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Outcomes of Patients Transferred to the University of Michigan Health System on a Short-Term Ventricular Assist Device for Cardiogenic Shock

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by

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DEDICATION

I dedicate this work to my wonderful husband, Dan, who goes along with me whenever I decide to change careers and my beautiful son, Bradley, who decided to come along in the middle of this journey.

ACKNOWLEDGEMENTS

I'd like to thank Dr. Pagani for his guidance in helping me develop this project and giving me the motivation to finish after seeing all the "red ink."

ABSTRACT

Short-term ventricular assist devices (VADs) are mechanical pumps that are used to temporarily support a patient who is in cardiogenic shock. These VADs are effective in sustaining a patient's life until he or she can been transferred to a tertiary cardiac center such as the University of Michigan Health System. The researcher examined patients' clinical status at the time of transfer and used univariate analysis to determine which factors are likely to predict a successful outcome. Multivariate analysis showed that younger age and better kidney function were prognostic variables in the patients' 30-day and long-term survival. These factors improve the chances of a patient becoming a heart transplant candidate and increase the probability of long-term survival.

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CHAPTER 1: Introduction

Introduction

Almost 80 million American adults have some form of heart disease, also known as cardiovascular disease (CVD). Many of these patients can be treated with medications and lifestyle changes, while others are prone to heart attacks, cardiogenic shock, and heart failure. Often the only hope of recovery for someone with severe heart failure is heart transplantation or ventricular assist device (VAD) therapy. However, many hospitals in the United States are not equipped to handle such operations or care for these patients. Therefore, many patients are not located near a major cardiac center when their disease progresses or when they are in an emergency situation. Physicians at smaller hospitals will often use a short-term VAD to stabilize patients until they can be transported to a tertiary medical center for further treatment. Relatively few studies have reported on the long-term outcomes of patients supported on short-term VADs and transferred to a tertiary center. Significantly more data are needed to determine whether patient selection and improvements in clinical management can improve survival for these patients. Identification of clinical variables prognostic in patient outcome could be invaluable to physicians not only at the tertiary centers but the referring hospitals as well. This study is an analysis of patients transferred to the University of Michigan Health System (UMHS) on a short-term ventricular assist device from 1997 – 2007.

Background

The heart functions to pump blood to all parts of the body so that oxygen can reach all of the cells, but there are many diseases and conditions that cause the heart to perform inadequately. The American Heart Association reports that cardiovascular disease is the leading cause of death in the United States, resulting in nearly 2400 deaths every day (2007). There are numerous

forms of CVD including hypertension, coronary heart disease, heart failure, and stroke. Sometimes these conditions can develop slowly over time and are influenced by genetics as well as environment. Other forms of CVD can develop more rapidly, such as viral cardiomyopathy or myocardial infarction.

Many people with heart disease are able to keep their condition under control with medications and lifestyle changes, such as diet modification and exercise. However, often the condition progresses and a patient may require a more invasive procedure, such as percutaneous coronary interventions (PCIs). PCIs include treatments such as angioplasty or stents, which are performed to open narrow or blocked arteries. Sometimes even PCI is not enough and surgery is required. One of the most common heart surgeries is coronary artery bypass grafting (CABG), which involves bypassing clogged arteries with another vessel.

Sometimes heart disease may progress into heart failure, a condition in which the heart fails to function properly. This can occur suddenly as a result of a myocardial infarction resulting in cardiogenic shock or can progress in a chronic fashion as a result of an underlying CVD.

Another cause of heart failure occurs when a patient fails to recover adequate heart function after being on cardiopulmonary bypass during a cardiac operation. This specific circumstance is called postcardiotomy heart failure. Treatment for heart failure, whatever the cause, may include surgery, implantation of mechanical assist devices, or heart transplantation.

There are more 2200 heart transplants performed each year in the United States; it is the fourth most common organ transplanted behind corneal, kidney, and liver transplants (U.S. National Library of Medicine and National Institutes of Health, 2006). There are many people on the waiting list for a heart transplant, but often a heart never becomes available due to the shortage of donor organs. Therefore, many physicians and patients have begun looking for

alternatives and other therapies to help patients either "hold on" long enough to wait for a heart or to help their heart recover in the hopes of not needing a heart transplant at all. One such therapy is the implantation of a VAD.

VADs are mechanical pumps that assist the heart in pumping blood when it is unable to do so due to heart failure. There are many different types and uses of VADs. Some are considered temporary and meant for shorter support times of hours or days. Other VADs are designed for long-term use and may be used for cardiogenic support for months or years. One common use of long-term VAD is for cardiogenic support while a patient is awaiting heart transplantation. An example of a temporary VAD is shown in Figure 1. It consists of an external device that is powered by a pneumatic console and is designed to support one or both of the ventricles for a short period of time.

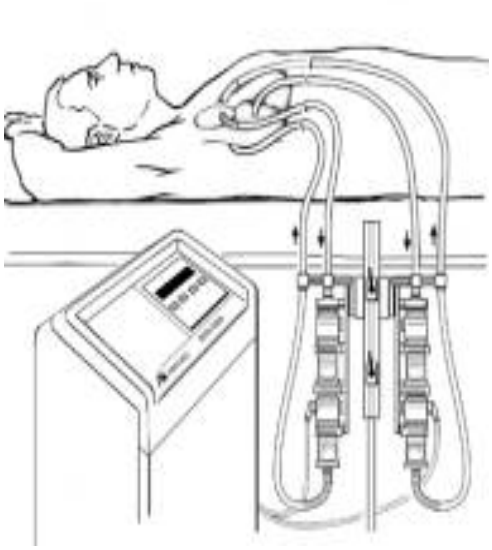


Figure 1. – Abiomed BVS5000; a temporary assist device

One major limitation of VAD and heart transplant therapy is that only a limited number of medical centers are able to provide this treatment. For a patient in a life-threatening situation and at a medical facility without these capabilities, there are typically few options available to

them. Short-term VADs have become more readily available at smaller facilities and are a feasible treatment for patients in cardiogenic shock. These VADs are designed to support patients until they can be transferred to a tertiary cardiac center for further treatment, which may involve recovery, implantation of a long-term VAD, or heart transplantation. This system of patient transfer is often referred to as a "hub and spoke," with the tertiary center as the hub receiving patients from the referring "spoke" hospitals. As more mechanical circulatory support devices are developed and studied, more centers will be able to report their success with this treatment, allowing physicians at both large and small hospitals to use the knowledge to better manage their heart failure patients.

Study Objective

The objective of this study is to identify prognostic variables based on patient information available within the first 24 hours of transfer to the University of Michigan Health System that may improve patient care and outcomes.

Study Goal

Suggesting prognostic variables to make patient care decisions to improve outcomes with short-term mechanical circulatory support is the goal of this research.

Hypothesis

Clinical characteristics of the patient's status within the first 24 hours of presentation with temporary VADs have significant prognostic value with respect to short- and long-term survival.

CHAPTER 2: Review of Literature

Mechanical pumps are becoming more common in the treatment of heart failure and cardiogenic shock. They are the subject of many clinical trials, most of which are designed to study the safety and effectiveness with the newer generations of VADs. Only a few centers have published their experiences of patients who are transferred to their institution from the referring hospital, commonly referred to as the "hub and spoke system."

Helman et al. (1999) published findings from Columbia-Presbyterian Medical Center after they established a referral network for patients who were potentially in need of a long-term VAD. They reported on 44 postcardiotomy patients, all of whom were being supported by a short-term VAD or other cardiogenic support therapies given at an outside hospital. They reported that 66% of the patients survived to discharge and that utilization of referral networks may substantially improve survival rates for postcardiotomy heart failure patients.

Years later, Kherani et al. (2003) reported further success of the hub and spoke system at Columbia-Presbyterian Medical Center. They performed a retrospective review of 46 patients with acute cardiogenic shock who had been transferred to their facility for further treatment. All patients received a long-term VAD for treatment, and their survival to discharge rate was 57%. This study also analyzed organ function tests as possible predictors to survival, although none were shown to be significant in this study. Not all patients in their study received a VAD at the spoke hospital, but it concluded that patients in cardiogenic shock may have better outcomes after referral to a large center.

R. J. Morris et al. (2005) conducted a prospective study of VAD supported patients at the University of Pennsylvania Hospital from 1997 to 2000. They separated their subjects into two cohorts: those who received a VAD at their institution (n= 76) or those who were transferred

from another hospital with a VAD already implanted for cardiac support (n=28). Analysis of their transferred patients showed a survival rate of 32%. All of these survivors went on to receive a heart transplant. This study differs from the Columbia experiences because they focused on only patients with VAD support. However, this study did not have many patients who were transferred to their hospital and also did not look at long-term survival.

Another study published by Gonzalez-Stawinski et al. (2006) examined the regional referral system for patients who were transferred to the Cleveland Clinic Foundation with an acute mechanical support device. This study reported the outcomes and variables that could influence survival of these patients. Thirty-nine patients were studied in a retrospective review from 1995-2003. The majority (85%) of the transferred patients were on VAD support, but the study also included patients who arrived on other types of cardiogenic support. Their survival rate was calculated to be 38%. Almost half were able to be weaned from support, while the others received long-term VAD support and/or heart transplantation. They concluded that patients who had undergone less complex surgical procedures were more likely to survive.

This study seeks to expand our knowledge of patient outcomes after transfer to a tertiary cardiac center with a short-term VAD for cardiogenic support. Examining patients' clinical status upon arrival and examining their survival may identify variables that are important in predicting survival for future patients. Most of the previous studies have not reported on the long-term outcomes of these patients, nor did they look at specific clinical variables such as laboratory tests, hemodynamics, and medications upon arrival.

CHAPTER 3: Research Design and Methodology

Study Design

This analysis is a single-center retrospective study of patients transferred to UMHS with a VAD for short-term cardiogenic support. The study was approved by the Eastern Michigan University Human Subjects Committee and the University of Michigan's IRBMED prior to data collection. A waiver of consent was granted for this study.

Study Population

Patients satisfying the study inclusion criteria were identified under the guidance of UMHS faculty advisor Francis D. Pagani, MD, PhD, Associate Professor of Surgery in the Section of Cardiac Surgery.

Inclusion/Exclusion Criteria

Subjects were included in this study if they were transferred to UMHS from an outside hospital after implantation of a short-term cardiac assist device for cardiogenic support. No age or other physiological limitation was established.

Patients on extracorporeal-membrane oxygenation (ECMO) were excluded from this study in order to maintain homogeneity of the subject population by eliminating patients who may be in respiratory failure.

Data Collection

Medical records were obtained for all subjects from the UMHS Health Information Management Department and the CareWeb system of electronic records at UMHS. Outside hospital records were reviewed only if they were already part of the patient's medical record at UMHS. Intensive Care Unit (ICU) critical care sheets were reviewed for the patients' first 24 hours at UMHS in order to determine their clinical status at the time of transfer. Variables that

were captured included, but were not limited to, demographics, medical history, outside hospital information, clinical status upon transfer, laboratory test results, and hospitalization times.

Patient outcomes were ascertained by review of current medical records or collection of a death certificate. Patients who had not been seen by a UMHS healthcare member since their discharge and did not have current information in their medical records were considered alive if they were not identified in the Social Security Death Index.

Data Analysis

SPSS (SPSS Inc, Version 15.0) and Microsoft Excel were utilized for Data Analysis. Statistical analysis included examining overall study population characteristics using mean$\pm$standard deviation and proportions. Survival estimates were performed using Kaplan-Meier analysis. Univariable analysis of dichotomous variables was performed using a chi-square test. Continuous variables were subjected to univariable analysis by utilizing an independent t-test. Level of significance for inclusion into a multivariable model was defined at $p<0.05$. Multivariable analysis was performed by a Cox regression method importing values identified as significant by univariable analysis. Comparison of survival estimates was done by log rank analysis.

CHAPTER 4: Results and Data Analysis

Study Population

Forty-eight patients with a temporary VAD implanted for heart failure at an outside hospital and transferred to the University of Michigan Health System for further care were the subject of this analysis. All transfers occurred between September of 1997 and June of 2007. The age range of all patients was 14-77 years and the median age was 50.9 years. Figure 2 shows the age distribution of the population.

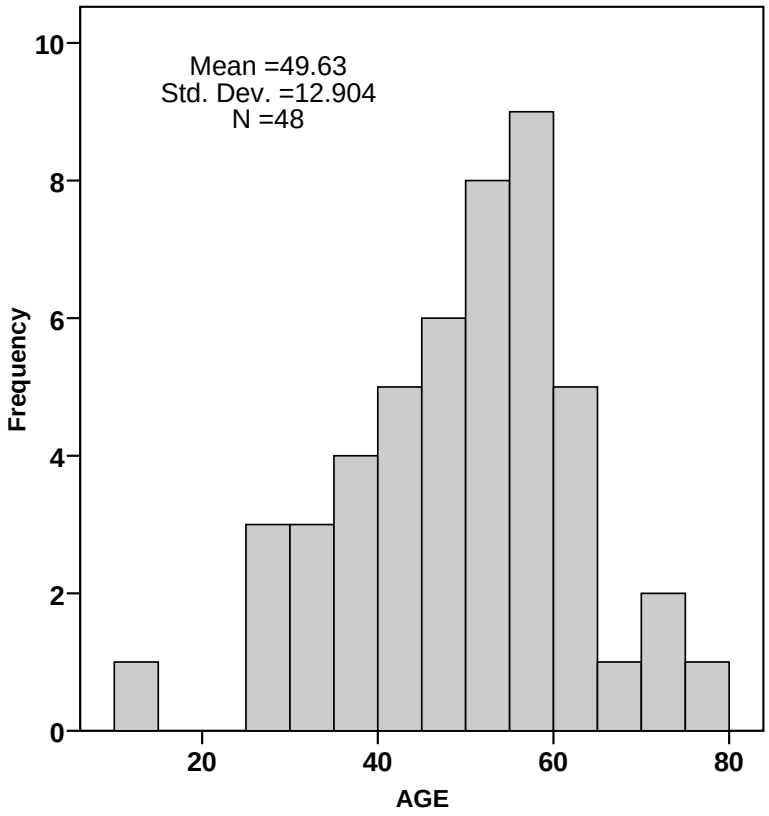


Figure 2. Age distribution.

The majority of these patients were Caucasian males in their late forties with ischemic heart disease and a history of hypertension and myocardial infarction (see Table 1). Analysis of their medical history showed that 60% of these patients did not have any cardiac procedures

prior to their implant, while those who had Coronary Artery Bypass Graft (CABG) surgery or percutaneous coronary interventions (PCI) were 15% and 25%, respectively.

Table 1

Demographics and Medical History

Variable	Overall No. (%)
Mean age (years)[a]	49.6 +/- 12.9
Range	14.8 – 77.3
Gender	
Male (%)	31 (65%)
Female (%)	17 (35%)
Race	
Caucasian (%)	39 (81%)
African American (%)	3 (6%)
Unknown (%)	6 (13%)
Body surface area (M^2)[a]	2.01 +/- 0.24
Body Mass Index	28.99 +/- 4.97
Co-morbidities	
Hypertension (%)	30 (63%)
Diabetes (%)	18 (38%)
COPD (%)	3 (6%)
Myocardial infarction (%)	35 (73%)
Etiology	
Ischemic (%)	40 (83%)
Nonischemic (%)	8 (17%)
Prior cardiac procedures	
None (%)	29 (60%)
PCI/PTCA[b] (%)	12 (25%)
CABG[c] (%)	7 (15%)

[a]Mean +/- Standard Deviation.
[b]PCI/PTCA = Percutaneous Coronary Interventions / Percutaneous Coronary Angioplasty
[c]CABG = Coronary Artery Bypass Graft

Implant Information

All patients presented to an outside hospital for either emergency service or routine care. During their visit they developed heart failure, and a temporary VAD was implanted for support. Table 2 shows that the majority of patients came from a large hospital. Experience and sophistication of medical care at the referring hospital was arbitrarily defined by the number of cardiac surgical procedures performed yearly at the referring institution. All hospitals were

located in Michigan or northwest Ohio and frequently refer patients to UMHS, which performs more than 800 cardiac procedures per year and is a regional transplant center.

Table 2

Information on Implant and Referring Hospital

Variable	Overall No. (%)
Referral Hospital[a]	
Small (0-200)	1 (2%)
Medium (201-500)	19 (40%)
Large (501+)	27 (56%)
Unknown	1 (2%)
Indication	
Cardiogenic Shock	11 (23%)
Postcardiotomy[b]	37 (77%)
Post-CABG	34 (71%)
Acute MI (< 7 days)	26 (54%)
Type of support	
Left (LVAD) only	18 (38%)
Right (RVAD) only	2 (4%)
Both (BiVAD)	28 (58%)
Specific Device	
ABIOMED BVS5000	46 (96%)
BioMedicus	2 (4%)
Days from Admission to Implant[c]	2.06 +/- 2.3
Days from Implant to Transfer[c]	2.1 +/- 3.4

[a]Based on number of cardiac procedures performed annually (in parentheses).
[b]Implantation occurring ≤ 24 hours after cardiac surgery.
[c]Mean +/- Standard Deviation

More than three-fourths of the patients required a VAD for postcardiotomy, which was defined as heart failure occurring within 24 hours of cardiac surgery. The majority of postcardiotomy patients were undergoing CABG surgery as treatment for their heart disease at the time of VAD implantation. More than one-half of all study patients were diagnosed as having had a heart attack within the seven days prior to receiving their implant.

Temporary VADs can be used to support either one of the ventricles or both ventricles depending on the severity of the heart failure. Most patients required biventricular support (BiVAD), meaning that two devices were implanted. The ABIOMED BVS5000 (ABIOMED,

Inc, Danvers, MA) is a popular device used in small hospitals to support patients in cardiogenic shock (see Figure 1). All but two of the patients transferred to UMHS were being supported by the ABIOMED BVS5000.

Clinical Status upon Presentation to UMHS

In order to identify variables that may be prognostic of survival, it was important to investigate the condition of a patient upon arrival from the referring hospital. Data were collected as close to transfer as possible. Table 3 shows the overall characteristics of this population including vital signs, hemodynamics, pump parameters, medication requirements, and other clinical factors.

The results show that every patient was in need of ventilator support (100%). Data on ventilator mode and rate were collected as well as PEEP and FiO_2 requirements. Intra-aortic balloon pumps (IABP) are devices placed in the aorta that increase blood flow to the heart. They are often used alone but may be used in combination with a VAD. One-fourth of the patients in this study arrived with an IABP in place.

Organ failure is a common risk of heart failure. When the kidneys are not functioning properly, dialysis is required. One type of dialysis used in these situations is continuous veno-venous hemofiltration (CVVH). Analysis showed that 23% of these patients required CVVH within the first 24 hours of presentation to UMHS.

Medication requirements upon arrival were collected from each patient's ICU flow sheet. Three categories of medications were used in this analysis. Inotrope medications help the heart beat stronger when it is incapable of doing so on its own. Vasoconstrictors contract the smooth muscle in blood vessels, causing them to constrict and restrict blood flow. Vasodilators

Table 3

Patient Status upon Arrival at UMHS

Variable	Value
Vital Signs/Hemodynamics	
Heart Rate (bpm)	89.0 +/- 22
Mean Systolic Blood Pressure	86.1 +/- 21
Temperature[a] (C)	37.2 +/- 0.8
Pulmonary Artery Pressure	28.3 +/- 11
Central Venous Pressure	18.7 +/- 8
Cardiac Output	4.9 +/- 1.1
LVAD flow (L/min)	4.6 +/- 0.7
RVAD flow (L/min)	4.6 +/- 0.9
Heart Rhythm	
Sinus	32 (67%)
Paced	8 (17%)
Atrial fibrillation	3 (6%)
Ventricular fibrillation	1 (2%)
Arterial Blood Gases	
O_2 Saturation (%)	93.4 +/- 6.1
pO_2	143.4 +/- 111
pCO_2	36.8 +/- 7.5
pH	7.41 +/- 0.1
Ventricular Support Required	48 (100%)
Ventilator Rate (breaths/min)	13.65 +/- 3.7
Ventilator Mode	
AC	20 (41.7%)
IMV	26 (54.2%)
PEEP (cmH_2O)	6.47 +/- 2.3
FiO_2 (%)	87.5 +/- 20.6
Intra-aortic Balloon Pump (IABP)	12 (25%)
Medication requirements	
Inotropes	28 (58.3%)
Vasoconstrictors	25 (52.1%)
Vasodilators	12 (25.0%)
Chest tube output (mL)[b]	537 +/- 483
Urine output (mL)[b]	1207 +/- 1276
Dialysis (CVVH)[c]	11 (22.9%)

[a]Tmax over first 24 hours.
[b]Over first 8 hours at UMHS.
[c]Within first 24 hours at UMHS.

act by opening blood vessels, which allows for more blood flow. More than half of the patients were on inotropic and/or vasoconstrictor support, while only 25% were on vasodilator support.

In addition to these clinical characteristics, laboratory values upon arrival were also explored. Those studied were chemistry panels, liver function tests, hematology, and coagulation. These tests are routinely done when a patient is brought to the hospital. Table 4 shows the mean, standard deviation, median, and range for the patient population.

Table 4

Laboratory Values upon Transfer to UMHS

Test	Mean	SD	Median	Range
Chemistry Panel				
Sodium (mMOL/L)	140.5	6.31	141.5	128 - 156
Potassium (mMOL/L)	4.29	0.813	4.2	2.4 - 6.5
Chloride (mMOL/L)	108.3	5.86	108.5	93 - 121
Bicarbonate (mMOL/L)	25.42	3.6	26.0	18 - 33
Urea Nitrogen (mg/dL)	25.6	12.23	23.0	8 - 60
Creatinine (mg/dL)	1.67	0.88	1.4	0.4 - 4
Glucose (mg/dL)	145.4	56.2	141.5	71 - 367
Calcium (mg/dL)	7.35	0.96	7.4	5.6 - 9.6
Phosphorus (mg/dL)	4.53	2.17	4.0	1.6 - 14.5
Protein – total (g/dL)	4.25	0.8	4.3	2.5 - 5.9
Liver Function				
Albumin (g/dL)	2.09	0.51	2.0	1.2 - 3.5
Aspartate Amino Transferase (IU/L)	1007	1592.8	379.0	25 - 7132
Alanine Amino Transferase (IU/L)	365.3	646.8	89.0	20 - 2797
Lactic Acid Dehydrogenase (IU/L)	1884.8	2307	936.5	292 - 8994
Alkaline phosphatase (IU/L)	66.62	52.11	50.0	25 - 322
Total Bilirubin (mg/dL)	2.21	2.41	1.2	0.4 -12.1
Hematology				
White Blood Cell Count (K/MM^3)	11.79	4.89	11.5	0.9 - 22.9
Hematocrit (%)	32.24	4.57	31.9	22.8 - 46.6
Hemoglobin (g/dL)	11.18	1.51	10.9	7.9 - 15.9
Platelet Count (K/MM^3)	104.6	49.25	97.0	31 - 231
Coagulation				
Prothrombin Time (sec)	15.7	13.5	12.3	10 - 100
International Normalized Ratio	1.56	1.4	1.2	0.9 - 10.1
Partial Thromboplastin Time (sec)	63.18	29.62	53.7	23.4 - 100

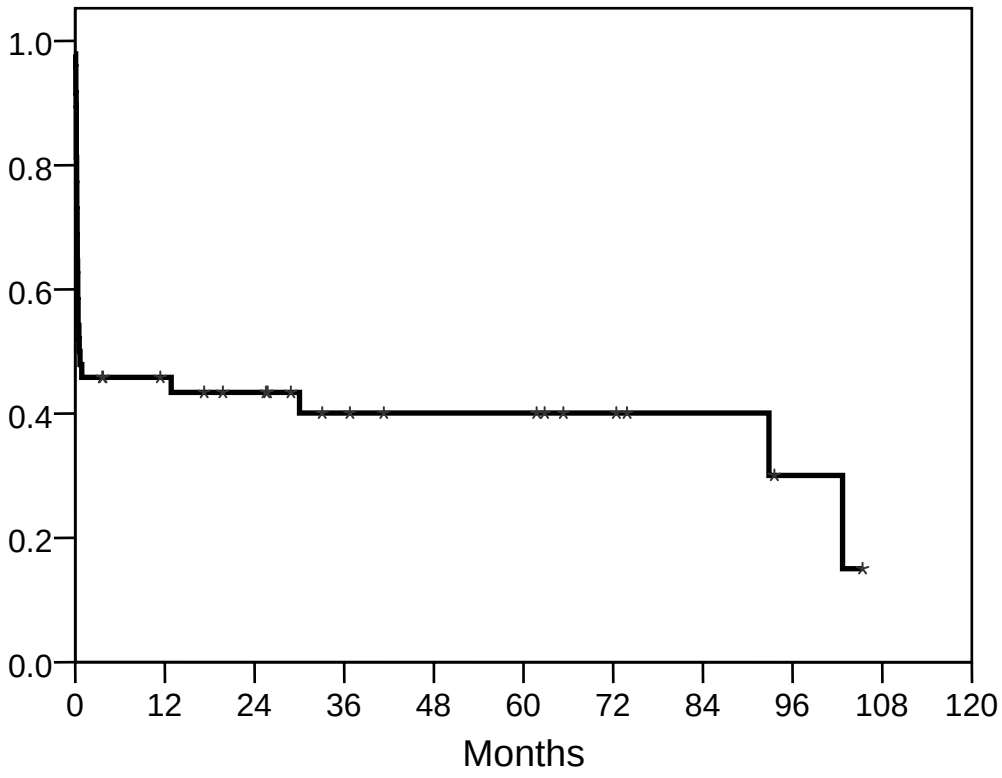
Overall Survival

Data captured from patient demographics, medical history, implant information, and clinical condition upon arrival all provide a clearer understanding of the condition in which these patients arrived for further care at UMHS.

After analysis of the patient's clinical condition, overall survival was examined. Twenty-eight of the patients had their deaths confirmed by the medical records. Thirteen patients were currently under the care of a UMHS physician and considered alive. The remaining seven patients were searched for in the Social Security Death Index. This national database was evaluated by Cowper, Kubal, Maynard, and Hayes (2002) and found to be a reputable source for researching morality. Two patients were listed as expiring. The remaining five patients were considered to be alive as of September 2007 and considered alive for data analysis. Median duration of follow-up for all patients was 18 days and survival to discharge from UMHS was calculated as 46%.

Figure 3 shows the Kaplan-Meier analysis of survival for all 48 patients following their temporary VAD implant. The analysis shows that the population appears to be divided into two roughly equal groups: those who die very soon after implant account for 54% of the population, and those who go on to live past 30 days after implant account for 46%.

The next step in the data analysis was to determine if any variables were significant between these two groups.



At risk:						
Month:	0	1	12	24	48	72
	48	22	19	16	9	6

Figure 3. Kaplan-Meier plot of survival in all patients.

Identification of Prognostic Variables of Survival at 30 Days Post-Implant

Univariable analysis was performed on all data points to determine which variables should be incorporated into a multivariable analysis to identify those factors prognostic of a patient's survival after implant. The population was separated into two groups for comparison: those who survived 30 days after implant of their temporary VAD (N=22) and those patients who expired prior to 30 days (N=26).

Table 5 shows the univariate analysis results of demographics and medical history. Age at the time of implant (p= 0.001) and a history of diabetes (p=0.000) were shown to be significant.

Table 5

Univariable Analysis of Demographics and Medical History for Those Surviving 30 Days Post Implant.

	30 Days Post Implant		
Variable	Survivors	Nonsurvivors	*p*
Mean age (years)[a]	43.2+/-12.6	55.1 +/- 10.5	0.001
Gender			
Male	12	19	0.232
Female	10	7	
Race			0.258
Caucasian	19	20	
African American	2	1	
Unknown	1	5	
Body Surface Area (M^2)[a]	1.96 +/- 0.23	2.06 +/- 0.25	0.167
Body Mass Index (kg/m^2)[b]	27.95 +/- 4.68	29.86 +/- 5.12	0.186
Co-morbidities			
Hypertension	13	17	0.768
Diabetes	2	16	0.0001
COPD	1	2	1.000
Myocardial infarction	17	18	0.746
Etiology			
Ischemic	16 (73%)	24	0.119
Nonischemic	6 (27%)	2	
Prior cardiac procedures			0.608
None (%)	14	15	
PCI/PTCA (%)	6	6	
CABG (%)	2	5	

[a]Calculated as √[(height in cm*weight in kg)/3600]
[b]Calculated as weight in kg/(height in m)^2

Information about the referring hospital and data relative to VAD implantation were also analyzed to determine if any of these factors might be predictive of a patient's status at 30 days (see Table 6). None of these variables were shown to be significant predictors of 30-day survival.

Table 6

Univariable Analysis of Implant and Referring Hospital for Short-term Survival

	30 Days Post Implant		
Variable	Survivors	Nonsurvivors	*p*
Referral Hospital			0.385
Small (0-200)	0	1	
Medium (201-500)	7	12	
Large (501+)	14	13	
Unknown	1	0	
Indication			
Cardiogenic Shock	16	21	0.732
Postcardiotomy[b]	6	5	
Post-CABG	13	21	0.122
Type of support			0.239
Left (LVAD) only	11	7	
Right (RVAD) only	1	1	
Both (BiVAD)	10	18	
Days from Admission to Implant	1.5 +/- 1.77	2.54 +/- 2.56	0.116
Days from Implant to Transfer	2.5 +/- 4.8	1.8 +/- 1.44	0.488

Clinical variables upon arrival were explored to determine if any were significant in a patient's survival at 30 days post-implant (see Table 7). Only two variables were calculated as being significant. One was the requirement for vasoconstrictor medications (p= 0.039). The other was the need for dialysis, specifically CVVH, within the first 24 hours at UMHS (p=0.006).

Table 7

Univariable Analysis of Variables Indicating Clinical Status upon Arrival

	30 Days Post Implant		
Variable	Survivors	Nonsurvivors	*p*
Vital Signs/Hemodynamics			
Heart Rate (bpm)	94 +/- 20	85.3 +/- 23	0.211
Mean Systolic Blood Pressure	88 +/- 19	85 +/- 23	0.620
Temperature[a] (C)	37.2 +/- 1.1	37.2 +/- 0.6	0.884
Pulmonary Artery Pressure	26.2 +/- 9.7	29.7 +/- 11.1	0.394
Central Venous pressure	18.9 +/- 7.0	18.6 +/-8.8	0.924
Cardiac output	4.66 +/- 0.7	5.03 +/- 1.4	0.297
LVAD flow (L/min)	4.59 +/- 0.7	4.68 +/- 0.7	0.714
RVAD flow (L/min)	4.61 +/- 0.9	4.62 +/- 0.9	0.993
Heart Rhythm			0.672
Sinus	14	18	
Paced	3	5	
Atrial fibrillation	1	2	
Ventricular fibrillation	1	0	
Arterial Blood Gases			
O2 Saturation (%)	94.4 +/- 4.9	92.6 +/- 7.0	0.304
pO2	129.9 +/- 72.6	154.8 +/- 135.6	0.445
pCO2	37.0 +/- 6.0	37.0 +/- 8.7	0.896
pH	7.42 +/- 0.1	7.40 +/- 0.1	0.497
Ventricular Support			
Ventilator Rate (breaths/min)	12.5 +/- 2.4	14.5 +/- 4.3	0.062
PEEP (cmH_2O)	6.3 +/- 2.1	6.6 +/- 2.5	0.671
Ventilator Mode			0.377
AC	7	13	
IMV	13	13	
FiO2 (%)	85.5 +/- 22.6	89.2 +/- 19.0	0.532
Intra-aortic Balloon Pump	3	9	0.095
Medication requirements			
Inotropes	13	15	0.543
Vasoconstrictors	7	18	0.039
Vasodilators	6	6	0.734
Chest tube output (mL)[b]	560 +/- 558	523 +/- 558	0.817
Urine output (mL)[b]	1079 +/- 967	1289 +/- 1453	0.614
Dialysis (CVVH)[c]	1	10	0.006

[a]Tmax over first 24 hours.
[b]Over first 8 hours at UMHS.
[c]Within first 24 hours at UMHS.

Values of laboratory blood tests were also tested in a univariable analysis, and the results are shown in Table 8. Univariate analysis showed that lower serum creatinine levels are significant (p=0.0001) in those that survive 30 days. Creatinine levels are used to determine kidney function, and a creatinine level of 0.7-1.3 mg/dL is considered normal. Two of the liver function tests were also shown to be significant by univariable analysis. AST (asparatate amino transferase) levels, which are often elevated in patients with cardiac disease, were significantly lower in survivors (p=0.041). The other significant test was LDH level (p=0.018), which is a measure of the amount of lactic dehydrogenase in the serum and an indicator of tissue damage.

Table 8

Univariable Analysis of Laboratory Variables

	30 Days Post Implant		
Variable	Survivors	Nonsurvivors	*p*
Chemistry Panel			
Sodium (mMOL/L)	139 +/- 5.6	142 +/- 6.8	0.195
Potassium (mMOL/L)	4.1 +/- 0.7	4.4 +/- 0.9	0.170
Chloride (mMOL/L)	108 +/- 6.6	108 +/- 5.3	0.939
Bicarbonate (mMOL/L)	25.8 +/- 3.5	25.1 +/- 3.7	0.534
Urea Nitrogen (mg/dL)	22.9 +/- 11.3	28.0 +/- 12.7	0.149
Creatinine (mg/dL)	1.19 +/- 0.46	2.07 +/- 0.96	0.000
Glucose (mg/dL)	130.6 +/- 40.0	157.9 +/- 65.1	0.094
Calcium (mg/dL)	7.1 +/- 0.7	7.5 +/- 1.1	0.120
Phosphorus (mg/dL)	4.5 +/- 1.6	4.5 +/- 2.8	0.962
Protein – total (g/dL)	4.4 +/- 0.7	4.1 +/- 0.9	0.329
Liver			
Albumin (g/dL)	2.11 +/- 0.4	2.07 +/- 0.6	0.782
AST(IU/L)	503.7 +/- 602	1449.9 +/- 2027	0.041
ALT (IU/L)	211 +/- 346	501+/- 810	0.126
LDH (IU/L)	976 +/- 541	2635 +/- 2894	0.018
Alkaline phosphatase (IU/L)	75.1 +/- 71.8	59.2 +/- 24.0	0.301
Total Bilirubin (mg/dL)	1.61 +/- 1.8	2.74 +/- 2.8	0.110
Hematology			
White Blood Cell Count (K/MM^3)	11.4 +/- 3.9	12.1 +/- 5.7	0.593
Hematocrit (%)	32.2 +/- 5.1	32.6 +/- 4.2	0.967
Hemoglobin (g/dL)	11.1 +/- 1.7	11.2 +/- 1.4	0.873
Platelet Count (K/MM^3)	118.5 +/- 43.4	92.8 +/- 51.6	0.071
Coagulation			
Prothrombin Time (sec)	12.9 +/- 3.1	18.0 +/- 17.9	0.193
International Normalized Ratio	1.27 +/- 0.35	1.8 +/- 1.86	0.189
Partial Thromboplastin Time (sec)	59.8 +/- 29.1	66.0 +/- 30.2	0.473

Multivariate Analysis to Determine Prognostic Variables of 30-Day Survival

Multivariate analysis was performed using those variables that were significant in the univariate analysis for 30 day survival. These variables are shown in Table 9. Variables that remained significant were age (p=0.015) and creatinine levels (p=0.004).

Table 9

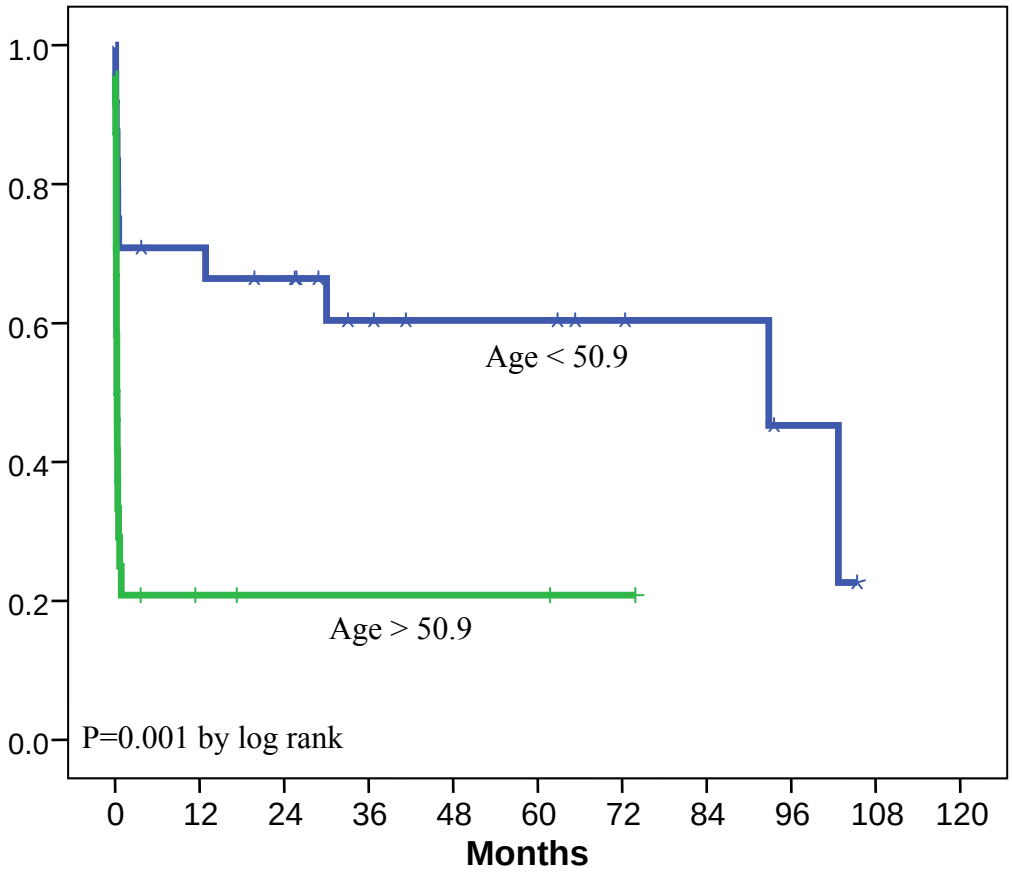
Multivariable Analysis of Variables Identified in Univariable Analysis of 30-Day Survival

Variable	30 Days Post Implant		
	Survivors (N=22)	Nonsurvivors (N=26)	*p*
Demographics/Medical History			
Age	43±13	55±11	0.015
Diabetes	2 (11%)	16 (53%)	0.087
Other support			
Dialysis (CVVH)	1 (5%)	10 (38%)	0.350
Vasoconstrictors	7 (32%)	18 (69%)	0.096
Laboratory values			
Creatinine	1.2±0.5	2.1±1.0	0.004
AST	503±601	1449±2027	0.510
LDH	976±540	2635±2894	0.196

Long-term Survival Based on Age and Serum Creatinine Levels

As previously shown, 54% of the patients transferred to UMHS with a temporary VAD did not survive 30 days after implant. Age and serum creatinine levels were shown to be significant prognostic variables of this survival based on multivariable analysis. Figure 4 shows a Kaplan-Meier analysis comparing patients who are younger or older than the median age of 50.9.

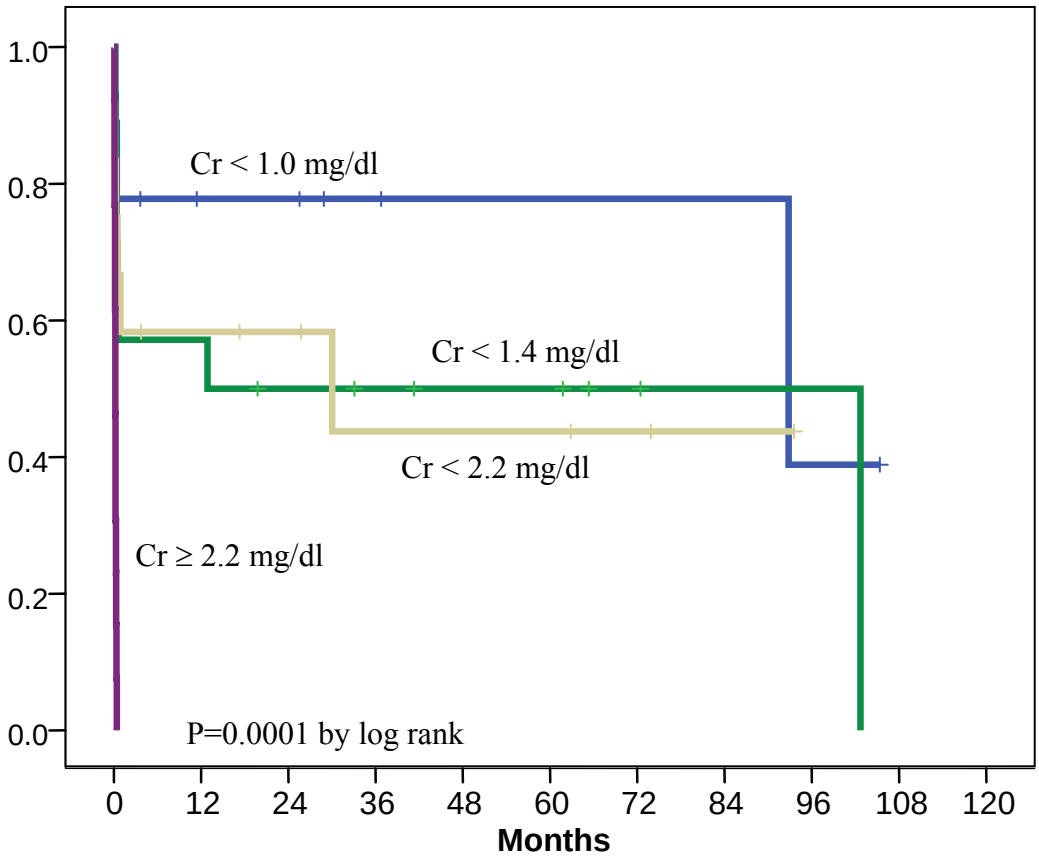
Statistical analysis reveals the survival of those younger than 50.9 to be significantly longer than those older than 50.9 ($p=0.001$).



At risk:						
Month:	0	1	12	24	48	72
< 50.9	24	17	16	14	7	5
> 50.9	24	5	3	2	2	1

Figure 4. Long-term survival dichotomized by median age

Creatinine levels were shown to be significant for 30-day survival. Kaplan-Meier analysis of the quartiles is shown in Figure 5. Patients with a creatinine level less than 1.0 mg/dl had an excellent chance of surviving not only 30 days after their implant, but also long term. None of the 13 patients with poor kidney function, as evidenced by their high creatinine levels (≥ 2.2 mg/dl), survived past 30 days.

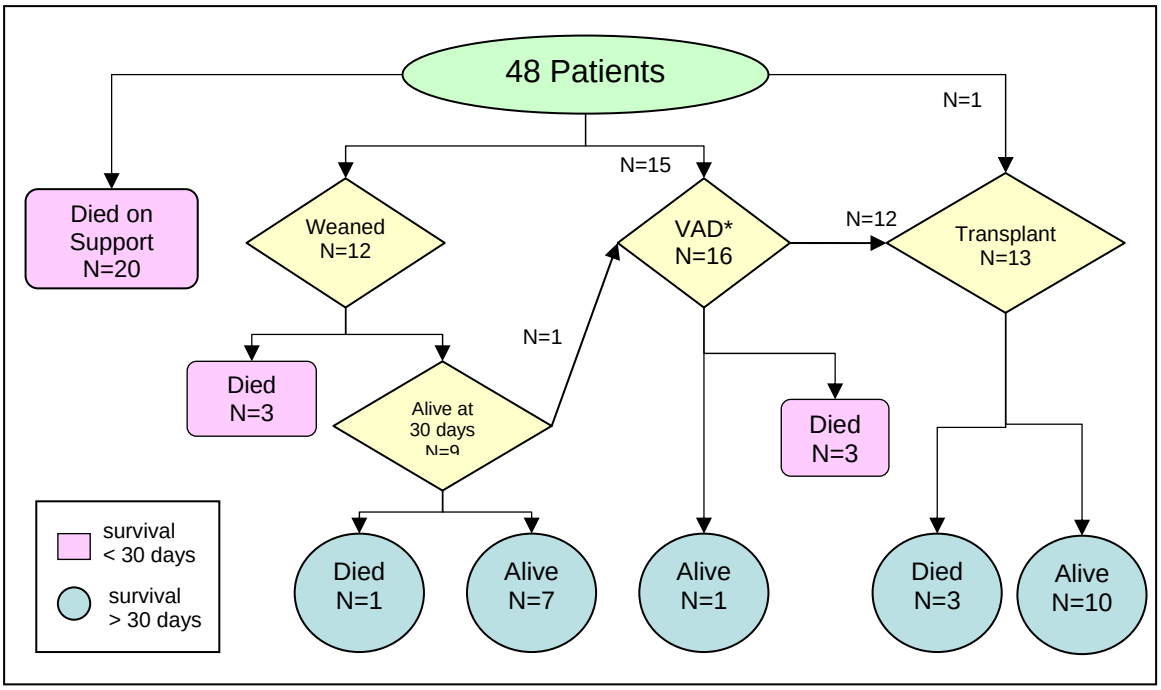


At risk:						
Month:	0	1	12	24	48	72
< 1.0 mg/dl	9	7	5	5	2	2
< 1.4 mg/dl	14	8	8	6	4	2
< 2.2 mg/dl	12	7	6	5	3	2
≥ 2.2 mg/dl	10	0	0	0	0	0

Figure 5. Long-term survival of patients based on serum creatinine levels (grouped by quartiles)

Patient Outcomes

Twenty patients in this study died while still on short-term mechanical support after being transferred to UMHS for further care. The six remaining patients who did not survive 30 days were either weaned (N=3) or received a more permanent VAD (N=3) but ultimately died from complications of their heart failure. A flowchart of all patient outcomes is shown in Figure 6.



*Long-term VADS

Figure 6. Patient outcomes (as of 09/17/2007)

Of the 22 patients who survived past 30 days post-implant, 16 went on to receive a long-term VAD. Thirteen of the survivors ultimately received a heart transplant, and 10 of the transplant recipients are still alive.

Further analysis of current survival revealed that most have lived past one year (see Figure 7). In addition, 82% (n=18) of those surviving 30 days post-implant are currently alive with the potential of living greater than 5 years and perhaps more.

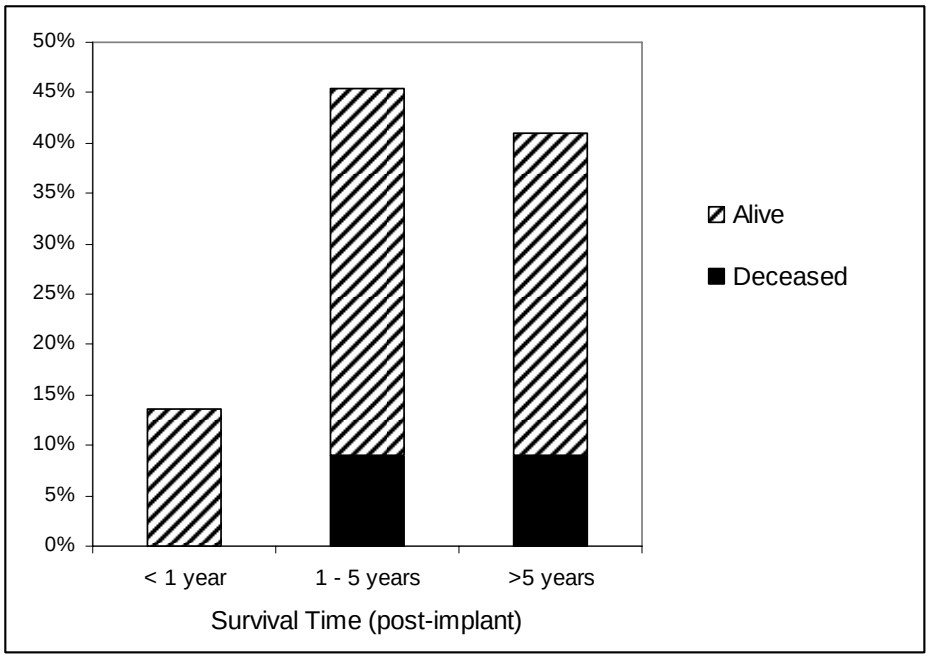


Figure 7. Current survival past implant of those surviving >30 days post-implant

CHAPTER 5: Discussion

Heart failure, either chronic from an underlying cardiovascular disease, or acute, such as failure to wean from cardiopulmonary bypass after heart surgery or cardiogenic shock from an MI, can cause sudden death if not treated immediately. Unfortunately, many people are not near a hospital when treatment is required and even fewer are near a tertiary cardiac center, where more options are available to them. This study was designed to examine those patients who received a short-term VAD for treatment of their heart failure at a hospital other than UMHS and were subsequently transferred to UMHS for further treatment.

The majority of patients in this study were Caucasian males with a median age of 50.9 years, a history of hypertension, myocardial infarction, and ischemic heart disease. Implantation of a short-term device was required due to postcardiotomy after CABG surgery and required biventricular support. Upon transfer to UMHS, more than half of them required inotrope therapy and vasoconstrictors, while less than one fourth required dialysis.

This is similar to the experiences of Gonzalez-Stawinski et al. (2006) at the Cleveland Clinic Foundation, in which their median age was 51 years and 85% required a temporary VAD for postcardiotomy. They did report a much smaller percentage with ischemic disease (46%) as compared to this analysis.

Kaplan-Meier analysis of the UMHS patients in this study showed that just over half died within the first 30 days after implantation of their short-term device. Gonzalez-Stawinski et al. (2006) reported their survival rate was 38%, and Morris et al. reported a survival rate of 32%. Separate centers are likely to have differing experiences, and results cannot necessarily be considered comparable. In addition, long-term treatments for heart failure are constantly improving, and the treatment given by the referring centers may impact the survival rate.

Identification of prognostic variables for short-term survival revealed age and kidney function, as shown by creatinine levels, as significant. Younger patients presenting to UMHS with better kidney function were more likely to survive 30 days post-implant. These patients were also most likely to be eligible for heart transplantation, thereby increasing the likelihood of long-term survival. Gonzalez-Stawinski et al. (2006) also reported that younger age, less complex surgery, and organ function were significant factors in their survival analysis.

Previous studies did not examine survival past one year. Patients in this study were very likely to live more than 5 years after implant if they survived the initial 30 days. The majority of them received a heart transplant during that time, most likely due to the fact that their younger age and better kidney function presented them as good candidates for transplant.

Experience at UMHS is consistent with these other reports that have shown that hub and spoke referral systems increase survival.

CHAPTER 6: Limitations

This study is a single center's experience on patients transferred with a short-term VAD for cardiogenic support. This study does have the limitations of being a retrospective. Some data elements were found to be missing or incomplete. In addition, this was a small study population, and some variables may truly be significant when examined in a larger population.

CHAPTER 7: Conclusion

Patients that go into cardiogenic shock are often treated by implantation of a temporary VAD at a community hospital. Once implanted, these patients will often be transferred to a tertiary care center for further treatment as part of a "hub and spoke" referral system. Identification of prognostic variables significant in survival of these patients could affect patient care decisions at both the referring and receiving hospital. The experience of previous patients transferred to the University of Michigan Health System with a temporary VAD for cardiogenic shock identified two variables that were indicative of survival. Patients who survived 30 days post-implant were generally younger and had better kidney function as measured by serum creatinine. The majority of the surviving patients eventually received a heart transplant, most likely because their younger age and better kidney function greatly improved their chances of being a transplant candidate and possibly increased their chances of survival after transplant.

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