Total Artificial Hearts and Implantable Ventricular Assist Devices

Description

Mechanical devices to assist or replace a failing heart have been developed over many decades of research. A ventricular assist device (VAD) is a mechanical support attached to the native heart and vessels to augment cardiac output. The VAD may be used as a bridge to heart transplantation or as destination therapy in those who are not candidates for transplantation. The VAD has also been used as a bridge to recovery in patients with reversible conditions affecting cardiac output.

Background

Heart failure may be the consequence of a number of differing etiologies, including ischemic heart disease, cardiomyopathy, congenital heart defects, or rejection of a heart transplant. The reduction of cardiac output is considered to be severe when systemic circulation cannot meet the body’s needs under minimal exertion. Heart transplantation improves quality of life and has survival rates at 1, 5, and 10 years of 89%, 75%, and 56%, respectively. (1) The supply of donor organs has leveled off, while candidates for transplants are increasing, compelling the development of mechanical devices.

Initial research into mechanical assistance for the heart focused on the TAH, a biventricular device which completely replaces the function of the diseased heart. An internal battery required frequent recharging from an external power source. Many systems use a percutaneous power line, but a transcutaneous power-transfer coil allows for a system without lines traversing the skin, possibly reducing the risk of infection. Because the heart must be removed, failure of the device is synonymous with cardiac death.

Left Ventricular Assist Devices (LVAD)

Implantable ventricular assist devices are attached to the native heart, which may have enough residual activity to withstand a device failure in the short term. In reversible conditions of heart failure, the native heart may regain some function, and weaning and explanting of the mechanical support system after months of use has been described. Ventricular assist devices can be classified as internal or external, electrically or pneumatically powered, and pulsatile or continuous flow. Initial devices were pulsatile, mimicking the action of a beating heart. Devices
that are more recent may utilize a pump, which provides continuous flow. Continuous devices may move blood in rotary or axial flow.

Surgically implanted ventricular assist devices represent a method of providing mechanical circulatory support for patients not expected to survive until a donor heart becomes available for transplant or for whom transplantation is otherwise contraindicated or unavailable. They are most commonly used to support the left ventricle, but right ventricular and biventricular devices may be used. The device is larger than most native hearts, and therefore the size of the patient is an important consideration: the pump may be implanted in the thorax or abdomen or remain external to the body. Inflow to the device is attached to the apex of the failed ventricle, while outflow is attached to the corresponding great artery (aorta for left ventricle, pulmonary artery for right ventricle). A small portion of ventricular wall is removed for insertion of the outflow tube; extensive cardiotomy affecting the ventricular wall may preclude VAD use.

Percutaneous Ventricular Assist Devices (pVAD)

Devices in which the majority of the system’s components are external to the body are for short-term use (6 hours to 14 days) only, due to the increased risk of infection and need for careful, in-hospital monitoring. Some circulatory assist devices are placed percutaneously, i.e., are not implanted. These may be referred to as percutaneous VADs. These devices are placed through the femoral artery. Two different pVADs have been developed, the TandemHeart™ (Cardiac Assist™, Pittsburgh, PA), and the Impella® device (AbioMed™, Aachen, Germany). In the TandemHeart™ system, a catheter is introduced through the femoral artery and passed into the left atrium via transseptal puncture. Oxygenated blood is then pumped from the left atrium into the arterial system via the femoral artery. The Impella device is also introduced through a femoral artery catheter. In this device, a small pump is contained within the catheter that is placed into the left ventricle. Blood is pumped from the left ventricle, through the device, and into the ascending aorta. Adverse events associated with pVAD include access site complications such as bleeding, aneurysms, or leg ischemia. Cardiovascular complications can also occur, such as perforation, myocardial infarction (MI), stroke, and arrhythmias.

There are several situations in which pVAD may offer possible benefits: 1) cardiogenic shock that is refractory to medications and intra-aortic balloon pump (IABP), 2) cardiogenic shock, as an alternative to IABP, and 3) high-risk patients undergoing invasive cardiac procedures who need circulatory support.

Intra-aortic balloon pumps are outside the scope of this policy.

Regulatory Status

A number of mechanical circulatory support devices have received approval or clearance for marketing by FDA. These devices are summarized in Table 1, and described further in following sections.
Table 1. Available Mechanical Circulatory Support Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Manufacturer</th>
<th>Date of Initial Approval</th>
<th>Method of FDA Clearance</th>
<th>Indication</th>
</tr>
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<tbody>
<tr>
<td>Ventricular assist devices</td>
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<tr>
<td>Thoratec® IVAD</td>
<td>Thoratec</td>
<td>Aug 2004</td>
<td>PMA supplement</td>
<td>Bridge to transplant and postcardiomy</td>
</tr>
<tr>
<td>DeBakey VAD® Child</td>
<td>MicroMed</td>
<td>Apr 2004</td>
<td>HDE</td>
<td>Bridge to transplant in children 5-16 y of age</td>
</tr>
<tr>
<td>HeartMate II®</td>
<td>Thoratec</td>
<td>Apr 2008</td>
<td>PMA</td>
<td>Bridge to transplant and destination</td>
</tr>
<tr>
<td>Centrimag®</td>
<td>Levitonix</td>
<td>Oct 2008</td>
<td>HDE</td>
<td>Postcardiomy</td>
</tr>
<tr>
<td>Berlin Heart EXCOR® Pediatric VAD</td>
<td>Berlin</td>
<td>Dec 2011</td>
<td>HDE</td>
<td>Bridge to transplant</td>
</tr>
<tr>
<td>HeartWare® Ventricular Assist System</td>
<td>HeartWare</td>
<td>Dec 2012</td>
<td>PMA</td>
<td>Bridge to transplant</td>
</tr>
<tr>
<td>Percutaneous ventricular assist devices</td>
<td></td>
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</tr>
<tr>
<td>Impella®</td>
<td>Abiomed</td>
<td>May 2008</td>
<td>510(k)</td>
<td>Partial circulatory support using extracorporeal bypass control unit for periods up to 6 h</td>
</tr>
<tr>
<td>TandemHeart®</td>
<td>Cardiac Assist</td>
<td>Sep 2005</td>
<td>510(k)</td>
<td>Temporary left ventricular bypass of ≤6 h</td>
</tr>
</tbody>
</table>

FDA: U.S. Food and Drug Administration; HDE: humanitarian device exemption; PMA: premarket approval.

Total Artificial Heart

In October 2004, device CardioWest™ Temporary Total Artificial Heart (SynCardia Systems, Tucson, AZ) was approved by FDA through the premarket approval process (PMA) for use as a bridge to transplant in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure. Also, the temporary CardioWest™ Total Artificial Heart (TAH-t) is intended for use inside the hospital. In April 2010, FDA approved a name change to SynCardia Temporary Total Artificial Heart. FDA product code: LOZ.

In September 2006, the AbioCor® Implantable Replacement Heart System (AbioMed, Danvers MA) was approved by FDA through the HDE process for use in severe biventricular end stage heart disease patients who are not cardiac transplant candidates and who:

- are younger than 75 years of age;
- require multiple inotropic support;
- are not treatable by left ventricular assist device (LVAD) destination therapy; and
- are not weanable from biventricular support if on such support.
In addition to meeting other criteria, patients who are candidates for the AbioCor® TAH must undergo a screening process to determine if their chest volume is large enough to hold the device. The device is too large for approximately 90% of women and for many men. FDA HDE: H040006.

**Ventricular Assist Devices**

In December 1995, the Thoratec® Ventricular Assist Device System (Thoratec Corp., Pleasanton, CA) was approved by FDA through the PMA process for use as a bridge to transplantation in patients suffering from end stage heart failure. The patient should meet all of the following criteria:

- candidate for cardiac transplantation,
- imminent risk of dying before donor heart procurement, and
- dependence on, or incomplete response to, continuous vasopressor support.

In May 1998, supplemental approval for this device was given for the indication for postcardiectomy patients who are unable to be weaned from cardiopulmonary bypass. In June 2001, supplemental approval was given for a portable external driver to permit excursions within a 2-hour travel radius of the hospital in the company of a trained caregiver. In November 2003, supplemental approval was given to market the device as Thoratec® Paracorporeal VAD. In August 2004, supplemental approval was given to a modified device to be marketed as the Thoratec® Implantable VAD for the same indications. In January 2008, supplemental approval was given to delete Paracorporeal VAD use.

In February 2004, FDA approved the DeBakey VAD® Child under the HDE approval process. According to FDA, this device is indicated under HDE for both home and hospital use for children between the ages of 5 and 16 years who have end stage ventricular failure requiring temporary mechanical blood circulation until a heart transplant is performed.

In April 2008, continuous flow device HeartMate® II LVAS (Thoratec, Pleasanton, CA) was approved by FDA through the PMA process for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from nonreversible left ventricular failure. The HeartMate II LVAS is intended for use both inside and outside the hospital. In January 2010, the device received the added indication as destination therapy for use in patients with New York Heart Association class IIIB or IV end-stage left ventricular failure who have received optimal medical therapy for at least 45 of the last 60 days and are not candidates for cardiac transplantation.

In October 2008, device Centrimag® Right Ventricular Assist Device (Levitronix, Zurich) was approved by FDA under the HDE to provide temporary circulatory support for up to 14 days for patients in cardiogenic shock due to acute right-sided heart failure.

In December 2011, the Berlin Heart EXCOR® Pediatric VAD was approved via HDE. The indications for this device are pediatric patients with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support.
In December 2012, FDA approved the HeartWare® Ventricular Assist System (HeartWare, Miami Lakes, FL) through PMA. The device is approved as a bridge to cardiac transplantation in patients at risk for death from refractory end stage left ventricular heart failure.

FDA product code: DSQ

Percutaneous Ventricular Assist Devices (circulatory assist devices)

The Impella® Recover LP 2.5 Percutaneous Cardiac Support System (Abiomed, Aachen, Germany) received FDA 510(k) approval in May 2008 for short-term (<6 hours) use in patients requiring circulatory support. The TandemHeart® (Cardiac Assist, Pittsburgh) received a similar 510(k) approval for short-term circulatory support in September 2005. FDA product code: KFM.

Several other devices are in clinical trials or awaiting FDA review.

Related Policies

7.03.08 Heart/Lung Transplant
7.03.09 Heart Transplant
8.01.60 Extracorporeal Membrane Oxygenation for Adult Conditions

Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Post-Cardiotomy Setting/Bridge to Recovery

Implantable ventricular assist devices with FDA approval or clearance may be considered medically necessary in the post-cardiotomy setting in patients who are unable to be weaned off cardiopulmonary bypass.

Bridge to Transplantation

Implantable ventricular assist devices with FDA approval or clearance may be considered medically necessary as a bridge to heart transplantation for patients who are currently listed as heart transplantation candidates and not expected to survive until a donor heart can be obtained, or are undergoing evaluation to determine candidacy for heart transplantation.

Ventricular assist devices with FDA approval or clearance, including humanitarian device exemptions, may be considered medically necessary as a bridge to heart transplantation in children aged 5 to 16 years who are currently listed as heart transplantation candidates and not expected to survive until a donor heart can be obtained, or are undergoing evaluation to determine candidacy for heart transplantation.
Total artificial hearts with FDA-approved devices may be considered **medically necessary** as a bridge to heart transplantation for patients with biventricular failure who have no other reasonable medical or surgical treatment options, who are ineligible for other univentricular or biventricular support devices, and are currently listed as heart transplantation candidates or are undergoing evaluation to determine candidacy for heart transplantation, and not expected to survive until a donor heart can be obtained.

**Destination Therapy**

Implantable ventricular assist devices with FDA approval or clearance may be considered **medically necessary** as destination therapy with end-stage heart failure patients who are ineligible for human heart transplant and who meet the following “REMATCH Study” criteria:

- New York Heart Association (NYHA) Class IV heart failure for >60 days, OR patients in NYHA Class III/IV for 28 days, received >14 days’ support with intra-aortic balloon pump or dependent on IV inotropic agents, with 2 failed weaning attempts.

In addition, patients must not be candidates for human heart transplant for 1 or more of the following reasons:
- Age >65 year; or
- Insulin-dependent diabetes mellitus with end-organ damage; OR
- Chronic renal failure (serum creatinine >2.5 mg/dL for >90 days; OR
- Presence of other clinically significant condition.

**Other Indications**

Other applications of implantable ventricular devices or total artificial hearts are considered **not medically necessary**. The use of non-FDA approved or cleared implantable ventricular assist devices is considered investigational.

Percutaneous ventricular assist devices (pVADs) are considered **not medically necessary** for all indications.

**Benefit Application**

The BCBS FEP contract stipulates that FDA-approved biologics, drugs and certain devices may not be considered investigational when used for their intended purpose and thus these products may only be assessed based on medical necessity.

**Policy Guidelines**

Only two ventricular assist device (VAD) has approval from the U.S. Food and Drug Administration (FDA) for the pediatric population. The DeBakey VAD® Child device has FDA approval (HDE process) for use in children ages 5 to 16 years who are awaiting a heart transplant, i.e., as a bridge to transplant. The Berlin EXCOR VAD is indicated for children with
severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support.

In general, candidates for bridge-to-transplant implantable ventricular assist devices (VADs) are those who are considered appropriate heart transplant candidates but who are unlikely to survive the waiting period until a human heart donor is available. Some studies have included the following hemodynamic selection criteria: either a left atrial pressure of 20 mm Hg or a cardiac index of <2.0 L/min/m while receiving maximal medical support. Patients with VADs are classified by the United Network for Organ Sharing (UNOS) as Status I, that is, persons who are most ill and are considered the highest priority for transplant.

The median duration for time on the device is between 20 and 120 days.

Contraindications for bridge to transplant VADs include conditions that would generally exclude patients for heart transplant. Such conditions are chronic irreversible hepatic, renal, or respiratory failure; systemic infection; coagulation disorders, and inadequate psychosocial support. Due to potential problems with adequate function of the VAD, implantation is also contraindicated in patients with uncorrected valvular disease. See policy 7.03.09 Heart Transplantation for further discussion of heart transplant candidacy.

In addition, patients must have sufficient space in the thorax and/or abdominal cavity for the device. In the case of the CardioWest™ temporary Total Artificial Heart, this excludes patients with body surface areas less than 1.7 m2 or who have a distance between the sternum and 10th anterior rib of less than 10 cm as measured by computed tomography scan.

**Rationale**

**Literature Review**

The literature review focuses on 3 types of devices: (1) left ventricular assist devices (LVADs), (2) total artificial hearts (TAHs), and (3) percutaneous VADs (pVADs). The literature review addresses short-term use of the devices as a bridge to recovery or transplantation. LVADs and TAHs are also evaluated as longer term destination therapy for patients who are not transplant candidates. Following is a summary of the key literature to date.

**Ventricular Assist Devices**

**VADS as Bridge to Recovery**

Five studies of the Centrimag Right Ventricular Assist Device (RVAS) included between 12 and 32 patients, the majority of whom received biventricular devices. (2-4) Indications (and numbers of patients) in these 5 studies were: support for post-cardiotomy cardiogenic shock (bridge to recovery, n=53), bridge to long-term device implantation (n=9), treatment of right heart failure in patients who previously received left ventricular assist devices (VADs) (n=15), bridge to later
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When neurologic status is clarified (n=16), and acute donor graft failure (n=6). The mean time on mechanical circulatory support ranged from 9.4 days to 46.9 days. The 30-day mortality rates were between 17% and 63%. The proportion of patients discharged from the hospital was between 30% and 83%. Major complications included bleeding requiring reoperation, sepsis, and stroke. No device failures were observed in these studies.

VADs may have a role in bridging patients to recovery, particularly if there is reverse remodeling of the left ventricle. A number of relatively small, noncomparative studies have evaluated VADs as bridge-to-recovery therapy. In a 2006 study, a series of 15 patients with severe heart failure due to nonischemic cardiomyopathy underwent implantation of LVADs, along with medical management designed to enhance myocardial recovery. Eleven of 15 patients had enough myocardial recovery to undergo LVAD explantation; 2 patients died after explantation. Among those who survived, the cumulative rate of freedom from recurring heart failure was 100% and 88.9%, respectively, at 1 and 4 years postexplantation. The same group subsequently reported results of their LVAD explantation protocol among patients with severe heart failure due to nonischemic cardiopathy who had nonpulsatile LVADs implanted. They included 20 patients who received a combination of angiotensin converting enzyme ACE-inhibitors, beta-blockers, and adosterol antagonists followed by the β2-agonist clenbuterol. One patient was lost to follow-up and died after 240 days of support. Of the remaining 19 patients, 12 (63.2%) were successfully explanted after a mean 286 days; estimated survival without heart failure recurrence was 83.3% at 1 and 3 years. In a prospective multicenter study to assess myocardial recovery in patients with LVAD implantation as a bridge to transplant, Maybaum et al evaluated 67 patients with heart failure who had undergone LVAD implantation for severe heart failure. After 30 days, patients demonstrated significant improvements compared with pre-LVAD state in left ventricular ejection fraction (17.1% vs 34.12%, p<0.001), left ventricular end-diastolic diameter (7.1 cm vs 5.1 cm, p<0.001), and left ventricular mass (320 g vs 194 g, p<0.001). However, only 9% of patients demonstrated enough recovery to have their LVAD explanted.

Takayama et al reported outcomes for a retrospectively defined cohort of 143 patients who received a CentriMag VAD as a “bridge to decision” for refractory cardiogenic shock due to a variety of causes. Patients were managed with a bridge-to-decision algorithm. Causes of cardiogenic shock included failure of medical management (n=71), postcardiotomy shock (n=37), graft failure post heart transplantation (n=2), and right ventricular failure postimplantable LVAD (n=13). The device configuration was biventricular in 67%, isolated right VAD in 26%, and isolated left VAD in 8%. After a mean duration of support of 14 days (interquartile range, 8-26 days), 30% of patients had myocardial recovery, 15% had device exchange to an implantable VAD, and 18% had a heart transplantation.

In a smaller single-center retrospective cohort study, Mohamedali et al reported outcomes for 48 patients treated with biventricular support with the CentriMag device as a “bridge to decision”, 18 of whom had biventricular support with venoarterial (VA) extracorporeal membrane oxygenation (ECMO), while the remainder received just biventricular VAD support. Overall, 23 patients were explanted, 9 to recovery, 14 to a durable LVAD, with 3 additional patients explanted for withdrawal.
of care. However, given that the study included patients who received VA ECMO, it is difficult to assess the relative impact of VAD support alone.

**Section Summary**

The studies previously outlined indicate that a subset of patients who receive a VAD as a bridge to transplant or as destination therapy demonstrate improvements in their cardiac function, sometimes to the point that they no longer require the VAD. However, questions remain about defining and identifying the population most likely to experience cardiac recovery with VAD placement. One clearly defined population in which the potential for myocardial recovery exists is in the postcardiotomy setting. The current evidence is insufficient to allow identification of other heart failure patient populations who might benefit from the use of an LVAD as a specific bridge-to-recovery treatment strategy. Ongoing research studies are addressing this question, along with protocols for transitioning patients off VAD use.

**Bridge to Transplant: Ventricular Assist Devices**

A 1996 Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) assessment concluded that left ventricular assist devices (VADs) could provide an effective bridge to transplantation. (9) Goldstein and colleagues published a more recent review. (10) It should be recognized that LVADs do not change the number of patients undergoing heart transplantation due to the fixed number of donor hearts. However, the VAD will categorize its recipient as a high-priority heart transplant candidate.

Published studies continue to report that the use of a VAD does not compromise the success of a subsequent heart transplant and, in fact, may improve post-transplant survival, thus improving the use of donor hearts. (11-14) Currently available implantable LVADs consist of pulsatile devices that require stiff power vent lines that perforate the skin and implantable pump chambers, as well as non-pulsatile axial flow systems of smaller size and lower noise levels. (15)

In 5 reports published from 2007 to 2008, with samples ranging from 32 to 279 patients, most participants received the continuous-flow device as a bridge to transplantation. (16-20) Survival rates at 6 months were between 67% and 87%, and between 50% and 80% at 1 year. These rates are similar to those observed in a recent report of a federal circulatory support device registry. (21) An additional report from INTERMACS comparing the HeartMate II with other LVAD devices for patients who received them with a bridge to transplantation indication reported that 91% and 80% of HeartMate II and other LVAD patients, respectively, reached transplant, cardiac recovery, or ongoing LVAD support by 6 months. (22) A study by Patel and colleagues compared HeartMate I and HeartMate II recipients at a single center, finding the same 1-year survival and similar rates of subsequent development of right heart failure. (19) Serious adverse events occurring after HeartMate II-implantation include bleeding episodes requiring reoperation, stroke, infection, and device failure.
A systematic review published in 2011 examined the evidence on the effect of VADs on post-transplant outcomes. (23) This review included 31 observational studies that compared outcomes of transplant in patients who did and did not have pretransplant VAD. Survival at 1 year was more likely in patients who had VAD treatment, but this benefit was confined to patients who received an intracorporeal device (relative risk [RR]=1.8, 95% confidence interval [CI], 1.53 to 2.13). For patients treated with an extracorporeal device, the likelihood of survival was not different from patients who were not treated with an LVAD (RR=1.08, 95% CI, 0.95 to 1.22). There was no difference in the risk of rejection between patients who did and did not receive VAD treatment.

Additional studies published since the systematic review continue to report high success rates in bridging to transplant. In 2011, Streeber et al (24) published a case series of 50 patients awaiting heart transplantation treated with HeartWare® VAD, which is a smaller, continuous flow centrifugal device that is implanted in the pericardial space. Patients were followed until transplantation, myocardial recovery, device explant, or death. The median duration of time on the VAD was 322 days. Nine patients died; 3 from sepsis, 3 from multiple organ failure, and 3 from hemorrhagic stroke. At the end of follow-up, 20 patients had undergone transplant (40%), 4 had the pump explanted (8%), and the remaining 17 continued on pump support (34%). The most common complications were infection and bleeding. A total of 21 patients had infections (42%), and 5 patients had sepsis (10%). Bleeding complications occurred in 15 patients (30%), 10 of whom (20%) required surgery for bleeding.

In 2012, Aaronson et al reported results of a multicenter, prospective study of a newer generation LVAD, the HeartWare®. (25) The study enrolled 140 patients who were awaiting heart transplantation who underwent HeartWare® implantation. A control group of 499 subjects comprised patients drawn from the INTERMACS database, which collects data on patients who receive FDA-approved durable mechanical circulatory support devices. The study’s primary outcome was defined as survival on the originally implanted device, transplantation, or explantation for ventricular recovery at 180 days. Secondary outcomes were comparisons of survival between groups and functional, quality of life, and adverse event outcomes in the HeartWare® group. Success occurred in 90.7% of the HeartWare® group and 90.1% of controls (p<0.001, noninferiority with a 15% margin). Serious adverse events in the HeartWare® group included, most commonly, bleeding, infections, and perioperative right heart failure.

In 2013, Slaughter et al reported combined outcomes for patients included in the HeartWare® bridge-to-transplant study previously described and a continued-access protocol granted by FDA.(26) The study included 322 patients with heart failure, eligible for heart transplant, who received the HeartWare® (140 patients from the original study; 190 patients in the continue-access protocol who were monitored to outcome or had completed 180 days of follow-up at the time of this analysis. Survival at 60, 180, and 360 days was 97%, 91%, and 84%, respectively. The most common adverse events were respiratory dysfunction, arrhythmias, sepsis, and driveline exit site infections. Patients generally had improvements in quality-of-life measures.

In 2014, Deo et al reported no significant differences in outcomes for 37 patients bridged to transplant with a VAD and 70 patients who underwent a heart transplant directly. (27)
Pediatric Patients

There is one FDA-approved device, the EXCOR Pediatric VAD, via the HDE process, available for use as a bridge to cardiac transplant in children. This HDE approval was based on data from children who were a part of the initial clinical studies of this device. (28) Publications have reported positive outcomes for children using VADs as a bridge to transplantation. Using the UNOS database, Davies et al reported on use of VADs in pediatric patients undergoing heart transplantation. (29) Their analysis concluded that pediatric patients requiring a pretransplantation VAD have similar long-term survival to those not receiving mechanical circulatory support.

Following the FDA approval, Fraser et al evaluated the EXCOR device among 48 children, aged 16 or younger with 2-ventricle circulation, who had severe heart failure, despite optimized treatment and were listed for heart transplant.(30) Patients were divided into 2 groups based on body surface area. A historic control group of children receiving circulatory support with extracorporeal membrane oxygenation (ECMO) from the Extracorporeal Life Support Organization registry, matched in a 2:1 fashion with study participants based on propensity-score matching. For participants in cohort 1 (body surface area <0.7 m²), the median survival time had not been reached at 174 days, while in the matched ECMO comparison group, the median survival was 13 days (p<0.001). For participants in cohort 2 (body surface area 0.7 to <1.5 m²), the median survival was 144 days, compared with 10 days in the matched ECMO group (p<0.001). Rates of adverse events were high in both EXCOR device cohorts, including major bleeding (in 42% and 50% of cohort 1 and cohort 2, respectively), infection (in 63% and 50% of cohort 1 and cohort 2, respectively), and stroke (in 29% of both cohorts).

In 2013, Almond et al reported results from a prospective, multicenter registry to evaluate outcomes in children who received the Berlin Heart EXCOR device as a bridge to transplant.(31) This study included a broader patient population than the Fraser et al study. All patients were followed up from the time of EXCOR implantation until transplantation, death, or recovery. The study included 204 children, 67% of whom received the device under compassionate use. Survival at 12 months on EXCOR support was 75%, including 64% who survived to transplantation, 6% who recovered (device explanted and patient survived 30 days), and 5% alive with the device in place. In a follow-up study that evaluated 204 children from the same registry, Jordan et al reported relatively high rates of neurologic events in pediatric patients treated with the EXCOR device (29% of patients), typically early in the course of device use. (32)

Section Summary

In adults, the evidence on the efficacy of VADs as bridge to transplant consists of numerous uncontrolled trials and trials comparing different VAD among patients who have no other treatment options. In children, the evidence consists of several uncontrolled trials and 1 trial with historical controls. These studies report that substantial numbers of patients survive to transplant in situations in which survival would not be otherwise expected. Despite the lack of high-quality controlled trials, this evidence is sufficient to determine that outcomes are improved in patients who have no other options for survival. The impact of pretransplant VADs on survival from
transplant is uncertain, with some studies reporting worse survival in patients receiving VADs, but other studies reporting similar or improved survival.

**VADS as Destination Therapy**

VADs as destination therapy based on the 2002 Blue Cross and Blue Shield Association TEC assessment (33) offers the following observations and conclusions:

- The available evidence comes from a single, well-designed and rigorously conducted randomized trial, known as the REMATCH study. (34) The study was a cooperative effort of Thoratec, Columbia University, and the National Institutes of Health.
- The randomized trial found that patients with end-stage heart failure who are not candidates for cardiac transplantation have significantly better survival on a VAD compared with treatment by optimal medical therapy. Median survival was improved by approximately 8.5 months. Serious adverse events were more common in the VAD group, but these appear to be outweighed by this group’s better outcomes on function; New York Heart Association (NYHA) class was significantly improved, as was quality of life among those living to 12 months.
- VAD patients spend a greater relative proportion of time inside the hospital than medical management patients do, but the survival advantage would mean a longer absolute time outside the hospital.

Park et al published an extended 2-year follow-up of patients in the REMATCH trial, which found that survival and quality-of-life benefits were still apparent. In addition, this study and other case series suggest continuing improvement in outcomes related to ongoing improvements in the device and in patient management. (35, 36) However, the durability of the HeartMate device used in the REMATCH trial is a concern; for example, at one participating institution, all 6 long-term survivors required device change-outs. Next generation devices consisting of smaller continuous flow devices are eagerly anticipated.

After publication of the REMATCH study results, Rogers et al published results from a prospective, nonrandomized clinical trial comparing LVAD as destination therapy with optimal medical therapy for patients with heart failure who were not candidates for heart transplant. (37) Fifty-five patients who had NYHA functional Class IV symptoms and who failed weaning from inotropic support were offered a Novacor LVAD; 18 of these did not receive a device due to preference or device unavailability and acted as a control group. The LVAD-treated patients had superior survival rates at 6 months (46% vs 22%; p=0.03) and 12 months (27% vs 11%; p=0.02), along with fewer adverse events.

In an FDA-required post approval study of the HeartMate II device for destination therapy, which included the first 247 HeartMate II patients identified as eligible for the device as destination therapy. Outcomes and adverse events did not differ significantly from those treated in the original trial, which compared patients who received the HeartMate II to earlier generation devices (Slaughter et al [2009], described next). (38) Survival in the post approval cohort was 82% and 69% at 1 and 2 years postoperatively, respectively.
Section Summary

The main piece of evidence on the efficacy of LVADs as destination therapy in patients who are not transplant candidates is from a multicenter randomized controlled trial (RCT), the REMATCH study. This trial reported that the use of LVADs led to improvements in survival, quality of life, and functional status. This evidence is sufficient to establish that health outcomes are improved for this patient population.

Comparative Efficacy of Continuous Flow versus Pulsatile Flow Devices

In December 2009, Slaughter et al published data from an unblinded randomized multicenter trial comparing a continuous flow device with a pulsatile device. (39) Subjects were randomly assigned to continuous-flow or pulsatile-flow devices on a 2:1 block-randomization basis. The primary outcome measured was a composite end point of 2-year survival, free of disabling stroke or need for device replacement. Continuous-flow patients (n=134) reached the primary outcome at a rate of 46% (95% CI, 38 to 55) compared with pulsatile-flow patients’ (n=66) rate of 11% (95% CI, 3 to 18), which was a significant difference (p<0.001). Analysis of constituent factors indicated that a lower rate of devices needing replacement in the continuous-flow group had the largest effect on the composite end point; 2-year death rate also favored this device (58% vs 24%, respectively; p=0.008). Stroke and death (within 2 years of implantation) were similar in the 2 groups (stroke rate 12% and death rate 36%). Quality-of-life scores were also similar in the 2 groups. Although unblinded, this randomized trial adds to the evidence favoring continuous-flow devices.

Nativi et al (40) published a nonrandomized comparison of pulsatile versus continuous flow devices using data from the registry of the International Society for Heart and Lung Transplantation on 8,557 patients undergoing transplant. Comparisons were made among patients receiving a pulsatile LVAD, a continuous flow LVAD, and no LVAD. Two time periods were used for analysis; the first was pre-2004, when nearly all LVADs were pulsatile devices, and post-2004 when continuous use devices began to be used in clinical care. Comparing the first time period to the second time period, there was a significantly greater risk of mortality in the first time period compared with the second time period RR=1.30, 95% CI, 1.03 to 1.65, p=0.03). When analysis was confined to the second time period, there was no significant improvement in survival for the continuous group compared with the pulsatile group (RR=1.25, 95% CI, 1.03 to 1.65, p=0.03).

Dell’Aquila et al compared outcomes for patients treated with a third-generation continuous flow device, the HeartWare device, with those for patients treated with earlier generation devices in a single-center study. (41) Comparison group patients received either an earlier generation continuous flow device or a pulsatile flow device. Of 287 patients who received VAD support from 1993 to 2012, 52 received a HeartWare device, 76 an earlier generation continuous flow device, and 159 a pulsatile device. Survival was significantly better for patients who received a third-generation device, with 24 month survival of 70.4%, compared with 33.7% for patients who received an earlier-generation continuous flow device and 33.8% for patients who received a pulsatile flow device (p=0.013). The difference in survival associated with third-generation devices was more pronounced for higher scores on the INTERMACs scale.
Other nonrandomized studies that have compared outcomes from different types of LVADs have been smaller and/or focused on physiologic outcomes. (42-45) In some of these studies, the continuous flow devices exhibit greater improvement in physiologic measures, but none of these studies have reported significant differences between devices in clinical outcomes.

**Section Summary**

The evidence on the comparative efficacy of different devices consists of one RCT and several nonrandomized comparative studies. The RCT reported fairly large differences in a composite outcome measure favoring the continuous flow devices, with increases in revision and reoperation rates for the pulsatile device group being the largest factor driving the difference in outcomes. Other nonrandomized comparative studies, including one database study with large numbers of patients, have not reported important differences between devices on clinical outcomes.

**Total Artificial Hearts**

*TAH as Bridge to Transplant*

The FDA approval of the CardioWest TAH was based on the results of a nonrandomized, prospective study of 81 patients. (46) Patients had failed inotropic therapy and had biventricular failure and thus were not considered appropriate candidates for an LVAD. The rate of survival to transplant was 79%, which was considered comparable with the experience with LVAD in patients with left ventricular failure. The mean time from entry into the study until transplantation or death was 79.1 days. Other case series have been reported on outcomes of the TAH as a bridge to transplant. For example, Copeland et al. (47) reported on 101 patients treated with the SynCardia artificial heart as a bridge to transplant. All patients either met established criteria for mechanically assisted circulatory support, or were failing medical therapy on multiple inotropic drugs. The mean support time was 87 days, with a range of 1 to 441 days. Survival to transplant was 68.3% (69/101). Of the 32 deaths before transplant, 13 were due to multiple organ failure, 6 were due to pulmonary failure, and 4 were due to neurologic injury. Survival after transplant at 1, 5, and 10 years, respectively, was 76.8%, 60.5%, and 41.2%.

*TAH as Destination Therapy*

Data concerning the artificial heart are available from information concerning the FDA approval (48) and from a published article describing results for the first 7 patients. (49) FDA indicated that their decision was based on the company’s laboratory and animal testing and on a small clinical study of 14 patients that was conducted by Abiomed. The patients had a 1-month survival prognosis of not more than 30%, were not eligible for cardiac transplants, and were felt to not benefit from VAD therapy. The study was reported to show that the device is safe and has likely benefit for people with severe heart failure whose death is imminent and for whom no alternative treatments are available. Of the 14 patients in the study, 12 survived surgery. Mean duration of support for the patients was 5.3 months. In some cases, the device extended survival by several months; survival...
was 17 months in 1 patient. Six patients were ambulatory; 1 patient was discharged home. Complications included postoperative bleeding and neurologic events. Device-related infection was "non-existent."

**Longer Term Follow-Up**

Torregrossa et al reported on 47 patients who received a TAH at 10 worldwide centers and had the device implanted for more than 1 year. (50) Patients were implanted for dilated cardiomyopathy (n=23), ischemic cardiomyopathy (n=15), and “other” reasons (n=9). Over a median support time of 554 days (range, 365-1373 days), 34 patients (72%) were successfully transplanted, 12 patients (24%) died while on device support, and 1 patient (2%) was still supported. Device failure occurred in 5 patients (10%). Major complications were common, including systemic infection in 25 patients (53%), driveline infections in 13 patients (27%), thromboembolic events in 9 patients (19%), and hemorrhagic events in 7 patients (14%). Two of the deaths occurred secondary to device failure.

**Section Summary**

There is a smaller amount of evidence on the use of TAH as a bridge to transplantation, or as destination therapy, compared with the use of LVADs. The type of evidence on bridge to transplant is similar to that for LVADs, ie, case series reporting substantial survival rates in patients without other alternatives. Therefore, this evidence is sufficient to conclude that TAH improves outcomes for these patients similar to LVADs, and is a reasonable alternative for patients who require bridge to transplantation but who are ineligible for other types of support devices. Although TAHs show promise for use as destination therapy in patients who have no other treatment options, the available data on their use is extremely limited. There is insufficient evidence on the use of TAH as destination therapy to support conclusions about the efficacy of TAH in this setting.

**Percutaneous Ventricular Assist Devices**

*pVADs as an Alternative to Intra-Aortic Balloon Pump in Cardiogenic Shock*

Three RCTs have been published that compare pVADs with intra-aortic balloon pumps (IABPs) for patients with cardiogenic shock, (51-53) along with a systematic review and meta-analysis of these 3 trials. (54) The meta-analysis was published in 2009 by Cheng et al. The 3 RCTs enrolled a total of 100 patients, 53 treated with a pVAD and 47 treated with an IABP. All 3 study populations included patients with acute MI and cardiovascular shock; one of the trials (32) restricted this population to patients who were postrevascularization in the acute MI setting. The primary outcomes reported were 30-day mortality, hemodynamic measures of left ventricular (LV) pump function, and adverse events.

None of the 3 trials reported an improvement in mortality associated with pVAD use. The combined analysis estimated the relative risk for death in pVAD patients as 1.06 (95% CI: 0.68-1.66, p=0.80). All 3 trials reported an improvement in LV hemodynamics in the pVAD group. On combined analysis, there was a mean increase in cardiac index of 0.35 L/min/m² for the pVAD
group, an increase in mean arterial pressure of 12.8 mm Hg (95% CI: 3.6-22.0, p<0.001), and a
decrease in pulmonary capillary wedge pressure of 5.3 mm Hg (95% CI: 1.2-9.4, p<0.05).
Complications were more common in the pVAD group. On combined analysis, patients in the
pVAD group had a significantly increased likelihood of bleeding events with a relative risk of 2.35
(95% CI: 1.40-3.93). Leg ischemia was also more common in the pVAD group, but this difference
did not meet statistical significance (relative risk [RR]: 2.59, 95% CI: 0.75-8.97, p=0.13).

O’Neill et al compared outcomes for patients with acute MI complicated by cardiogenic shock who
received pVAD support pre—percutaneous coronary intervention (PCI) with those who received
pVAD support post-PCI using data from 154 consecutive patients enrolled in a multicenter
registry. (55) Patients who received pVAD support pre-PCI had higher survival to discharge
compared with those who received pVAD support post-PCI (65.1% vs 40.7%; p=0.003). In
multivariable analysis, receiving pVAD support pre-PCI was associated with in-hospital survival
(odds ratio [OR], 0.37; 95% CI, 0.17 to 0.79; p=0.01). However, the potential for underlying
differences in patient groups other than the use of pVAD support makes the study’s implications
uncertain.

Case series of patients treated with pVADs as an alternative to IABP in cardiogenic shock have
been published, (56, 57) and report high success rates as a bridge to alternative therapies.
However, given the availability of RCT evidence these studies add a limited amount to the body of
evidence on efficacy of pVADs for the management of cardiogenic shock.

**pVADS as Bridge to Recovery in Cardiogenic Shock Refractory to IABP**

Case series of patients with cardiogenic shock refractory to IABP who were treated with pVAD
have also been published. In the largest series, Kar et al. (58) treated 117 patients who had
severe, refractory cardiogenic shock with the TandemHeart® System. Eighty patients had
ischemic cardiomyopathy and 37 had nonischemic cardiomyopathy. There were significant
improvements in all hemodynamic measures following LVAD placement. For example, cardiac
index increased from 0.52±0.8 L/min/m² to 3.0±0.9 L/min/m² (p<0.001), and the systolic blood
pressure (BP) increased from 75±15 mm Hg to 100±15 mm Hg (p<0.001). Complications were
common post-LVAD implantation. Thirty-four patients had bleeding around the cannula site
(29.1%) and 35 developed sepsis during the hospitalization (29.9%). Groin hematoma occurred in
6 patients (5.1%); limb ischemia in 4 patients (3.4%); femoral artery dissection or perforation in 2
patients (1.7%); stroke in 8 patients (6.8%); coagulopathy in 13 patients (11.0%).

**pVADS Ancillary Support in High – Risk Patients Undergoing Invasive Cardiovascular Procedures**

The PROTECT trial intended to evaluate whether the Impella® 2.5 system improved outcomes
for patients undergoing high-risk percutaneous coronary intervention (PCI) procedures.
PROTECT I (59) was a feasibility study of 20 patients who had left main disease or last patent
coronary conduit that required revascularization but who were not candidates for coronary artery
bypass graft (CABG) surgery. High-risk PCI was performed using the Impella® system for
circulatory support. All of the procedures were completed successfully without any hemodynamic
compromise during the procedures. There were 2 patient deaths within 30 days (10%) and 2 patients had a periprocedural MI (10%). An additional 2 patients had evidence of hemolysis, which was transient and resolved without sequelae.

The PROTECT II trial was planned as an RCT to compare the Impella® system with IABP in patients undergoing high-risk PCI procedures. Enrollment was planned for 654 patients from 50 clinical centers. The primary end point was the composite of 10 different complications occurring within 30 days of the procedure, with the authors hypothesizing a 10% absolute decrease in the complication rate for patients in the pVAD group. The trial was discontinued prematurely in late 2010 due to futility, after an interim analysis of the first 327 patients enrolled revealed that the primary end point could not be reached. At the point that the data safety and monitoring board stopped the study, 452 patients had been enrolled, and of whom 3 withdrew consent and 1 died. Results were published by O’Neill et al in 2012.(60) The study’s primary analysis was intention to treat and included all 448 patients randomly assigned to the Impella® system (n=225) or IABP (n=223). The primary composite end point of major adverse effects at 30 days occurred in 35.1% of Impella® patients and in 40.1% of the IABP patients (p=0.277). There was no significant difference in the occurrence of in-hospital death, stroke, or MI between the Impella® patients and the IABP patients.

In a prespecified subgroup analysis of the PROTECT II trial, Kovacic et al compared outcomes for the Impella system compared with IABP among 325 patients with 3-vessel disease with LVEF less than or equal to 30%. (61) In the 3-vessel disease subgroup, 167 subjects were randomized to PCI with Impella support and 158 to PCI with IABP support. PCI characteristics differed in that rotational atherectomy was more aggressively used in the Impella-support group, with more passes per patient (5.6 vs 2.8, p=0.002) and more passes per coronary lesion (3.4 vs 1.7, p=0.001). Acute procedural revascularization results did not differ between groups. At 30 days, the major adverse event rate did not differ significantly between groups (32.9% of Impella patients vs 42.4% of IABP patients, p=0.078). At 90 days, Impella patients had a significantly lower major adverse event rate compared with IABP patients (39.5% vs 51.0%, p=0.039). The 90-day event rates for the individual components of the composite major adverse event score differed only for severe hypotension requiring treatment, which was more common in patients treated with IABP (7.6% vs 2.4%, p=0.029).

In a post hoc analysis, results of the PROTECT II trial were reanalyzed by Dangas et al, using a revised definition of MI in the determination of patients with major adverse events and major adverse cardiac and cerebral events. (62) In contrast to the original trial, which used a cutoff of 3 times the upper limit of normal for biomarker elevation to define periprocedural MI, the authors used a cutoff of 8 times the upper limit of normal for biomarker elevation or the presence of Q waves to define periprocedural MI. In multivariable analysis, compared with IABP, treatment with the Impella system was associated with freedom from 90-day major adverse events (OR=0.75; 95% CI, 0.61 to 0.92; p=0.007) and major adverse cardiac and cerebral events (OR=0.76; 95% CI, 0.61 to 0.96; p=0.020).
A few other case series have described pVAD use in high-risk patients undergoing an invasive cardiac procedure. Sjauw et al (63) performed a retrospective analysis of 144 consecutive patients undergoing high-risk PCI with pVAD support (Impella® system) from a European registry. Endpoints included successful device function and incidence of adverse events at 30 days. The device was successfully implanted in all 144 patients. There was one periprocedural death and 8 deaths at 30 days for a mortality rate of 5.5%. Bleeding requiring transfusion or surgery occurred in 6.2% of patients, and vascular access site complications occurred in 4.0%. There was 1 stroke (0.7%) and no MIs were reported. Maini et al (64) performed a similar retrospective analysis of 175 patients undergoing high-risk PCI with pVAD support with the Impella® 2.5 circulatory support system. The primary safety end point was the incidence of major adverse cardiac events at 30 days. Secondary end points included device safety and efficacy and patient outcomes at 30 days and 12 months. Angiographic revascularization was successful in 99% of patients. At 30-day follow up, the major adverse cardiac event rate was 8%; survival was 96%, 91%, and 88% at 30 days, 6 months, and 12 months, respectively. Secondary safety end points occurring most frequently included acute renal dysfunction (2.8%), hypotension on support (3.4%), ventricular tachycardia, or cardiopulmonary resuscitation (2.8%); other vascular complications such as vessel dissection and arteriovenous fistula (3.4%), hematomas ipsi- or contra-lateral to the device insertion site (8.6%), infection (5.1%), and blood transfusion (9.7%).

Reddy et al reported outcomes for a series of 66 patients enrolled in a prospective, multicenter registry who underwent ventricular tachycardia (VT) ablation with a pVAD or IABP. (65) Twenty-two patients underwent ablation with IABP assistance, while 44 underwent ablation with either the TandemHeart or Impella pVAD device (non-IABP group). Compared with patients who received support with an IABP, those who received support with a pVAD had greater numbers of unstable VTs that could be mapped and ablated (1.05 vs 0.32, p<0.001), greater numbers of VTs that could be terminated by ablation (1.59 vs 0.91, p=0.001), and fewer numbers of VTs that were terminated with rescue shocks (1.9 vs 3.0, p=0.049). More pVAD-supported patients could undergo entrainment/activation mapping (82% vs 59%, p=0.046). Mortality and VT recurrence did not differ over the study follow-up period (average, 12 months).

In a retrospective study, Aryana et al reported procedural and clinical outcomes for 68 consecutive unstable patients with scar-mediated epicardial or endocardial VT who underwent ablation with or without pVAD support. (66) Thirty-four patients had hemodynamic support periprocedurally with a pVAD. pVAD- and non-pVAD-supported patients were similar at baseline, with no differences in procedural success rates between groups. Compared with non-pVAD-supported patients, patients in the pVAD group had a longer maximum time in unstable VT (27.4 vs 5.3 min, p<0.001), a greater number of VT ablations per procedure (1.2 vs 0.4, p<0.001), a shorter radiofrequency ablation time (53 vs 68 seconds, p=0.022), and a shorter hospital length of stay (4.1 vs 5.4 days, p=0.013). Over a follow-up period of 19 months, rates of VT recurrence did not differ between groups.
Section Summary

pVADs have been tested in RCTs and uncontrolled studies of patients with cardiogenic shock and in patients undergoing high-risk cardiac interventions. The RCTs do not consistently report a benefit for use of pVADs. In addition, both the RCTs and case series report high rates of adverse events that may outweigh any potential benefits. As a result, the evidence on pVADs does not demonstrate that pVADs are associated with improvements in health outcomes for patients with cardiogenic shock or in patients undergoing high-risk cardiac interventions.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this policy are listed in Table 2.

Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<td>NCT01187368</td>
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<td>20</td>
<td>Jul 2016</td>
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<td>NCT01966458a</td>
<td>A Prospective, Randomized, Controlled, Unblinded, Multi-Center Clinical Trial to Evaluate the HeartWare® Ventricular Assist Device System for Destination Therapy of Advanced Heart Failure</td>
<td>429</td>
<td>Oct 2016</td>
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<tr>
<td>NCT01774656a</td>
<td>Remission From Stage D Heart Failure (RESTAGE-HF)</td>
<td>40</td>
<td>Dec 2017</td>
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<tr>
<td>NCT02387112</td>
<td>Early Versus Emergency Left Ventricular Assist Device Implantation in Patients Awaiting Cardiac Transplantation</td>
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<td>Dec 2022</td>
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<tr>
<td>Unpublished</td>
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<td>NCT01369407a</td>
<td>The Randomized Evaluation of VAD InterVEntion Before Inotropic Therapy (REVIVE-IT)</td>
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<td>Suspended</td>
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</tbody>
</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

The American College of Cardiology/American Heart Association (ACC/AHA) released guidelines for the management of heart failure in October 2013 that include recommendations related to the use of for mechanical circulatory support, including both durable and nondurable mechanical circulatory support (MCS) devices.(67) The guidelines categorize percutaneous and extracorporeal VADs as nondurable MCS devices. The following Class IIA guidelines are made related to MCS devices:

- MCS is beneficial in carefully selected patients with stage D heart failure with reduced ejection fraction (HFrEF) in whom definitive management (e.g., cardiac transplantation) or cardiac recovery is anticipated or planned. (Level of Evidence: B)
Nondurable MCS, including the use of percutaneous and extracorporeal VADs, is reasonable as a “bridge to recovery” or “bridge to decision” for carefully selected patients with HFrEF with acute, profound hemodynamic compromise. (Level of Evidence; B)

Durable MCS is reasonable to prolong survival for carefully selected patients with stage D HFrEF. (Level of Evidence: B)

The AHA/ACC guidelines note: “Although optimal patient selection for MCS remains an active area of investigation, general indications for referral for MCS therapy include patients with LVEF <25% and NYHA class III–IV functional status despite GDMT, including, when indicated, CRT, with either high predicted 1- to 2-year mortality (e.g., as suggested by markedly reduced peak oxygen consumption and clinical prognostic scores) or dependence on continuous parenteral inotropic support. Patient selection requires a multidisciplinary team of experienced advanced HF and transplantation cardiologists, cardiothoracic surgeons, nurses, and ideally, social workers and palliative care clinicians.”

In 2012, the American Heart Association published recommendations for the use of MCS. (68) These guidelines define nondurable MCS as intraballoon pumps, extracorporeal membrane oxygenation, extracorporeal VADs, and pVADs. The following recommendations were made regarding indications for use of MCS, including durable and nondurable devices:

- MCS for bridge-to-transplant indication should be considered for transplant-eligible patients with end-stage heart failure who are failing optimal medical, surgical, and/or device therapies and at high risk of dying before receiving a heart transplantation. (Class I; Level of Evidence B).

- Implantation of MCS in patients before the development of advanced heart failure is associated with better outcomes. Therefore, early referral of heart failure patients is reasonable. (Class IIa; Level of Evidence B).

- MCS with a durable, implantable device for permanent therapy or destination therapy is beneficial for patients with advanced heart failure, high 1-year mortality resulting from heart failure, and the absence of other life-limiting organ dysfunction; who are failing medical, surgical, and/or device therapies; and who are ineligible for heart transplantation. (Class I; Level of Evidence B).

- Elective rather than urgent implantation of destination therapy can be beneficial when performed after optimization of medical therapy in advanced heart failure patients who are failing medical, surgical, and/or device therapies. (Class IIa; Level of Evidence C).
  - Urgent nondurable MCS is reasonable in hemodynamically compromised heart failure patients with end-organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with time and restoration of an improved hemodynamic profile. (Class IIa; Level of Evidence C).
  - These patients should be referred to a center with expertise in the management of durable MCS and patients with advanced heart failure. (Class I; Level of Evidence C).
• Patients who are ineligible for heart transplantation because of pulmonary hypertension related to heart failure alone should be considered for bridge to potential transplant eligibility with durable, long-term MCS. (Class IIa; Level of Evidence B).

The Heart Failure Society of America published guidelines in 2010 on surgical approaches to the treatment of heart failure. (69) The following recommendations were made regarding left ventricular assist devices:

• Patients awaiting heart transplantation who have become refractory to all means of medical circulatory support should be considered for a mechanical support device as a bridge to transplant. (Strength of Evidence = B)

• Permanent mechanical assistance using an implantable assist device may be considered in highly selected patients with severe HF refractory to conventional therapy who are not candidates for heart transplantation, particularly those who cannot be weaned from intravenous inotropic support at an experienced HF center. (Strength of Evidence = B)

• Patients with refractory HF and hemodynamic instability, and/or compromised end-organ function, with relative contraindications to cardiac transplantation or permanent mechanical circulatory assistance expected to improve with time or restoration of an improved hemodynamic profile should be considered for urgent mechanical circulatory support as a "bridge to decision." These patients should be referred to a center with expertise in the management of patients with advanced HF. (Strength of Evidence = C)

European Society of Cardiology

In 2012, the European Society of Cardiology issued guidelines for the diagnosis and treatment of acute and chronic heart failure, (70) which were an update to previous guidelines published in 2008 and 2010. These guidelines make the following recommendation regarding VADs:

• An LVAD or BiVAD is recommended in selected patients with end-stage heart failure despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplant, to reduce the risk of heart failure hospitalization for worsening heart failure and to reduce the risk of premature death while awaiting transplant. (Class I, Level B recommendation).

• An LVAD should be considered in highly selected patients with end-stage heart failure despite optimal pharmacological and device therapy and who are not suitable for heart transplant, but are expected to survive greater than 1 year with good functional status, to improve symptoms and to reduce the risk of heart failure hospitalization and of premature death. (Class IIa, Level B recommendation).

Summary of Evidence

There is a substantial body of evidence from clinical trials and observational studies supporting implantable VADs as a bridge to transplant in patients with end stage heart failure, possibly improving mortality, as well as quality of life. A well-designed clinical trial, with 2 years of follow-up data, demonstrates an advantage of implantable VADs as destination therapy for patients who are
ineligible for heart transplant. Despite an increase in adverse events, both mortality and quality of life appear to be improved for these patients. Therefore, left ventricular assist devices (LVADs) may be considered **medically necessary** as a bridge to transplant and as destination therapy in patients who are not transplant candidates.

The evidence for the total artificial heart (TAH) in these settings is less robust. However, given the limited evidence from case series and the lack of medical or surgical options for these patients, TAH is likely to improve outcomes for a carefully selected population with end stage biventricular heart failure awaiting transplant who are not appropriate candidates for an LVAD. TAH may be considered **medically necessary** for this purpose.

There is insufficient evidence on the use of TAH as destination therapy, and TAH is considered **not medically necessary** for this purpose.

Ventricular assist devices with FDA approval or clearance, including humanitarian device exemptions, may be considered **medically necessary** as a bridge to heart transplantation in children aged 5 to 16 years who are currently listed as heart transplantation candidates and not expected to survive until a donor heart can be obtained, or are undergoing evaluation to determine candidacy for heart transplantation.

The evidence on percutaneous VADs (pVADs) does not support that these devices improve health outcomes. Three RCTs of pVAD versus intra-aortic balloon pump (IABP) for patients in cardiogenic shock failed to demonstrate a mortality benefit and reported higher complications associated with pVAD use. A fourth RCT comparing pVAD with IABP as an adjunct to high-risk percutaneous coronary interventions was terminated early due to futility; analysis of enrolled subjects did not demonstrate significant improvements in the pVAD group. Case series of patients with cardiogenic shock refractory to IABP have reported improved hemodynamic parameters following pVAD placement. However, these uncontrolled series cannot determine if pVAD improves mortality, and high rates of complications are reported with pVAD use. Observational studies have evaluated the use of pVAD support as an adjunct to ventricular tachycardia ablation procedures. While these studies show some differences in procedural specifics and hospital length of stay, no differences in long-term ablation success or mortality were reported. Because of the lack of demonstrated benefits in clinical trials, and the high complication rates reported, the use of pVAD for all indications is considered **not medically necessary**.

**Medicare National Policy**

Medicare has a national coverage determination policy for LVADS as a bridge to transplant.

The national coverage policy mandates coverage for VADs in the **post-cardiotomy setting** as long as the following conditions are met:

- The VAD has approval from FDA for post-cardiotomy support.
- The VAD is used according to the FDA-approved labeling instructions.
The national coverage policy also mandates coverage for VADs as a bridge-to-transplant as long as the following conditions are met:

- The VAD has approval from FDA for the bridge-to-transplant indication.
- The VAD is used according to the FDA-approved labeling instructions.
- The patient is approved and listed as a candidate for heart transplantation by a Medicare-approved heart transplant center.
- The implanting site, if different than the Medicare-approved transplant center, must receive written permission from the Medicare-approved heart transplant center under which the patient is listed prior to implantation of the VAD.

The national coverage policy mandates coverage for VADs as destination therapy as long as the following conditions are met:

- The VAD has approval from FDA for the destination therapy indication.
- Patient selection: VADs are covered for patients who have chronic end-stage heart failure (New York Heart Association Class IV end-stage left ventricular failure) who are not candidates for heart transplantation, and meet all of the following conditions:
  - Have failed to respond to optimal medical management (including beta-blockers and ACE inhibitors if tolerated) for at least 45 of the last 60 days, or have been balloon pump-dependent for 7 days, or IV inotrope-dependent for 14 days; and,
  - Have a left ventricular ejection fraction (LVEF) <25%, and,
  - Have demonstrated functional limitation with a peak oxygen consumption of ≤14 ml/kg/min unless balloon pump- or inotrope-dependent or physically unable to perform the test.
- Facility criteria: As of an October 30, 2013, decision memo on a National Coverage Analysis for VADs, the Centers for Medicare & Medicaid Services (CMS) concluded that the evidence is sufficient to conclude that VADs implanted in facilities that meet certain criteria improve health outcomes. Facilities currently credentialed by the Joint Commission for placement of VADs as DT [destination therapy] may continue as Medicare-approved facilities until October 30, 2014. At the conclusion of this transition period, these facilities must be in compliance with the following criteria as determined by a credentialing organization. As of the effective date, new facilities must meet the following criteria as a condition of coverage of this procedure:
  - Beneficiaries receiving VADs for DT must be managed by an explicitly identified cohesive, multidisciplinary team of medical professionals with the appropriate qualifications, training, and experience. The team embodies collaboration and dedication across medical specialties to offer optimal patient-centered care. Collectively, the team must ensure that patients and caregivers have the knowledge and support necessary to participate in shared decision making and to provide appropriate informed consent. The team members must be based at the facility and must include individuals with experience working with patients before and after placement of a VAD. The team must include, at a minimum, all of the following:
    - At least one physician with cardiothoracic surgery privileges and individual experience implanting at least 10 durable, intracorporeal, left ventricular VADs as
BTT [bridge to transplant] or DT over the course of the previous 36 months with activity in the last year.
- At least one cardiologist trained in advanced heart failure with clinical competence in medical and device-based management including VADs, and clinical competence in the management of patients before and after heart transplant.
- A VAD program coordinator.
- A social worker.
- A palliative care specialist.
- Facilities must be credentialed by an organization approved by CMS.

The national coverage policy mandates coverage for artificial hearts as bridge to transplant or destination therapy when performed under coverage with evidence development when a clinical study meets the criteria outlined in the Medicare policy and addresses one of the following questions:

- Were there unique circumstances such as expertise available in a particular facility or an unusual combination of conditions in particular patients that affected their outcomes?
- What will be the average time to device failure when the device is made available to larger numbers of patients?
- Do results adequately give a reasonable indication of the full range of outcomes (both positive and negative) that might be expected from more widespread use?

Clinical trials that meet the above requirements will be listed on the CMS website (http://www.cms.gov/MedicareApprovedFacilitie/06_artificialhearts.asp).

References

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<tr>
<th>Section:</th>
<th>Surgery</th>
<th>Effective Date:</th>
<th>April 15, 2016</th>
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<tr>
<td>Subsection:</td>
<td>Transplant</td>
<td>Original Policy Date:</td>
<td>September 13, 2012</td>
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70. McMurray JJ, Adamopoulos S, Anker SD, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J. Jul 2012;33(14):1787-1847. PMID 22611136
Policy History

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<th>Date</th>
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<td>September 2012</td>
<td>New Policy</td>
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<td>December 2014</td>
<td>Update Policy</td>
<td>Policy updated with literature review, adding references 5, 6, 20, 21, 24, 27, 28, 40-44, 47, 49, 50 &amp; 51 and deleting others. Policy updated to include total artificial hearts as medically necessary as a bridge to transplant for patients with biventricular failure until a donor can be obtained. The policy name was revised to add Total Artificial Hearts.</td>
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Keywords

Assist Devices, Ventricular Devices, Ventricular Assist, as a Bridge to Heart Transplantation
Ventricular Assist Devices as a Bridge to Heart Transplantation
Percutaneous Ventricular assistive device
LVAD
pLVAD
pVAD

This policy was approved by the FEP<sup>®</sup> Pharmacy and Medical Policy Committee on March 18, 2016 and is effective April 15, 2016.

Signature on file
Deborah M. Smith, MD, MPH