVAD therapy on functional status. Significant functional gains were demonstrated in patients supported by LVAD throughout the first year with most improvement in distance walked and peak oxygen consumption demonstrated in the first 6 months. Interventions to enhance exercise performance have had inconsistent effects on functional status. Poor exercise performance was associated with increased risk of adverse events. Functional status improved with LVAD therapy, though performance remained substantially reduced compared to age adjusted norms. There is tremendous need to enhance our understanding of factors influencing functional outcomes in this high-risk population.

Keywords: Heart-Assist Device, Functional Status, Quality of Life, Outcomes, Left Ventricular Assist Device

Background

Left Ventricular Assist Devices Improve Functional Status

According to the American Heart Association in 2014 there were 5.1 million Americans adults diagnosed with heart failure (HF).(1) This growing number is attributable to the aging of the population as well as overall improvements in HF management. Of patients with advanced HF, less than 4,000 are on the waiting list for heart transplant.(2,3) Though 2,506 Left Ventricular Assist Devices (LVAD) were implanted in 2013 in the US, it is estimated that between 40,000 - 200,000 HF patients may benefit from the support of an LVAD.(4,5) The number of patients receiving LVAD is anticipated to increase because of the limited availability of hearts for transplantation and the growing body of evidence supporting the use of LVAD as destination in addition to bridge to transplant therapy.(6)

Left Ventricular Assist Devices have been demonstrated to improve functional status and quality of life (QOL) over medical management through the REMATCH trial and other LVAD clinical trials.(7–14) A systematic review of the literature regarding QOL has been reported, but the current state of the science with regard to functional status in patients supported by LVAD has not been published.(15) The purpose of this article is to provide a current review of functional status in patients supported by LVAD.

Search Methods

A systematic literature search of the PUBMED and CINAHL databases was conducted. Search terms included the MESH term “heart-assist device” as well as “left ventricular”. For functional status, the terms “functional capacity”, “functional status”, “exercise capacity”, “exercise tolerance” and “exercise performance” were used. “Quality of life” was added to the search list because in HF QOL is often measured with a parallel functional measure. In addition, the references of the articles were reviewed to identify supplementary articles of interest.

The search was limited to studies published from 2007 through February 2014. This limitation was in consideration of the vast technological improvements to LVADs, in particular the transition from pulsatile LVADs to continuous-flow devices. Continuous flow LVADs, used in current practice, are more reliable and patients with these LVADs have less thrombotic events than those with pulsatile devices.(16) Articles were limited to English language and international studies were included. Studies were included if they reported original research with a sample including at least 1/3 LVAD patients. Also for inclusion, functional measures were measured or functional outcomes were reported (in qualitative studies). Studies were excluded if the emphasis was on molecular or surgical function, right-sided HF or if a case study was reported. Titles and abstracts (n=331) were reviewed and 241 were excluded. Sixty additional articles were excluded after article review. Thirty studies met criteria for inclusion in this review. Several large cohort studies had overlapping samples with smaller studies. Of the 30 articles selected for review, three categories emerged. Articles focused on describing functional progress, interventions to improve functional status and alternative approaches to understanding functional status. The results are categorized according to these themes.

Describing Functional Progress

Functional Gains Measured by a Six Minute Walk Test

Prior to LVAD insertion most HF patients were classified New York Heart Association (NYHA) class IV with many dependent on inotrope therapy, therefore unable to perform exercise testing.(14) Studies mapping the recovery and functional gains of LVAD recipients found an increase of cardiac output within 2 days of insertion.(17) Functional gains were demonstrated as early as one month.(14,18–20) NYHA class improved to I-II in nearly half of the sample at one month post-implantation in a study by Adamson et al.(19) However, overall surgical recovery and gains were more apparent 3 to 6 months after insertion.(13,14,20) Patients demonstrated marked increase of distance walked during the 6MWT. Distance walked at 1 month ranged from 225 to 367 meters.(14,18,20) By 6 months distance walked increased to 327 to 430 meters.(14,20,21) Between men and women there was a significant difference in distances at each time point, but overall improvement was similar (men improved from 247m to 356m and women from 219m to 327m).(14,20) At later time periods, 6MWT distance further improved at 12 months and remained stable at 24 months for those who could perform the test.(14) At 1 year, Allen et al reported mean 6MWT distance of 393±290m and at 24 months Rogers et al reported stable 6MWT for destination therapy patients.(13,14) These and other findings are summarized in Tables 1 and 2.

Functional Gains Measured by a Cardiopulmonary Exercise Testing

In addition to distance walked, cardiopulmonary exercise (CPX) testing demonstrated that over time patients supported by LVAD increased peak VO_2. Only one study reported CPX testing at 1 month; mean peak VO_2 was 10.5 ± 2.3 in a group assigned for a physical training intervention and 12.4 ± 1.7 in the control group.(18) Mean peak VO_2 at 3 months increased to a range from 12.66 to 18.3 mL/kg/min across several studies.(18,22–24) By 6 months, peak VO_2 ranged from 12.7 to 18.7 mL/kg/min.(21,24–26) Percentage of predicted norms reflected these increases with percentages increasing from 48-61% at 1 month to 42-66% at 12 months.(24–28) These large improvements illustrated that patients function better after LVAD, however function remained significantly below age-adjusted norms.

The studies reviewed had a variety of comparison groups. Pulsatile devices were compared to continuous-flow devices, though this comparison has limited relevance as pulsatile devices have limited use at this time. Patients with LVADs were also compared to heart transplant patients, and heart transplant patients consistently demonstrated greater improvements in functional measures. In Germany, a study comparing CPX testing in LVAD and heart transplant recipients found similar increases in workload between groups, but higher peak VO2 and self-rated QOL in the heart transplant group.(27) This is similar to findings reported in the US.(10)

Prediction of whom among LVAD recipients will have the best overall outcomes remains difficult. Outcomes do not appear to be associated consistently with disease severity, age, gender or race.(10,14,29) Hasin et al used 6MWT performance to group patients into performance groups (< 300m or > 300m).(30) This study used the first 6MWT (mean 4.1 months) after LVAD surgery to predict adverse outcomes, showing a 21% increase in mortality for every 10m less than 300m walked during the test.

Peak exercise capacity has been favored as an objective measure with multiple diagnostic and prognostic applications. The increase of exercise capacity over time in LVAD patients is impressive, but further research is needed to understand how best to help low-scoring patients improve. No published prospective studies have reported serial CPX testing with the same sample and no studies have focused on interventions to support low-functional status LVAD patients. The peak VO_2 improvements, supported by reported gains in quality of life and other functional measure data in the articles reviewed, contribute to the growing body of literature demonstrating the long-term benefit of LVAD therapy.

Functional status was measured using CPX and/or 6MWT in the studies reviewed, but the timing of the exercise testing after surgery was often not standardized. The 2013 International Society for Heart and Lung Transplantation Guidelines suggest CPX or 6MWT at regular intervals: an initial assessment post-op to guide rehab, 3 months, and every 6 months until 2 years after LVAD placement with yearly assessments after that.(31) Future collaborative research will need to further assess the appropriateness and utility of these intervals for functional capacity testing in larger populations of patients.

Interventions to Improve Functional Status

Physical Training Shows Modest Benefit in Small Studies

Interventional studies were conducted in various countries to examine the effect of physical training and other lifestyle-related interventions on functional status. Intervention studies are summarized in Table 3. Physical training studies utilized multi-faceted intervention strategies to enhance functional status, although no two studies used the same combination of strategies.(18,21,28) Intervention strategies included: dietary coaching, psychosocial counseling, aerobic training, strength training and inspiratory muscle training. These studies based their selection of intervention strategies on other cardiac surgery rehabilitation interventions. The multiple modality approach addresses physical recovery multi-dimensionally, however it does not provide evidence of the strength of any individual component of the multi-faceted intervention among LVAD patients. .

All physical training interventional studies demonstrated within group improvements in functional status measures for both control and intervention groups.(18,21,27) Intervention groups realized greater improvements in exercise tolerance and 6MWT distance and less weight gain than control groups.(21,28) With an intervention for inspiratory muscle training, Laoutaris et al saw significant within-group improvements in peak VO2, 6MWT and pulmonary function testing in the intervention group while no significant gains were made in the control group.(21) Between group comparisons of change in each functional measure were not statistically significant.(18,21,27) Some of the improvements seen over time were attributable to recovery from the operative procedure and the LVAD benefit of improved cardiac output, however in spite of non-significant findings in these small studies trends towards significance demonstrate an area for continued intervention and investigation. Despite functional improvements made in these studies of physical training interventions, functional status remained far below predicted norms for age groups.

The interventional studies were each conducted at single-sites with small samples; with small studies limited in power to detect differences between groups. Although there may be some methodological benefits to having a comparison group or in some cases, randomizing, the lack of differences between control and intervention groups may be attributed to dividing an already small sample into smaller groups. Another limitation in these studies was that patients entered the intervention programs at different points in their recovery. For instance, in the Hayes et al intervention study patients were included in the intervention after they were able to walk one complete lap on the surgical unit (mean days since implant was 32).(18) Functional status improvements may represent not only the intervention but also time since surgery or complications.

This body of evidence is insufficient to support specific interventions that can produce higher functional outcomes in LVAD patients. Modest benefits were seen in all exercise intervention studies reviewed. The 2013 Guidelines suggest that all capable LVAD patients should be involved in programs for cardiac rehabilitation.(31) Although the guidelines are not specific about intervention methods, articles reviewed here suggest a multi-modal approach of dietary guidance, inspiratory muscle, strength and endurance training may be of benefit.

Pump Speed Alterations

Exercise testing also was used to measure peak exercise performance with LVAD pump speed alterations. Exercise performance was evaluated before and after an LVAD pump speed decrease of 30% in two studies.(32,33) Cardiac output drop commensurate with the pump speed alteration as well as other similar effects were observed in both studies. However, Noor et al further compared change in pump speed by dividing the sample based on an ejection fraction of 40%.(33) Those in the higher ejection fraction group did not significantly drop cardiac output with a pump speed decrease, demonstrating native heart function.

Two studies examined increasing pump speed with exercise (400 rpm per exercise stage) and compared results with the same group of patients performing an exercise test at usual fixed pump speed.(34,35) Brassard et al showed cardiac output increased at submaximal exercise with increased pump speed (at rest cardiac output was 6 ± 2.1 L/min; submaximal exercise 60W cardiac output was 8.7 ± 1.1 L/min).(34) But, this study did not demonstrate significant differences at maximal exercise between the increased pump speed and constant pump speed groups. However, in a follow-up study, Jung et al demonstrated the benefit of increasing pump speed to support maximal exercise.(35) A significant increase of speed of pump (control group 9,357 ± 238 rpm to pump increase group 10,843 ± 835 rpm) resulted in peak VO2 that was significantly higher in the group with increased pump speed (control group 14.1 ± 6.3 ml/kg/min; pump increase group 15.4 ± 5.9 ml/kg/min). The earlier study used a Swan Ganz catheter to capture cardiac output, but this approach may have limited the participants from reaching maximum exhaustion.(34) Jung et al did not use invasive catheterization to measure cardiac output.(35) They did, however, have an older sample with longer mean days of support.

This important area of research merits further investigation as it may produce a means to support higher activity level in LVAD patients. The possibility of developing pump algorithms to support increased demand could be realized with confirmatory studies in larger samples. Here it is also important to highlight the debated relevance of peak versus submaximal exercise. Peak VO_2, even after 6-12 months of recovery, is still poor enough in most LVAD patients to suggest the need for transplant. In a recent study, 6MWT was approximately 80m further in patients with LVAD compared to heart failure patients medically managed with the same peak VO_2.(36) Submaximal exercise testing during CPX and 6MWT may more clearly reflect the functional gains that patients experience and require for improved ability to execute activities of daily living, participate in active hobbies and recreation and even return to work.

Functional Status Improves During Inpatient Rehabilitation

Three retrospective studies examined the effect of inpatient rehabilitation, a common discharge setting for patients following LVAD surgery, by comparing functional status, using the Functional Independence Measure (FIM), at admission and discharge.(37–39) The FIM is a reliable tool that quantifies several domains of function including: self-care, motor control, ambulation, etc.(40) All three of these studies demonstrated gains in FIM and FIM efficiency (FIM/length of stay) (depicted in Table 3).(37–39) These studies were limited by quasi-experimental design and measurement of few outcomes. However, more research efforts focusing on this discharge setting may help address concerns of a group of LVAD users at increased risk, i.e., those who cannot safely go home with a single caregiver or have increased supervision and physical activity and/or nursing care needs.

The value of early mobilization and increased physical activity post LVAD has been well supported.(41) However, acute complications can limit functional recovery and ability to engage in rehabilitation, leading to poor outcomes. Acute complications were addressed in several of the articles reviewed and particularly in the studies evaluating inpatient rehabilitation. Complications during inpatient rehabilitation were varied but included: acute, symptomatic anemia, epistaxis, depression, and stroke.(37–39) These complications demonstrated the necessity for patient and provider education regarding signs and symptoms of complications, evaluating discharge practices and understanding the burden of the medical complexity of these patients.

Alternative Approaches to Understanding Functional Status

Most studies used approaches to measure functional status that focused on physiologic measures (as the 6MWT, CPX), but several qualitative studies sought to broaden the understanding of what 'function' meant to LVAD patients and examined functional disruptions. Individuals living with LVAD struggled after discharge with bathing independently, interrupted sleep and returning to pleasurable and meaningful activities including sexual intercourse and driving, which negatively affected both functional status and QOL.(42–47) These findings suggest a need to further explore the specific stressors that cause functional limitations and trouble LVAD patients.

Casida et al explored the relationship between sleepiness, daytime function and QOL. QOL was negatively correlated with sleepiness and positively correlated with daytime function.(42) Sleepiness was found to improve from baseline (1 month post-implantation) to time 2 (6 months), though LVAD patients were still more sleepy at 6 months post-implantation than the age-adjusted norms. Sleep disturbance has been directly related to symptoms of cardiopulmonary congestion and pain in heart failure patients. These have been demonstrated to impact depression which can have additional effects on functional and QOL outcomes.(48) The importance of sleep for LVAD patients is not well understood and should be further investigated in future research.

Functional status has been measured under the assumption that physical exercise (maximal or submaximal) represents the effort of performing ADLs and other functional requirements. The work of Casida and others draws attention that measuring functional status and QOL likely does not capture the ways that life with an LVAD is functionally difficult. There have been few studies with an emphasis on nutrition, BMI, sleep, frailty and other topics that are likely to be important influences on functional status. Continued research is necessary to create a comprehensive understanding of barriers and facilitators of good functional outcomes in patients supported by LVAD.

Recommendations for Future Research

While functional gains are dramatic for those measured, a large number of LVAD patients die in the early peri-operative period and within the first year.(13,23,25) In addition, only the LVAD patients that are assessed to be physically capable are included in exercise testing. Thus, the patients with greatest illness severity likely are not represented and therefore the findings have limited generalizability. Research methodologies and reporting should continue to provide clarity about how many patients are unable to participate in measurement of functional outcomes. As the use of LVAD increases, understanding who is most at risk to have poor outcomes will influence studies that examine patient selection for LVAD placement, LVAD care coordination and interventions to maximize functional and QOL outcomes.

Addressing health disparities is a priority for both the American Heart Association and the National Institutes of Health. However, due to the predominantly white, male LVAD population, the diversity of LVAD research samples has been limited. According to Interagency Registry for Mechanically Assisted Circulatory Support women receive about 21% of LVADs.(49) This inequality may be attributable to the greater age at which women develop late stage HF. LVAD research participation reflects this gender gap. In addition to gender disparities, there is little LVAD research done comparing racial groups, although some work has been done comparing African-Americans and Caucasians.(29) Also, it was noted that mean age of participants, particularly in the intervention studies, was lower than the mean age of the LVAD program population from which they were selected, suggesting a potential selection bias related to age. Although there may be many reasons these disparities in research participation exist, future LVAD research will need to broaden samples to enhance generalizability, particularly as it is anticipated that LVAD programs will move out of academic centers and into the community.(50)

In accordance with the 2013 guidelines, LVAD programs will begin to gather functional status and quality of life data at regular intervals.(31) As programs grow, future research will need to continue to assess these intervals and functional gains to determine the appropriateness of the intervals and the measures. More comparisons will need to consider implant strategy, bridge to transplant versus destination therapy. Functional gains up to 6 months are clearly and consistently demonstrated, but interventions should be developed and tested to help enhance these gains throughout LVAD therapy. This review also demonstrates opportunities for improved understanding of how changes in pump settings can improve functional outcomes.

Finally, years of single-center studies have been published reporting LVAD outcomes. Multi-center collaborations are necessary to advance the science of caring for this advanced heart failure population with high healthcare utilization to improve prediction models, functional outcomes and the lives of the patients and families receiving LVAD therapy.

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Table 1: Functional Gains Over Time

	Pre-op	**1 month**	**3 months**	**6 months**	**12 months**	**18 months**	**24 months**
NYHA class (I-IV)							
Rogers*	~III-IV	~II-III	~I-III	~I-III	~I-III		
McDiarmid (mean)	3.6 ± 0.5			2.3 ± 0.7	1.7 ± 0.8		
Bogaev	0% of sample class I			83-85% of sample class I			
Allen					1.4±0.6		
Adamson							
< 70 years	I-II – 0%	I-II – 48%	I-II – 86%	I-II – 100%			
> 70 years	I-II – 0%	I-II – 42%	I-II – 90%	I-II – 89%			
Peak VO$_2$ (ml/kg/min)							
McDiarmid	9.9 ± 2.1			14.3 ± 5.1	14.6 ± 4.6		
Leibner	11.16 ± 3.1		12.66 ±3.52		10.74 ± 2.7	11.18 ± 1.7	
Pruijsten			18.3 ± 4.8				
Haft			15.6 ± 4.7				
Hayes^{+}							
IGr		10.5 ± 2.3	14.8 ± 4.9				
CGr		12.4 ± 1.7	15.3 ± 4.4				
Martina				18.7± 5.8	18.8 ± 5.7		
Laoutaris^{+}							
IGr				16.8 ± 3.7	19.3 ± 4.5		
CGr				14.9 ± 4	14.8 ± 4.2		
Percentage of Predicted peak VO$_2$ (%)							
McDiarmid	32.3 ± 7.4			41.4 ±12.7	42 ± 15		
Leibner	40.4 ± 9.3		46.94 ± 10.2		46.81 ± 11.5	50.09 ± 6.1	
Pruijsten			49 ± 11				
Martina				51 ± 13	52 ± 13		
Haft			49.1 ± 13.6				
Kugler		~48		~56			
Kugler^{+}		59-61		58-62	61-66	62-69	
IGr							
CGr							
6MWT (meters)							
Rogers							
DT	204 ± 150	~225	~280	350 ± 198 372	~325	360±210	~350
BTT	214 ± 125	~250	~350	± 199			
Bogaev							
Female	219 ± 173	238 ± 108	306 ± 147	327 ± 114 356			
Male	247 ± 112	275 ± 162	351 ± 163	± 179			
Adamson							
< 70 years	256 ± 96	188 ± 113	354 ± 162	275 ± 135			
>70 years	233 ± 100	162 ± 114	256 ± 100	295 ± 97			
Allen					393 ± 290		
Laoutaris^{+}							
IGr				462 ± 88	527 ± 76		
CGr				430 ± 41	448 ± 55		
Hayes^{+}							
IGr		351 ± 77	531 ± 131				
CGr		367 ± 129	489 ± 95				
SF-36 (patient-rated Physical Health only)							
Kugler (Physical Function)		50 ± 3.8		55 ± 5.5			
Kugler^{+}							
IGr		34.7 ± 1.5		~37	~39	~40	
CGr		30.4 ± 1.4		~37	~36	~35	
Hayes^{+}							
IGr		23.4 ± 8.9	53.7±23.8				
CGr		33 ± 10.4	47.7 ± 9.4				

Key:
~ data is obtained from graphs and is approximate
+ exercise intervention study
IGr Intervention Group
CGr Control Group

Table 2: LVAD Functional Outcomes

Study (country)	Sample	Design	Findings
Functional Gains Measured by Six Minute Walk Test			
Adamson et al, (2011) (US)	LVAD type: HMII N LVADs: 55 Female: not reported Mean age in years: < 70: 56.7 ± 14.3 > 70: 76.3 ± 3.9	Retrospective HMII trial participants compared outcomes for patients > 70 years and < 70 years old.	- Within group improvements were similar across time and there was no statistical difference between groups for QOL, 6MWT and METs - No difference in the incidence of adverse events for this small sample. - Survival was comparable across time regardless of age - Demonstrated value of LVAD therapy for patients > 70 years
Bogaev et al, (2011) (US)	LVAD type(s): HMII N LVADs: 465 Female: 22% Mean age in years: Men 52.4±12.8 Women 49.6±14.2	Retrospective Compared outcomes by gender	- Men and women had similar improvements in 6MWT and NYHA class at 6 months. - 6MWT at 6 months compared to baseline pre-op (most patients could not perform pre-op 6MWT): Women improved from 219 to 327m and men improved from 247 to 356m. -NYHA I or II at 6 months - 83% women and 85% men (0% NYHA I or II at baseline for men or women) - Distance walked at all times was greater for men ($p=0.037$).
Rogers et al,(2010) (US)	LVAD type(s): HMII N LVADs: 655 Female: BTT – 24% DT – 27% Mean age in years: BTT - 50±13 DT - 63±12	Prospective 2 years Compared BTT vs DT	- Dramatic improvement in distance walked up to 6 months, leveling from 6-24 months - Only 14% BTT and 34% DT were able to do 6MWT pre-op -DT improved 6MWT +146m at 24 months from baseline pre-op - 80-82% in NYHA class I-II from 6-24 months - 60% of DT rated exercise ability moderate-very high
Allen et al, (2010) (US)	LVAD type(s): HMII and others (not specified) N LVADs: 103 Female: survivors – 27% died in 1st year – 21% Mean age in years: survivors – 48.2±12.4 died in 1st year – 49.8±13.7	Retrospective Compared 1-year survivors with those who died in the 1st year	-Survivors were more likely to have had HMII, planned DT (not BTT), and did not have intra-aortic balloon pump pre-op. - Mean days of support for those who died in the 1st year was 148±153. - Among survivors at 1 year, mean 6MWT 393±290m and mean NYHA 1.4±0.6. - Survivors spent 87.3% ± 14% of time out of hospital, but 23/30 survivors required re-operation.
Loforte et al, (2009) (Italy)	LVAD type: HMII N LVADs: 18 Female: 28% Mean age in years: 52± 8	Retrospective Reported Progress Over Time	-30-day mortality 27.7% -12/18 discharged NYHA class I -Mean Cardiac Index improved from 1.8 to 3.5 by 48 hours post-op (no p-value reported) -Greater proportion able to complete 6MWT and go further distance at 30 days (no number reported)
Hasin et al, (2012) (US)	LVAD type: HMII N LVADs: 65 Female: 17% Mean age in years: 65.92	Retrospective Examined risk for mortality based on 6MWT results	-21% increased mortality for every 10m less than 300m - Poor performers were older, had diabetes and hypertension comorbidity, decreased glomerular filtration rates, required prolonged inotropy, had increased ventilator time, increased length of stay, and increased Right Atrial Pressures at 1 month. -Created 3 risk predictor categories: pre-op issues, peri-op issues and 1 month echo result indicators
Functional Gains Measured by CardioPulmonary Exercise Testing			
McDiarmid et al, (2013) (UK)	LVAD type: Heartware N LVADs: 30 Female: 27% Mean age in years:	Retrospective Compared 2 timepoints – approximately	-By 12 months, improved NYHA from 3.6 to 1.7 -Improved VO_2 from 9.9 ± 2.1 to 14.6 ± 4.6 -Improved from 32.3% predicted norm for peak VO_2 to 42% of predicted norm

	47±12	6 (mean 201 ± 86 days) and 12 months (mean 351 ± 86 days)	
Leibner et al, (2013) (US)	LVAD type: Heartware and HMII N LVADs: 31 Female: 24% Mean age in years: 63.9 ±11.3	Retrospective Compared multiple timepoints: pre-LVAD, 3-6 and 12 months and >1 year	-No significant change in peak VO_2 across timepoints -% predicted norm did improve, but still severe functional limitation -Only 10 living at > 1 year time
Martina et al, (2013) (Netherlands)	LVAD type: HMII N LVADs: 30 Female: 23% Mean age in years: 43 ± 14	Prospective Compared 2 timepoints - 6 and 12 months	- Peak VO2 was stable at 6 and 12 months(18.7±5.8 and 18.8±5.7 mL/min, respectively). - Main focus of study was on changes in hemodynamics: from rest to max exercise HR, BP, TCO increased and SVR decreased. - Older age and gender affected exercise capacity (BP increased significantly in men compared to women).
Pruijsten et al, (2012) (Netherlands)	LVAD type: HMI (prior to 2005) and HMII (2006-present) N HMI: 42 HMI Female: 10% HMI Mean age in years: 39 ± 12 N HMII: 33 HMII Female: 21% HMII Mean age in years: 44 ± 12	Retrospective Compared pulsatile (HMI) vs continuous-flow (HMII) LVADs	-No difference in peak VO_2 after adjusting for BMI -Labs: Significant improvement in all lab values esp BNP and Creatinine, Hemoglobin improved in both groups by 3months -Echo: greater decrease in dimensions of LV in pulsatile group (80±10mm vs 72 ±12mm; p=0.005)
Kugler et al, (2011) (Germany)	LVAD type: HMII N LVADs: 27 N HTx: 54 Female: 3% Mean age in years: 47±13	Prospective Compared LVAD and HTx recipient outcomes	-Peak VO_2 increased 7% LVAD, 10% HTx (p=0.01) -7% increase in BMI-adjusted workload LVADs vs 8% HTx at 6 months (P=0.01)
Jakovljevic et al, (2010) (UK)	LVAD type: HMII N LVADs: 27 N Explanted: 54 N HF: 20 Female: 0% Mean age in years: 39±14 (LVAD group)	Retrospective Compared 3 groups: Heart Failure, Implanted LVAD and Explanted LVAD patients	-Peak CPO and exercise performance are best in explanted patients - No difference at rest between groups in CPO or VO_2 - No precision of timing of exercise test Cardiac Power Output: peak: Explant & LVAD > HF Cardiac Output at rest: LVAD>HF (by 1.4 L/min or 25%) -Peak VO_2: Explant> LVAD>HF -% Max predicted O2 Consumption: Explant 83% > LVAD 57% > HF 46% Exercise Duration: LVAD>HF – stopped due to fatigue or dyspnea
Pruijsten et al, (2008) (Netherlands)	LVAD type: HMII N LVADs: 44 N HTx: 29 of the 44 Female: not reported Mean age in years: Not reported	Retrospective Compared outcomes 3 months after LVAD to 3 months after HTx in same patients	-Mean peak VO_2 3 months post-LVAD insertion is compatible with ADLs -50% mean predicted VO_2 for age and gender in both groups -Post transplant VO_2> post-LVAD -Normalized BNP and renal function 3 months after LVAD
Haft et al, (2007) (US)	LVAD type: HMXVE and HMII N LVADs: 34	Retrospective Compared HMXVE and	- Peak VO_2 15.4±4 HMXVE and 15.6±4.7 HMII at 3 months - Peak % predicted 46.8 HMXVE and 49.1 HMII

Female: 6% HMXVE and 17% HMII Mean age in years: 52 ± 14 years	HMII outcomes	- Exercise time 10:25±3 minutes HMXVE and 9:31±3 minutes HMII -No difference between devices in hemodynamic support and exercise capacity - HMXVE had improved left ventricular unloading

Key: HMII, Heartmate II Continuous Flow LVAD; HMXVE, Heartmate XVE Pulsatile LVAD; TAH, Total Artificial Heart; HTx, Heart Transplant; BTT, Bridge to Transplant; DT, Destination Therapy; 6MWT, 6 Minute Walk Test; NYHA, New York Heart Association Heart Failure Functional Classification; FS, Functional Status; QOL, Quality of Life; METS, Metabolic Equivalent Test Score; CPX, Cardiopulmonary Exercise Testing; CPO, Cardiac Power Output

Table 3: Interventions to Improve Functional Outcomes

Study(country)	Sample	Design	Findings
Physical Training Interventions			
Kugler et al, (2012) (Germany)	LVAD type(s): Continuous Flow N LVADs: 70 Female: 14% Mean age in years: 52±2	Randomized control trial Intervention included dietary counseling, home ergometry and psycho-social counseling for 8 weeks	-Intervention prevented weight gain in IGr, CGr BMI increased by mean of 5.9 kg/m^2 ($p<0.02$) -Exercise Tolerance was higher in IGr -Both exercise capacity and QOL remained below predicted norms in both groups despite improvement over time
Laoutaris et al, (2011) (Greece)	LVAD type(s): LVAD and BiVAD N LVADs: 15 Female: 7% Mean age in years: 37.2 ± 17.7 (IGr)	Randomized control trial Intervention included mod-intensity aerobic & inspiratory muscle training for 10 weeks	-Peak VO_2 increased in IGr only (+15%) ($p<0.008$) -6MWT increased in IGr only (+14%, $p<0.005$) - Pulmonary Function increased significantly in IGr only ($p<0.008$)
Hayes et al, (2012) (Australia)	LVAD type(s): VentrAssist N LVADs: 14 Female: 14% Mean age in years: 48.7 ± 14.5 (IGr)	Randomized control trial Intervention included gym-based aerobic and strength training for 8 weeks	-Both groups had significant improvement of peak VO_2, workload and 6MWT, but no difference between groups -Early mobilization without any acute complications
Altering Pump Speed			
Jung et al, (2014) (Denmark)	LVAD type(s): HMII N LVADs: 16 Female: 14% Mean age in years: 55 ± 13 Mean support days: 465 ± 483	Intervention – paired randomization Compared fixed pump speed with incremental increases in pump speed in the same group of LVAD patients	- Mean peak VO_2 was significantly greater in the test with incremental increases in pump speed versus fixed speed (15.4±5.9 mL/kg/min vs. 14.1±6.3 mL/kg/min; $P=0.012$) - Mean Baseline fixed pump speed was 9,357±238 rpm. Mean Increased pump speed to 10,843 ± 835rpm, increase of 9.2% in increments of 400rpm/2min. - No differences between tests for exercise time work-load or post-exercise blood lactate
Noor et al, (2012) (UK)	LVAD type(s): HMII N LVADs: 30 Female: 7% Mean age in years: 35 ± 13	Intervention Compared Clinical pump speed (9000rpm) with lowest speed (6000rpm) and EF <40% to EF >40%	- Peak VO2 was lower in the low EF group at both clinical and reduced speeds (21.4 ±4.8 mL/kg/min and 14.7 ± 5.9 mL/kg/min, respectively). - At low speed, peak VO2 dropped by 2.5mL/kg/min in the low EF group - No significant change in peak VO2 in >40% EF group with change in pump speed.
Brassard et al, (2011) (Denmark)	LVAD type(s): HMII N LVADs: 8 Female: 12.5% Mean age in years: 39 ± 18 Mean support days: 329 ± 190	Intervention – paired randomization Compared fixed pump speed with incremental increases in pump speed of 400 rpm in the same group of LVAD patients	- During light exercise, increased pump speed was associated with increased cardiac output and cerebral perfusion. - No difference noted at max exertion between group with increased LVAD speed compared to fixed speed -Transcranial Doppler showed 80% of normal cerebral blood flow at rest and an increase with light exertion -High patient burden – only 3 patients with Swan Ganz catheter and femoral sheath
Jakovljevic et al, (2010) (UK)	LVAD type(s): HMII N LVADs: 12 Female: 0% Mean age in years: 33 ± 13	Intervention Compared Normal LVAD speed (9000-9600 revs/min) vs. reduced speed (6000 revs/min)	-With reduction in LVAD speed: CPO decreased by 39% at peak exercise ($p<0.001$) CO decreased by 30% at peak exercise ($p<0.001$) -Additional significant changes in VO2, SVR, BP, VE slope, SV, HR and exercise time -CPO is sensitive to changes in LVAD speed
Inpatient Rehabilitation			

Kohli et al, (2011) (US)	LVAD type(s): HMII N LVADs: 12 N TAH: 30 Female: 17% Mean age in years: 51.2 ± 13.6 (HMII)	Retrospective Compared LVAD and TAH	-Greater BP response in LVADs vs TAH -Mean arterial pressure positively correlated with Metabolic equivalents in LVADs (p=0.04) -LVAD was comparison group – not all results for LVAD disclosed
Nguyen (2013) (US)	LVAD type(s): HMII N LVADs: 11 Female: 27% Mean age in years: 61.8 ± 11.9	Retrospective	- Mean FIM increase from Admission to Discharge: 22.1 - Mean Length of Stay: 11.6 days - FIM efficiency = FIM/LOS = 2.4 - Discharge setting: 7/11 home and 4/11 hospital - LVAD patients safely completed 3 hours of rehab for 5 days of the week.
English (2012) (US)	LVAD type(s): HMII N LVADs: 20 Female: not reported Mean age in years: 60.6 ± 10.4	Retrospective	- Mean FIM increase from Admission to Discharge: 27 - Mean Length of Stay: 11.3 days - FIM efficiency = FIM/LOS = 2.8 - Discharge setting: 16/20 home and 4/20 hospital

Key: HMII, Heartmate II Continuous Flow LVAD; HMXVE, Heartmate XVE Pulsatile LVAD; TAH, Total Artificial Heart; HTx, Heart Transplant; BTT, 6MWT, 6 Minute Walk Test; NYHA, New York Heart Association Heart Failure Functional Classification; IGr, Intervention Group; CGr, Control Group; BMI, Body Mass Index; BP, Blood Pressure; FIM, Functional Independence Measure

Chapter 3: Adaptation and Coping in Patients Living with an LVAD: A Meta-synthesis

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Abstract

Background: Left Ventricular Assist Device (LVAD) patients have shown improvements in measures of quality of life and functional status compared to those who are medically managed. Qualitative research has not yet been meaningfully integrated.

Aim: To synthesize and convey information to inform components of LVAD education programs that support the coping and adaptation of patients living with an LVAD and to identify opportunities for future interventions.

Methods: Qualitative meta-synthesis using Lazarus and Folkmans' Transactional Model of stress and coping

Results: Four distinct stages of adaptation were identified: Pre-LVAD, Implant Hospitalization, Early Home Adaptation and Late Home Adaptation. Each stage includes tasks related to physical, psychological and social domains. Further, two themes emerged: 1) Primary Appraisal: Every stage is a new challenge and 2) Secondary Appraisal: Routines are achievable, emotions are more difficult.

Conclusions: The emotional challenges LVAD patients face including fear and anxiety related to living with a life limiting illness and changed social roles need to be honestly addressed. Individuals living with LVAD can achieve a sense of independence and enjoy social interactions and activities that are important to them through addressing practical and emotional problems to facilitate effective coping.

Keywords: Adaptation, Coping, Left Ventricular Assist Device, LVAD, heart failure

Background

Left Ventricular Assist Devices (LVADs) are pumps that assist the failing heart and are powered through a driveline that attaches externally to batteries or non-portable sources of power. They are used as a bridge to heart transplantation and increasingly, as destination therapy, meaning that the patient will use this therapy until death.[1] Seventy-eight percent of LVAD recipients live for at least one year and nearly 50% survive four or more years with the LVAD, extending life much longer than medical management alone.[1,2] In addition to surviving longer, patients experience functional and quality of life (QOL) gains during the first year of therapy and these gains remain stable for the duration of therapy.[3] However, in comparison to age-adjusted norms and heart transplant patients, LVAD patients have been found to have worse QOL and functional status.[4,5]

Qualitative research has suggested unique aspects of life with an LVAD that may be stressful, including alteration in body image, managing the batteries and device, limitations of bathing and swimming, driving restrictions, and effects on intimacy.[6–8] Emotional distress, adjustment disorders, and disability have been identified after device implant.[9,10]

The complexity of care and changes in lifestyle for LVAD patients likely contributes to a unique adaptive process.[11] While functional status and patient reported outcomes, including quality of life, have been reviewed in the literature, no single study has provided a holistic account regarding the ways in which patients experience and adapt to living with an LVAD. The purpose of this review is to synthesize and convey information to inform components of LVAD education programs that support the coping and adaptation of patients living with an LVAD and identify opportunities for future interventions.

For the purposes of this synthesis, we used the Lazarus and Folkman Transactional Model of Stress and Coping to inform our analysis. This model asserts that coping processes mediate the relationships between stress and outcomes.[12–14] Key components of this model include primary and secondary appraisals which inform emotion and problem-focused coping strategies.

Search Methods

A meta-synthesis was conducted to enhance our understanding of individuals' experiences and processes involved in living with a LVAD for the purpose of designing and delivering services to support patient coping with living with LVAD. An electronic database search of Pubmed, Cinahl, Medline and PsycINFO was undertaken in May 2015. Ex. ((heart-assist device (MESH term) OR LVAD OR mechanical circulatory support) AND (qualitative OR adjustment OR adaptation OR coping)). The titles and abstracts of articles were independently reviewed by 2 researchers, both cardiac nurses (MA & MC). Studies were included if they involved adult LVAD patients and used qualitative data collection and analysis methods (see Figure 1). Studies were excluded if they focused on caregivers, used mixed methods or were published before 2007. The last criterion reflects the dramatic improvement in LVAD technology in recent years. A landmark study was conducted in 2007 that resulted in the transition from pulsatile to continuous-flow devices.[15,16] Seven articles met inclusion and exclusion criteria.

Each paper was independently evaluated according to the Critical Appraisal Skills Program (CASP) (see Table 1). [17,21] The articles were read multiple times by two independent reviewers who are both nurses with experience caring for LVAD patients in the intensive care unit (MA and RP). A thematic synthesis of qualitative literature was undertaken using the methods of Thomas and Harden.[17] Two articles, with high qualitative rigor according to the CASP, were selected to create a codebook.[7,8] After each reviewer coded the text from two articles, the reviewers met to discuss and create a combined spreadsheet organized into descriptive themes. Components of the Transactional Model of Stress and Coping were used to organize the coding framework.[12–14] Coding continued on the remaining 5 articles. Discrepancies between coders were discussed and a consensus code was created. Themes were drawn from the codes both within and across studies. A clear audit trail was maintained through the use of memos and notes. As a further measure of analytic rigor, a third researcher (MD) performed an independent analysis of the results of the seven articles. Analytical themes were then synthesized from the descriptive themes. Any discrepancies in the analysis were resolved through discussion.

Results

Of the seven articles included in the review, two articles reported results from a single sample, yet asked different research questions.[7,18] All studies reported methods to maintain qualitative rigor as measured by the CASP, but the article by Sandau was most transparent, reporting attributes of the non-clinician interviewers and more details regarding the grounded theory approach (see Table 1).[7,8,18–22] Sample sizes ranged from 5-12 patients with a total of 59 patients included in the 7 studies (see Table 2). The mean age of participants was 52.3 years and 25% (n=15) were women. Two of the studies were conducted in the United Kingdom[20,19], four in the United States[7,18,21,22] and one in Denmark[8]. The two studies in the United Kingdom included participants' recall of living with an LVAD after they had been explanted, meaning that at the time of the interview, the LVAD had been removed because of recovery or transplantation.[20,19] Each study sample was drawn from a single LVAD center. As yet, no qualitative studies have recruited patient participants from multiple LVAD centers.

Four studies described the implant strategy (bridge to transplant or destination therapy); however, none of the studies used implant strategy to compare findings.[7,18,21] One study included only destination therapy participants, yet little is known about how adaptation may differ by implant strategy of patients living with an LVAD.[21] Although these studies span a period of less than 10 years, recommendations for care of LVAD patients have evolved in that time. For instance, one study commented on the extensive involvement of the palliative care team in their program, which although called for in recent recommendations for care, is still an unmet goal in many programs.[21,23,24] No studies included sick or hospitalized LVAD patients who may have a very different perspective on aspects of life with an LVAD.

As we read the seven studies, it became clear that patients remember their journey in 4 distinct stages: Pre-LVAD, the time from first discussions for the device to surgery, Implant Hospitalization, Early Home Adaptation and Late Home Adaptation. These stages were identified through thematic analysis and were organized based on the Transactional Model of Stress and Coping (see Figure 2) including physical, psychological and social domains (see Table 3).[14] Further, two themes emerged: 1) Primary Appraisal: Every stage is a new challenge and 2) Secondary Appraisal: Routines are achievable, emotions are more difficult.

Primary Appraisal: Every stage is a new challenge

Primary appraisal, as described by Lazarus and Folkman, involves the evaluation of harm, threat and challenge to determine if the stress has a significant impact on well-being.[14] This appraisal is a constant process but is more pronounced at times of transition. The initial implant of an LVAD, the transition to home and then dealing with the device in the long term were stages in which LVAD patients appraised new challenges, threats to normalcy and independence.

For LVAD patients who participated in these studies, a repeated theme was that being dependent on another person is undesirable.[7,8,18–22] Previous roles and the personal identity were threatened by dependence. However, LVAD patients recognized their need for a caregiver and that learning to live with the device would be nearly impossible without their support.[7,8,21] The pursuit of independence was discussed particularly in the hospital, early home and late home stages. It is likely that preoccupation with symptom burden made this less relevant during the pre-LVAD stage.

Individuals living with LVAD consider ‘normal life’ to be their life before the LVAD was implanted and often their life before significant heart failure symptom limitations.[7,8,18–22] They felt that learning to find normalcy while living with an LVAD was difficult, particularly if LVAD lifestyle changes were dissonant with developmental stage.[8,22] Finding a “new normal” was hampered by unexpected hospitalizations and poor outcomes (ie. gastrointestinal bleeding, stroke or even vision loss).[20,22] In addition, LVAD patients were plagued with concerns that the LVAD itself would have device problems or that infection might develop.[8,19] They also had concerns about body image and difficulty with managing transplant expectations.[7,18,19,22]

Pre-LVAD stage

As patients reflected on their experiences during the pre-LVAD stage, many talked about their heavy symptom burden (Table 3).[21,19] Their strong need to be relieved of their symptoms affected the decision-making process as they learned about LVADs and went through the evaluation process. LVAD patients felt that although they were offered the choice of LVAD or medical treatment, many felt that there was only one choice – to live.[21,22] Patients needed to take time to reflect on the experiences and decisions that led to the device placement. For some, who received the device emergently, and had no recollection of this period, it was necessary to cognitively and emotionally process events that were out of their control prior to implantation during later stages of recovery.[8,20,19]

Implant Hospitalization stage

The hospital stage of the adaptation process includes a high level of dependence on the care team while recovering from surgery and learning basic LVAD skills.[7,21] In the hospital many talked about the impact of seeing their bodies with scars and the driveline.

"I look at myself now in the mirror. Before I didn't have any scars. Now I'm covered in scars. It doesn't really bother me." [19]

Learning basic LVAD skills during the hospitalization was a key activity and was overwhelming for many.[7,8,18–22] Emphasis on mastery of skills was placed on the caregiver with the expectation that the patient would later master VAD-related skills.[7,21] The basic skills include learning to manipulate the battery pack, using supportive gear to wear the device and methods for bathing, dressing and driveline dressing changes.[7,8,21,22] Alarms and vibrations of the device were frightening at first and those who had more frequent alarms struggled with fear and anxiety about device failure.[19]

"They give you a lot of information on that first [visit], and they put it into a folder, and they treat you like a scared hog in a packing plant but they do it right."[21]

Early Home stage

Early Home Adaptation involves the early testing and development of routines for activities of daily living while slowly initiating steps of independence. However, in this stage the necessary dependence on the family caregiver (instead of the professional team) is a significant change from the hospital experience and even the pre-LVAD disease state. LVAD coordinators were available by phone and mentioned as good communicators through this transition.[21,19] All of the skills acquired in the hospital must be adapted for the home environment.[7,8,19,21,22] The home environment needed to be changed to support the patient. For example some homes required electrical work. The privacy of being back at home allowed some to re-explore sexual intimacy described as a significant benefit.[18]

However, the stress of the early home stage was also influenced by the frequency of clinic visits and related testing or travel.[7,21] LVAD patients mentioned that they did not understand prior to surgery how much follow-up care would be necessary.[21]

Late Home Stage

Lastly, in the Late Home Adaptation phase, patients discussed a change in their sense of normalcy and an acceptance, even gratitude, for the LVAD. This stage was characterized by increasing confidence in device manipulation and increased independence in self-management. This new confidence allowed for increased sexual intimacy.[18,22] However, it was difficult for LVAD patients to return to work and resume previous roles, which are considered to be priorities to achieve normalcy.[8] For instance, only 4 LVAD patients across 6 studies were described as working at the time of data collection.[7,8,18–20,22] (1 study did not

describe any return to work, but the average age of participants was over 70 and this may not have been a relevant consideration.[21])

"Well I think I was fairly comfortable mentally, because I'm good at accepting things and working from there…it took about 6 months to adjust to daily life with the [LVAD]."[8]

"The whole thing about it is feeling better; going to bed with this equipment, getting up with this equipment, um, is living."[7]

Secondary Appraisal: Routines are achievable, emotions are more difficult

Secondary appraisal is the cognitive process of evaluating what steps can be taken to decrease the challenges. [14] Problem-focused, emotion-focused and spiritual coping strategies may be used to cope with threats. Coping with life with an LVAD was described as extremely challenging in all of the studies.

Problem focused coping

Problem focused coping included focusing on the skills required to be more independent.[13,14] Routines for activities of daily living, such as bathing and dressing, helped establish a sense of control and independence for the individual living with an LVAD. Having control over life situations was seen as highly desirable for patients who had experienced many symptom burden-related losses of control. Routines serve as an important key to adapting to life with an LVAD.[7,8,18–22]

"I prefer to [change my own bandages]. If I don't, I feel sick, like I can't do anything, then I feel disabled."[8]

"I didn't want to be alone just after I got the [LVAD], so I moved in with my aunt, who was home all day."[8]

Patients stated that having a full-time caregiver and the support of family or social networks addressed the problem of loneliness and isolation for them.[7,8,18–22] Involving friends and family in the adaptation process helped distract from fears and worry. Returning to social

activities also supported a sense of normalcy and LVAD patients reported feeling closer to their families and social networks. But some transitioned to having family gatherings at their own home to limit the need for exhausting travel. Patients also discussed the benefit of participating in professional counseling.[19]

Some patients reported having a deeper intimate connection with their sexual partner and described how they and their partners coped with the practical challenges of adapting their intimate routines to the encumbering device and cords.[18,22] Men preferred the flexibility of battery use, while women felt they were more comfortable knowing they were attached to AC power.[18]

''We keep on changing positions a little bit, but (laugh) it's good, I mean it's a little slower, little more awkward but you adapt to it.''[18]

Emotion-focused Coping

Patients reported that over time, they were able to develop confidence by increasing their independence, developing safe routines, and coping with uncertainty.[7,8,19–22] Managing expectations about timing for each stage began as soon as the decision to implant the device was made while patients awaited implant surgery and was especially difficult for patients with longer implant hospitalizations waiting to go home.[21] Some of the coping mechanisms involved intentionally keeping a positive attitude, having a sense of humor, religious involvement and prayer.[7,8,18–22] Several patients pointed out the value of meeting with other LVAD patients and families in a support group or one-on-one.[8,21] One patient described finding value and meaning in being the LVAD mentor and reaching out to hospitalized patients with newly implanted devices.

"…it's getting better, but you got to learn to lift your feet and you got to learn not to make a fast turn."[21]

Sandau et al (2014) highlighted the way that participants used their spiritual beliefs to cope with existential distress and find peace with decisions that were made, events that had

transpired and to cope with the uncertainty of the future.[22] Social support may be enhanced through religious affiliation.

"I believe in a Higher Power and the strength from that….those around you where you can find your strength."[22]

Finally, prayer, meditation and even the quiet of a day spent fishing were ways that LVAD patients found to still their anxieties and establish a sense of peace.[7,22]

Participants also identified several factors that made coping difficult. Living with the LVAD left some feeling exposed or vulnerable.[7,8,18–22] This was reinforced when, despite best attempts to maintain a clean driveline site, they experienced driveline infections or a VAD malfunction.[19] Some LVAD patients also reported that the over-protection of their caregiver and family prevented them from having any feeling of control.[7] Focusing on the differences between life before significant illness and after the LVAD was distressing, but some were unable to avoid it.[7,8,18–22] Noticing that although they were able to be social, they had less visitors than usual was a challenge.[7,8] Similarly, it was difficult for some patients to accept that there are some activities that cannot be done with the LVAD in place, like taking a bath or swimming.[8] Some chose to intentionally test limits of batteries or ignore advice of providers to avoid favorite activities such as boating.[8,22] There was also a definite sense of physical restriction that was related to the need for battery power during outings.[7,8,21] Although LVAD patients are taught to carry additional batteries and the charger for long trips, concern for battery life had an impact on patients' sense of return to normalcy and life satisfaction. Finally, some were embarrassed of the attention the LVAD and their scars attracted, expressing that when in a public area, people would often stare and ask questions.[19,22]

"I think I am emotionally scarred…I am not 100% right, but I think it is all in the mind"[19]

Discussion

A gap exposed by this synthesis is that there is very little discussion of avoidant behaviors or non-compliant patients. No patients were hospitalized and the perspective of those LVAD patients who are frequently hospitalized is relatively absent from the literature. All of the studies had a very positive, upbeat tone, but many LVAD patients have very adverse outcomes and the lifestyle changes for the most fragile VAD patients are poorly understood. A strength of the qualitative approach is that it is amenable to discussing outliers. In using non-clinician interviewers Sandau et al (2014) was more successful at eliciting the breadth of positive and negative experiences. Using clinician interviewers may leave studies vulnerable to social desirability bias. More qualitative work should be done to explore the coping of LVAD patients who experience poor outcomes including functional status and quality of life. Casida et al. (2011) introduced the idea of early and late stage adjustment to living with an LVAD.[7] Our expanded view of the temporal sequence of primary appraisal (Table 3) offers a more comprehensive understanding of patients' progression from pre-implantation to late adaptation living with the device. While it is not possible to directly compare these findings to outcomes literature, it is likely that continued improvement in perceptions of quality of life observed in the first 3-6 months of LVAD therapy are related to the transition from the early to late home adaptive stages.[3,4,25,26] As physiologic improvements occur over time, each adaptive phase may coincide with functional improvements. Rather than a linear process, adaptation has been elsewhere characterized as an iterative process with mini-regressions which, in the case of LVAD patients, may be associated with unexpected hospitalizations or complications.[14]

A recent study of educational materials available to LVAD patients and their families found that while 100% of materials discussed benefits of the device only 38% discussed lifestyle considerations, 12% provided information for caregivers and 3% presented any information about palliative care.[24] Because of this, some patients may have high expectations that following LVAD implantation, they will return to pre-HF functioning. Managing such expectations is an important component of pre- and post-implant education for recipients and caregivers and helps normalize the experience since very few VAD patients improve to a pre-HF level of function. This synthesis has identified that it is common for LVAD patients to seek reassurance of normal progress with recovery. Based on these findings, LVAD patients may need more education about expectations throughout surgical recovery and initial adjustment to living with the device. Helping patients and families to manage expectations may also help them manage emotions and improve coping.

Limitations

The studies included in this synthesis used convenience samples from single LVAD centers. Few of the studies mentioned a qualitative theory or conceptual framework, although all of them described methods to provide qualitative transparency. Additionally, the diversity of perspectives was narrow; samples across studies were primarily white, educated men. Some of the studies included patients who received pulsatile devices, which are no longer in use. In addition, across studies the samples varied by implant strategy. Patients were primarily bridge to transplant, but included some explanted LVAD patients and some destination therapy patients. Considering that destination therapy is now the most prevalent reason for implantation in the US, future studies should consider implant strategy to ensure that the perspective of destination therapy patients is better understood.[1] Finally, LVAD programs may vary significantly between countries, limiting comparability for synthesis and transferability to other LVAD populations. However, the involvement of an international, interdisciplinary team for this meta-synthesis is a strength.

Implications

This synthesis draws attention to the need to foster a sense of independence and normalcy for LVAD patients. It is clear that LVAD programs have been successful at helping patients establish routines related to LVAD care, which contributes to independence. However, developing and providing additional materials that explain the recovery and adaptation process may help promote emotional coping and help patients regain a sense of normalcy. Little is known about how different LVAD centers educate patients and the efforts of LVAD coordinators to provide education. Because stress is a commonly used term in the community, the stress model may help LVAD patients and caregivers better interpret their own responses. An educational program that incorporates the concepts of stress and coping, while presenting typical tasks at each transitional stage would provide a theory-based format for delivering LVAD education. Studies should be conducted to support the development of best practices and guidelines. In addition, more research is needed for destination therapy patients and examining the perspective of LVAD patients who have had the device for greater than 1 year, particularly as more patients are surviving several years on the device.[27] This synthesis suggests that interventions to support emotional coping, spiritual coping and body image recovery may also be needed. Finally, as research moves forward to further understand adaptation and develop interventions to improve lifestyle adaptation for LVAD patients, it will be important to increase the focus on patients with mal-adaptive coping responses and poor outcomes.

The Authors declare that there are no conflicts of interest.

Table 1: Analysis of Qualitative Rigor per CASP

*Same sample

Author/ Title/ Year	**Sandau et al.** **Conceptual Definition of Quality of Life 2014**[22]	**Ottenberg et al. Choices for Patients "Without a Choice" 2014**	**Overgaard et al. Illness and Vocational Adjustment 2012**[24]	**Marcuccilli et al. Sex and Intimacy* 2011**[26]	**Casida et al. Lifestyle Adjustments* 2011**[25]
Was there a clear statement of the aims of the research?	Yes - To allow patients to share impressions and experiences about life after receiving and living with DT	Yes - To allow patients to share impressions and experiences about life after receiving and living with DT	Yes – Explore the lived experience of patients living with LVAD	Yes – explore the experience of adults living with LVAD including the effect on their intimate and sexual functioning	Yes - Explore and describe the lifestyle adjustments of adults living with LVAD through lived experience
Is a qualitative methodology appropriate?	Yes	Yes	Yes	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes Grounded theory With in-depth interviews, individual or paired with an average of 6 weeks between interviews	Yes No qualitative approach discussed, although phenomen-ological approaches were used	Yes No qualitative approach discussed, although phenomen-ological approaches were used	Yes Hermeneutic phenomenology	Yes Hermeneutic phenomeno-logy
Was the recruitment strategy appropriate to the aims of the research?	Purposive, convenience sample: - 3/11 women - diverse implant strategies	Purposive, convenience sample: - inclusion based on availability and cognitive/ physical appropriateness	Purposive, convenience sample: - sample included the most females - 4/10 females	Purposive, convenience sample: (may have enhanced study to purposively select more female perspective although most LVAD patients are men)	Purposive, convenience sample: - only two women - wide range of time with LVAD
Were the data collected in a way that addressed the research issue?	Yes - disclosed interview questions - interviews were audio taped and transcribed - described audit trail - saturation of data with 11 participants	Yes - disclosed interview questions - tape recorded interviews - many qualitative techniques discussed but did not use term 'saturation'	Yes	Yes - disclosed interview questions - tape recorded interviews -did not discuss transcription methods -saturation of data with 9 participants	Yes - disclosed interview questions - tape recorded interviews -transcribed verbatim -saturation of data with 9 participants
Has the relationship between researcher and participants been adequately considered?	Yes Heart Center Staff did not conduct interviews	Yes Disclosed author experiences related to heart failure and LVAD care.	Not addressed	Yes Bracketing	Yes Bracketing
Have ethical issues been taken into consideration?	Yes Institutional Review Board	Yes Institutional Review Board	Yes Ethical Considerations thoroughly addressed	Yes Institutional Review Board	Yes Institutional Review Board

Was the data analysis sufficiently rigorous?	Yes Thorough description audit trail, transcription and thematic analysis and non-clinicians conducted interviews to reduce bias	Yes Thorough description audit trail, inter-rater reliability, transcription and thematic analysis	Yes Thorough description of credibility, transfer-ability, dependability and confirmability	Yes Thorough description of credibility, transferability, dependability and confirmability	Yes Thorough description of credibility, transferability, dependability and confirmability
Is there a clear statement of findings?	Yes 5 Themes organized by QOL domains: Physical, Emotional, Social, Cognitive and Spiritual	Yes 6 themes: preparedness planning, new lease on life, optimizing support networks, systemic limitations, reflections on time, and communication matters	Yes Table describing themes: transition to illness, transition to LVAD, Life with LVAD and Life with Transplant	Yes 3 themes: improved sexual relations with the LVAD, sexual adjustment and non-sexual intimacy	Yes 1 theme and 2 sub-themes: adjustment takes time -early adjustment: changes in everyday life -late adjustment: new way of living
How valuable is the research?	First study to explore the unique attributes of QOL in the LVAD population	First qualitative study to consider only the Destination Therapy Patient perspective	Using the Lifestage Development Model is innovative and provides valuable insight	High level of importance to patients, first to report patient perspectives, implications discussed	Significant contribution to what was previously reported. Confirms prior studies and adds early/late stage adjustment themes

Table 1: Analysis of Qualitative Rigor per CASP (continued)

Author/ Title/ Year	**Hallas et al. Psychological Experience 2008[23]**	**Chapman et al. Psychosocial Issues 2007[21]**
Was there a clear statement of the aims of the research?	Yes - Identify Psychological processes that patient use to make sense of adjustment to LVAD and consider adjustment construct	Yes – Determine the impact of LVAD on body image, psychological functioning and social support
Is a qualitative methodology appropriate?	Yes	Yes
Was the research design appropriate to address the aims of the research?	Yes Grounded theory With in-depth interview with f/up phone call	Yes Interpretive Phenomeno-logical Analysis
Was the recruitment strategy appropriate to the aims of the research?	Purposive, stratified sampling: - VAD in situ, explanted, transplanted	Purposive stratified sample: - VAD in situ and transplanted
Were the data collected in a way that addressed the research issue?	Topics of discussion were disclosed, but not interview questions	No disclosure of questions - interviews were audio taped and transcribed - described audit trail - no mention of saturation
Has the relationship between researcher and participants been adequately considered?	Not addressed	Not addressed
Have ethical issues been taken into consideration?	Yes Ethical approval	Yes Research Ethics Committee
Was the data analysis sufficiently rigorous?	Yes Audit trail, inter-rater reliability addressed	No Audit trail is mentioned - Coding methods are not addressed
Is there a clear statement of findings?	Yes Theme of control with 6	Yes 2 major themes: body/self and trust

	sub-categories: normality, uncertainty, emotional state, identity of illness, impact of LVAD, Independence	
How valuable is the research?	Highlights importance of perceived control and independence in advanced heart failure patient care.	Supportive care mentioned as part of discussion

Table 2: Study Characteristics

Author/ Title/ Year/ Country	Purpose	Sample	Design	Paradigm/ Framework
Sandau et al. Conceptual Definition of Quality of Life 2014[22] United States	To develop a conceptual definition of quality of life (QoL)with LVAD.	N = 11 3/11 female 10/11 White 4/11 DT 6/11 BTT 1/11 BTR	Qualitative design with in-depth Interviews	Grounded Theory
Ottenberg et al. Choices for Patients "Without a Choice" 2014[21] United States	To allow patients to share impressions and experiences about life after receiving and living with DT	N = 12 1/12 female 1/12 Asian 11/12 White DT only	Qualitative design with in-depth Interviews	None identified
Overgaard et al. Illness and Vocational Adjustment 2012[8] Denmark	Explore the lived experience of patients living with LVAD	N = 10 4/10 female No race reported BTT only	Qualitative explorative design with in-depth interviews	Life Span Development model
Marcuccilli et al. Sex and Intimacy* 2011[18] United States	Explore the experience of adults living with LVAD including the effect on their intimate and sexual functioning	N = 9 2/9 female 2/9 Black 6/9 White 1/9 other 2/9 DT 7/9 BTT	Qualitative Design with in-depth interviews	Hermeneutic Phenomenology
Casida et al. Lifestyle Adjustments* 2011[7] United States	Explore and describe the lifestyle adjustments of adults living with LVAD through lived experience		Qualitative Design with in-depth interviews	Hermeneutic Phenomenology
Hallas et al. Psychological Experience 2008[20] United Kingdom	Identify Psychological processes that patient use to make sense of adjustment to LVAD and consider adjustment construct	N = 11 3/11 female No race reported 4 with LVAD in situ 4 LVAD explanted 3 s/p heart transplant	Prospective, cross-sectional qualitative design with in-depth interviews	Grounded Theory
Chapman et al. Psychosocial Issues 2007[19] United Kingdom	Determine the impact of LVAD on body image, psychological functioning and social support	N= 6 2/6 female 4/6 s/p heart transplant 2/6 LVAD explanted	Qualitative Idiographic approach with in-depth interviews	Phenomenology

DT – Destination Therapy, BTT – Bridge to Transplant, BTR – Bridge to Recovery

Table 3: Temporal sequence of primary appraisal tasks: physical, psychological and social domains

	Pre-LVAD	Implant Hospitalization	Early Home	Late Home
Physical	• Very low functioning[7,8,18,19] • Very severe lifestyle-limiting symptoms[7,8,18,19,21,22] • Waiting for the device until "sick enough"[7,8,18,19]	• Pain and surgical recovery[8] • Drastic changes in physical body including disfiguring scars[8,18,20–22] • Learning basics of device and safety routines:[7,8,19–22] ○ Frequent practice ○ Becoming used to vibration of device ○ Alarms – confidence effected by alarm frequency	• HF symptom management, but symptoms improving[21,19] • Surgical recovery continues[7,21] • Frequent appointments require exhausting travel[21] • Need to create and adapt safe routines to home environment:[7,8,18–22] • ADLs ○ Medication ○ Batteries ○ Driveline care ○ Sleeping ○ Clothing comfort	• Routines become normal[7,8,21,22] • Learn to make time for necessary device care[7,8,19] • Testing limits of device[8,22] • Improving mobility and energy[7,18]
Psychological (cognitive, emotional and spiritual)	• Trauma[8,20,19] • Lack of memory[8,20] • Facing mortality[8,21,20,19] • Waiting for the device[8,21,20]	• Early body-image[7,8,18,19,22] • Feeling different from others[7,18,22] • Grappling with meaning of life – existence = device dependency[7,8] • Fear and anxiety related to device (ie. alarms and disconnecting driveline)[7,8,18]	• Fear of complications[7,8,19] • Confidence with basic device builds[7,8,20,19] • Poor memory, unfocused thoughts[22]	• Reflection[7,20,22] • Making peace with decisions and life with LVAD[7,20,22] • Anger when others don't understand[22] • Fear diminishes as routines are normalized and time passes without complications[7,18–22] • Feeling grateful[7,8,18,21,22] • Increased intimacy[7,18,19,22]
Social	• Patient role changes with increased illness[21,20] • Family providing support at home and has large role in decision making[8,21,20]	• Dependence on care team[8,19] • Early discussions with family can be supportive or stressful[8,21,20]	• Dependence transitions from hospital team to caregiver[7,8,21,20] • Importance of LVAD coordinator[7,21] • Change in home roles[7,8,18,21,22]	• Outings are valuable but require:[7,8,21,20,19] ○ need to come to terms with body image and embarrassment ○ anxiety regarding new environments • Return to work[8,20,22]

Figure 1: Literature Review and Inclusion

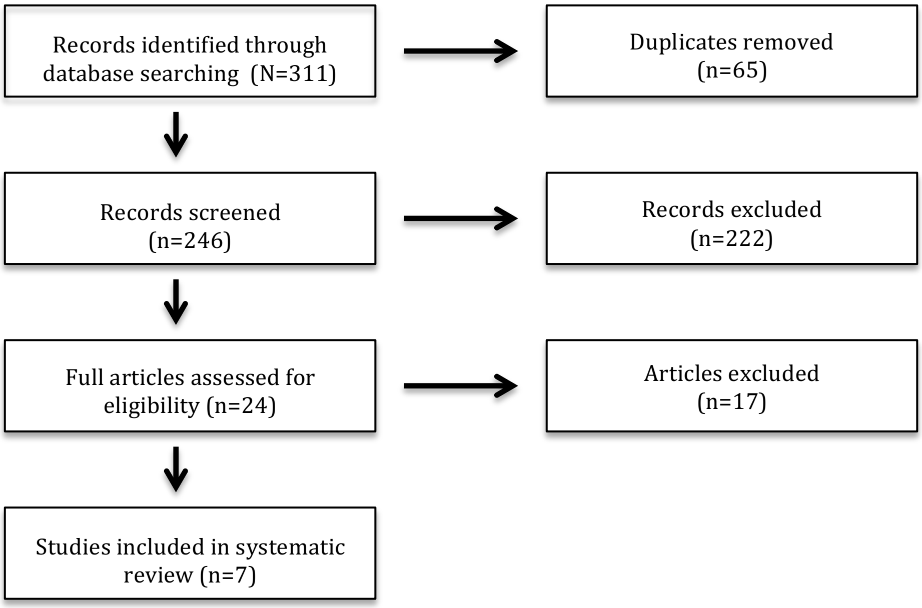
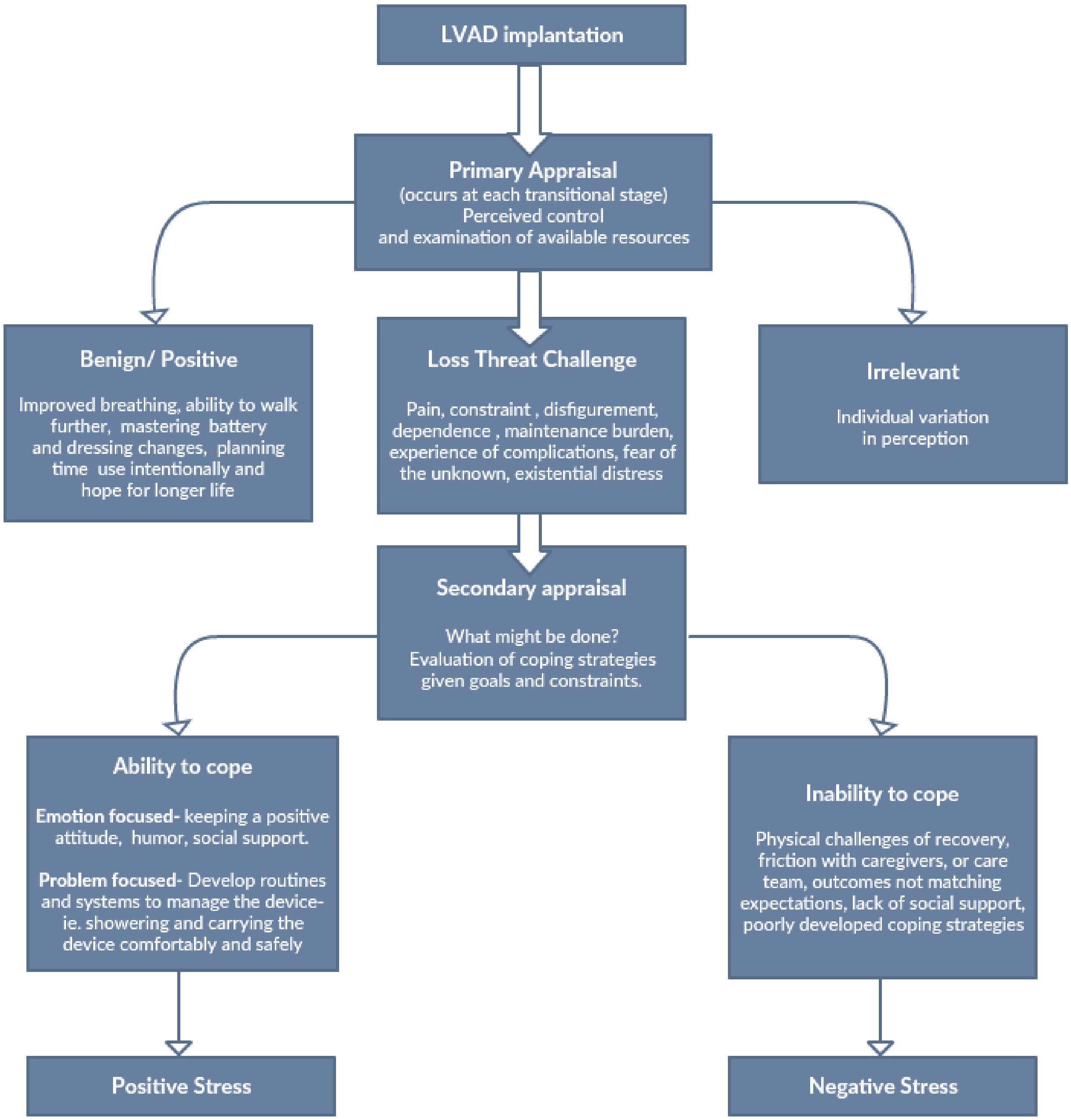


Figure 2: LVAD Transactional Model of Stress and Coping



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Chapter 4: The Role of Psychological Stress, Sleep Quality and Social Support on Outcomes in Patients with a Left Ventricular Assist Device

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Abstract

Background

The implant of a left ventricular assist device (LVAD) has significant emotional and psychological sequelae that impact health related quality of life (HRQOL). The purpose of this study was to examine relationships among sleep quality, psychological stress, social support and LVAD patient outcomes including HRQOL, exercise capacity and healthcare utilization.

Methods

A cross-sectional study design was used and patients were recruited from 2 outpatient clinics. Clinical and sociodemographic data were collected and standardized measures administered.

Results

The sample (N=62) was male (78%), black (47%), married (66%), (mean=56.5± 13 years). An average of 3 stressful life events were reported; most commonly personal illness (51%); changes in eating (21%), finances (19%), and social activity (19%); and death in the family (19%). Increased perceived stress was associated with worse sleep quality, fatigue, depression and maladaptive coping ($p< 0.001$). Overall HRQOL was good (mean 73±14.6); 6MWT mean distance was 287 ± 193 meters. Patients had 6.5 ± 4.6 days of outpatient visits in the 6 months prior to study. Regression analysis demonstrated perceived stress and fatigue were significant correlates of overall HRQOL (adj. $R^2=0.41$, $p < 0.0001$). Social support moderated the relationship between perceived stress and HRQOL when controlling for fatigue ($R^2 = 0.49$, $p < 0.001$). Regression analysis showed no significant multivariate models for exercise capacity or healthcare utilization.

Conclusions

LVAD patients with increased stress had poor sleep quality, worse depression, fatigue, maladaptive coping, and HRQOL. This underscores the importance of a comprehensive management plan to address physical, social and psychological factors.

Background

The numbers of individuals living with a left ventricular assist device (LVAD), both destination therapy and bridge to transplant is increasing, underscoring the importance of examining psychological as well as physiological and clinical outcomes.[1] Living with advanced heart failure (HF) and an LVAD is stressful.[2] Serious emotional and psychological impacts are present due to challenges of LVAD self-care (e.g., adapting to dependence on a power source and manipulation of the device), impaired sleep, pain, limitations on bathing and management of complex medication regimen.[3]

Stress has been defined as the experience of appraising events as exceeding personal resources that result in a sense of threat to person.[4] Psychological stress response may be characterized by perceived stress, depression, fatigue and poor sleep quality among other factors. Although little is known about the psychological stress experienced by LVAD patients, perceived stress and depression have been associated with poor health outcomes among cardiac patients.[5,6] In addition, increased perceived stress has been related to decreased physical activity, which is also a prevalent limitation for patients living with an LVAD.[7] Similarly, depression in HF negatively impacts functional outcomes, social isolation and self-care and is also associated with impaired cognition.[8]

Poor sleep quality and sleep disturbances have been associated with worse functional status and worse QOL in HF patients.[9,10] LVAD patients experience poor sleep quality which is known to be associated with depression, increased symptom burden and even increased risk of mortality, however there has only been one study to date that has measured sleep quality among LVAD patients.[11–13] Sleeping with the LVAD components presents sleep challenges, however little is known about sleep in LVAD patients after they have adjusted to sleeping with the LVAD equipment.

Coping, the cognitive and behavioral efforts to manage stressful events and chronic stress can take adaptive and maladaptive forms.[4] Few studies have examined coping strategies among LVAD patients, but similar to other populations, acceptance and optimism were related to improved HRQOL.[14] Maladaptive coping strategies, such as denial and avoidance, are associated with worse outcomes in HF patients.[8] One important adaptive coping strategy evaluated by transplant committees is social support. Typically, each LVAD patient must have a caregiver, identified prior to implantation, however, the caregiver-patient relationship, demonstrated in qualitative studies, can be strained by changes in levels of independence, roles and relationships. [3,15,16] Higher levels of social support have been associated with better outcomes including HRQOL and HF self-care in HF studies.[17,18]

The purpose of this study was to describe and examine the relationships among measures of psychological stress, sleep quality, and coping, and key LVAD patient outcomes including HRQOL, exercise capacity, and healthcare utilization. In addition, we tested the role of social support as a moderator of the relationships between psychological stress response and HRQOL.

Methods

Study Design

A cross-sectional study design was used to describe psychological stress response, sleep quality and coping among patients living with an LVAD. The conceptual framework for this study is an adaptation of the Lazarus and Folkman Stress Model (see figure 1) in which the economics of stress suggests that as stress increases, the demand for coping increases.[4] Poor outcomes result from the inability of the body to meet the demands of the stress. In this conceptual framework, individual characteristics of LVAD patients (implant strategy, emergent implantation, time since implant, stressful life events) are expected to influence psychological stress response (i.e, perceived stress, depression and coping) and sleep quality. Psychological stress response is expected to impact LVAD patient outcomes (HRQOL, exercise capacity and healthcare utilization).

Sampling

Patients living with LVAD and served by the LVAD clinic at two large tertiary care centers in the mid-Atlantic region of the United States were included in the study. Institutional Review Boards at both hospitals approved this study. Convenience sampling was used to recruit patients living with an LVAD from both centers. Informed consent was obtained in person during clinic visits. We recruited individuals at >2 months post-implant or any time after that. The timing of inclusion was based on an understanding that early surgical recovery is very stressful with functional and HRQOL improvements that change rapidly.[19] Eligibility criteria included: patients were treated in the LVAD clinic, over 21 years of age, had a Montreal Cognitive Assessment (MoCA) score $\geq$17 (no severe cognitive impairment)[20] and can speak and understand English. No proxy was used for the completion of survey data and patients were not seen during acute hospitalizations or if being treated in inpatient rehabilitation.

Sample Size

A power analysis was conducted to determine the sample size needed to sufficiently power the study based on the co-variates in the model and estimated effect sizes. Based on the power analysis for a linear regression analysis, an estimated effect size of $f^2=0.25$, $\alpha=0.05$, and power of 80%, we planned to recruit a target sample of 80 patients.

Study Procedures and Measurement

Patients were recruited and consented on scheduled clinic visit days. Surveys were administered on paper and collected at the end of the visit if completed but often, at a subsequent clinic visit. Survey of demographic characteristics and measurement instruments was self-administered, which took about 20 minutes to complete. Widely validated instruments were selected based on their use with HF populations and relevance to the conceptual model. Table 1 includes a summary of measures.

In addition to survey data, the Six Minute Walk (6MWT), a test of exercise capacity at submaximal level, was administered according to the American Thoracic Society Protocol. This test has a reported reliability of 0.86[21–23] and is used in "standard of care" in many LVAD centers. Also, healthcare utilization was operationalized as number of outpatient visits, number of days hospitalized and number of number of outpatient procedures. Relevant data were captured from the electronic medical record for the 6 months prior to the date of survey completion or since the date of LVAD implant. A STROBE diagram is presented in figure 2 to demonstrate completion rates.[24]

Data analysis

Data were checked for quality and consistency. All statistical analyses were done with Stata version 14 (StataCorp, College Station, Texas). Descriptive statistics and graphical displays were used to summarize data by perceived stress level. We examined the distribution of perceived stress and ranked low (0-11), moderate and high (12-40), using approximately the upper two quartiles to designate moderate and high stress. A correlation matrix was created to examine relationships between continuous variables. All other variables were tested using chi-square tests. A multiple linear regression model was then tested using only variables with $p<0.20$ from the correlation analysis. This analysis was followed by tests for multi-collinearity between model variables using variance inflation factor analysis. The assumptions of this parametric analysis were met. The final model includes only variables with $p<0.05$ significance level.

The moderation of social support was tested using two additional models. To test these relationships we dichotomized social support at the median of 20. Interaction terms were created for 1) social support and perceived stress, then 2) social support and fatigue. Building on the multiple linear regression models, social support and interaction terms were tested in the models using likelihood ratio testing.

Results

Descriptive findings

The 62 patients who completed the survey were predominantly male (78%), black (47%), and married (66%) with mean age 56.5± 13.0 years. (See Table 2) Patients were evenly distributed by implant strategy (DT 50%, BTT 50%) and mean length of LVAD support was 25.3 ± 24.5 months. (See Table 3) Forty-nine percent were Intermacs Profiles 1 and 2, implanted emergently.

On the Holmes & Rahe stressful life event inventory 17 participants (27%) had a summed weighted score greater than 150, the hi-risk threshold. (See Table 3) Most common life stress events in all LVAD patients were: major illness, death in the family, change in health of a family member, changes in finances, change in social and family activities, change in sleeping habits and revision of personal habits, especially eating.

Mean perceived stress for the sample was 11.7 ± 7. (See Table 4) The overall sample seemed to have a moderate stress profile: moderate perceived stress (mean 11.7 ± 7), few depressive symptoms (mean 3.2 ± 3.9) and moderate fatigue (mean 14.3 ± 9.1). Sleep quality was rated poor overall (6.2 ± 3.4) with a high number of nightly sleep disturbances (2.3 ± 0.5). Both adaptive and mal-adaptive coping strategies were commonly used by all participants but acceptance and religious coping strategies (mean 6.2 ± 2 and 5.3 ± 2.3, respectively) were reported most commonly and substance use (mean 2 ± 0) reported the least commonly. Patients reported very high social support (mean 19.9 ± 5.4).

Overall HRQOL was rated good, 73 out of 100. Of the HRQOL domains, LVAD patients reported that their HF symptom frequency had little impact on their HRQOL (88 out of 100) and that social limitation domain had the greatest impact on HRQOL (65.5 out of 100). Mean 6MWT distance was 287 meters overall. Participants spent an average of 6.5 ± 4.6 days or 8% of days in the 6 months prior to the study in the hospital or attending outpatient visits.

Higher Perceived Stress is related to Worse Sleep, Depression, Fatigue and HRQOL

When comparing psychological stress response by perceived stress level, the higher stress group had mean depressive symptoms of 5.2, greater than the cutoff of 5 for mild depression on the PHQ-9, while the lower stress group had an average of 1.2 depressive symptoms. The higher perceived stress group had worse fatigue ($p< 0.001$) and was more likely to use maladaptive coping strategies ($p< 0.003$). Social support was rated lower in the higher stress group ($p < 0.003$). In addition, overall HRQOL as well as all domains of HRQOL were worse in the higher stress group ($p<0.05$). There were no demographic differences between groups, but the higher stress group included 6/31 participants with a history of depression. There were also no differences between groups by implant strategy, emergent implantation, time since implant, 6MWT distance or healthcare utilization.

Multi-variate Modeling

In multivariate regression analysis, perceived stress and fatigue each were independent predictors of HRQOL. Using the model for HRQOL we tested social support as a moderator of the relationships between psychological stress response and HRQOL. High social support moderated the relationship between perceived stress and HRQOL when controlling for fatigue ($R^2 = 0.49$, $p < 0.001$). (See Table 5 & Figure 3) Regression analysis showed no significant multivariate models for exercise capacity or healthcare utilization.

Discussion

We found that most LVAD patients had a moderate level of perceived stress, mild depression, moderate fatigue and poor sleep quality. Those with higher perceived stress had worse depression, fatigue, sleep quality and more frequently used mal-adaptive coping compared with those with lower stress. In multivariate analysis, high perceived stress and fatigue were associated with poor HRQOL and this relationship was moderated by social support.

Overall, this sample of community dwelling LVAD patients appears similar in HRQOL and exercise capacity compared to previous findings. In past studies LVAD patients have reported HRQOL between 6-12 months, with a plateau after dramatic early improvement. KCCQ average scores for this plateau range between 66 and 75.[19,25,26] HRQOL in this study was within this range, which is nearly double reported KCCQ values prior to LVAD implant and exceeds the minimal clinically important difference for the KCCQ.[25,27,28] Exercise capacity was also within range of findings from Intermacs.[25,1] Hospital length of stay has been reported in the literature, but we did not identify any other studies that considered outpatient visits in LVAD healthcare utilization. The frequency of outpatient visits may vary by region and LVAD program as a function of the distance from the patient's home to clinic, use of outreach strategies and stability of the patient, which we did not capture in this study.

Overall scores on perceived stress, depression and fatigue revealed a moderate stress profile in most LVAD patients. The perceived stress mean score was similar to the age-adjusted normal value of 12, which has been reported for the general population and similar to those reported in other cardiac populations.[29] Those with higher ratings of perceived stress also reported worse sleep quality, high levels of fatigue, more depressive symptoms, more frequent use of mal-adaptive coping strategies and worse HRQOL. Further investigation is warranted to examine the role of perceived stress in LVAD patients, the mechanisms for these effects and the possible impact on adverse events and survival. Still, these findings suggest that enhanced clinical assessment of psychosocial factors and sleep quality is important for understanding LVAD outcomes. This is a challenge as LVAD patient visits are frequently full, including physical exams and equipment checks. However, early referral for sleep study, psychological counseling and even palliative care may reduce the burden felt by patients and providers.

Our study confirms most LVAD patients report poor sleep quality, with sleep disturbances as a primary contributor to sleep quality scores. In a longitudinal study of LVAD patients (N = 12) from pre-implant to 6 months post-implant, average sleep quality was poor and no change was seen over time.[12] Poor sleep quality has been linked to depression and increased symptom burden in the general heart failure population; impaired sleep also affects neurohormonal regulation.[9,11,30] It is unclear what are the causes of sleep disturbances among LVAD patients, although nocturia and sleeping with the LVAD equipment are likely contributers. Further quantitative, especially longitudinal, and qualitative investigation may improve our understanding of sleep quality and factors contributing to poor sleep quality in this population, revealing opportunities for sleep interventions.[31]

In LVAD patients, optimisitic, supportive and religious coping were used most frequently and viewed as most helpful to patients.[14] We did not see a relationship between coping strategies and HRQOL, however we did find that more frequent use of adaptive and mal-adaptive coping strategies was associated with a worse psychological stress response. This is consistent with the Lazarus and Folkman description of the economics of stress - as stress increases, the demand for coping increases.[32] Thus, those with higher levels of perceived stress also reported more frequent use of both mal-adaptive and adaptive coping strategies because more coping is required when more stress is experienced. The brief COPE does not evaluate effectiveness of coping strategies, only frequency of use. Understanding how LVAD patients cope with stress is important for understanding issues of adherence and self-management and for determining ways to support patients and families throughout LVAD therapy to promote adaptive coping.

Social support was reported at a comparable level to previously reported cardiac populations who were partnered.[33] This was expected, as LVAD patients are required to have caregivers available for initial implant care, to support clinic attendance and to manage LVAD care. Multi-variate modeling and moderation analysis revealed that, when comparing those with the same level of perceived stress, those with high social support had a higher HRQOL than those with low social support after controlling for fatigue. This moderation analysis provides evidence for the importance placed on social support when considering advanced HF patients for VAD implantation. However, it was not possible to determine in this study if the caregiver, healthcare team or other sources are responsible for the perceived level of social support. Support is provided by LVAD programs through 24/7 access to providers. Yet, patients and caregivers have reported variable levels of satisfaction with the support provided by LVAD programs, suggesting a need to explore additional ways to increase the type(s) and level of support provided.[34] Specifically, it is not clear how programs are assessing patient stress or helping patients manage stress. Resources vary between institutions, although some offer support groups and other activities for LVAD patients and caregivers. Support strategies that are tailored to the individual patients' needs may be most effective.

Strengths and Limitations

This is the first study to examine sleep quality in this large of an LVAD patient sample, providing important interventional targets for future work. In addition, we evaluated important psychosocial factors and their impact on outcomes in a diverse, multi-center population. Finally, we have introduced evidence that supports LVAD program policies related to social support. To expand these findings, the next step will be to conduct a longitudinal study to examine how sleep and psychosocial factors change over time and to establish approaches to tailoring and optimal timing for future interventions. Further qualitative work should explore LVAD patient stress, sleep and factors promoting resilience.

This study has several limitations. As a cross-sectional study, no causal relationships can be drawn from this analysis. Further we had several challenges in completion rates. Long patient clinic visits often meant that patients who consented did not complete the survey on the day of consent. In the following days, several patients experienced hospitalizations, changes in mental status and a few received transplants, which prevented them from completing the study. This may have resulted in a self-selection bias and in the under-estimation of variables related to stress and over-estimation of HRQOL compared to the total LVAD population. This concern is consistent with other survey data collected from the LVAD population.[35] In addition, the patients in our sample had an average of almost 2 years of LVAD support, which also may have resulted in lower reported stress and higher HRQOL than the overall LVAD population. Another limitation is that we used a HF-specific measure for HRQOL. This measure is not specific to having a VAD, however as of yet there are no VAD-specific measures of HRQOL.

Conclusions

LVAD patients experienced moderate level of perceived stress, mild depression, moderate fatigue and poor sleep quality. Increased stress was reported by almost one-third of the sample and was related to worse depression, fatigue, mal-adaptive coping, sleep quality and worse HRQOL. Further, the influence of high levels of social support to improve HRQOL despite fatigue is confirmation of the need to continually assess the social support available to LVAD patients. Thorough, ongoing assessment by healthcare providers and social workers may uncover stressful conditions requiring increased monitoring. Future studies should test the effects of interventions designed to improve sleep and stress management on adaptive coping, HRQOL and other LVAD outcomes.

Tables and Figures

Table 1: Instrument Description

Variable Instrument	# Items Sub-scales	Scoring: Score range, Significance of high score, Diagnostic cutoffs	Reliability Cronbach's alpha
Stressful Life Events Holmes and Rahe Stressful Life Events Scale	43 Total Weighted Score	0 - 450 Higher total weighted score indicates higher stress. Scores >150 are associated with higher health risk.	0.90
Sleep Quality Pittsburgh Sleep Quality Index	19 Subjective Sleep Quality Sleep Latency Habitual Sleep Efficiency Sleep Duration Sleep Disturbances Use of Sleeping Meds Daytime Dysfunction Global PSQI	0 - 21 Higher score indicates worse sleep quality Score greater than 5 indicates poor sleep quality	0.83
Perceived Stress Perceived Stress Scale	10 Total Score	0 – 40 Higher score indicates worse stress No diagnostic cutoff	0.82
Depression Perceived Health Questionnaire	9 Total Score	0 - 25 Higher score indicates worse depressive symptoms 5 = mild, 10 = moderate depression	0.89
Fatigue Multidimensional Assessment of Fatigue	16 Global Fatigue Index	1 – 50 A higher score indicates worse fatigue and impact on activities of daily living.	0.93
Coping Brief COPE	28 Adaptive Coping: (task-focused, seeks social support, religion & acceptance) Maladaptive Coping: (behavioral disengagement, substance abuse & self-blame)	Adaptive Coping: 0 - 64 Maladaptive coping: 0 - 48 Higher Score indicates more frequent use of more strategies. No diagnostic cutoffs	0.72
Social Support ENRICHD	10 Emotional, Instrumental, Informational and Appraisal	0 – 25 Higher score indicates more social support No diagnostic cutoffs	0.88
Health-related Quality of Life Kansas City Cardiomyopathy Questionnaire	12 Physical Limitation, Symptoms, Quality of Life, Social Limitation Overall	0 – 100 Higher score indicates better quality of life 50-75 good QOL, > 75 excellent QOL	0.92

Figure 1: Stress in Patients living with LVAD Conceptual Framework

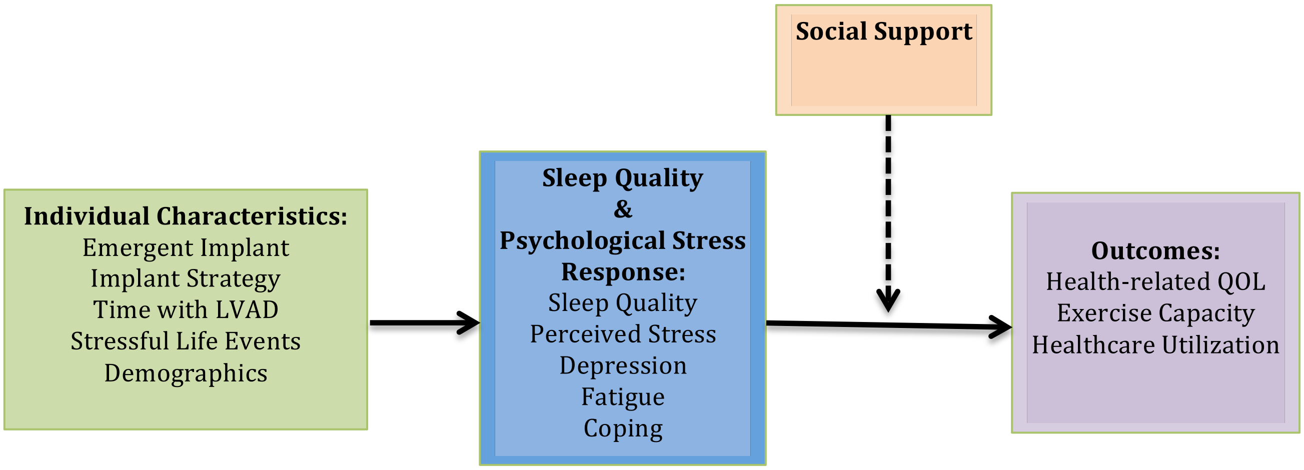


Figure 2: STROBE diagram of participant selection and inclusion

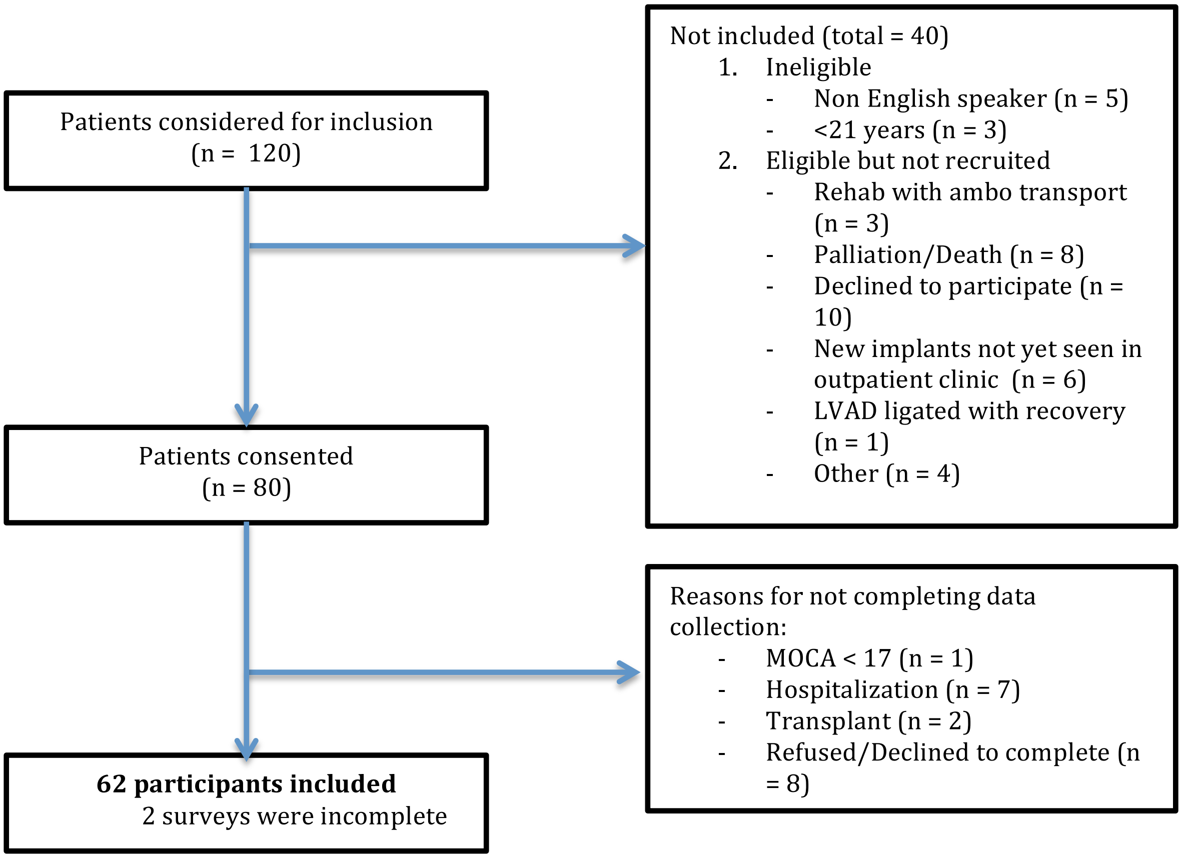


Table 2: Sample Characteristics by Perceived Stress Level

		Perceived Stress		
	n (%)	**Low (n = 31) n (%)**	**Moderate to High (n = 31) n (%)**	**T-test or chi^2 p-value**
Gender				
Male	48 (77)	24 (50)	24 (50)	1.00
Female	14 (23)	7 (50)	7 (50)	
Age				
Mean	56.7 ± 13.0	58.2 ± 12.6	55.3 ± 13.2	0.38
Median	58.8	60.6	56.5	
Race				
Black	29(47)	16 (55)	13 (45)	
White	25 (40)	12 (48)	13 (52)	0.65
Other	8 (13)	3 (38)	5 (62)	
Marital Status				
Married or Living with Partner	40 (66)	19 (48)	21 (52)	0.72
Other	21 (34)	11 (52)	10 (48)	
Annual Household Income				
< $30,000	16 (25)	9 (56)	7 (44)	0.53
$30, 000-60,000	9 (15)	3 (33)	6 (67)	
>$60,000	37 (60)	19 (51)	18 (49)	
Highest Level of Education				
<= high school	14 (23)	8 (57)	6 (43)	0.52
technical school or some college	18 (30)	7 (39)	11 (61)	
graduated college or beyond	28 (47)	15 (54)	13 (46)	
Co-morbidities				
Diabetes	20 (32)	9 (45)	11 (55)	0.59
Chronic Renal Disease	19 (31)	11 (58)	8 (42)	0.41
Depression	6 (10)	0 (0)	6 (100)	**0.01**
Right heart failure	5 (8)	3 (60)	2 (40)	0.64

Table 3: LVAD and Individual Characteristics

		Perceived Stress		
	n (%)	Low (n = 31) n (%)	Moderate to High (n = 31) n (%)	T-test or chi^2 p-value
Device				
Heartware	23 (37)	12 (52)	11 (48)	0.97
Heartmate II	37 (60)	18 (49)	19 (51)	
Heartmate III	2 (3)	1 (50)	1 (50)	
Implant Strategy				
Bridge to Transplant	31 (49)	15 (48)	16 (52)	0.80
Destination Therapy	32 (51)	16 (52)	15 (48)	
Emergent Implant				
Intermacs 1 or 2	30 (49)	14 (47)	16 (53)	0.61
Intermacs > 2	32 (51)	17 (57)	15 (43)	
Stressful Life events				
Mean	111.9 ± 91.8	90.9 ± 79.8	133 ± 99.3	0.07
Median	97.5	82	128	
Months since initial implant				
Mean	25.3 ± 24.5	25.3 ± 4.4	25.2 ± 4.5	0.98
Median	18.5			
Complications				
Gastrointestinal bleed	16 (27)	6 (38)	10 (62)	0.25
Stroke	13 (21)	7 (54)	6 (46)	0.76
Driveline Infection	10 (16)	5 (50)	5 (50)	1.00
Right Heart Failure	4 (7)	2 (50)	2 (50)	1.00
Pump replaced	4 (7)	2 (50)	2 (50)	1.00
Sepsis	4 (7)	1 (25)	3 (75)	0.30
Tracheostomy	3 (5)	1 (33)	2 (67)	0.55

Table 4: Psychosocial Stress Response, Sleep Quality and Outcomes

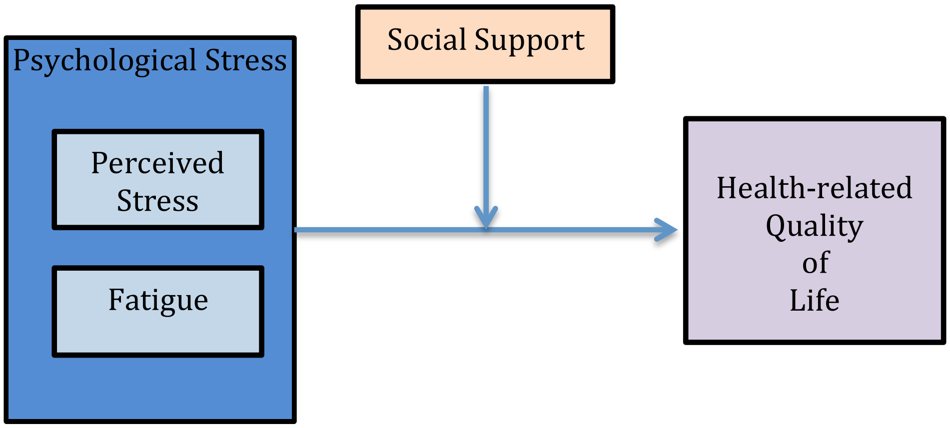
		Perceived Stress		
	Mean ± SD	**Low (n = 31) Mean ± SD**	**Moderate to High (n = 31) Mean ± SD**	**T-test or chi^2 p-value**
Psychosocial Stress Response, Sleep Quality, Social Support				
Depression	3.2 ± 3.9	1.2 ± 1.6	5.2 ± 4.5	**<0.01**
Fatigue	14.3 ± 9.1	8.4 ± 8	18.8 ± 7.4	**<0.01**
Coping				
Adaptive Strategies	37.4 ± 11.9	35.2 ±13.4	39.6 ± 10.0	0.14
Mal-adaptive Strategies	15.5 ± 4.4	13.6 ± 3.8	17.4 ± 4.1	**<0.01**
Sleep Quality	6.2 ± 3.4	4.9 ± 0.5	7.4 ± 0.6	**<0.01**
Social Support	19.9 ± 5.4	21.9 ± 4.8	18 ± 5.3	**<0.01**
Outcomes				
Quality of Life				
Physical limitation	66.4 ± 16.0	70.4 ± 14.8	62.5 ± 16.3	**0.05**
Symptom frequency	88 ± 14.7	91.8 ± 11.8	84.4 ± 16.5	**0.05**
QOL	73.7 ± 23.8	83.5 ± 19.1	63.9 ± 24.3	**<0.01**
Social Limitation	64.4 ± 20.3	74.6 ± 11.8	54.5 ± 22.0	**<0.01**
Overall	73 ± 14.6	80.1 ± 9.5	66.3 ± 15.2	**<0.01**
Six Minute Walk Test Distance (meters)	287 ± 193	270 ± 187	306 ± 200	0.46
Healthcare Utilization*				
Days of Outpatient Visits	6.5 ± 4.6	5.4 ± 3.5	7.5 ± 5.2	0.08
Days Hospitalized	9.9 ± 14.2	10.9 ± 16.4	9 ± 12.0	0.60
Total healthcare days	16.8 ± 15.7	15.8 ± 17.5	17.8 ± 14.0	0.62
#days hospitalized/#days with LVAD	0.08 ± 0.13	0.09 ± 0.16	0.07 ± 0.11	0.59

Legend: *Healthcare utilization was calculated for the 6 months prior to study date or in the time since LVAD implant.

Table 5: Social Support Moderation Model, $R^2 = 0.49$, DF = 59, p< 0.001

	Beta Coefficient	**Standard Error**	**P-value**
Perceived Stress	-0.99	0.33	**<0.01**
Fatigue	-0.62	0.19	**<0.01**
Social Support (Dichotmized at median = 21.5)	-4.54	5.5	0.41
Perceived Stress * Social Support	0.86	0.42	**0.04**

Figure 3: Final Multi-variate Quality of Life Model ($R^2 = 0.49$, $p < 0.01$)



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Chapter 5: Salivary Biomarkers, Sleep Quality and Stress are related to Key Outcomes Among People living with a Left Ventricular Assist Device

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Abstract

Background: Advanced heart failure patients with left ventricular assist device (LVAD) have experienced emotional distress and psychological sequelae following implant. However, few studies have examined stress among patients with LVAD. The purpose of this study was to describe physiological and psychological stress response and then to examine relationships between physiological and psychological stress response and outcomes (quality of life (QOL), functional status and healthcare utilization) in patients with LVAD.

Design: A descriptive observational study design was used to examine physiological and psychological stress response among LVAD patients.

Methods: Data was collected for patients more than 3 months post-LVAD implantation (N = 44). Relationships among indicators of physiological (salivary cortisol, sleep quality) and psychological stress, (perceived stress, depression and fatigue) and outcomes (quality of life, functional status as measured by Six Minute Walk Test (6MWT) and healthcare utilization, using hospitalization rate) were examined using descriptive statistics and logistic regression models.

Results: The sample was average age 57.7 years, mostly male (73%), married (70.5%) and racially diverse (white 46%, black 43%, other 11%). Median LVAD support was 18.2 months. Normal cortisol awakening response was seen in most participants (61%). LVAD patients reported moderate levels of psychological stress and sleep quality and enjoy a good quality of life (73 out of 100, SD ± 13.5). At the bivariate level, normal cortisol awakening response was correlated with low depressive symptoms ($p < 0.02$). Poor sleep quality was correlated with increased psychological stress response and QOL ($p < 0.01$).

Conclusions: This is the first report of salivary cortisol and perceived stress in outpatients with LVAD. Associations were seen between sleep quality, psychological stress response and QOL. Future research should explore if those with a higher stress profile (abnormal cortisol awakening response, worse sleep quality, perceived stress, depression, fatigue) would benefit from tailored supportive interventions to lower perceived stress, improve sleep quality and improve QOL.

Background

As prevalence of heart failure is approaching 6 million in the United States, left ventricular assist devices (LVAD) help patients live longer than medicine alone.[1,2] LVADs are placed as a bridge to transplant (BTT) or 'destination therapy' (DT), meaning that it is expected that the patient will be supported by the LVAD until death. Although the decision for implant strategy is handled differently by each institution, many physiological and psychosocial considerations are reviewed to make a determination. However, there is little evidence on which to base these decisions as few studies have compared physiological and psychosocial responses to LVAD in these two implant strategy groups.

Following LVAD implant emotional distress and psychological sequelae have been reported.[3] More studies examining the lived experiences and stress of transitioning to living with the LVAD have been done with BTT than DT patients. For instance, among BTT patients managing the extra burden of transplant-related appointments and managing the uncertainty of waiting for the heart have been identified as difficult and stressful.[4] There is also some literature that points to the challenge of 'accepting' the LVAD for those who know that they are transplant-listed.[4–6] However, the destination therapy population may be more impacted by existential distress and awareness of their mortality.[7]

The stress experienced by LVAD patients is important to understand because psychological stress response, characterized by high levels of perceived stress and depression, has been associated with poor health outcomes among cardiac patients.[8,9] Increased perceived stress has also been related to decreased physical activity, a prevalent limitation for patients living with an LVAD.[10] When the brain perceives a stressful event, it will stimulate both physiological and psychological responses.[11] Actual or interpreted threats to an individual's homeostatic balance initiate the hypothalamic–pituitary–adrenal (HPA) axis secretion of glucocorticoids, which then mobilizes fight-or-flight responses through release of energy.[12] Increased cortisol is an independent predictor of mortality and cardiac events in HF patients.[13] Although, unloading of the left ventricle with LVAD support may result in decreased myocardial stress and inflammation, the inflammatory biomarker profile of LVAD patients is abnormal.[14]

Neurohormonal activity is intrinsically connected to sleep; many neurohormones vary with the diurnal cycle. In addition, sleep quality is an important indicator of physiological stress and may have a particular impact on LVAD patients who must sleep with LVAD equipment.[15] Sleep quality is poor among HF patients, and in a small study was shown to be poor among LVAD patients.[15,16] Sleep quality, stress biomarkers, perceived stress, depression and fatigue are indicators of physiological and psychological stress and likely influence QOL, functional status and healthcare utilization, but there is little evidence to understand these relationships in the LVAD population.

Despite the stress LVAD patients face, outcomes such as quality of life and functional status improve throughout the first 6 months of therapy and remain stable between 12-24 months post-implant. However, there is still significant room for deepening our understanding of factors that contribute to QOL and functional status outcomes in patients living with an LVAD, which are worse than heart transplant outcomes.[17–19] The disparities in outcomes between transplant eligible and ineligible patients is particularly important for patients and providers to understand the impact of destination therapy. Further, patients living with an LVAD are often hospitalized and many patients living with an LVAD require re-operations.[20] Healthcare utilization, including hospitalizations and outpatient visits, and related impact on the experience of stress among patients living with an LVAD has not been well-examined in the literature.

Therefore, the purpose of this study was to describe physiological and psychological stress by implant strategy and to examine relationships between physiological stress response (cortisol, CRP and sleep quality), psychological stress response (perceived stress, depression and fatigue) and outcomes (QOL, functional status and healthcare utilization).

Methods

Study Design

A cross-sectional study design was used to describe physiological and psychological stress response among patients living with an LVAD. Our conceptual framework was based on the Allostatic Load Model which posits that psychological, behavioral and physiological influences result in the burden of stress patients experience.[21] For this study, we focused on the psychological and physiological aspects of stress. (See Figure XXX) Patients living with LVAD and served by the LVAD clinic at two large tertiary care centers in the Baltimore-Washington Metropolitan area were included in the study. Institutional review boards at both institutions approved this study.

Sampling

Convenience sampling was used to recruit patients living with an LVAD from both centers. Informed consent was obtained in person during clinic visits. We recruited individuals after their initial implant hospital discharge and after they had been seen in the outpatient LVAD clinic at least once. This study examined how patients respond to the stress of living with an LVAD after early recovery, therefore newly implanted patients were seen at around 3 months after implant. Patients from the 2 LVAD centers met inclusion criteria if they: were over 21 years of age, had a Montreal Cognitive Assessment (MoCA) score ≥17 (mild to no cognitive impairment), and could speak and understand English. A MoCA score ≥ 17 was used so that only patients who can reliably self-report were included.[22] Patients were not seen during acute hospitalizations and no proxies were used for the completion of survey data.

Measurement

We collected both physiological and psychological data to comprehensively investigate the stress experienced by LVAD patients. Physiologic data included salivary biomarkers to assess stress level. In addition to salivary samples, demographics, medical characteristics and survey data were collected using validated study instruments, which took about 20 minutes to complete.

Salivary Biomarkers – Cortisol and C-reactive protein (CRP) were collected from salivary specimens participants collected at home. Cortisol changes with the diurnal rhythm, peaking about 30 minutes after waking with lowest levels expected in the evening.[23] Cortisol can also vary significantly based on acute stressors. Therefore participants were asked to collect 3 samples per day for 2 days on days when they expected to have a 'normal' routine. Samples were collected at waking, 30 minutes after waking and prior to going to bed. Participants documented time and date of sample collection along with a short log of what was happening at the time of each sample collection. Specimens were frozen to protect against enzymatic action and bacterial growth.

Samples for salivary cortisol and CRP were aliquoted into separate tubes and labeled for freezing at -20°C until batch assayed in duplicate for the respective measurements. Saliva samples were measured using enzyme immunoassay (EIA) kits from Salimetrics (St. College, PA). The intra-assay coefficient of variation was less than 7% for levels of cortisol and 6% for CRP. Plates were read using a Packard Spectra Count microplate photometer.

Sleep Quality - Sleep Quality was measured using the Pittsburgh Sleep Quality Index (PSQI), a 19-item instrument. Respondents provide common wake and sleep times and the remainder of items are ranked from "poor" to "good" sleep quality, measuring seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction over the last month. A global score is calculated from the 7 domains, with a typical cutoff score of 5 indicating poor sleep quality. The PSQI has been used in heart failure populations and has good reliability (Cronbach's alpha 0.83).[24]

Psychological Stress Response - The Perceived Stress Scale (PSS) contains 10 items with Likert scale rating of influence of stress from "never" to "very often". It is a general measure of the cognitive appraisal and perceptions of stress over the last month. There are no diagnostic cutoffs for this instrument; scores range from 0-40 (Cronbach's alpha 0.82).[25–27]

The Perceived Health Questionnaire (PHQ-9) is a 9-item, well-validated scale that measures depressive symptoms (Cronbach's alpha 0.89).[28,29] Respondents consider the previous two weeks and answer questions with a four point Likert scale rating each item from "not at all" to "nearly every day". A total score of 5 a cutoff for uncontrolled depressive symptoms. There is also a screen for suicidality.

The Multidimensional Assessment of Fatigue (MAF) uses a Likert scale to measure 4 dimensions of fatigue: severity, distress, interference with ADLs and timing.[30] The instrument is 16 items and is validated in chronic conditions (Cronbach's alpha 0.93).[16,30]

Quality of life - The Kansas City Cardiomyopathy Questionnaire (KCCQ-12) measures four domains of QOL: physical limitation, symptoms, QOL, social limitation. This instrument has been routinely measured in standard of care in the LVAD population as part of the Intermacs registry (Cronbach's alpha 0.92).[31,32] High QOL was defined as >75 on the overall score, based on literature relating this cutoff to the highest cardiac event-free survival.[33]

Functional status - The Six Minute Walk (6MWT) is a non-invasive, valid and reliable test of functional status at submaximal level (Reliability: 0.86).[34–36] According to the American Thoracic Society Protocol, standard verbal prompts are given after every minute of walking. This test approximates the functional level required in activities of daily living, which usually do not require maximal effort.[37] This measure is used as a part of standard of care in many LVAD centers. High Functional status was defined as 6MWT distance > 300m, based on literature supporting worse outcomes below this threshold.[38]

Healthcare utilization – Healthcare utilization was operationalized as number of outpatient visits, number of days hospitalized and number of number of outpatient procedures. Relevant data were captured from the electronic medical record for the 6 months prior to the date of survey completion or since the date of LVAD implant.

Attrition and Sample Size

While the data collected was essentially cross-sectional, it took a minimum of 3 days to provide informed consent, complete the survey, 6MWT and salivary biomarker sample collection. Despite multiple attempts for follow-up there was a 22% rate of attrition from this study, explained in figure 2. Of those who completed the survey, 71% completed salivary sample collection. There were no statistically significant differences between those who completed and those who did not complete all study procedures. Reasons for never starting study procedures after consent included many hospitalizations, refusing because they "had too much going on" and 2 participants were transplanted before they began the study. Several participants were physically unable to complete the 6MWT, but most participants who did not complete did not respond to study staff requests (by phone or in clinic) to complete. Due to this attrition and small sample size, non-parametric analysis is reported, and modeling work is for exploratory purposes only.

Data analysis

Data were checked for completeness, quality and consistency. A random data check was done independently by a research assistant. Appropriate graphical displays, frequency (percent) for categorical variables, and mean (standard deviation) and median for continuous variables were used for data summary.

Change in cortisol was summarized by calculating the area under the curve by using the mean of the cortisol level for each sample for day 1 and day 2. A Spearman's rank correlation matrix was created to examine relationships between continuous variables. Non-parametric testing was used including Mann-Whitney two group comparisons to examine the difference between implant strategy groups for continuous variables. Categorical comparisons were done using Chi^2 tests. An exploratory logistic regression modeling was used with physiological and psychological stress response variables as independent variables and the outcomes as dichotomous dependent variables. Because of the cross-sectional nature of this study, only correlations and not causation can be implied. All statistical analyses used Stata version 14 (StataCorp, College Station, Texas). Descriptive statistics and graphical displays were used to summarize data.

Results

Sample characteristics

The sample (N = 44) was average age 57.7 years, male (73%), white (45.5%) and married (70.5%). This sample of LVAD patients from 2 centers was similar to the overall LVAD population in distribution of age and gender, but was more racially diverse.[39,40] The percentage of LVAD patients who had been implanted emergently, in Intermacs profiles 1 or 2 was 59%, slightly over the current Intermacs report of 52% Intermacs 1 and 2.[41] Most patients had been managing their device for more than a year. Median time since implant in the overall sample was 18.2 months with 6 participants managing their LVAD for more than 4 years. Typical co-morbidity profiles were noted, 34% diabetes, 27% chronic renal disease and 9% had a history of depression. Most participants were implanted with a Heartmate II device (63.6%); more DT patients had a Heartmate II in this sample ($p < 0.02$). Two patients were implanted with Heartmate III through the Momentum trial.

Descriptive Findings

For our samples, the intra-assay coefficient of variation was less than 5.7% for levels of cortisol. Most participants (27/44) had a normal cortisol awakening response; salivary cortisol levels peaked 30 minutes after waking, followed by a trough in the evening which dropped below waking cortisol levels (Figure 3). Mean area under the curve for the overall group was 322.3 ± 225. Mean salivary CRP was 1196 ± 823 pg/mL.

Overall, LVAD patients experienced poor sleep quality (median 5.5), getting approximately 7 hours of sleep per night, but getting out of bed or waking up at least twice per night. Very few reported the use of sleep aids. Among psychological stress response variables, LVAD patients reported moderate levels of perceived stress (11.8 ± 7.0), few depressive symptoms (3.4 ± 3.8) and moderate fatigue (15.1 ± 8.7).

In this sample, LVAD patients rated QOL 73 (SD ± 13.5) out of 100. In the symptom domain, they ranked heart failure symptoms as rarely impacting their QOL. The physical and social limitation domains were ranked the worst, with the physical limitations domain disproportionately affecting the DT group ($P < 0.02$). Average walking distance on the 6MWT was 318.5 meters including those who did not attempt the 6MWT. Among those who completed the 6MWT, average distance was 389 meters.

In terms of healthcare utilization, LVAD patients had an average of 7 days in the hospital and 6 outpatient visits. This does not include lab testing or rehabilitation visits which could not be captured from clinic medical record for all patients. This does include initial implant hospitalizations from the date of implant for the participants who had their VAD less than 6 months. Finally, there were no differences by implant strategy in outcomes: overall QOL, 6MWT distance or HCU.

No Differences in Physiological or Psychological Stress by Implant Strategy

Physiological stress as measured by cortisol level and CRP did not differ by implant strategy. There were also no significant differences in subjective sleep quality, perceived stress, depression or fatigue by implant strategy. However, DT patients had their device about twice as long as BTT patients (35 months vs. 17 months, $p < 0.02$) and were more likely to be implanted with a Heartmate II device ($p < 0.02$). There were no significant differences between BTT and DT groups among demographic characteristics including age, race, marital status, income and education.

Relationships between Physiological, Psychological Stress and Outcomes

When comparing those with normal versus abnormal cortisol awakening response, Chi^2 testing showed significant relationships between normal cortisol awakening response and low levels of depressive symptoms ($p < 0.02$, Figure 4). No other relationships were evident between physiological (cortisol, CRP, sleep quality) and psychological stress response variables. Cortisol mean AUC was positively associated with overall QOL, 6MWT distance and healthcare utilization ($p < 0.05$). Worse sleep quality and psychological stress response (including perceived stress, depression and fatigue) were associated with worse QOL ($p < 0.05$), but not with 6MWT nor healthcare utilization. Exploratory logistic regression analysis of outcomes did not produce significant multi-variate models (Table 6).

Discussion

Examination of physiological and psychological stress response variables among community-dwelling LVAD patients revealed no significant differences in physiological or psychological stress response by implant strategy. We did see a relationship between normal cortisol awakening response and depression. Also, salivary cortisol was related to QOL, functional status and healthcare utilization. In addition, poor sleep quality and psychological stress response variables (perceived stress, depression and fatigue) were each related to QOL in univariate analysis, however no multivariate models were produced after logistic regression analysis.

Physiological and psychological Stress were not different by implant strategy

This study presents important findings, that BTT and DT patients experience similar levels of stress. Further, we have shown that with or without the hope of transplant, cortisol levels are associated with key outcomes among LVAD patients. Many LVAD patients suffer from moderate levels of stress, fatigue, mild depression and poor sleep quality. In light of these findings, all LVAD patients should be assessed for symptoms of physiological and psychological stress, with special attention to the role of sleep quality. We expected to see differences based on implant strategy because the literature has suggested unique difficulties in each group. It may be that key stressor differences between groups are related to variables not measured in this study such as hope related to transplant, existential distress and other variables.[3–5,7] Stress and coping may also differ by implant strategy at the time of implant strategy decision, but less after the patients have adapted to the decision.[4,42] Previous studies have suggested that the uncertainty in decision-making is very stressful.[4,42,43] Adjustment to home after a long hospitalization may also be particularly difficult for LVAD patients and caregivers, but after home routines are established, living with an LVAD becomes less challenging.[3,5] Although it is not clear if there are differences by implant strategy, this study confirms that stress has a significant role in LVAD patient psychosocial health. However, there is still a need to further explore how implant strategy relates to stress and coping and when these differences are most apparent.

Cortisol awakening response and depression are related in LVAD patients

This study confirms subjectively reported psychological symptoms with objectively measured physiological measures. This corroboration serves as a reminder to healthcare providers that improving psychological symptoms may also improve physiological measures. In our study, most patients (27/44) had normal cortisol awakening response and normal cortisol awakening response was associated with low levels of depression. This relationship is consistently demonstrated in the literature.[44] In healthy older adults abnormal cortisol awakening response, characterized by a decrease in cortisol 30 minutes after waking, has been associated with increased depression and decreased QOL, however we did not see a relationship between abnormal cortisol awakening response and QOL.[44] Salivary biomarkers are useful measures because patients can collect them in the home rather than in a lab. There is little known value in measuring salivary cortisol or CRP diagnostically or without simultaneously measuring other variables. However, these biomarkers could be used as part of a toolkit to explore inflammatory stress response in heart failure and LVAD patients. Recent studies have shown promise examining serum biomarkers including oxidative stress, BNP and cytokines.[45–47]

Sleep quality and psychological stress response

Overall sleep was rated poor, exceeding the cutoff of 5 for poor sleep quality on the PSQI. One explanation is that patients reported about 2 sleep disturbances per night. These disturbances may be more disruptive for LVAD patients than other populations. If an LVAD patient wakes, they may do a quick equipment check or require a change from AC power to battery power to get up to use the bathroom. Sleep disruption and poor sleep quality among general HF patients have been associated with 2.5 times increased odds of short cardiac-event-free survival compared to those with good sleep quality.[48] LVAD patients with poor sleep may be at risk, however more prospective research is needed to examine sleep and outcomes in this population.

The significant relationships between sleep quality, perceived stress, depression, fatigue, QOL provide an important insight into patient perception during LVAD therapy. Those that experience worse psychological stress and sleep also report worse quality of life. Supportive care for those that have difficulty managing stressful life events, stress related to treatment, mood and emotions is critical. It also highlights the need to provide high quality mental health assessment prior to implant so that appropriate services can be provided throughout care. Creating a holistic approach to LVAD care needs to encompass connecting patients to mental health services. Some programs provide support groups where patients and caregivers can meet together to discuss the unique challenges of managing the stress of living with an LVAD. In addition, online groups on Facebook and websites like myLVAD.com provide forums for patient engagement. However, it is likely that there is a need to increase psychological assessment and therapies to support mental and emotional health during LVAD support.

Strengths and Limitations

This study has several strengths including prospective design, recruitment from multiple sites with racial diversity and the biobehavioral approach to considering stress among LVAD patients. This study provides a snapshot of the stress managed by chronic LVAD patients living in the community and being treated in outpatient LVAD clinics. It is the first to incorporate inflammatory stress salivary biomarkers with measures of psychological stress in the LVAD population. We have demonstrated that BTT and DT patients experience similar levels of stress, but questions remain about when differences between implant strategy groups may impact outcomes. Future work should include longitudinal methods to evaluate the role of stress and sleep quality using this biobehavioral approach.

This study has limited generalizability due to its limited sample size. LVAD centers struggle to make meaningful research contributions due to the small LVAD populations that are served. To combat this we recruited from 2 LVAD centers. It is likely that the attrition in the study was due to illness and/or stress that was not captured, making the extra tasks of completing salivary sample collection seem like a burden. The study team picked up samples from the participant's home, to eliminate the need for an extra trip to the clinic; still, about one third of those who consented did not complete this task. Also, because we did not include patients hospitalized, at rehab centers or in the first 2 months after implant, we likely did not capture certain stress profiles in the LVAD population. However, since much of the focus in the LVAD literature has been around the response to implant, we have provided an important contribution to our understanding of the role of stress in the community dwelling LVAD population. As a cross-sectional study no causal relationships may be inferred.

Conclusions

This study reveals important links between physiological and psychological stress response among LVAD patients. We did not find differences by implant strategy in any of our variables of interest, suggesting that chronic LVAD patients experience similar stress response, regardless of implant strategy. This was the first study to examine salivary biomarkers in this population and we identified relationships between cortisol, depression and outcomes. This study provides new insight into the significant role of sleep quality in LVAD patient physical and psychological health. Finally, links in sleep quality, psychological stress response and quality of life may describe a stress profile that requires tailored mental health interventions.

Tables

Table 1: Sample Demographic Characteristics by Implant Strategy (N = 44)

		Implant Strategy		
	Total (n=44) **%(n) or** Mean ± SD	**BTT** **(n = 24)** **% (n) or** Median	**DT** **(n = 20)** **% (n) or** Median	**Mann-Whitney or Chi²** **p-value**
Gender				
Female	73% (32)	50% (16)	50% (16)	0.32
	27% (12)	67% (8)	33% (4)	
Age (years)				
Median	59.5	59.2	63.4	0.16
Race				
White	45% (20)	45% (9)	55% (11)	
Black	43% (19)	68% (13)	32% (6)	0.27
Other	11% (5)	40% (2)	60% (3)	
Marital Status				
Married or Living with Partner	70% (31)	61% (19)	39% (12)	0.17
Other	29% (13)	38% (5)	62% (8)	
Annual Household Income				
< $30,000	25% (11)	36% (4)	64% (7)	
$30, 000-60,000	15% (7)	43% (3)	57% (4)	0.21
>$60,000	60% (26)	65% (17)	35% (9)	
Highest Level of Education				
<= high school	26% (11)	45% (5)	55% (6)	
technical school or some college	28% (12)	50% (6)	50 % (6)	0.52
graduated college or beyond	46% (20)	65% (13)	35% (7)	
Co-morbidities				
Diabetes	34% (15)	40% (6)	60 % (9)	0.16
Chronic Renal Disease	27% (12)	42% (5)	58% (7)	0.29
Depression	9% (5)	40% (2)	60% (3)	0.49
PulmHTN/RightHF	9% (5)	40% (2)	60% (3)	0.85

Table 2: Individual and VAD Characteristics by Implant Strategy

	Total (n=44) Median or % (n)	**BTT (n = 24) % (n)**	**DT (n = 20) % (n)**	**Mann-Whitney or Chi^2 p-value**
Device				
HMII	64% (28)	39% (11)	61% (17)	
Heartware	32% (14)	79% (11)	21% (3)	**0.02**
HMIII	4% (2)	100% (2)	0% (0)	
Emergent Implant (Intermacs 1 or 2)	59% (26)	54% (14)	46% (12)	0.90
Months since implant (median)	18.2	11.4	30.7	**0.02**
Complications after VAD				
GI bleed	27% (12)	42% (5)	58% (7)	0.29
Stroke	21% (9)	33% (3)	66% (6)	0.76
Driveline Infection	16% (7)	29% (2)	71% (5)	0.13
RHF	3% (1)	0% (0)	100% (1)	0.27
Re-implant	3% (1)	0% (0)	100% (1)	0.27
Sepsis	7% (3)	33% (1)	66% (2)	0.45
Trach	5% (2)	50% (1)	50% (1)	0.90

Table 3: Physiological and Psychological Stress by Implant Strategy

	Overall		**Implant Strategy**		
	(n=44) Mean± SD	**(n=44) Median**	**BTT (n = 24) Median**	**DT (n = 20) Median**	**Mann-Whitney p-value**
Physiological Stress: Biomarkers					
Cortisol (mg/dL)					
Waking	0.26 ± 0.12	0.23	0.21	0.29	**0.03**
30 minute after waking	0.31 ± 0.18	0.30	0.29	0.30	0.55
Bedtime	0.12 ± 0.11	0.08	0.08	0.10	0.37
Area under the curve	322.3 ± 226	263.7	253.7	271.5	0.45
C-reactive protein (pg/mL)	1196 ± 823	1003.6	1329.9	980.6	0.63
Physiological Stress: Sleep Quality					
Global sleep quality (0 = best - 21 = worst)	6.2 ± 3.5	5.5	6	5	0.81
Psychological Stress					
Perceived Stress Scale (0 = no stress – 40 = maximum)	11.8 ± 7.0	12	12	11.5	0.93
Depression PHQ-9 (0 = No symptoms – 10 = maximum depressive symptoms)	3.4 ± 3.8	2	2	2.5	0.46
Fatigue MAF total (1 = no fatigue – 50 = severe fatigue)	15.1 ± 8.7	16.6	18.5	14.3	0.46
Quality of Life					
KCCQ Overall (0 = poor – 100 = excellent QOL)	73.0 ± 13.5	74.6	75.6	71.0	0.44
Functional Status					
6 Minute Walk Test Distance (meters)	337.9 ± 162	368.1	367.3	374.9	0.87

Figure 1: Stress in Patients living with LVAD Conceptual Framework

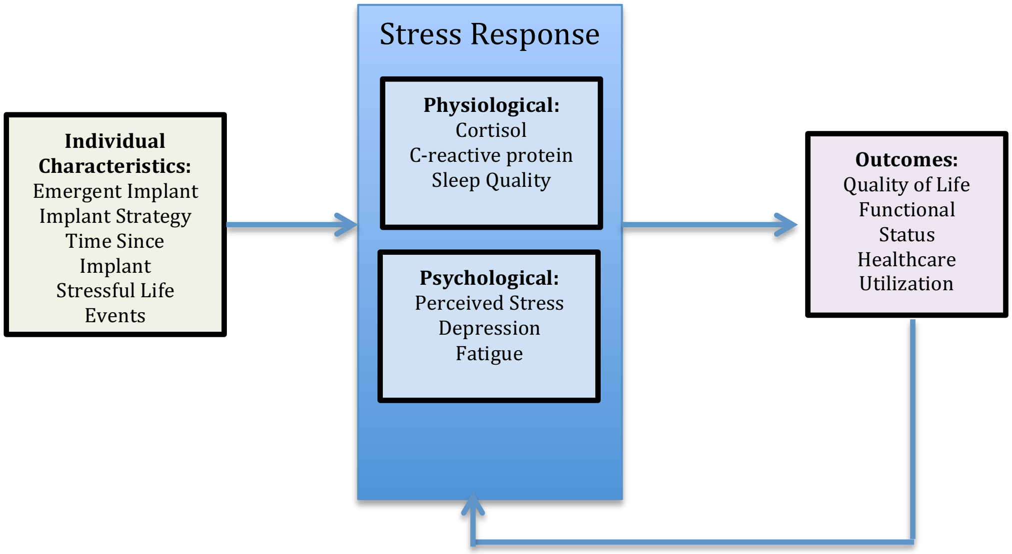

Figure 2: STROBE diagram Study Inclusion, Attrition and Sample Size

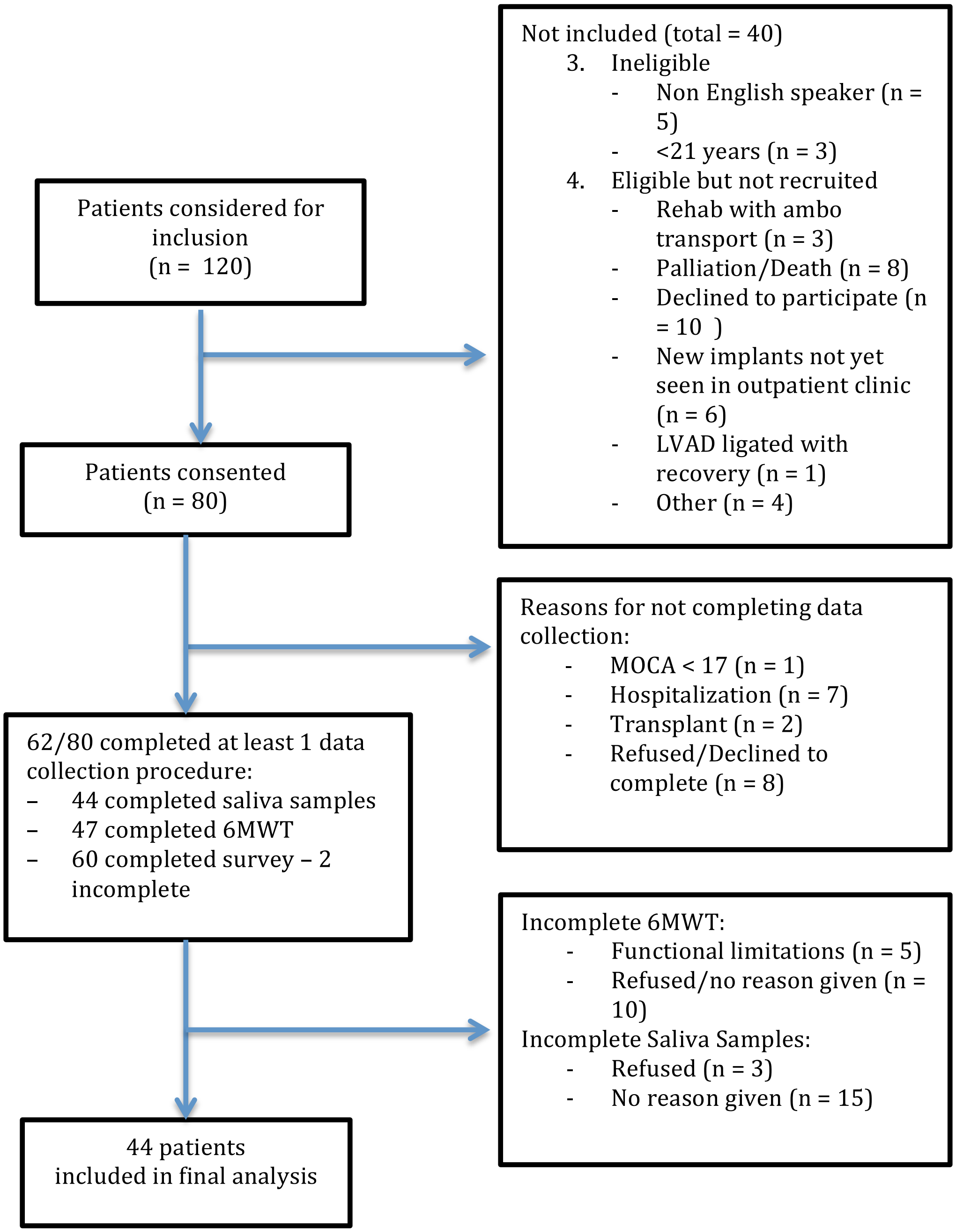

Figure 3: Cortisol Awakening Response (CAR)

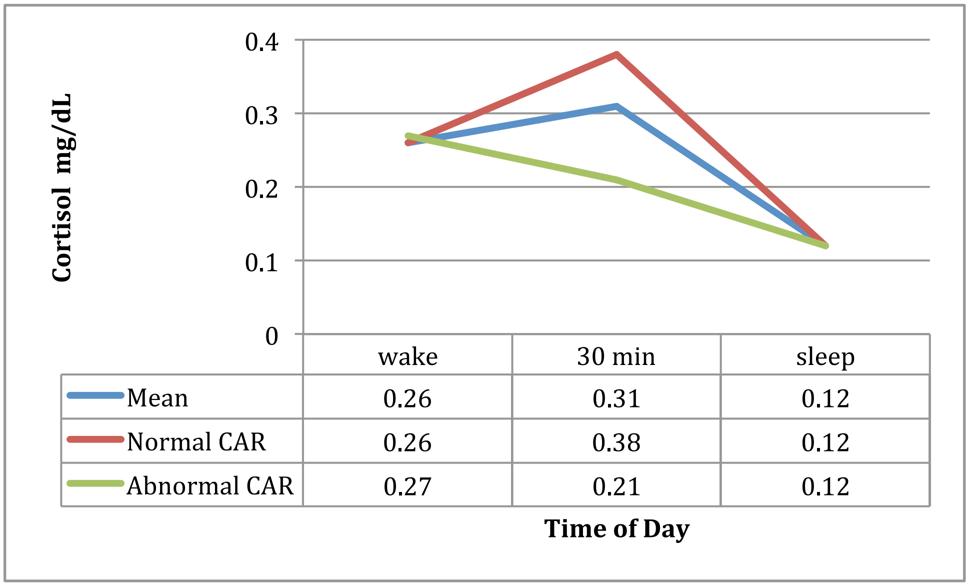

Figure 4: Relationships between Cortisol Awakening Response and Depressive Symptoms

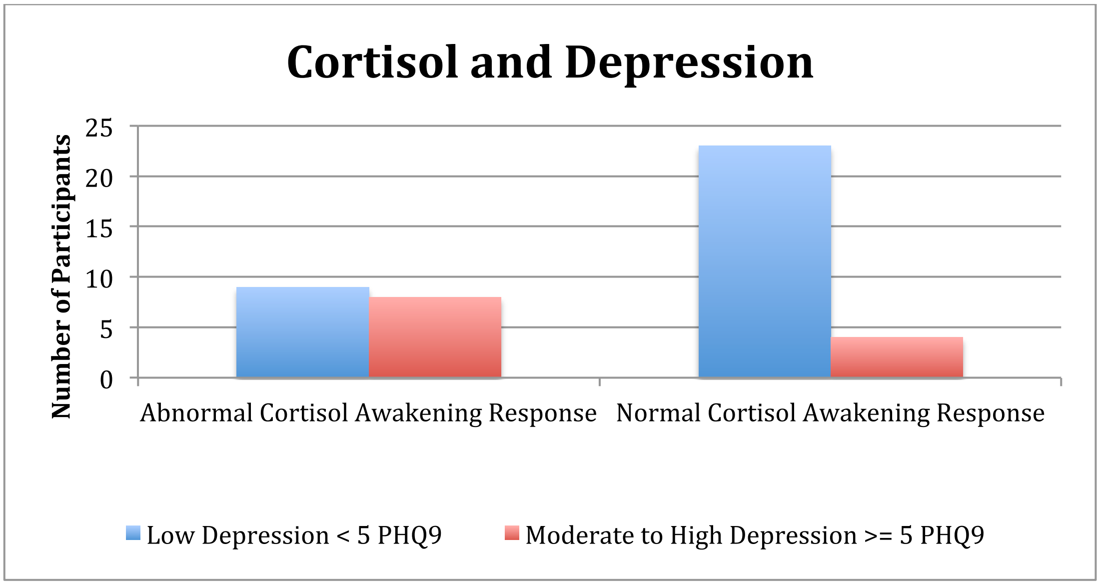

Table 5: Final Models for Logistic Regressions of Quality of Life and Functional Status

	Unadjusted Univariate Models			**Adjusted Multivariate Models**			
	Odds Ratio	**SE**	**p-value**	**Adj. Odds Ratio**	**SE**	**95% CI**	**p-value**
Outcome 1: Quality of Life (Hi QOL >75)							
Predictor				**Pseudo R^2 = 0.29, Chi^2 p= 0.004**			
Cortisol (mean AUC)	1.003	0.002	0.07	1.003	0.002	1.00 – 1.01	0.11
C-reactive protein	1.00	<0.001	0.89	-	-	-	-
Sleep Quality	0.79	0.1	**0.02**	0.86	0.13	0.64-1.17	0.35
Perceived Stress	0.87	0.05	**0.01**	0.94	0.07	0.81-1.09	0.40
Depression	0.80	0.09	**0.04**	1.08	0.17	0.79-1.47	**0.62**
Fatigue	0.86	0.05	**<0.01**	0.89	0.07	0.79-1.00	**0.06**
Outcome 2: Functional Status (Hi 6MWT >300m)							
Predictor				**Pseudo R^2 = 0.27, Chi^2 p= 0.005**			
Cortisol (mean AUC)	1.01	0.003	**0.01**	1.01	0.003	1.00 – 1.01	**0.04**
C-reactive protein	1.00	<0.001	**0.05**	1.00	<0.001	0.99 – 1.00	**0.09**
Sleep Quality	0.90	0.08	0.26	0.94	0.12	0.74 – 1.2	**0.64**
Perceived Stress	1.01	0.05	0.79	-	-	-	-
Depression	1.04	0.10	0.66	-	-	-	-
Fatigue	0.97	0.04	0.50	-	-	-	-

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Chapter 6: Discussion

Summary of Findings

This was the first study to examine stress in LVAD patients chronically managed in the outpatient setting using a bio-behavioral approach. We are the first to report the cortisol awakening response using salivary cortisol in this large sample of LVAD patients. Further perceived stress, fatigue and sleep quality have not been reported previously in a sample of this size. By examining these variables in this vulnerable population we have identified several key findings.

The sample was predominantly male, married and average age 57 years. We recruited a racially diverse sample from 2 large LVAD centers that have experience supporting the chronic management of LVAD patients. This was an experienced cohort of LVAD patients with about 2 years mean duration of LVAD support (median 18.2 months).

Most have a low stress profile

The overall sample had a moderate stress profile: moderate perceived stress, few depressive symptoms and moderate fatigue, with a lot of social support. To assess contributors to stress we also used a stressful life events inventory. About half of the sample reported personal illness as a recent stressor, but despite LVAD use, half of the sample did not report personal illness in the last year. The average stressful life events weighted sum was high, however it did not exceed the clinical threshold. This data provides further quantitative evidence to support previous qualitative findings that once patients cope with the changes in lifestyle required early after implant, developing routines to tackle LVAD tasks, most are able to establish a "new normal".[1,2] Our data confirms that most patients are experiencing low stress and have adequate social support while chronically managing their LVAD in the outpatient setting.

However, for those with moderate to high perceived stress ($n = 30$), worse sleep quality, fatigue, depression and maladaptive coping and quality of life were evident ($p < 0.05$). Regression analysis demonstrated perceived stress ($p < 0.008$) and fatigue ($p < 0.005$) were independent predictors of overall QOL (adj. $R^2 = 0.41$, $p < 0.0001$). VAD literature has examined QOL extensively and previous studies have found demographic characteristics, pre-implant conditions and clinical complications to be predictive.[3] We did not find strong relationships between demographics or pre-implant condition (defined by intermacs profile 1 or 2) and psychological stress or QOL. It is possible that some of these factors contribute to perceived stress but were not detectable given our sample size. Higher perceived stress has been associated with worse 2-year outcomes in the acute MI population.[4] Examining the relationships between perceived stress and future outcomes has not been done in the LVAD population, however depression, conceptualized as a psychological stress response in our study, has been associated with worse outcomes, particularly QOL.[5,6]

Cortisol is related to depression and outcomes

Two-thirds of the overall sample also completed salivary biomarker sample collection (N=44). Normal cortisol awakening response was seen in over half of the sample and was associated with low depressive symptoms ($p< 0.02$). This relationship has been reported in other older adult populations.[7] Cortisol, along with other neurohormones, has been studied early after LVAD implant and in association with glucose management. One previous study examined serum cortisol reported high levels after implant (N = 6) that decreased at 30 days after implant. Another study found that after LVAD implant type II diabetics (N = 28) had significantly lower cortisol and required less insulin than prior to implant.[8] Although salivary cortisol has been demonstrated to be highly correlated to unbound free cortisol levels in plasma and serum, these studies did not report the diurnal variation of the hormone, making comparison difficult.[9,10]

Interpretation of the non-normal cortisol awakening response is challenging due to several confounders which we could not account for. Abnormal variation could be attributed to difficulties in sample collection, medications, infection or other sources of inflammation. Inability to complete the tasks associated with sample collection is concerning as these patients must complete tasks to maintain the LVAD such as battery changes, medication management and infection prevention.

In addition, to analyzing the cortisol awakening response, we also examined the mean area under the curve (AUC) for the two days of cortisol samples. Mean AUC was associated with QOL, functional status and healthcare utilization ($P < 0.05$). No other variable in the study was associated with all three outcomes. The utility of salivary cortisol is limited, however this data provides an important link between a physiological inflammatory measure and outcomes in LVAD patients. In heart failure patients high serum cortisol levels increased mortality risk 3.4 fold.[11] Considering the challenges in predicting outcomes in LVAD patients and the inflammatory mechanisms at play in heart failure, future studies should consider including cortisol among other biomarkers.[12]

LVAD patients have poor sleep quality

The relationships between cortisol and sleep were not statistically significant, however sleep was correlated with perceived stress, depression, fatigue and QOL. On average despite 7 hours of sleep, LVAD patients experience poor sleep quality and have about 2-3 sleep disturbances per night. We found only one other study that included sleep variables. In a longitudinal study of LVAD patients ($N = 12$) from pre-implant to 6 months post-implant, average sleep quality was poor and no change was seen over time.[13] Sleep disordered breathing has been associated with worse functional status, however there have been mixed findings relating sleep disordered breathing and self-reported sleep quality.[14,15] LVAD patients benefit from decreased heart failure symptoms, but it is likely that sleeping with the LVAD components present additional sleep challenges. In our study, cortisol and sleep quality were independent predictors of functional status when controlling for psychological stress response variables ($R^2 = 0.33$, $chi^2 = 0.002$). In addition, there was a trend towards significance in depression as a third predictor in the model. Interventions to improve sleep quality may also result in improved depression, fatigue, perceived stress and outcomes such as QOL and functional status.

Finally, healthcare utilization was determined from chart review of the 6 months prior to the survey completion. Days hospitalized, outpatient visits and outpatient procedures were examined. Participants spent an average of 8% of days in the 6 months prior to the study in the hospital or attending outpatient visits. There was no statistical difference in healthcare utilization between perceived stress groups, but the higher stress group had a trend toward more outpatient visits than the lower stress group ($p < 0.08$). This is consistent with prior literature in heart failure suggesting that depressed patients are more likely to seek care and less likely to use self-management strategies.[16,17] LVAD and transplant patients are highly monitored by coordinators, but very little research has been done to reveal the impact of coordinator and efforts to reduce hospitalizations for LVAD patients. In challenging economic times, cost effectiveness research may reveal ways coordinators and clinicians can prioritize their efforts to help keep patients enjoying their life outside of the healthcare system.

Implications

This study highlights the need for ongoing clinical assessment of stress in LVAD patients. Although, most attention is given to patients during the first 6 months after implant, this study highlights that for patients managed long-term, physiological and psychological stress, social support and outcomes are inter-related. Although we did not see a difference by implant strategy, those with moderate to high stress may benefit from increased monitoring, pharmacotherapeutic and non-pharmacologic interventions. In addition, clinicians should consider adding questions regarding sleep to general assessment.

This study also points to several opportunities for future research to shape our understanding of the LVAD patient experience and possibly intervene to improve outcomes. Longitudinal studies are needed to examine the LVAD patient trajectory using a bio-behavioral lens. Further qualitative work should explore LVAD patient stress and resilience factors which may reveal intervention targets and educational opportunities. Finally, interventions are needed to improve sleep quality and reduce stress in this highly vulnerable population.

LVAD therapy is extremely costly, but remarkable benefits are demonstrated. This research provides evidence to support the LVAD program policies that require social support through a dedicated caregiver for LVAD patients. Transplant committees may need to consider the findings of this study and future work related to psychosocial outcomes as they make policies related to LVAD implant and implant strategy decision making.

Limitations and Strengths

This study is limited by the cross-sectional study design, which precludes causal inference. In addition, despite recruitment from 2 centers, the limited sample size resulted in analysis that could not control for co-variates that may be related to study variables. We also experienced a high rate of incomplete salivary samples. To ease patient burden, samples were picked up from patient homes and transported on ice back to the lab. Still, collection of biomarkers was challenging for many. Despite these limitations, we have provided the largest study to date examining important stress-related predictors of outcomes in the LVAD population with meaningful insights for future intervention.

Conclusions

This study reveals important links between physiological and psychological stress response among LVAD patients. The overall sample seemed to have a minimal stress profile: low perceived stress, few depressive symptoms and mild fatigue, with a lot of social support. We did not find differences by implant strategy but did identify patterns of cortisol awakening response related to depression and functional status. In addition, higher perceived stress was related to worse sleep quality, depression, fatigue and mal-adaptive coping. Subjective sleep quality, psychological stress response and quality of life may describe a stress profile that may require tailored mental health interventions. Further, the influence of high levels of social support to improve QOL despite fatigue is confirmation of the need to continually assess the social support available to LVAD patients. Finally, though LVAD patients face significant stressors, many demonstrate remarkable resiliency and enjoy a good quality of life.

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Appendix: Study Instruments

Thank you so much for your willingness to participate in this study. We are trying to better understand physiological and psychological stress among people living with a left ventricular assist device. Please answer each question as honestly as you can. Try not to overthink your answers.

Demographic Information

Identifiers
First name:
Last name:

What is your race?
○ African American
○ Asian
○ Native American
○ Pacific Islander
○ White/Caucasian
○ Other

What is your ethnicity?
○ Hispanic
○ Non-hispanic

What is your current marital status?
○ Single
○ Living with partner
○ Married
○ Separated
○ Divorced
○ Widowed

What is your combined annual household income?
○ under $20,000
○ 20,000-29,999
○ 30,000-39,999
○ 40,000-49,999
○ 50,000-59,999
○ 60,000-69,999
○ 70,000-79,999
○ 80,000-89,999
○ 90,000-99,999
○ 100,000+

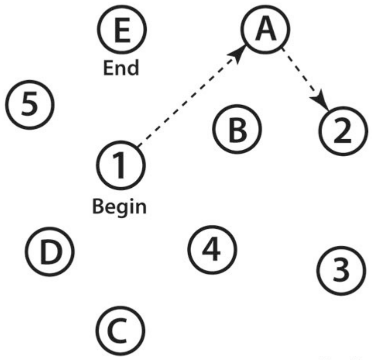
What is your highest level of education?
○ some high school
○ graduated high school
○ technical school
○ some college
○ graduated college
○ some graduate school
○ graduate degree

MONTREAL COGNITIVE ASSESSMENT (MOCA)
`Version 7.1 Original Version`

NAME :
Education : Date of birth :
Sex : DATE :

POINTS

VISUOSPATIAL / EXECUTIVE



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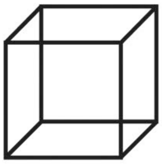
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NAMING


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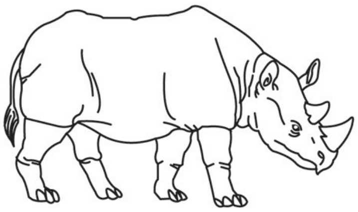
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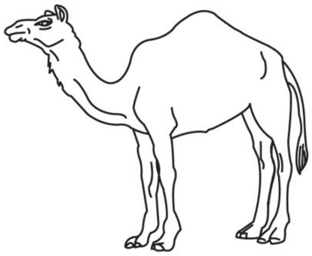
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___/3

MEMORY

Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful.
Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION

Read list of digits (1 digit/ sec.).
Subject has to repeat them in the forward order [ ] 2 1 8 5 4
Subject has to repeat them in the backward order [ ] 7 4 2
___/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors
[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B
___/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**
___/3

LANGUAGE

Repeat : I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]
___/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)
___/1

ABSTRACTION

Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler
___/2

DELAYED RECALL

		FACE	VELVET	CHURCH	DAISY	RED	
	Has to recall words **WITH NO CUE**	[ ]	[ ]	[ ]	[ ]	[ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

___/5

ORIENTATION

[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City
___/6

www.mocatest.org
Normal ≥ 26 / 30
TOTAL ___/30
Add 1 point if ≤ 12 yr edu

Administered by: ____________________

Subject's Initials________________ID#__________________Date_______________Time_____AM PM

PITTSBURGH SLEEP QUALITY INDEX

INSTRUCTIONS:
The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. Please answer all questions.

---

1. During the past month, what time have you usually gone to bed at night?

BED TIME ___________

2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?

NUMBER OF MINUTES ___________

3. During the past month, what time have you usually gotten up in the morning?

GETTING UP TIME ___________

4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.)

HOURS OF SLEEP PER NIGHT ___________

For each of the remaining questions, check the one best response. Please answer all questions.

5. During the past month, how often have you had trouble sleeping because you . . .

a) Cannot get to sleep within 30 minutes

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Wake up in the middle of the night or early morning

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Have to get up to use the bathroom

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Cannot breathe comfortably

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Cough or snore loudly

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

f) Feel too cold

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

g) Feel too hot

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

h) Had bad dreams

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

i) Have pain

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

j) Other reason(s), please describe____

____

How often during the past month have you had trouble sleeping because of this?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

6. During the past month, how would you rate your sleep quality overall?

Very good ___________

Fairly good ___________

Fairly bad ___________

Very bad ___________

7. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all __________

Only a very slight problem __________

Somewhat of a problem __________

A very big problem __________

10. Do you have a bed partner or room mate?

No bed partner or room mate __________

Partner/room mate in other room __________

Partner in same room, but not same bed __________

Partner in same bed __________

If you have a room mate or bed partner, ask him/her how often in the past month you have had . . .

a) Loud snoring

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

b) Long pauses between breaths while asleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

c) Legs twitching or jerking while you sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

d) Episodes of disorientation or confusion during sleep

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

e) Other restlessness while you sleep; please describe__________________________________

____

Not during the past month_____	Less than once a week_____	Once or twice a week_____	Three or more times a week_____

Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: Psychiatry Research, 28:193-213, 1989.

MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE

Instructions: These questions are about fatigue and the effect of fatigue on your activities.

For each of the following questions, circle the number that most closely indicates how you have been feeling during the past week.

For example, suppose you really like to sleep late in the mornings. You would probably circle the number closer to the "a great deal" end of the line. This is where I put it:

Example: To what degree do you usually like to sleep late in the mornings?

1	2	3	4	5	6	7	[✓ 8]	9	10
Not at all									A great deal

Now please complete the following items based on the past week.

---

1. To what degree have you experienced fatigue?

1	2	3	4	5	6	7	8	9	10
Not at all									A great deal

If no fatigue, stop here.

2. How severe is the fatigue which you have been experiencing?

1	2	3	4	5	6	7	8	9	10
Mild									Severe

3. To what degree has fatigue caused you distress?

1	2	3	4	5	6	7	8	9	10
No distress									A great deal of distress

CONTINUED ON NEXT PAGE →

MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE (Continued)

Circle the number that most closely indicates to what degree fatigue has interfered with your ability to do the following activities <u>in the past week</u>. For activities you don't do, for reasons other than fatigue (e.g. you don't work because you are retired), check the box.

In the past week, to what degree has fatigue interfered with your ability to:

(NOTE: Check box to the left of each number if you don't do activity)

☐ **4. Do household chores**

1 2 3 4 5 6 7 8 9 10

Not at all A great deal

☐ **5. Cook**

1 2 3 4 5 6 7 8 9 10

Not at all A great deal

☐ **6. Bathe or wash**

1 2 3 4 5 6 7 8 9 10

Not at all A great deal

☐ **7. Dress**

1 2 3 4 5 6 7 8 9 10

Not at all A great deal

☐ **8. Work**

1 2 3 4 5 6 7 8 9 10

Not at all A great deal

☐ **9. Visit or socialize with friends or family**

1 2 3 4 5 6 7 8 9 10

Not at all A great deal

CONTINUED ON NEXT PAGE →

MULTIDIMENSIONAL ASSESSMENT OF FATIGUE (MAF) SCALE (Continued)

(NOTE: Check box to the left of each number if you don't do activity)

☐ **10. Engage in sexual activity**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **11. Engage in leisure and recreational activities**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **12. Shop and do errands**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **13. Walk**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

☐ **14. Exercise, other than walking**

1 2 3 4 5 6 7 8 9 10
Not at all A great deal

15. Over the past week, how often have you been fatigued?

4 Every day
3 Most, but not all days
2 Occasionally, but not most days
1 Hardly any days

16. To what degree has your fatigue changed during the past week?

4 Increased
3 Fatigue has gone up and down
2 Stayed the same
1 Decreased

Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

The following questions refer to your **heart failure** and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity	**Extremely** Limited	**Quite a bit** Limited	**Moderately** Limited	**Slightly** Limited	**Not at all** Limited	Limited for other reasons or did not do the activity
a. Showering/bathing	○	○	○	○	○	○
b. Walking 1 block on level ground	○	○	○	○	○	○
c. Hurrying or jogging (as if to catch a bus)	○	○	○	○	○	○
	1	2	3	4	5	6

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○
1	2	3	4	5

3. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○	○	○
1	2	3	4	5	6	7

4. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○	○	○
1	2	3	4	5	6	7

5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○
1	2	3	4	5

Rev. 2012-04-11

6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
○	○	○	○	○
1	2	3	4	5

7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
○	○	○	○	○
1	2	3	4	5

8. How much does your **heart failure** affect your lifestyle? Please indicate how your **heart failure** may have limited your participation in the following activities over the past 2 weeks.

Activity	**Severely** Limited	Limited **quite a bit**	**Moderately** limited	**Slightly** limited	**Did not** limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	○	○	○	○	○	○
b. Working or doing household chores	○	○	○	○	○	○
c. Visiting family or friends out of your home	○	○	○	○	○	○
	1	2	3	4	5	6

Perceived Stress Scale

Instructions: The questions in this scale ask you about your feelings and thoughts during the last month. In each case, please indicate your response representing how often you felt or thought a certain way.

1. How often have you been upset because of something that happened unexpectedly?
○ Never
○ Rarely
○ Sometimes
○ Often
○ All of the Time

2. How often have you felt that you were unable to control the important things in yourlife?
○ Never
○ Rarely
○ Sometimes
○ Often
○ All of the Time

3. How often have you felt nervous and “stressed”?
○ Never
○ Rarely
○ Sometimes
○ Often
○ All of the Time

4. How often have you felt confident about your ability to handle your personal problems?
○ Never
○ Rarely
○ Sometimes
○ Often
○ All of the Time

5. How often have you felt that things were going your way?
○ Never
○ Rarely
○ Sometimes
○ Often
○ All of the Time

6. How often have you found that you could not cope with all the things that you had to do?
- ○ Never
- ○ Rarely
- ○ Sometimes
- ○ Often
- ○ All of the Time

7. How often have you been able to control irritations in your life?
- ○ Never
- ○ Rarely
- ○ Sometimes
- ○ Often
- ○ All of the Time

8. How often have you felt that you were on top of things?
- ○ Never
- ○ Rarely
- ○ Sometimes
- ○ Often
- ○ All of the Time

9. How often have you been angered because of things that were outside your control?
- ○ Never
- ○ Rarely
- ○ Sometimes
- ○ Often
- ○ All of the Time

10. How often have you felt difficulties were piling up so high that you could not overcomethem?
- ○ Never
- ○ Rarely
- ○ Sometimes
- ○ Often
- ○ All of the Time

Perceived Health Questionnaire

Instructions: Answer the following questions for how often in the last 2 weeks you have been bothered by any of the following problems.

1. Little interest or pleasure in doing things
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

2. Feeling down, depressed, or hopeless
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

3. Trouble falling or staying asleep, or sleeping too much
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

4. Feeling tired or having little energy
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

5. Poor appetite or overeating
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

6. Feeling bad about yourself - or that you are a failure or have let yourself or your familydown
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

7. Trouble concentrating on things, such as reading the newspaper or watchingtelevision
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

8. Moving or speaking so slowly that other people could have noticed? Or the opposite -being so fidgety or restless that you have been moving around a lot more than usual
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

9. Thoughts that you would be better off dead or of hurting yourself in some way
○ Not at all
○ Several days
○ More than half the days
○ Nearly every day

10. If you checked off any problems, how difficult have these problems made it for you to doyour work, take care of things at home, or get along with other people?
○ Not difficult at all
○ Somewhat difficult
○ Very difficult
○ Extremely difficult

Brief COPE

Instructions: Brief COPE State how often you have used each of the following coping methods in the last month.

1. I've been turning to work or other activities to take my mind off things.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

2. I've been concentrating my efforts on doing something about the situation I'm in.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

3. I've been saying to myself "this isn't real."
○ Not at all
○ A little bit
○ a medium amount
○ a lot

4. I've been using alcohol or other drugs to make myself feel better.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

5. I've been getting emotional support from others.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

6. I've been giving up trying to deal with it.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

7. I've been taking action to try to make the situation better.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

8. I've been refusing to believe that it has happened.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

9. I've been saying things to let my unpleasant feelings escape.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

10. I’ve been getting help and advice from other people.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

11. I've been using alcohol or other drugs to help me get through it.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

12. I've been trying to see it in a different light, to make it seem more positive.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

13. I’ve been criticizing myself.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

14. I've been trying to come up with a strategy about what to do.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

15. I've been getting comfort and understanding from someone.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

16. I've been giving up the attempt to cope.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

17. I've been looking for something good in what is happening.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

18. I've been making jokes about it.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

19. I've been doing something to think about it less, such as going to movies, watching TV,reading, daydreaming, sleeping, or shopping.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

20. I've been accepting the reality of the fact that it has happened.
- ○ Not at all
- ○ A little bit
- ○ a medium amount
- ○ a lot

21. I've been expressing my negative feelings.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

22. I've been trying to find comfort in my religion or spiritual beliefs.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

23. I’ve been trying to get advice or help from other people about what to do.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

24. I've been learning to live with it.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

25. I've been thinking hard about what steps to take.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

26. I’ve been blaming myself for things that happened.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

27. I've been praying or meditating.
○ Not at all
○ A little bit
○ a medium amount
○ a lot

28. I've been making fun of the situation.

○ Not at all
○ A little bit
○ a medium amount
○ a lot

ENRICHD Social Support

Instructions: Answer the following questions regarding the support available to you (in general).

1. Is there someone available to whom you can count on to listen to you when you need totalk?
○ None
○ A little
○ Some
○ Most of the time
○ All of the time

2. Is there someone available to you to give you good advice about a problem?
○ None
○ A little
○ Some
○ Most of the time
○ All of the time

3. Is there someone available to you who shows you love and affection?
○ None
○ A little
○ Some
○ Most of the time
○ All of the time

4. Is there someone available to help with daily chores?
○ None
○ A little
○ Some
○ Most of the time
○ All of the time

5. Can you count on anyone to provide you with emotional support (talking over problemsor helping you make a difficult decision)?
○ None
○ A little
○ Some
○ Most of the time
○ All of the time

6. Do you have as much contact as you would like with someone you feel close to, someonein whom you can trust and confide in?

- ○ None
- ○ A little
- ○ Some
- ○ Most of the time
- ○ All of the time

7. Are you currently married or living with a partner?

- ○ yes
- ○ No

1. What are the top 3 challenges regarding life with an LVAD?

2. What are the top 3 benefits of life with an LVAD?

3. Knowing what you know now about life with an LVAD, would you do itagain?

○ yes
○ No

4. Why or why not?

Thank you so much for your time and willingness to share experiences. I hope you continue to improve and are able to find ways to alleviate your stress.

Data Collector: ____

Participant Name: ____

Participant ID: ____

6MWT

Oxygen? Yes/no Flow____________________L/min Type________________

Borg Scale

0 = Nothing, 1 = very slight, 2 = slight, 3 = moderate, 4 = somewhat severe, 5 = severe, 6, 7 = very severe, 8, 9, 10 = very, very severe (maximal)

Vital Signs

	Baseline	End of test
Time	:	:
Blood Pressure		
Heart Rate		
Dyspnea (Borg)		
Fatigue (Borg)		
SpO_2 (%)		

Encouragements after…

1 min – "You are doing well. You have 5 minutes to go."
2 min - "Keep up the good work. You have 4 minutes to go."
3 min - "You are doing well. You are halfway done."
4 min - "Keep up the good work. You have only 2 minutes left."
5 min - "You are doing well. You have only 1 minute to go."
15 seconds left - "In a moment I'm going to tell you to stop. When I do, just stop right where you are and I will come to you."
End of test - "Stop! I'll come to you, mark the distance and get your vitals. Do you need to sit?"

If the patient stops walking during the test and needs a rest, say this:

"You can lean against the wall if you would like; then continue walking whenever you feel able."

Stopped or paused before 6 minutes? Yes/no
Reason____

Symptoms at end of exercise:
angina/dyspnea/dizziness/claudication/other________________________
(Number of laps ________________X 60 meters) + final partial lap____________meters = 6MWT_________

Comments:

Interpretation:

Lap Counter: 1 2 3 4 5 6 7 8 9 10
11 12 13 14 15 16 17 18 19
20

VAD Stress Study

What is this study about?

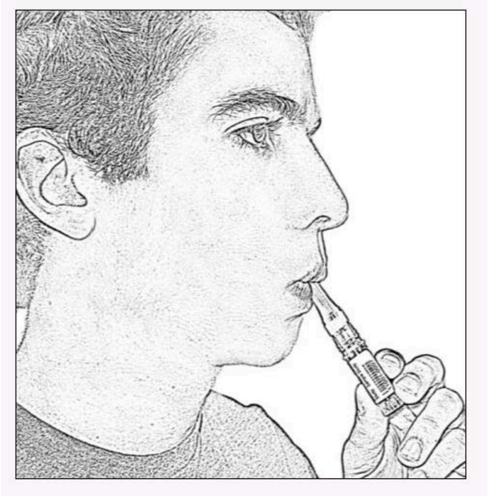
We are trying to understand how VAD patients react to the stress of daily life. We want to know how the body reacts (saliva) and how you think about it (surveys).

Why saliva?

Saliva contains some important lab values just like your blood. We are asking you to collect these samples because we would like to avoid needle sticks as part of this study.

Questions?

Please call the Study Coordinator, Martha Abshire, MS, RN at 443-340-6201.

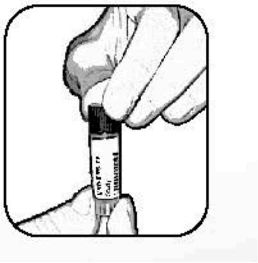


Saliva Sample Schedule:

Day 1	Day 2
Waking	Waking
30 minutes after you wake up	30 minutes after you wake up
Bedtime	Bedtime

Each day:

1. Place the tubes by your bed the night before you collect the saliva samples.
2. Saliva sample 1 is collected by passive drool when you wake up.
3. Rest in bed for 30 minutes. Don't brush your teeth, eat breakfast or exercise until after the sample is collected.
4. Saliva sample 2 is collected by passive drool 30 minutes after waking up.
5. Place sample 1 and 2 in the Ziploc bag in the freezer.
6. Saliva sample 3 is collected by passive drool at bedtime.
7. Place sample 3 in the Ziploc bag in the freezer.



How to collect the Saliva Samples:
In your kit, you have 6 tubes. Each tube is labelled with your ID number for the study and timing of the sample.

- Place straw in tube.
- Imagine you are chewing a favorite food
- Slowly moving your jaws in a chewing motion
- Tilt your head forward and place straw between your lips, allowing the saliva to enter the tube.
- Cap the tube tightly.
- Put your tube in the bag and the bag in the freezer.
- Write down the time for each sample and write a few words about what is going on during that part of your day.

Please, do NOT:

- ➢ Do not eat, drink or brush your teeth 15 minutes before each saliva sample.
- ➢ Do not eat chips or cheese 1 hour before saliva sample or drink milk or alcohol.
- ➢ Do not exercise 1 hour before the saliva sample.

Timing is important…

- ➢ If you forget the wake-up sample, just start over the next day.
- ➢ If you miss a sample later in the day, please collect the sample as soon as you remember and make a note on your log.

When you are finished collecting the samples:

- Make sure you put all of your tubes into the freezer in the bag provided.
- Add your log to the bag.
- Call the study coordinator, Martha at 443-340-6201 when you are finished.
- A research study team member will come to collect your samples at a time you agree on. If you can't keep the time you arranged at the clinic, just let the study coordinator know.

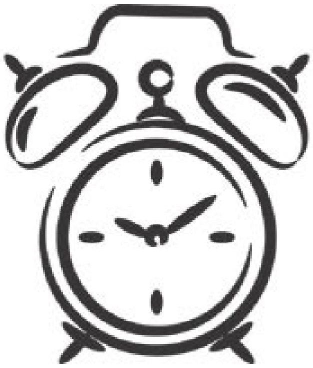
Your time is so valuable and we really appreciate it!
The information from this study will help us understand stress in VAD patients.
We hope to use this data to develop programs to help reduce VAD patient stress.

Questions?

Please call the Study Coordinator, Martha Abshire, MS, RN at 443-340-6201.

Log for Spit Samples – Day 1

When you first wake up:



Date:____________________

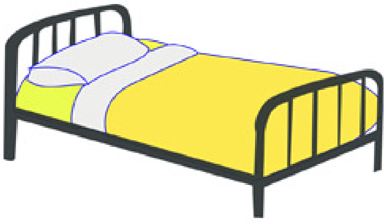
Day 1 – Wake up sample

ne:____________________

What's happening?________________________________

____

30 minutes after you wake up:



Time:____________________

Day 1 – 30 min. sample

What's happening?________________________________

____

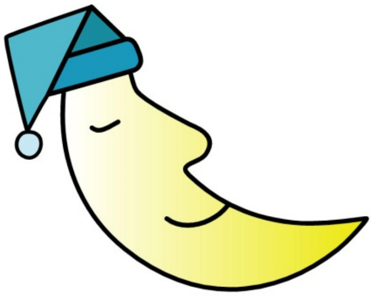
Bedtime:

Time:____________________

Day 1 – bedtime sample

What's happening?________________________________

____

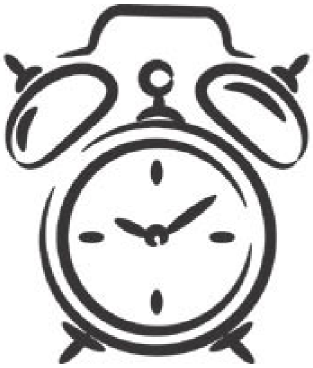


Questions?

Please call the Study Coordinator, Martha Abshire, MS, RN at 443-340-6201.

Log for Saliva Samples – Day 2

When you first wake up:



Date:____________________

Day 2 – Wake up sample

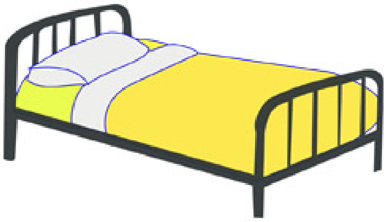
ne:____________________

What’s happening?________________________________

____

30 minutes after you wake up:

Time:____________________

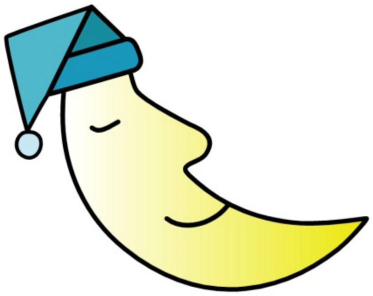


Day 2 – 30 min. sample

____

____

Bedtime:



Time:____________________

Day 2 – bedtime sample

What’s happening?________________________________

____

Questions?

Please call the Study Coordinator, Martha Abshire, MS, RN at 443-340-6201.

Curriculum Vitae

Part I

PERSONAL DATA

Martha Abshire, 443.340.6201, mabshir1@jhu.edu

EDUCATION

2012-present, PhD candidate, Johns Hopkins University School of Nursing, Baltimore, MD
planned graduation May 2017

2006, MS in Clinical Nurse Leadership, University of Maryland at Baltimore School of Nursing, Baltimore, MD

1998, BA in Modern Language and Linguistics, University of Maryland Baltimore County, Catonsville, MD

CURRENT LICENSE AND CERTIFICATION

2007-present, RN, State of Maryland Board of Nursing #R176549

PROFESSIONAL EXPERIENCE

2016	PRN LVAD Coordinator	Johns Hopkins Hospital, Baltimore, MD
2013-2016	PRN RN, CVPCU	Johns Hopkins Hospital, Baltimore, MD
2012-2013	PRN RN, ICU	Johns Hopkins Hospital IntraStaff, Baltimore, MD
2012	Travel RN, BMT ICU	Johns Hopkins Hospital, Baltimore, MD
2012	Travel RN, MICU	Yale New Haven Hospital, New Haven, CT
2009-2012	Staff RN, CCU	University of MD Medical Center, Baltimore, MD
2007-2010	Staff RN, Med/Surg	Carroll Hospital Center, Westminster, MD
2000-2004	Cryptanalyst	National Security Agency, Ft. Meade, MD
1999-2000	Teacher	Spanish II, Aberdeen High School, Aberdeen, MD

HONORS AND AWARDS

2016 Nursing Research Award, 2nd place, and Travel Award, HFSA
2015-2016 Margaret Tyson Scholarship, Nurses Educational Funds, $5,000
2014-15 President, Doctoral Student Organization, Johns Hopkins University School of Nursing
2014-15 Professional Development Award, Johns Hopkins University School of Nursing, $2000
2013-14 Social Chair (Appointed), Doctoral Student Organization, Johns Hopkins University School of Nursing
2013 Sigma Theta Tau Induction
2013 Graduate Nursing Faculty Scholarship and Living Expenses Grant
2012 Silver Beacon Award – Writing Committee Member for the CCU at UMMC
2009 Daisy Award awarded at Carroll Hospital Center for Extraordinary Nursing Care
2009 Team of the Month Award for initiating Walking Rounds through Best Practice Committee
2007-2009 Multiple Spot and WOW awards for excellence in care given to patients.
2005-2006 UMB SON Academic Scholarship
2003 Cash Award for Contributions made during Operation Iraqi Freedom
2003 Time Off Award for leadership of boot camp course
2001 Time Off Award for contributions during September 11th Crisis
1994-1998 Presidential Scholar, Honors college Fellow, Dean's List, Palomares Award for Service and Excellence in Language

RESEARCH

2015 – 2017 F31 1 F31 NR015179-01A1 (PI: Abshire, M) Physiological and Psychological Stress in Left Ventricular Assist Device Patients $43,120

2014-2016 Heart Failure Society of America Nursing Research Grant (PI: Abshire, M) $10,000

2014 – 2015 TL1 Fellow Predoctoral Clinical Research Training Program

2012-2014 T32 Fellow Interdisciplinary Training in Cardiovascular Health Research, National Institute of Nursing Research (T32 NR012704)

2014-2016 Recruitment and Retention Strategies in Large, Longitudinal Studies
Research assistant. Collaboration with Dr. Dale Needham, Dr. Cheryl Dennison Himmelfarb and Dr. Michelle Eakin. Recruited and performed in-depth interviews, data analysis and currently drafting a manuscript. (manuscript submitted)

2013-2015 End-of-Life Heart Failure Symptoms Study
Secondary analysis of quantitative and qualitative data, studying the relationships between symptoms and fear in heart failure patients at end-of-life. Mentored in this work by Dr. Marie Nolan, an expert in end-of-life research. (See publication below)

2013-2015 Research Residency in Cardiovascular Risk Management among HIV Infected People. Study Coordinator. Emphasis on: Study planning, implementation, mentorship of baccalaureate nursing student, IRB submission, focus groups. Abstract was accepted for oral presentation at STTI Research Congress 2015 in San Juan, Puerto Rico (See presentation below)

2013-2014 Research Residency in Heart Failure. Emphasis on: IRB submission, data management and collection.

SCHOLARSHIP

Abshire M, Dinglas VD, Cajita MIA, Eakin MN, Needham DM, Dennison Himmelfarb C. Participant retention practices in longitudinal clinical research studies with high retention rates. *BMC Medical Research Methodology*. 2017; In Press.

Casida, J. M., Wu, H. S., **Abshire, M**., Ghosh, B., & Yang, J. J. (2016). Cognition and adherence are self-management factors predicting the quality of life of adults living with a left ventricular assist device. *The Journal of Heart and Lung Transplantation*.

Abshire, M., Prichard, R., Cajita, M., DiGiacomo, M., & Himmelfarb, C. D. (2016). Adaptation and coping in patients living with an LVAD: A metasynthesis. *Heart & Lung: The Journal of Acute and Critical Care*, *45*(5), 397-405.

Abshire M, Xu J, Baptiste D, Almansa JR, Xu J, Cummings A, et al. Nutritional Interventions in Heart Failure: A Systematic Review of the Literature. *J Card Fail.* 2015;21(12):989-999. doi:10.1016/j.cardfail.2015.10.004.

Xu J, **Abshire M,** Han H-R. Decision Making Among Persons Living With Heart Failure. *J Cardiovasc Nurs*. December 2015. doi:10.1097/JCN.0000000000000312.

Abshire, MA, Xu, J, Dennison Himmelfarb, CR, Davidson, PM, Sulmasy, D, Kub, J, Hughes, M, Nolan, M. Symptoms and fear in patients with heart failure approaching end of life: a mixed methods study. *Journal of Clinical Nursing*, *24*(21-22), 3215-3223.

Abshire, MA, Dwyer, D. Palliative Care Considerations for LVAD patients, American Association of Heart Failure Nurses newsletter, July 2015.

Abshire, Martha, Cheryl R. Dennison Himmelfarb, and Stuart D. Russell. "Functional Status in Left Ventricular Assist Device–Supported Patients: A Literature Review." Journal of cardiac failure, 20(12), 973-983.

Abshire, Martha A., and Cheryl R. Dennison Himmelfarb. "Go With the Flow: Progress in Mechanical Circulatory Support." Journal of Cardiovascular Nursing 29.4 (2014): 364-366.

Abstract and Podium Presentation

Abshire, M, Davidson, PM, Desai, SD, Budhathoki, C, Russell, SD, Dennison Himmelfarb, C. Increased Perceived Stress and Fatigue are associated with Worse Quality of Life in Patients with a Left Ventricular Assist Device, International Society of Heart and Lung Transplantation 2017, San Diego, CA, planned April 2017

Abshire, MA, Wu, H & Casida, JM. Depression Predicts of Quality of Life in Adults with Long Term Left Ventricular Assist Device, American Heart Association 2016 Scientific Sessions, New Orleans, Louisiana, November 14, 2016.

Abshire, MA, Dennison Himmelfarb, CR. Depression, Fatigue and Sleep Quality are associated with Quality of Life among Patients with Left Ventricular Assist Device, Heart Failure Society of America, Orlando, FL. *Sept 19, 2016. *Nursing Research Award, 2nd place*

Abshire, MA, Commodore-Mensah, Y, Farley, JE, Dennison Himmelfarb, CR. Provider Cardiovascular Risk management in an Urban HIV Practice: Challenges and Opportunities, Sigma Theta Tau International Research Congress, San Juan, Puerto Rico. July 23-26, 2015.

Abshire, MA, Xu, J, Dennison Himmelfarb, CR, Davidson, PM, Sulmasy, D, Kub, J, Hughes, M, Nolan, M. Symptoms and fear in patients with heart failure approaching end of life: a mixed methods study, Southern Nurses Research Society, Tampa, FL. Feb 28, 2015.

Baptiste, DL, **Abshire, MA**, Increasing scholarly productivity through a heart failure journal club: Be accountable, improve your science and collaborate! International Network for Doctoral Education in Nursing Biennial Conference, San Juan, Puerto Rico. July 22-3, 2015.

Abstract and Poster Presentation

Abshire, M, Page, GG, Davidson, PM, Han, HR, Desai, SD, Budhathoki, C, Russell, SD, Dennison Himmelfarb, C. Physiological and Psychological Stress Response are related to Quality of Life and Functional Status Among People living with a Left Ventricular Assist Device, Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke 2017 Scientific Sessions, planned for April 2, 2017, Arlington, VA

Abshire, MA & Dennison Himmelfarb, CR. Physiological and Psychological Stress Among Left Ventricular Assist Device Patients, Translational Science, Washington, DC. April 16, 2015.

EDITORIAL ACTIVITIES

2014-present	Reviewer, American Journal of Cardiology, Circulation Outcomes, International Journal of Nursing Studies and Heart & Lung, Advances in Nursing Doctoral Education and Research
2013	Ad Hoc Journal Article Review with Dr. Marie Nolan for *Journal of Palliative Medicine*
2013	Ad Hoc Journal Article Review with Yvonne Commodore-Mensah, PhD (candidate) for *European Journal of Cardiovascular Nursing*
2012	Ad Hoc Journal Article Review with Dr. Marie Nolan for *Progress in Transplantation*

PROFESSIONAL ACTIVITIES

2016-2017	International Network for Doctoral Education in Nursing Conference Planning
2016-2017	Student Board Member International Network for Doctoral Education in Nursing
2015-2016	Philanthropy Chair, Sigma Theta Tau International, Nu Beta Chapter
2013-2015	Executive Director International Network for Doctoral Education in Nursing
2014-2015	Student Representative, SNRS Board of Directors

Curriculum Vitae
Part II

EDUCATIONAL ACTIVITIES

2017	Professionalism in Nursing, JHU SON, 2 credits, 45 students
2016	Conference Steering Committee - Inaugural Partnering with Patients, Shared Decision Making Conference June 2016
2015	Research Honors Mentor – 2015 mentored an Honors student in conducting a pilot study
2013-15	Biostatistics tutor, PhD Program, Johns Hopkins University School of Nursing
2014	Teaching Assistant and Course Development, Johns Hopkins University School of Nursing, Anatomy and Physiology, online courses
2013	Lab Instructor, JHU SON, Health Assessment, 8 students
2009-13	Adjunct Faculty, UMB SON: Senior Practicum – 8 credits, 10-11 students Lab Instructor, Health Assessment and Fundamentals, 10-12 students Clinical Instructor, Fundamentals clinical in Assisted Living Facilities, 8-12 students

Martha Allison Abshire
Born June 19, 1976
Patuxent River, Maryland, USA