Efficacy of the HeartWare Ventricular Assist System in Bridging Adult Heart Failure Patients to Transplantation: A Systematic Review.

Annie Mastrandrea
Pacific University
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Abstract
Background: Heart failure has a high mortality rate with 20% dying within the first year after diagnosis. The gold standard of treatment has been cardiac transplant however the shortage of donors continues to be a problem. Left ventricular assist devices (LVAD) have been bridging patients to transplantation, but they come with many complications. The HeartWare HVAD system is a promising new smaller LVAD that will hopefully improve the survival of heart failure patients awaiting transplant. The evidence of the clinical trials in this review was evaluated using the GRADE system.

Method: An exhaustive search of available medical literature was conducted using Medline, CINHAL, and Evidence-Based Medicine Reviews Multifile. The terms used in the search included the words, “Heartware, HVAD, and transplant” with limits set for human subjects, the English language, and articles published since the year 2000. After one clinical trial was found the author of that trial was searched to find the second article then included in this review.

Results: Two studies were reviewed in this systematic review. Both found that the HeartWare device was effective and safe in bridging end-stage heart failure patients to transplantation. The first study showed survival was 91% at 180 days and 86% at one year and the second study showed survival was 90% at 180 days, 84% at one year, and 79% at two years.

Conclusion: The HeartWare HVAD system is effective and safe in bridging end-stage heart failure patients to transplantation.

Keywords: HeartWare, HVAD, transplant, heart failure

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Annie Mastrandrea

A course paper presented to the College of Health Professions in partial fulfillment of the requirements of the degree of Master of Science

Pacific University School of Physician Assistant Studies

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Faculty Advisor: Dr. Mark Pedemonte
Clinical Graduate Project Instructors: Torry Cobb, DHSc, MPH, PA-C & Annjanette Sommers MS, PAC
Biography

Annie Mastrandrea is a native of Oregon where she majored in Biology and minored in music at Linfield College. After completion of her undergraduate degree, she worked as an oral and maxillofacial surgical assistant for two years where she discovered a love of working in medicine with patients. She was accepted into the Pacific University Physician Assistant Program and will be graduating in August, 2011. She is excited to start her career as a Physician Assistant and to get back into her passion of vocal performance.

Acknowledgements

To Pacific Faculty: Thank you for your endless amount of time and passion to teach us budding Physician Assistants. We will make you all proud.

To my parents: Thank you for your love and support throughout these busy, stressful years. I could not have done any of it without your support. Thank you for instilling in me a passion to serve. You both mean the world to me.
ABSTRACT

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INTRODUCTION

Background

According to the Centers for Disease Control, heart failure in the United States affects approximately 5.8 million people (Lloyd-Jones et al., 2010). The average American has a one in five lifetime risk of developing heart failure after the age of forty (Lloyd-Jones et al., 2010). Once diagnosed with heart failure, one in five people will die from the disease in less than one year (Lloyd-Jones et al., 2010). Heart failure is an epidemic affecting the worldwide population and the number of people being diagnosed with the disease is continuing to climb (Strueber et al., 2011). With this anticipated steady rise of people diagnosed with heart failure, it is imperative that current treatments are improved and new treatments are developed.

Heart failure is failure of the heart muscle to effectively pump blood to the vital organs of the body, which can lead to multiple organ failure, and eventually death. The two different types of heart failure are diastolic and systolic and both types are caused by dysfunctional ventricles of the heart (Colucci, 2009). Symptoms of heart failure include shortness of breath on exertion, dyspnea while laying down, edema in the legs and feet, and fatigue (Colucci, 2009). The most common causes of heart failure in the U.S. include, but are not limited to, coronary artery disease, hypertension, and diabetes (Lloyd-Jones et al., 2010).

Treatment for heart failure as the disease progresses can be thought of as a continuum. Often treatment is determined by the New York Heart Association (NYHA) functional classification system. The NYHA classification categorizes
patients with heart failure into four classes based on how many physical limitations a patient has from their disease. A heart failure patient with no physical limitations is a class I and a heart failure patient with severe physical limitations is a class IV (Colucci & Pina, 2011). Goals for heart failure treatment include symptom control, stopping or reversing myocardial dysfunction, and reducing mortality (Colucci, 2009). Initial treatment, if applicable, is aimed at correcting the underlying cause of the heart failure, such as hypertension, coronary artery disease, and/or valvular disease. Patients should then be treated with lifestyle modifications like smoking cessation, sodium restriction, and weight reduction if overweight (Colucci, 2009). The most common pharmacologic therapies to be started include in order: loop diuretics for fluid overload control, ACE inhibitors or angiotensin II receptor blockers (ARBs) for hemodynamic benefit, and beta blockers that are cardio-protective (Colucci, 2009).

Unfortunately, there are some patients who do not respond to these pharmacologic therapies. These patients have refractory heart failure and they require different treatments due to the severity of their illness. Therapy is guided towards use of intravenous inotropes and vasodilators, which require these patients to be hospitalized (Colucci, 2010). Inotropes and vasodilators will help relieve symptoms and improve hemodynamics in these patients. Another treatment is ultrafiltration which moves fluid from the interstitial compartment into the vascular space and then from the body (Colucci, 2010). If still refractory to treatment then cardiac transplantation and/or mechanical cardiac support should be considered.
Cardiac transplantation is reserved for those patients with end-stage heart failure or NYHA class III or IV. Transplantation can improve survival and the quality of life for many of them. In one study, survival after transplantation was 85% after one year and 79% after three years (Colucci, 2010). Unfortunately, there is a higher need for organs than there are donors by a factor of 10 and thus, many patients die awaiting transplantation (Colucci & Pina, 2011).

Mechanical assist devices are designed to add support to failing left and/or right ventricles of the heart. These ventricular assist devices have even been shown to improve contractile properties of the heart, reverse the down-regulation of beta receptors in the heart, and correct anatomical abnormalities of the heart. There are many different types of mechanical support device that are designed for either short-term use as in a bridge to transplant, or for long-term use as in destination therapy when a patient is ineligible for transplantation (Jeevanandam & Eisen, 2010).

The short-term devices consist of paracorporeal ventricular assist devices that are located outside the body such as the Thoratec Ventricular Assist Device and the Abiomed AB 500 (Jeevanandam & Eisen, 2010). Both of these devices can be configured to assist the left and/or right ventricles and are FDA approved. There are many complications with these two devices that involve bleeding, infection, and thromboembolism and thus they should only be used as temporary solutions (Jeevanandam & Eisen, 2010).

The long-term devices can be used for either bridge to transplant or as destination therapy alone. The three major FDA approved left ventricular assist
devices (LVAD) used today, are the WorldHeart Novacor and the Thoractec HeartMate XVE, and HeartMate II (Jeevanandam & Eisen, 2010). The HeartMate XVE and the Novacor pumps produce a pulsatile flow of blood mimicking the heart, whereas the HeartMate II pump produces a continuous axial flow (Jeevanandam & Eisen, 2010). All of these devices are implanted internally below the diaphragm and are connected to the left ventricle and aorta with a pump mechanism in between. To place these devices requires a sternotomy and creation of a pump pocket in the abdominal cavity. As with the short-term devices these devices also have complications with bleeding, infection, and thromboembolism (Jeevanandam & Eisen, 2010).

The newest LVAD systems include the HeartWare HVAD, Ventrocor VentrAssist LVAD, and the Terrumo Duraheart which are all currently involved in clinical trials in the U.S. and thus, are not currently FDA approved. These devices have a different mechanism of action than the other LVADs and provide a centrifugal continuous flow. These devices are also more energy efficient, less prone to cause thromboembolism, easier and faster to insert resulting in less time on the bypass machine, and are more durable possibly as long lasting as 10 years (Jeevanandam & Eisen, 2010).

In January 2009, the HeartWare HVAD system was approved in Europe (CE Mark authorized) and has since started undergoing clinical trials in the U.S. (LaRose, Tamez, Ashenuga, & Reyes, 2010). This system is very promising as a device for a bridge to transplant and even as a destination therapy for those ineligible for transplantation. The system is very small, weighing only 145 grams,
and is implanted in the pericardial space, eliminating the need for a pump pocket in the abdominal cavity which would be a second surgical incision (LaRose et al., 2010). It has a broad-based impeller that is suspended in between the two housing pieces. This is unique to this product since the impeller does not come into contact with either of the housing pieces, eliminating wear on the device (LaRose et al., 2010). The impeller is the only moving part of the device and is powered by electromagnetic force. The device is powered by either an AC/DC power source or lithium-ion batteries that will last up to 12 hours (LaRose et al., 2010). It also has a touch screen tablet PC that shows how the system in operating and monitors battery life. The batteries and tablet PC maybe worn on a belt or carried over the patient’s shoulder allowing mobility (LaRose et al., 2010). This system has the capacity to be the next best LVAD on the market due to the ease of implantation, small size, durability, longevity of cardiac support, and the ease of mobility for the patient.

Purpose of the Study

The purpose of this paper is to perform a systematic review of the literature on the use of the HeartWare Ventricular Assist System in bridging heart failure patients to transplantation. The body of evidence will be evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool developed by the GRADE Working Group (Guyatt et al., 2008).

METHOD
An extensive literature search was conducted using Medline, CINHAL, and Evidence-Based Medicine Reviews Multifile. These databases were accessed through the Pacific University Library system. The keywords searched, individually and in combination, included: “HeartWare, HVAD, and transplant”. The search was limited to human subjects, the English language, and articles published since the year 2000. Only the articles that included “HeartWare, HVAD, and transplant” in combination were included. This resulted in four articles and, of these, only one was a clinical trial which was included in this systematic review. To find more articles, the first clinical trials’ primary author G.M. Wieselthaler was searched which resulted in 19 articles. Of these articles only two were clinical trials on the HeartWare Ventricular Assist System, one was the first clinical trial found and the other article was new and is included in the review.

RESULTS

The first clinical trial reviewed titled the “Initial Clinical Experience With a Novel Left Ventricular Assist Device With a Magnetically Levitated Rotor in a Multi-Institutional Trial” was a prospective, non-randomized, single-arm clinical trial for the HeartWare HVAD system (Wieselthaler, O’Driscoll, Jansz, Khaghani, & Strueber 2010). The goal of the study was to look at the efficacy of the HVAD system as a bridge to cardiac transplantation for patients with refractory end-stage heart failure. There were 23 participates that were enrolled during the period between March 2006 and November 2007 at five centers located in Europe and Australia (Appendix A. Table 1). At the time of enrollment, all of the
participants were in NYHA class IV heart failure and were receiving intravenous
inotropic therapy (Appendix B. Table 2). The primary end point of the study was
survival to cardiac transplantation or to 180 days on the pump. If the patients
remained on the pump longer than 180 days then they were followed up to one
year. All of the pumps were implanted using the same procedure, through a
standard sternotomy and patients were put on a normothermic cardiopulmonary
bypass machine. Post-operatively the patients were anti-coagulated with
unfractionated heparin which was later replaced with warfarin to achieve an INR
of 2.5-3.0. (Wieselthaler et al., 2010)

The results of this first study showed that survival was 91% at 180 days
and 86% at one year (Wieselthaler et al., 2010). The mean duration of support of
the device was 167 ± 143 days. After one year from the start of the study, five
patients received a cardiac transplant, 14 were still on the HVAD device, one
patient was weaned off the device, two patients died from multi-organ failure
caused by septicemia, and another patient died of an intracranial hemorrhage.
The adverse events after one year from the start of the study included, infections
(not related to the device), bleeding, cardiac arrhythmias, hemolysis, pleural
effusions, pneumonia, device replacement, renal dysfunction, right heart failure,
and cerebrovascular accidents. Thrombus formation occurred inside the pump
leading to replacement in six of the first 13 implants. This was suspected to be
due to a manufacturing defect which was later fixed and no other issues have
occurred since. The mean time on the cardiopulmonary bypass machine was 67
minutes and there were no complications with the implant procedures. There
were 21 patients that were able to be discharged home and only nine post-implant re-admissions to the hospital for complications. Prior to the study year, this same group of patients had been admitted to the hospital for heart failure treatment $2.7 \pm 3$ times per patient-year (Wieselthaler et al., 2010). The authors of the study state that this study has comparable results in initial clinical trials of other left ventricular assist devices, which demonstrates efficacy of the device. They also talk about how this is an important device in the context of support to heart failure patients awaiting transplantation in countries where the wait time can be as long as 269 days (Wieselthaler et al., 2010). Their conclusion was that the HVAD system is effective and safe as a bridge to transplantation and is comparable with other left ventricular assist devices. The study also showed that the pump provided great hemodynamic support and that myocardial recovery is possible when the device is used for at least one year (Wieselthaler et al., 2010).

The second clinical trial included in this review entitled, “Multicenter Evaluation of an Intrapericardial Left Ventricular Assist System” was the same type of study, had the same goals, took place in the same locations, and patients underwent the same implant procedure as in the first study (Strueber et al., 2011). The trial enrolled 50 NYHA class IV participants between March 2006 and December 2008 (Appendix A. Table 1). All of the patients enrolled were receiving intravenous inotropic therapy (Appendix B. Table 2). The patients were followed up until June 2009 for adverse events or until they reached the end points. The primary end points were survival to cardiac transplant, survival to 180 days, or cardiac recovery enough to explant the pump. The study was done in compliance
with the U.S. Food and Drug Administration guidelines. Anti-coagulation therapy was initiated post-operatively with IV heparin. Patients were then transitioned to warfarin (achieved an INR of 2.0-3.0) and aspirin or clopidogrel. After implantation, patients were given rehabilitative care and education about the device (Strueber et al., 2011).

The survival rates to transplantation, cardiac recovery with device explant, or ongoing cardiac support with the device was 90% at 180 days, 84% at one year, and 79% at two years (Strueber et al., 2011). These results were compared with the Seattle Heart Failure Model (SHFM) which estimated survival of the study group with only medical therapy. The SHFM estimated the cohort survival to 180 days at 73 ± 3%, 58 ± 4% at one year, and 40 ± 4% at two years. The mean duration on the device was 348 days. As of May 2010, 20 patients had cardiac transplants, four patients had cardiac recovery and the device was explanted, and 17 were still supported on the device. Nine patients died while on the support device between 13-515 days on the device. Causes of these deaths include sepsis, multi-organ failure, and hemorrhagic stroke. Other adverse events included infection at the driveline exit site, sepsis, bleeding, ventricular arrhythmias, ischemic and hemorrhagic stroke, transient ischemic attacks, device replacement, and right heart failure requiring right ventricular assist devices. Forty-seven patients were able to be discharged home and there were 53 re-admissions to the hospital. This was a 74% reduction of re-admission to the hospital compared with the average re-admission rate of the cohort a year prior to the study (Strueber et al., 2011). The authors of this study concluded that the
HVAD system can effectively and safely bridge end-stage heart failure patients to transplantation. They commented that the two-year survival rate on the HVAD system was similar to that of a cardiac transplant, which could open the doors to using this device as a destination therapy. They also stated that the patients on the device had improvements in circulation and had low adverse events. The size and location of the device was of benefit as well, eliminating the need for entry into the abdominal cavity for placement of a pump pocket. Less time on the cardiopulmonary bypass machine was needed as a result of the size and location of the device.
DISCUSSION

Today, transplantation continues to be the best option for the treatment and survival of end-stage heart failure. However, there is a 10-fold difference in the number of patients needing a heart transplant and those who will actually receive one before it is too late (Lloyd-Jones et al., 2010). The need for improved ventricular assist devices or other treatment strategies for end-stage heart failure has never been more apparent.

The HeartWare HVAD system is a promising ventricular assist device for the support of patients to transplantation as shown by the two clinical trials in this review. The first clinical trial reviewed entitled, “Initial Clinical Experience With a Novel Left Ventricular Assist Device With a Magnetically Levitated Rotor in a Multi-Institutional Trial” was a prospective, non-randomized, single-arm clinical trial (Wieselthaler et al., 2010). This means that the trial is an observational study and, more specifically, a prospective cohort study. Cohort studies follow patients who receive a particular treatment or intervention and compare them with a similar population of patients that did not receive the intervention. In this case, this study did not directly compare the group of patients that received the HVAD with a group of patients that did not receive the HVAD device, making it a single arm study. The study was also prospective meaning the patients were involved in the study prior to the intervention. The outcomes of this first study are very promising showing that 91% of the patients had survived on the device until 180 days and that 86% had survived on the device for one year (Wieselthaler et al., 2010). Some of those patients have received cardiac transplants. This study also
concluded that the patients had fewer re-admissions to the hospital, even though
the data that shows this is confusing to interpret. This is just one of the multiple
limitations of the study. Another limitation was the small number of patients
involved and the study design. The study would have been of higher quality if
there were two groups of patients randomized to two different interventions
instead of one group all receiving the same intervention. By not comparing this
intervention with either medical therapy alone or another LVAD device the
outcomes of the study stand alone and do not show how survival is effected with
the HVAD device as a bridge to transplant. A major limitation to the study was
the fact that G.M. Wieselthaler (one of the study’s authors) is a member of the
Medical Advisory Board of HeartWare Inc. and his hospital receives grants from
the company (Wieselthaler et al., 2010). This means that there is a potential for
bias in how the study was conducted, who was involved, and how the data was
reported in the study.

The second clinical trial reviewed entitled, “Multicenter Evaluation of an
Intrapericardial Left Ventricular Assist System” was also a non-randomized,
single arm, prospective cohort study (Strueber et al., 2011). The outcomes of this
trial were very similar to those of the first study, showing that there was a 90%
survival rate to 180 days, 84% survival rate at one year, and 79% survival rate at
two years on the device (Strueber et al., 2011). In this trial the results were
compared with the Seattle Heart Failure Model (SHFM) which estimated the
survival of the study group during the same time with only medical therapy. The
SHFM estimated the cohort survival to 180 days was approximately 73%, 58% at
one year, and 40% at two years (Strueber et al., 2011). If these estimates are correct then this study does show survival was improved with the use of the HVAD device. However these estimates are theory and are not as powerful as a randomized two arm control trial would be. This would be considered a limitation to the study. Another limitation includes the study design not being randomized or blinded. The study does state, that, after the first trial it would be unethical to randomize patients to the HVAD device or continued medical support since there was already data showing that survival was improved with the HVAD device. Even though this study had more patients than the first, it was still a very small group of patients. Other limitations that were stated include patient selection bias and variability in how the patients were cared for while in the hospital (Strueber et al., 2011). A large limitation to this study is that fact that HeartWare Inc., the manufacturer of the system, was the financial sponsor of the study (Strueber et al., 2011). Unlike the first study, this study does not have a paragraph at the end of the paper stating that G.M. Wieselthaler (one of the authors) is a member of the Medical Advisory Board of HeartWare Inc. and his hospital receives grants from the company. This information was written in very small text font at the bottom of the first page. In contrast to the first study, this paper points out that the authors M. Strueber, P. Jansz, and A. Khaghani are Principle Investigators to HeartWare Inc. (Strueber et al., 2011). Authors M. Strueber is a consultant to HeartWare Inc., G. O’Driscoll is a HeartWare advisory board member and W. Levy has received research funding from HeartWare Inc. (Strueber et al., 2011).
It is concerning that every author of this study has a connection to the manufacturer of the HeartWare HVAD system, either financially or as an advisor.

The purpose of this systematic review was to review the literature on the efficacy of the HVAD system in bridging end-stage heart failure patients to transplant. To evaluate the literature the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used. It was developed by the GRADE Working Group for evaluating the quality of outcomes and recommendations of clinical trials (Guyatt et al., 2008). The GRADE system is an important tool for helping practitioners evaluate the strength of recommendations and whether or not they should implement the recommendations into their practice. The GRADE system works by categorizing the trials together with the same outcomes. For each outcome the quantity and type of clinical studies are factored together to determine a starting grade. The high starting grade is awarded to randomized control trials (RCT) and the low starting grade is awarded to observational studies. From there the starting grade is either increased or decreased based on different factors that affect the quality of evidence. At the end of the table all of the outcomes and grades are factored together to give one grade of either ‘high, moderate, or low’ quality of evidence (Guyatt et al., 2008). From here the recommendations are either categorized into ‘strong’ or ‘weak’ recommendations based on the quality of evidence and the benefits and harms of the intervention (Guyatt et al., 2008). As with many grading systems the GRADE system is subject to individual biases of the grader. Yet this system claims to be superior to many other systems because it was developed
by an international group of guideline developers and is used by many world renown organizations including the World Health Organization, the American College of Physicians, UpToDate, and the Cochrane Collaboration to name a few (Guyatt et al., 2008).

The GRADE table for the clinical trials in this review can be found in the appendices (Appendix C. Table 3). The table will be discussed in detail to help the reader better understand how the overall grade for the studies was determined. The comparison and purpose of this review is the efficacy of the HVAD system on bridging end-stage heart failure patients to transplantation. The two separate outcomes that were used to compare across the trials was ‘survival to transplantation’ and ‘survival 180 days on the device’. Since both of the articles addressed these outcomes they both were placed as observational studies in the quantity and type of evidence. Given that both of the studies are observational the starting grades for both outcomes are ‘low’ (Guyatt et al., 2008). Due to the fact that observational studies start out ‘low’ they cannot be downgraded any further by the study quality, consistency, directness, precision, or publication bias even if they apply. Observational studies can be upgraded if there is a large magnitude effect, dose-response, and/or with confounders. These clinical trials did have a large magnitude effect and were given a +1 in that category. A large magnitude effect means that even though a study may have been done with a small population the population represents the type of patients that would be seeking the intervention (Guyatt et al., 2008). It also means that the same results would be found if the study was re-done with a larger
population. This determination of a large magnitude of effect was due to the fact that most of the patients receiving the intervention were either going to wait in the hospital on IV inotropic therapy for a transplant or die waiting. This intervention will only be used in patients awaiting transplantation on IV inotropic therapy who are in end-stage heart failure (NYHA class IV). The GRADE of evidence for these outcomes up to this point are the same and have been upgraded from ‘low’ to ‘moderate’. This means the overall GRADE of evidence for these two outcomes is ‘moderate’. A moderate quality GRADE means that further research is likely to have an important impact on the estimate of effect which may change (Guyatt et al., 2008). This warrants higher quality trials like randomized control trials with other LVAD devices to be done in the future to help strengthen these recommendations. Fortunately these types of trials are currently being conducted in the United States. The recommendation of using the HVAD system was considered ‘strong’ based on the fact that the quality of evidence is moderate and the benefits of this intervention outweigh the harms.

Heart failure is a debilitating disease with a high mortality rate within the first year of diagnosis. Cardiac transplantation is really the only treatment at this point in time, but with the shortage of donors and long wait time it can be less than ideal. Today left ventricular assist devices are starting to help bridge the gap between end-stage heart failure and transplantation. As technology continues to advance and improve, so does the success of these devices in helping to prolong lives. The HeartWare HVAD system is a new type of LVAD that is considerably smaller than its competitors and more durable, allowing it to function for a longer
period of time. In the first clinical trials, the system is shown to have comparable, if not better survival rates than other LVADs with end-stage heart failure patients awaiting transplantation. The GRADE system showed that these trials have a 'moderate' quality of evidence for use in similar patient populations. In conclusion the HeartWare HVAD system has been shown to be safe and effective in bridging adult heart failure patients to transplantation. Hopefully, this system will soon finish with the U.S. clinical trials so that it can be used to help prolong the lives of heart failure patients awaiting transplant.
REFERENCES


of Heart and Lung Transplantation, 29, 1218-1225. doi: 10.1016/j.healun.2010.05.016
## APPENDICES

### APPENDIX A

Table 1: Pre-operative Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Clinical trial 1</th>
<th>Clinical trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary angioplasty</td>
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<td>13</td>
</tr>
<tr>
<td>Previous Sternotomy</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Pacemaker and/or Implantable Cardioverter</td>
<td>16</td>
<td>41</td>
</tr>
<tr>
<td>Pacemaker and/or Implantable Defibrillator</td>
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<td></td>
</tr>
<tr>
<td>Moderate-severe right ventricular dysfunction</td>
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<td>19</td>
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<tr>
<td>Diabetes</td>
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<td>7</td>
</tr>
<tr>
<td>Inotropic support</td>
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<td>50</td>
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<td>Previous Myocardial infarction</td>
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<td>10</td>
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<tr>
<td>Arrhythmias</td>
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<td>25</td>
</tr>
<tr>
<td>Hypertension</td>
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## Baseline Characteristics of the patients in the clinical trials

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Clinical trial 1</th>
<th>Clinical trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (years)</td>
<td>48</td>
<td>48.5</td>
</tr>
<tr>
<td>Gender</td>
<td>20 males, 3 females</td>
<td>43 males, 7 females</td>
</tr>
<tr>
<td>Signed informed consent</td>
<td>Meets</td>
<td>Meets</td>
</tr>
<tr>
<td>Body Surface Area mean (m²)</td>
<td>1.98</td>
<td>1.9</td>
</tr>
<tr>
<td>Body Mass Index mean (kg/m²)</td>
<td>27.6</td>
<td>25.6</td>
</tr>
<tr>
<td>Heart Failure cause:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) idiopathic cardiomyopathy</td>
<td>14 patients</td>
<td>22 patients</td>
</tr>
<tr>
<td>2) Ischemic cardiomyopathy</td>
<td>7 patients</td>
<td>20 patients</td>
</tr>
<tr>
<td>3) Familial or congenital</td>
<td>Not measured</td>
<td>5 patients</td>
</tr>
<tr>
<td>cardiology/ congenital cardiomyopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) Myocarditis</td>
<td>2 patients</td>
<td>3 patients</td>
</tr>
<tr>
<td>Inotropic Support</td>
<td>100% of the patients</td>
<td>100% of the patients</td>
</tr>
</tbody>
</table>

### Hemodynamic Parameters

<table>
<thead>
<tr>
<th>Hemodynamic Parameters</th>
<th>Clinical trial 1</th>
<th>Clinical trial 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Ventricular Ejection Fraction (%)</td>
<td>20.6 ± 7.4</td>
<td>18.7 ± 5.9</td>
</tr>
<tr>
<td>Left ventricular end-diastolic dimension (mm)</td>
<td>68.4 ± 7.5</td>
<td>68.6 ± 8.0</td>
</tr>
<tr>
<td>Cardiac Index (L/min/m²)</td>
<td>1.9 ± 0.5</td>
<td>1.94 ± 0.54</td>
</tr>
<tr>
<td>Pulmonary Capillary Wedge Pressure (mm Hg)</td>
<td>23.1 ± 7</td>
<td>23.7 ± 6.5</td>
</tr>
<tr>
<td>Central Venous Pressure (mm Hg)</td>
<td>13 ± 5.7</td>
<td>12.3 ± 5.9</td>
</tr>
<tr>
<td>Mean Systolic Blood Pressure (mm Hg)</td>
<td>105 ± 15.8</td>
<td>101.5 ± 13.9</td>
</tr>
<tr>
<td>Mean Diastolic Blood Pressure (mm Hg)</td>
<td>67 ± 8.9</td>
<td>64.2 ± 10.9</td>
</tr>
<tr>
<td>Systolic Pulmonary Artery Pressure (mm Hg)</td>
<td>52.7 ± 17.2</td>
<td>47.6 ± 15.7</td>
</tr>
<tr>
<td>Diastolic Pulmonary Artery Pressure (mm Hg)</td>
<td>28.1 ± 9.3</td>
<td>27.7 ± 9.3</td>
</tr>
</tbody>
</table>
## APPENDIX C

### Table 3: GRADE Table

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Outcome</th>
<th>Quantity and type of evidence</th>
<th>Findings</th>
<th>Starting grade</th>
<th>Decrease GRADE</th>
<th>Increase GRADE</th>
<th>Grade of Evidence for Outcome</th>
<th>Overall GRADE of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy of the HeartWare Ventricular Assist System in bridging adult heart failure patients to transplantation</td>
<td>Survival to transplant</td>
<td>2 cohort (observational)</td>
<td>High survival</td>
<td>Low</td>
<td>0 0 0 0 0</td>
<td>+1 0 0</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Survival 180 days on device</td>
<td>2 cohort (observational)</td>
<td>High survival</td>
<td>Low</td>
<td>0 0 0 0 0</td>
<td>+1 0 0</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
</tbody>
</table>