
Medical Policy



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***Current Policy Effective Date: 5/1/21**
(See policy history boxes for previous effective dates)

Title: Total Artificial Hearts and Implantable Ventricular Assist Devices

Description/Background

A ventricular assist device (VAD) is a mechanical support attached to the native heart and vessels to augment cardiac output. The total artificial heart (TAH) replaces the native ventricles and is attached to the pulmonary artery and aorta; the native heart is typically removed. Both the VAD and TAH 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.

Heart Failure

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, 3, and 5 years of 91%, 85%, and 78%, respectively.¹ The supply of donor organs has leveled off, while candidates for transplants are increasing, compelling the development of mechanical devices.

Treatment

Ventricular Assist Devices

Implantable VADs are attached to the native heart, which may have enough residual capacity to withstand a device failure in the short term. In reversible heart failure conditions, the native heart may regain some function, and weaning and explanting of the mechanical support system after months of use has been described. VADs 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. More recent devices may use a pump, which provides continuous flow. Continuous devices may move blood in a rotary or axial flow.

At least one VAD system developed is miniaturized and generates an artificial pulse, the HeartMate 3 Left Ventricular Assist System.²

Surgically implanted VADs 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 contraindicated or unavailable. VADs 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 the left ventricle, a pulmonary artery for the right ventricle). A small portion of the ventricular wall is removed for insertion of the outflow tube; extensive cardiomy affecting the ventricular wall may preclude VAD use.

Total Artificial Hearts

Initial research into mechanical assistance for the heart focused on the TAH, a biventricular device that completely replaces the function of the diseased heart. An internal battery required frequent recharging from an external power source. Many systems utilize 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 native heart must be removed, failure of the device is synonymous with cardiac death.

A fully bioprosthetic TAH, which is fully implanted in the pericardial sac and is electrohydraulically actuated, has been developed and tested in 2 patients, but is currently experimental.³

Percutaneous Ventricular Assist Devices (pVAD)

Devices in which most 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 (pVADs). pVADs 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 vein 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 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, hemolysis, 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 (IABPs) 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

Device	Manufacturer	Date of Initial Approval	Method of FDA Clearance	Indication
Ventricular assist devices				
Thoratec® IVAD	Thoratec	Aug 2004	PMA supplement	Bridge to transplant and postcardiotomy
DeBakey VAD® Child	MicroMed	Apr 2004	HDE	Bridge to transplant in children 5-16 y of age
HeartMate II®	Thoratec	Apr 2008	PMA	Bridge to transplant and destination
Centrimag®	Levitronix	Oct 2008	HDE	Postcardiotomy
Berlin Heart EXCOR® Pediatric VAD	Berlin	Dec 2011	HDE	Bridge to transplant
HeartWare® Ventricular Assist System	HeartWare	Dec 2012	PMA	Bridge to transplant
HeartMate 3™ Left Ventricular Assist System	Thoratec	Aug 2017	PMA	Bridge to transplant and destination
Percutaneous ventricular assist devices				
Impella® Recover LP 2.5	Abiomed	May 2008	510(k)	Partial circulatory support using extracorporeal bypass control unit for periods up to 6 h
TandemHeart®	Cardiac Assist	Sep 2005	510 (k)	510(k) Temporary left ventricular bypass of ≤6 h
Impella 2.5 System	Abiomed	Mar 2015	PMA	Temporatrty ventricular support for ≤6 h

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

Ventricular Assist Devices

In 1995, the Thoratec® Ventricular Assist Device System (Thoratec Corp.) was approved by the FDA through the premarket approval process as a bridge to transplantation in patients with 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 1998, supplemental approval for this device was given for the indication of post cardiotomy patients 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 when accompanied by a trained caregiver. In 2003, supplemental approval was given to market the device as Thoratec® Paracorporeal VAD. In 2004, supplemental approval was given to a modified device to be marketed as the Thoratec® Implantable VAD for the same indications. In 2008, supplemental approval was given to rescind Paracorporeal VAD use.

In August 2016, HeartWare® recalled its VAD Pumps due to a design flaw that was deemed by the FDA as potentially causing serious injuries or death (class I recall). The devices affected were manufactured and distributed from March 2006 and May 2018. FDA product codes 204 and 017.

A class I recall was issued for the HeartMate 3™ in April 2018 affecting all manufacturing dates. FDA product code: DSQ.

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. In addition, 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;
- Requiring multiple inotropic support;
- Not treatable by left ventricular assist device (LVAD) destination therapy; and
- 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.

Percutaneous Ventricular Assist Devices (Circulatory Assist Devices)

Table 2. Available Mechanical Circulatory Support Devices

Device	Manufacturer	Approval Date	FDA Clearance	PMA, 510(k) No.	Indication
TandemHeart®	Cardiac Assist	Sep 2005	510(k)	K110493	Temporary left ventricular bypass of ≤6 hr
Impella® Recover LP 2.5	Abiomed	May 2008	510(k)	K063723	Partial circulatory support using extracorporeal bypass control unit for ≤6 hr
Impella 2.5 System	Abiomed	Mar 2015	PMA	P140003	Temporary ventricular support for ≤6 hr

FDA: U.S. Food and Drug Administration; PMA: premarket approval

Comparative Efficacy of Left VAD Devices

The mechanism of operation of left VADs has changed since their introduction. The earliest devices were pulsatile positive displacement pumps. These pumps have been largely replaced by axial continuous-flow pumps. More recently centrifugal continuous-flow pumps have also been introduced.

The evidence of the comparative efficacy of centrifugal continuous-flow vs axial continuous-flow devices consists of two randomized controlled trials of two different centrifugal continuous-flow devices.^{4,5} The MOMENTUM 3 trial compared HeartMate 3 centrifugal continuous-flow device with the HeartMate II axial continuous-flow device in patients indicated for circulatory support as a bridge to transplant or destination therapy. HeartMate 3 received PMA approval as a bridge to transplant therapy in August 2017 and as destination therapy in October 2018. The destination therapy indication was based on 2-year results from MOMENTUM 3, which showed superiority of the HeartMate 3 device compared to HeartMate II on the composite primary outcome, survival at 2 years free of disabling stroke or reoperation to replace a malfunctioning device (relative risk 0.84; 95% confidence interval 0.78–0.91, $p < 0.001$).⁶ Prevalence of stroke at 2 years was lower in the HeartMate 3 than the HeartMate II group (10.1% vs. 19.2%; $P = 0.02$).⁷ Measures of functional capacity and Health-Related Quality of Life did not differ between the two devices at six months.⁸ The ENDURANCE trial compared HeartWare centrifugal continuous-flow device with the HeartMate II axial continuous-flow device in patients indicated for circulatory support as destination therapy. HeartWare is FDA-approved as a bridge to transplantation device. Both trials found the centrifugal device to be noninferior to the axial device for the primary, composite outcome including measures of survival, freedom from disabling stroke, and freedom from device failure. While there are fewer device failures with the centrifugal devices without a significant increase in disabling stroke, the HeartWare device was associated with increased risk of any stroke over a period of two years.

The evidence on the comparative efficacy of continuous-flow vs. pulsatile-flow devices consists of a randomized controlled trial and several nonrandomized comparative studies.^{9,10,11,12,13} The randomized controlled trial 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 a database study with large numbers of patients, have not reported important differences in clinical outcomes between devices.

Medical Policy Statement

The safety and effectiveness of *implantable* ventricular assist devices and total artificial hearts have been established. They are useful therapeutic options for patients meeting specified selection criteria.

The safety and effectiveness of the use of a *percutaneous* ventricular assist device (pVAD) have been established for a subset of patients. They are useful therapeutic options for patients meeting specified selection criteria.

All other uses for pVADs are considered experimental/investigational. The evidence on the use of pVADs does not support the conclusion that these devices improve health outcomes for any other situations.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

I. Implantable ventricular assist devices (VADs)-(must be FDA-approved)

Inclusions:

For Post-cardiotomy Setting /Bridge to Recovery

- For patients in the post-cardiotomy setting who are unable to be weaned off cardiopulmonary bypass.

For Use as a Bridge to Transplantation

- Implantable ventricular assist devices with FDA approval or clearance when used as a bridge to heart transplantation 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.
- Implantable ventricular assist devices with FDA approval or clearance, including HDEs, in children 16 years of age or younger 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.

For use as Destination therapy

- For patients with end-stage heart failure 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
 - NYHA Class III/IV heart failure for 28 days, received with over 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 over 65 years; 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

Exclusions:

- Patients not meeting the above patient selection guidelines.
- The use of non-FDA approved or cleared ventricular assist devices. For patients under age 16, HDE approval is acceptable.

II. Percutaneous Ventricular Assist Device (must be FDA-approved)

Inclusions:

- For providing short term circulatory support for patients with severe cardiogenic shock who are unstable to the point where IABP support would not be tolerated or effective.
- As an adjunct to percutaneous coronary intervention in the following high-risk patients:
 - Patients with a cardiac ejection fraction of less than 35% who are undergoing unprotected left main or last-remaining-conduit PCI.
 - Patients with three-vessel disease and ejection fraction less than 30 percent.

The Impella® 2.5 Circulatory Support System is intended for partial circulatory support using an extracorporeal bypass control unit, for periods up to 6 hours. It is also intended to be used to provide partial circulatory support (for periods up to 6 hours) during procedures not requiring cardiopulmonary bypass.

Exclusions:

The use of a pVAD for any other indication not listed above.

III. Total artificial hearts (must have FDA approval or clearance)

Bridge to Transplantation only

Inclusions:

When used as a bridge to heart transplantation for patients with biventricular failure who have no other reasonable medical or surgical treatment options, *AND*

- Who are ineligible for other univentricular or biventricular support devices, *AND*
- Who are currently listed as heart transplantation candidates or undergoing evaluation to determine candidacy for heart transplantation and not expected to survive until a donor heart can be obtained.

Exclusions:

- Patients not meeting the above patient selection guidelines.
- The use of non-FDA approved or cleared implantable ventricular assist devices or total artificial hearts
- The use of total artificial hearts as destination therapy.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

0051T	0052T	0053T	33927	33928	33929
33975	33976	33977	33978	33979	33980
33990	33991	33992	33993	33995	33997
L8698					

Other codes (investigational, not medically necessary, etc.):

N/A

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable

intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The literature review focuses on 3 types of devices:

- 1) Ventricular assist devices (VADs),
- 2) Total artificial hearts (TAHs), and
- 3) Percutaneous ventricular assist devices (pVADs).

The literature review addresses short-term use of the devices as a bridge to recovery or transplantation. VADs 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 as a Bridge to Heart Transplant for End-Stage Heart Failure

Clinical Context and Therapy Purpose

The purpose of VADs as a bridge to heart transplant in patients who have end-stage heart failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a VAD as a bridge to heart transplant improve the net health outcome in individuals with end-stage heart failure?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with end-stage heart failure. A subset of patients who receive a VAD as a bridge to transplantation have demonstrated improvements in their cardiac function, sometimes to the point that they no longer require the VAD. This results in the use of VAD as a bridge to recovery.

Interventions

The therapy being considered is a VAD as a bridge to heart transplant.

Implantation of a VAD is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapy is currently being used to make decisions about individuals with end-stage heart failure: optimal medical therapy without VADs.

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Time-to-transplant is of interest, as is the short-term outcome ranging from 30 days to 1 year.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

VADs as Bridge to Recovery

Prospective Studies

VADs may have a role in bridging patients to recovery, particularly if there is reverse remodeling of the left ventricle (LV). Several studies have investigated the role of VADs in bridging patients to decision for transplant eligibility. One clearly defined population in which the potential for myocardial recovery exists is in the post-cardiotomy setting.

In 2016, Acharya et al reported on patients who underwent VAD placement in the setting of acute myocardial infarction (AMI) who were enrolled in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry, a prospective national registry of FDA-approved durable mechanical circulatory support devices.¹⁴ Patients who had an AMI as the admitting diagnosis or a major myocardial infarction (MI) as a hospital complication that resulted in VAD implantation (n=502) were compared with patients who underwent VAD implantation for non-AMI indications (n=9727). Patients in the AMI group were generally sicker at baseline, with higher rates of smoking, severe diabetes, and peripheral vascular disease, but had fewer cardiac surgeries and recent cardiovascular hospitalizations. Most AMI patients (53.8%) were implanted with a “bridge-to-candidacy” strategy. At 1 month post-VAD, 91.8% of the AMI group was alive with the device in place. At 1 year post-VAD, 52% of the AMI group were alive with the device in place, 25.7% had received a transplant, 1.6% had their VAD explanted for recovery, and 20.7% died with the device in place.

Two additional 2016 publications from the INTERMACS registry reported on cardiac recovery in patients implanted with LVADs. Wever-Pinzon et al (2016) included adults registered between March 2006 and June 2015 excluding those who had a right VAD only, TAH, or prior heart transplant (n=15631). One hundred twenty-five of these patients had an a priori bridge to recovery LVAD strategy. Cardiac recovery occurred in 192 (1.3%) of the LVAD patients overall and in 14 (11.2%) of the bridge to recovery patients. Topkara et al (2016) reported a similar analysis of 13454 INTERMACS adults with implants between June 2006 and June 2015 without TAH or pulsatile-flow LVAD or heart transplant. Device explant rates for cardiac recovery were 0.9% at 1-year, 1.9% at 2-year, and 3.1% at 3-year follow-up. An additional 9% of patients demonstrated partial cardiac recovery.

In a prospective multicenter study to assess myocardial recovery in patients with LVAD implantation as a bridge to transplant, Maybaum et al (2007) evaluated 67 patients with heart failure who had undergone LVAD implantation for severe heart failure.¹⁵ 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.

Retrospective Studies

In 2018, Agrawal et al produced a retrospective cohort study evaluating the 30-day readmissions of 2510 patients undergoing LVAD implantation.¹⁶ Of the patients who met the inclusion criteria, 788 (31%) were readmitted within 30 days after surviving initial index hospitalization. Cardiac causes accounted for 23.8% of readmissions, 13.4% due to heart failure, and 8.1% to arrhythmias. Infection (30.2%), bleeding (17.6%), and device-related causes (8.2%) comprised the 76.2% of noncardiovascular causes for readmission. The study's limitations relate to the nature of nonclinical data collection and gaps in current subject knowledge.

Takayama et al (2014) 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.¹⁷ Patients were managed with a bridge-to-decision algorithm. Causes of cardiogenic shock included failure of medical management ($n=71$), post-cardiotomy shock ($n=37$), graft failure post heart transplantation ($n=2$), and right ventricular failure post-implantable 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 heart transplantation.

Section Summary: VADs as Bridge to Recovery

There has been interest in prospectively identifying subsets of patients who might benefit from a temporary VAD with the goal of bridging to recovery. Available studies have indicated that a subset of patients who receive a VAD as a bridge to transplant or as destination therapy have demonstrated 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 post-cardiotomy 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.

VADs as Bridge to Heart Transplant

The insertion of a VAD will categorize its recipient as a high-priority heart transplant candidate. The available evidence on the efficacy of VADs in bridging patients with refractory heart failure to transplant includes single-arm series, which generally have reported high success rates in bridging to transplant.

Adult Patients

Systematic Reviews

Several older systematic reviews have that VADs can provide an effective bridge to transplantation.^{18,19}

Prospective Studies

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.²⁰ 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 continued-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.

Case Series

In 2011, Strueber et al 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.²¹ 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.

In 2012, Aaronson et al reported results of a multicenter, prospective study of a newer generation LVAD, the HeartWare®.⁴⁰ The study enrolled 140 patients who were awaiting heart transplantation that underwent HeartWare® implantation. A control group of 499 subjects comprised patients drawn from the INTERMACS database, which collects data on patients who receive U.S. Food and Drug Administration (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 five 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.²²⁻²⁶ Survival rates at 6 months were between 67% and 87%, and between 50% and 80% at 1 year. These rates are similar to those reported in a recent report of a federal circulatory support device registry, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).²⁷ A study by Patel et al 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.²⁵ Serious adverse events occurring after HeartMate II-implantation include bleeding episodes requiring reoperation, stroke, infection, and device failure.

In 2018, Aissaoui et al published an observational study comparing 224 patients in Germany and France with end-stage heart failure who received VAD (group I, n=83) or heart

transplantation or medical therapy as first treatment options (group II, n=141). The estimated 2-year survival was 44% for group I and 70% for group II ($p < 0.001$).²⁸

Pediatric Patients

There is one FDA-approved device, the EXCOR Pediatric VAD, via the humanitarian device exemption (HDE) process, available for use as a bridge to cardiac transplant in children. The HDE approval was based on data from children who were a part of the initial clinical studies of this device.³¹ Publications have reported positive outcomes for children using VADs as a bridge to transplantation.

Registry Studies

Bulic et al (2017) identified all U.S. children between 1 and 21 years of age at heart transplant between 2006 and 2015 for dilated cardiomyopathy who were supported with an LVAD or vasoactive infusions alone at the time of heart transplant from the Organ Procurement and Transplant Network registry (n=701).³² Children receiving LVAD were older, on a higher level of hemodynamic support, more likely to be on dialysis and waited long to receive a donor heart than children receiving vasoactive infusions. Functional status as measured by the median Karnofsky Performance Scale at heart transplant was higher for children receiving LVAD compared with vasoactive infusion (6 vs. 5, $p < 0.001$) and children receiving LVAD were more likely to be discharged from the hospital at the time of transplant. The percent of children having stroke at the time of transplant was higher in those receiving LVAD (3% vs. 1%, $p = 0.04$).

Also in 2016, Wehman et al reported on post-transplant survival outcomes for pediatric patients who received a VAD, extracorporeal membrane oxygenation (ECMO), or no mechanical circulatory support (MCS), in the pre-transplant period.³³ The study included 2777 pediatric patients who underwent heart transplant from 2005 to 2012 who were identified through the United Network for Organ Sharing Database, of whom 428 were bridged with VADs and 189 were bridged with ECMO. In unadjusted analysis, the actuarial 5-year survival was highest in the direct-to-transplant group (77%), followed by the VAD group (49%) and then the ECMO group (35%). In a proportional hazards model to predict time to death, restricted to the first 4 months post-transplant, ECMO bridging was significantly associated with higher risk of death (adjusted hazard ratio [HR] 2.77 vs. direct-to-transplant, 95% CI 2.12 to 3.61, $P < 0.0001$). However, a model to predict time to death excluded deaths in the first 4 months post-transplant, the bridging group was not significantly associated with risk of death.

Fraser et al (2012) evaluated the EXCOR device among 48 children, aged 16 or younger with 2-ventricle circulation, which had severe heart failure, despite optimized treatment and were listed for heart transplant.³⁴ 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, $< 0.7 \text{ m}^2$), 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, $0.7 \text{ to } < 1.5 \text{ m}^2$), 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).

Noncomparative Studies

In 2016, Blume et al published the first analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS), which is a prospective, multicenter registry which collects data on patients who are under age 19 at the time of implant, and includes patients implanted with either durable or temporary VADs.³⁵ At the time of analysis, the registry included 241 patients; of these, 41 were implanted with a temporary device only, leaving 200 patients implanted with VADs for the present study. Most patients (73%) had an underlying diagnosis of cardiomyopathy. At the time of implantation, 64% were listed for transplant, while an additional 29% were implanted with a “bridge to candidacy” strategy. A total of 7% were implanted with a destination therapy strategy. Actuarial survival at both 6 months and one year was 81%. At 6 months, 58% of patients were transplanted.

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.³⁶ 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.³⁷

In 2016, Chen et al reported on a retrospective, single-center series of pediatric patients with continuous flow VADs, with a focus on outpatient experiences.³⁸ The series included 17 children implanted with an intracorporeal device from 2010 to 2014. Eight of those patients (47%) were discharged from the hospital after a median hospitalization duration post-implant of 49 days. Adverse events were common in outpatients, most frequently major device malfunction (31%, 5/16 events) and cardiac arrhythmias (31%, 5/16 events). At the time of analysis, 4 patients had received an orthotopic heart transplant, 2 were on ongoing support, and 1 each was transferred or died.

In 2016, Conway et al conducted a retrospective, single-center series of pediatric patients reported on outcomes for patients treated with short-term continuous flow VADs, which including the Thoratec PediMag or CentriMag, or the Maquet RotaFlow.³⁹ From 2015 to 2014, 27 children were supported with one of these devices, most commonly for congenital heart disease (42%). The median duration of support was 12 days, and 67% of all short term continuous flow VAD runs (19 of 28 runs) lead to hospital discharge.

Effects of Pretransplant VADs on Transplant Outcomes

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.⁴⁰⁻⁴³ A systematic review published in 2011, by Alba et al, examined the evidence on the effect of VADs on post-transplant outcomes.⁴⁴ 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], 0.95 to 1.22). There was no difference in the risk of rejection between patients who did and did not receive LVAD treatment.

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.⁴⁵ Data from the United Network for Organ Sharing, reported by Grimm et al (2016), suggests that patients bridged to transplant with an LVAD have better outcomes than those bridged with TAH or biventricular assist devices.⁴⁶ Using the United Network for Organ Sharing (UNOS) database, Davies et al reported on use of VADs in pediatric patients undergoing heart transplantation.⁴⁷ Their analysis concluded that pediatric patients requiring a pretransplantation VAD have similar long-term survival to those not receiving mechanical circulatory support.

Section Summary: VADs as Bridge to Transplant for End-Stage Heart Failure

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 post-cardiotomy setting. The current evidence is insufficient to identify other heart failure patient populations that might benefit from the use of an LVAD as a specific bridge to recovery treatment strategy.

In adults, the evidence on the efficacy of VADs as bridge to transplant consists of uncontrolled trials registry studies and case series. 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 is historically low. Despite the lack of high-quality controlled trials, this evidence is sufficient to determine that outcomes are improved in patients given they have no other options.

VADs as Destination Therapy for End-Stage Heart Failure

Clinical Context and Therapy Purpose

The purpose of VADs as destination therapy in patients who have end-stage heart failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a VAD as destination therapy improve the net health outcome in individuals with end-stage heart failure?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with end-stage heart failure.

Interventions

The therapy being considered is a VAD as destination therapy.

Implantation of a VAD is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapy is currently being used to make decisions about managing individuals with end-stage heart failure: optimal medical therapy without VADs.

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Time of interest ranges from 6 months to 2 years following implantation of VAD as destination therapy.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

Systematic Reviews

The evaluation of VADs as destination therapy is based on a 2002 TEC Assessment that offered the following observations and conclusions:⁴⁸

- The available evidence comes from a single, well-designed and rigorously conducted randomized trial, known as the REMATCH study.⁴⁹ 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 (2005) 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.^{50,51} 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.

Nonrandomized Comparative Studies

A subsequent prospective observational study, called the Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients study, comparing LVAD support (n=97) with optimal medical therapy (n=103) for patients with heart failure not requiring inotropes also reported superior survival and health-related quality of life in LVAD-treated patients.⁵² Twelve-month, as treated, event-free actuarial survival was 80% in the LVAD group, compared with 63% in the best medical therapy group (P=0.022). Two-year results were reported by Starling et al (2017).⁵³ At the end of 2

years, 35 (34%) medical therapy patients and 60 (62%) LVAD patients were alive on their original therapy; 23 medical management patients received LVADs during the 2 years. The LVAD-treated patients continued to have higher as-treated, event-free actuarial survival (70% vs. 41%, $p < 0.001$) although there was no difference in intention to treat survival (70% vs. 63%, $p = 0.31$).

In an FDA-required post approval study of the HeartMate II device for destination therapy,⁵⁴ which included the first 247 HeartMate II patients identified as eligible for the device as destination therapy, Jorde et al (2014) found that outcomes and adverse events did not differ significantly from those of the original trial, which compared patients who received the HeartMate II with earlier-generation devices. Survival rates in the post approval cohort were 82% and 69% at 1 and 2 years postoperatively, respectively.

After publication of the REMATCH study results, Rogers et al (2007) 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.⁵⁵ 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 six months (46% vs. 22%; $p = 0.03$) and 12 months (27% vs. 11%; $p = 0.02$), along with fewer adverse events.

Section Summary: VADs as Destination Therapy for End-Stage Heart Failure

The highest quality 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.

Total Artificial Heart as a Bridge to Transplant for End-Stage Heart Failure

Clinical Context and Therapy Purpose

The purpose of a total artificial heart (TAH) as a bridge to heart transplant in patients who have end-stage heart failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a TAH as a bridge to heart transplant improve the net health outcome in individuals with end-stage heart failure?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with end-stage heart failure.

Interventions

The therapy being considered is a TAH as a bridge to heart transplant.

Implantation of a TAH as a bridge to transplant is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapy is currently being used to make decisions about managing individuals with end-stage heart failure: optimal medical therapy without a TAH.

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Implantation of a VAD is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

Nonrandomized Trials

FDA approval of the CardioWest™ TAH was based on the results of a nonrandomized, prospective study of 81 patients.⁵⁶ 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 to 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.

Case Series

Other case series have been reported on outcomes of the TAH as a bridge to transplant. For example, Copeland et al (2012) reported on 101 patients treated with the SynCardia artificial heart as a bridge to transplant.⁵⁷ 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 1-441 days. Survival to transplant was 68.3% (69/101). Of the 32 deaths prior to 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%.

Section Summary: Total Artificial Heart as a Bridge to Transplant for End-Stage Heart Failure

There is a smaller amount of evidence on the use of TAH as a bridge to transplantation, or as destination therapy, compared to the use of LVADs. The type of evidence on bridge to transplant is similar to that for LVADs, (i.e., case series reporting substantial survival rates in patients without other alternatives). Therefore, similar to LVADs, this evidence is sufficient to

conclude that TAH improves outcomes for these patients and TAH is a reasonable alternative for patients who require a bridge to transplantation but who are ineligible for other types of life-sustaining support devices.

TAH as Destination Therapy for End-Stage Heart Failure

Clinical Context and Therapy Purpose

The purpose of a TAH as destination therapy in patients who have end-stage heart failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a TAH as destination therapy improve the net health outcome in individuals with end-stage heart failure?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with end-stage heart failure.

Interventions

The therapy being considered is a TAH as destination therapy.

Implantation of a TAH as destination therapy is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapy is currently being used to make decisions about managing individuals with end-stage heart failure: optimal medical therapy without TAHs.

Time of interest ranges from six months to two years following implantation of a TAH as destination therapy.

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

Case Series

Data on the artificial heart are available from information concerning the FDA approval⁵⁸ and from a published article describing results for the first seven patients.⁵⁹ FDA indicated that their

decision was based on the company's laboratory and animal testing and on a small clinical study of 14 patients 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. No device-related infections were reported.

Torregrossa et al (2014) reported on 47 patients who received a TAH at 10 worldwide centers and had the device implanted for more than 1 year.⁶⁰ 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: Total Artificial Hearts as Destination Therapy for End-Stage Heart Failure

There is a less evidence on the use of TAH as destination therapy compared with the use of LVADs. Although TAHs show promise as destination therapy in patients who have no other treatment options, the available data on their use is extremely limited. Currently, the evidence base is insufficient to support conclusions about TAH efficacy in this setting.

Percutaneous Ventricular Assist Devices (pVAD) For Cardiogenic Shock

Clinical Context and Therapy Purpose

The purpose of pVADs in patients who have cardiogenic shock is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a pVAD as a bridge to heart transplant improve the net health outcome in individuals with end-stage heart failure?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with cardiogenic shock.

Interventions

The therapy being considered is a pVADs.

Implantation of a pVAD is performed in a hospital setting with specialized staff equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapy is currently being used to make decisions about managing individuals with cardiogenic shock: intra-aortic balloon pump (IABP).

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Timing of interest ranges from perioperative events to 30-day mortality outcomes.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

Systematic Reviews

Romeo et al (2016) reported on a systematic review and meta-analysis that evaluated a variety of percutaneous mechanical support methods, including pVADs, for patients with cardiogenic shock due to AMI who were undergoing revascularization (Tables 3 and 4).⁶¹ This review included the 3 RCTs (described above) comparing pVADs with intra-aortic balloon pumps (IABPs), along with 3 observational studies. In the comparison of pVADs with IABP, the reviewers found that in-hospital mortality (the primary outcome of the analysis) was nonsignificantly increased in the pVAD group.

Table 3. Characteristics of a Systematic Review Evaluating pVADs vs. IABPs for Cardiogenic Shock

Study	Dates	Trials	Participants	N	Design
Romeo et al (2016) ⁶¹	1997-2015	6	Patients receiving IABP or pVADs	271	3 RCT and 3 observational

pVAD: percutaneous ventricular assist device; IABP: intra-aortic balloon pump; RCT: randomized controlled trial.

Table 4. Results of a Systematic Review Evaluating pVADs vs. IABP for Cardiogenic Shock

Study	In Hospital Mortality
Romeo et al (2016) ⁶¹	
RCTs	
Total N	100
Risk ratio (95% CI)	1.06 (0.68, 1.66)
I^2	0% (0.83)
Observational Studies	
Total N	171
Risk ratio (95% CI)	1.16 (0.92, 1.47)
NNH per 100 patients	8
I^2 (p)	0% (0.062)
All studies	
Total N	271

Risk ratio	1.14 (0.93, 1.41)
I^2 (p)	0% (0.92)

pVAD: percutaneous ventricular assist device; IABP: intra-aortic balloon pump; N: sample size; CI: confidence interval; NNH: number needed to harm; RCT: randomized controlled trial.

Randomized Controlled Trials

A total of 4 RCTs have compared pVADs with IABPs for patients who had cardiogenic shock; 3 were included in the Romeo et al (2016) systematic review described above^{62,63,64} and 1 was published after Romeo et al (2016).⁶⁴ The 4 RCTs enrolled a total of 148 patients, 77 treated with a pVAD and 71 treated with an IABP. All four trial populations included patients with AMI and cardiovascular shock; one trial restricted its population to patients who were post-revascularization in the AMI setting. The primary outcomes reported were 30-day mortality, hemodynamic measures of left ventricle pump function, and adverse events. The trials are summarized in Tables 5 and 6. Some trials reported improvements in hemodynamic and metabolic parameters but none found any reductions in 30-day mortality. The IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK (IMPRESS) trial reported 6-month mortality outcomes and also found no difference between groups. Bleeding events and leg ischemia were more common in the pVAD groups.

Table 5. Characteristics of RCTs Evaluating pVADs and IABPs for Cardiogenic Shock

Study	Trial (Registration)	Countries	Sites	Dates	pVAD	Key Eligibility Criteria
Ouweneel et al (2017) ⁶⁴	IMPRESS (NTR3 450)	Netherlands, Norway	2	2012-2015	Impella CP	AMI and severe CS in the setting of immediate PCI; receiving mechanical ventilation
Seyfarth et al (2008) ⁶³	ISAR-SHOCK (NCT00417378)	Germany	2	2004-2007	Impella LP 2.5	AMI <48h and CS
Burkhoff et al (2006) ⁶²	TandemHeart (NR)	U.S.	12	2002-2004	TandemHeart	CS <24 h due to MI or heart failure
Thiele et al (2005) ⁶⁵	NR	Germany	1	2000-2003	TandemHeart	AMI with CS and intent to revascularize with PCI

AMI: acute myocardial infarction; CS: cardiogenic shock; IABP: intra-aortic balloon counterpulsation; IMPRESS: Impella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK; ISARSHOCK: Efficacy Study of LV Assist Device to Treat Patients With Cardiogenic Shock; MI: myocardial infarction; NR: not reported; PCI: percutaneous coronary intervention; pVAD: percutaneous ventricular assist device; RCT: randomized controlled trial.

Table 6. Results of RCTs Evaluating pVADs and IABPs for Cardiogenic Shock

Study	30-Day Mortality	60-Day Mortality	Bleeding	Leg Ischemia	Other Outcomes
Ouweneel et al (2017) ⁶⁴ IMPRESS					Rehospitalization
N	48	48	48		48
pVAD	46%	50%	33%		21%
IABP	50%	50%	8%		4%
HR (95% CI)	0.96 (0.42 to 2.18)	1.04 (0.47 to 2.32)			
Seyfarth et al (2008) ⁶³ ISAR-SHOCK					Increase in cardiac index (L/min/m ²)

N	26	26	26	
pVAD	46%	8%	0.49	
IABP	46%	0%	0.11	
Burhkoff et al (2006) ⁶² TandemHeart				<i>At least 1 adverse event:</i>
N	33	33	33	33
pVAD	47%	42%	21%	95%
IABP	36%	14%	14%	71%
Thiele et al (2005) ⁶⁵				<i>Final cardiac index (W/m²)</i>
N	41	41	41	41
pVAD	43%	90%	33%	0.37
IABP	45%	40%	0%	0.28

CI: confidence interval; HR: hazard ratio; IABP: intra-aortic balloon counterpulsation; IMPRESS: IMPella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK; ISAR-SHOCK: Efficacy Study of LV Assist Device to Treat Patients With Cardiogenic Shock; pVAD: percutaneous ventricular assist devices; RCT: randomized controlled trial.

^a Values are hazard ratio (95% confidence interval).

^b Major bleeding.

Observational Studies

Results of a recent comparative observational study conducted by Schrage et al (2019) were consistent with previous evidence in showing no mortality benefit for pVAD over IABP.⁶⁶ Using registry data, the researchers retrospectively identified 237 patients who had been treated with the Impella device and matched them to patients who had received IABP as part of an RCT. There was no significant difference between groups in 30-day all-cause mortality (48.5% vs. 46.4%, P=0.64). Severe or life-threatening bleeding (8.5% vs. 3.0%, P<0.01) and peripheral vascular complications (9.8% vs. 3.8%, P=0.01) occurred significantly more often in the Impella group.

Case Series

Case series of patients treated with pVADs as an alternative to IABP in cardiogenic shock have reported high success rates as a bridge to alternative therapies.⁶⁷⁻⁷⁰

Section Summary: Percutaneous VADs for Cardiogenic Shock

Four RCTs comparing pVAD with IABP in patients with cardiogenic shock and meta-analyses evaluating three of these RCTs failed to demonstrate a mortality benefit for pVAD use and reported higher complication rates associated with pVAD use.

Percutaneous VADs for High-Risk Cardiac Procedures

Clinical Context and Therapy Purpose

The purpose of pVADs in patients who undergo high-risk cardiac procedures is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a pVAD improve the net health outcome in individuals who undergo high-risk cardiac procedures?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals undergoing high-risk cardiac procedures.

Interventions

The therapy being considered is a pVAD.

Implantation of a pVAD is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapy is currently being used to make decisions about managing individuals who undergo high-risk cardiac procedures: IABP.

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Timing of interest ranges from perioperative events to 30-day mortality outcomes.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

Percutaneous VADs as Ancillary Support for High-Risk Percutaneous Coronary Intervention

Systematic Reviews

Two recent systematic reviews have evaluated pVAD as ancillary support for patients undergoing high-risk PCI. Table 7 shows a comparison of the RCTs included in each. Only one RCT (PROTECT II) was included in both reviews. In addition to PROTECT II, Ait Ichou et al (2018) included 3 RCTs in patients who received emergent PCI post-MI: IMPRESS, IMPRESS in STEMI, and ISAR-SHOCK. Ait Ichou et al (2018) conducted a systematic review of the Impella device compared to IABP for high-risk patients undergoing PCI (Tables 7 and 8).⁷¹ The researchers included 4 RCTs, 2 controlled observational studies, and 14 uncontrolled observational studies published between 2006 and 2016, with a total of 1287 patients. Individual study results were reported with no pooled analyses.

Table 7. Comparison of RCTs Included in SRs Evaluating pVAD as Ancillary Support for High-Risk PCI

Study ²	Ait Ichou et al (2018) ⁷¹	Briasoulis et al (2016)
O'Neill et al (2012) ⁷² PROTECT II	•	•
Ouweneel et al 2016 ⁶⁴ IMPRESS	•	
Ouweeneel et al (2016) IMPRESS in STEMI ⁷⁰	•	

RCT: randomized controlled trial; SR: systematic review; pVAD: percutaneous ventricular assist device; PCI: percutaneous coronary intervention.

The range of results identified in the controlled and uncontrolled studies as reported by Ait Ichou et al (2018) are summarized in Table 8. The RCTs found similar rates of all-cause mortality between the Impella device and IABP. One RCT reported higher rates among patients randomized to Impella (7.6% vs. 5.9%) but the difference was not statistically significant (P=0.47). Two of the 3 controlled observational studies found higher 30-day mortality rates in patients receiving Impella but the differences were not statistically significant. There was a reduction in major cardiovascular adverse events at 90 days with the Impella device reported in one RCT (odds ratio vs. IABP: 0.79, 95% CI: 0.64–0.96). Among uncontrolled studies, the rates of all-cause mortality and adverse events were heterogeneous due to differences in study populations and their underlying cardiovascular risk.

Risk of bias assessment determined that three of the four RCTs were at a low-risk of bias, but they had insufficient power to detect a difference in clinical outcomes. One RCT (IMPRESS in STEMI) was rated as a high-risk of bias due to early termination and widening of inclusion criteria over time. The two controlled observational studies had methodological limitations leading to a serious risk of bias, and the other observational studies were at a high-risk of bias due to their uncontrolled study design. After exclusion of low-quality studies, the rates of 30-day mortality, major bleeding, and MI did not change substantially. However, in the group of low-risk of bias studies, the vascular complication rate was higher.

An earlier systematic review and meta-analysis conducted by Briasoulis et al (2016) included studies of both Impella and TandemHeart.⁷³ Reviewers identified 18 nonrandomized observational studies and a single RCT (PROTECT II).⁷² Results are shown in Table 9. In the observational studies, the sample sizes ranged from 7 to 637 patients. In a pooled analysis of the observational trial data, the 30-day mortality rate following Impella-assisted high-risk PCI was 3.5% (95% CI, 2.2% to 4.8%; $I^2=20\%$), while that for TandemHeart-assisted high-risk PCI was 8% (95% CI, 2.9% to 13.1%; $I^2=55\%$). The pooled vascular complication rates were 4.9% (95% CI, 2.3% to 7.6%) and 6.5% (95% CI, 3.2% to 9.9%) for the Impella and the TandemHeart, respectively. This meta-analysis did not compare pVAD to IABP or other interventions.

Table 8. Characteristics of SRs Evaluating pVAD as Ancillary Support for High-Risk PCI

Study	Dates	Trials	Participants	Devices Included	N (Range)	Design	Duration
Ait Ichou et al (2018) ⁷¹	Inception 2016	20	High-risk patients undergoing PCI	Impella	1287 (10-225)	4 RCT, 2 controlled observational, 14 uncontrolled observational	1-42 months
Briasoulis et al (2016)		Impella: 12 TandemHeart: 8	High-risk patients undergoing PCI	Impella and TandemHeart	Impella: 1350 (10-637) TandemHeart: 252 (7-68)	Impella: TandemHeart:	Impella: TandemHeart:

SR: systematic review; pVAD: percutaneous ventricular assist device; PCI: percutaneous coronary intervention; N: sample size; RCT: randomized controlled trial.

Table 9. Results of SRs Evaluating pVAD as Ancillary Support for High-Risk Percutaneous Coronary Intervention

Study	All-Cause Mortality (30 days)	All-Cause Mortality (3 months)	All-Cause Mortality (12 months)	Stroke (30 days)	Stroke (3 months)	Stroke (12 months)	Major Adverse Events (30 days)	Major Adverse Events (3 months)	Major Adverse Events (12 months)	Vascular Complications
Ait Ichou et al (2018)										
Range of effect (controlled studies)										
Impella	7.6%-46%	12.1%-50%	15.3%-26%	0%	0.9%-8%	8%	15%-35.1%	26%-40.6%	37%	
IABP	0%-46%	8.7%-50%	11%-25.8%	0%-1.8%	0%-4%	0%	40%-40.1%	33%-49.3%	47%	
Range of effect (uncontrolled studies)										
Impella	0%-74%	--	10%-45.5%	0%-2%	--	--	0%-20%	--	30%	
Briasoulis et al (2016) ⁷³										
Impella	54/1346						Major bleeding 126/1346		89/1346	
Pooled effect (95% CI)	0.35 (0.022, 0.048)						0.71 (0.043, 0.99)		0.049 (0.023, 0.076)	
I ² (p)	20% (0.243)						63% (0.002)		78% (<0.001)	
TandemHeart	22/212						11/205		15/205	
Pooled effect (95% CI)	0.080 (0.029, 0.131)						0.036 (0.011, 0.061)		0.065 (0.032, 0.099)	
I ² (p)	55% (0.030)						0% (0.581)		0% (0.865)	

SR: systematic review; pVAD: percutaneous ventricular assist device; IABP: intra-aortic balloon pump; CI: confidence interval.

Section Summary: Percutaneous VADs for High-Risk PCI

Percutaneous VADs have been assessed in 1 RCT (PROTECT II) and subsequent trial data analyses and in uncontrolled studies of high-risk patients undergoing high-risk cardiac interventions such as PCI. The RCT and other nonrandomized studies and accompanying post hoc analyses have not consistently reported a benefit for the use of pVADs. Registry studies have described pVAD use in high-risk patients undergoing an invasive cardiac procedure, but given trial design lacking comparators, these studies add little to suggest the efficacy of pVAD use in this population.

Percutaneous VADs for High-Risk VT Ablation

Reddy et al (2014) reported on outcomes for a series of 66 patients enrolled in a prospective, multicenter registry who underwent VT ablation with a pVAD or IABP.⁷⁴ Twenty-two patients underwent ablation with IABP assistance, while 44 underwent ablation with 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 more unstable VTs that could be mapped and ablated (1.05 vs. 0.32, p<0.001), more VTs than could be terminated by ablation (1.59 vs. 0.91, p=0.001), and fewer VTs 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 (average, 12 months).

In a retrospective study, Aryana et al (2014) 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.⁷⁵ Thirty-four patients had hemodynamic support periprocedurally with a pVAD. Percutaneous VAD- and non-pVAD-supported patients had similar procedural success rates. Compared with non-pVAD-supported patients, patients in the pVAD group had a longer maximum time in unstable VT (27.4 minutes vs. 5.3 minutes, $p<0.001$), more VT ablations per procedure (1.2 vs. 0.4, $p<0.001$), shorter radiofrequency ablation time (53 seconds vs. 68 seconds, $p=0.022$), and a shorter hospital length of stay (4.1 days vs. 5.4 days, $p=0.013$). Over a follow-up of 19 months, rates of VT recurrence did not differ between groups.

Section Summary: Percutaneous VADs for High-Risk VT Ablation

Two nonrandomized studies have compared VT ablation with pVAD or IABP. In both studies, patients who had pVAD support spent less time in unstable VT than patients without pVAD support. Rates of recurrence of VT was comparable between groups for both studies. The current evidence based does not support conclusions about the use of pVAD for VT ablation.

Percutaneous VADs for cardiogenic shock refractory to IABP Therapy

Clinical Context and Therapy Purpose

The purpose of pVADs in patients who have cardiogenic shock refractory to IABP therapy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of a pVAD improve the net health outcome in individuals with cardiogenic shock refractory to IABP?

The following **PICOTS** were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with cardiogenic shock refractory to IABP therapy.

Interventions

The therapy being considered is the use of a pVAD.

Implantation of a pVAD is performed in a hospital setting with specialized staff who are equipped to perform the surgical procedure and manage postsurgical intensive care.

Comparators

The following therapies are currently being used to make decisions about managing individuals with cardiogenic shock refractory to IABP: optimal medical therapy without IABP and other MCS.

Outcomes

The general outcomes of interest are overall survival, device malfunction, heart failure, respiratory dysfunction, arrhythmias, and infection.

Timing of interest ranges from perioperative events to 30-day mortality outcomes.

Study Selection Criteria

To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for RCTs and systematic reviews of RCTs.

In the absence of such trials, we included comparative observational studies, with a preference for prospective studies.

To assess long-term outcomes and adverse effects, we included single-arm studies that captured longer periods of follow-up and/or larger populations.

Case Series

Case series of patients with cardiogenic shock refractory to IABP therapy who were treated with pVAD have been published. In a large series, Kar et al (2011) treated 117 patients who had severe, refractory cardiogenic shock with the TandemHeart System.⁷⁶ Eighty patients had ischemic cardiomyopathy and 37 had nonischemic cardiomyopathy. There were significant improvements in all hemodynamic measures following LVAD placement. For example, the cardiac index increased from 0.52 L/min/m² to 3.0 L/min/m² (p<0.001), and systolic blood pressure increased from 75 mm Hg to 100 mm Hg (p<0.001). Complications were common after LVAD implantation. Thirty-four (29.1%) patients had bleeding around the cannula site, and 35 (29.9%) developed sepsis during hospitalization. Groin hematoma occurred in 6 (5.1%) patients; limb ischemia in 4 (3.4%) patients; femoral artery dissection or perforation in 2 (1.7%) patients; stroke in 8 (6.8%) patients; and coagulopathy in 13 (11.0%) patients.

Section Summary: Percutaneous VADs for Cardiogenic Shock Refractory to IABP Therapy

Percutaneous VADs have been assessed in uncontrolled studies of patients with cardiogenic shock including those refractory to IABP therapy. The case series have reported high rates of adverse events that may outweigh any potential benefits. As a result, the evidence on pVADs does not demonstrate that the use of pVADs is associated with improvements in health outcomes for patients with cardiogenic shock refractory to IABP therapy.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this policy are listed in Table 10.

Table 10. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing NCT01633502	Effects of Advanced Mechanical Circulatory Support in Patients With ST Segment Elevation Myocardial Infarction Complicated by Cardiogenic Shock. The Danish Cardiogenic Shock Trial	360	Jan 2023
NCT01187368 ^a	Prospective Multi-Center Randomized Study for Evaluating the EVAHEART®2 Left Ventricular Assist System: the COMPETENCE Trial	399	Dec 2024
NCT01966458 ^a	A prospective, randomized, controlled, unblinded, multi-center clinical trial to evaluate the HeartWare® VAD for	494	Aug 2020

	destination therapy of advanced heart failure.		
NCT01187368 ^a	A prospective study to evaluate the safety and efficacy of the EVAHEART LVAS for use as bridge-to-transplant	20	Dec 2020
NCT02468778 ^a	Supporting Patients Undergoing high-Risk PCI Using a High-Flow percutaneous Left Ventricular Support Device (SHIELD II)	716	Dec 2020
NCT02232659	SynCardia 70cc Temporary Total Artificial Heart (TAH-t) for Destination Therapy (DT)	38	Dec 2020
NCT02326402	THEME Registry: TandemHeart Experiences and Methods	200	Dec 2020
NCT02459054	SynCardia 50cc Temporary Total Artificial Heart (TAH-t) as a Bridge to Transplant	72	Jun 2024
NCT01627821 ^a	Evaluation of the Jarvik 2000 left ventricular assist system with post-auricular connector—destination therapy study	350	Dec 2020
NCT01369407	REVIVE-IT registry (REVIVAL: registry evaluation of vital information for VADs in ambulatory life)	400	Jun 2019
NCT02387112	Early versus emergency left ventricular assist device implantation in patients awaiting cardiac transplantation	500	Dec 2022

NCT: national clinical trial

^a Denotes industry-sponsored or cosponsored trial.

SUMMARY OF EVIDENCE

Ventricular Assist Device

For individuals who have end-stage heart failure who receive a VAD as a bridge to transplant, the evidence includes single-arm trials and observational studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. 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 reducing mortality as well as improving quality of life. These studies have reported that substantial numbers of patients have survived to transplant in situations in which survival would not be otherwise expected. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end-stage heart failure who receive a VAD as destination therapy, the evidence includes a trial and multiple single-arm studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. A well-designed trial, with 2 years of follow-up data, has demonstrated an advantage of implantable VADs as destination therapy for patients ineligible for heart transplant. Despite an increase in adverse events, both mortality and quality of life appear to be improved for these patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Total Artificial Heart

For individuals who have end-stage heart failure who receive a TAH as a bridge to transplant, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. Compared with VADs, the evidence for TAHs in these settings is less robust. However, given the lack of medical or surgical options for these patients and the evidence case series provide, 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 a left VAD. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end-stage heart failure who receive a TAH as destination therapy, the evidence includes 2 case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, and treatment-related mortality and morbidity. The body of evidence for TAHs as destination therapy is too limited to draw conclusions. The evidence is insufficient to determine the effects of the technology on health outcomes.

Percutaneous Ventricular Assist Device

For individuals with cardiogenic shock or who undergo high-risk cardiac procedures who receive a pVAD, the evidence includes randomized controlled trials. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, quality of life, and treatment-related mortality and morbidity. Four randomized controlled trials of pVAD vs IABP for patients in cardiogenic shock failed to demonstrate a mortality benefit and reported higher complication rates with pVAD use. Another randomized controlled trial 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. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with cardiogenic shock refractory to IABP therapy who receive a pVAD, the evidence includes case series. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, quality of life, and treatment-related mortality and morbidity. Case series of patients with cardiogenic shock refractory to IABP have reported improved hemodynamic parameters following pVAD placement. However, these uncontrolled series do not provide evidence that pVADs improve mortality, and high rates of complications have been reported with pVAD use. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, BCBSA received input from two physician specialty societies and five academic medical centers while this policy was under review in May 2014. Vetting focused on the use of percutaneous VADs in accordance with the American Heart Association /American College of Cardiology guidelines (2013) and the use of TAH as destination therapy. All of those providing input supported the use of implantable VADs as destination therapy subject to the guidelines in the policy statements. Most of those providing input considered TAHs investigational for destination therapy; reviewers noted that there is limited clinical trial data to support the use of TAHs as destination therapy.

Most of those providing input considered pVADs to be investigational as a “bridge to recovery” or “bridge to decision” and for all other indications. Some reviewers noted that pVADs may improve patients’ hemodynamics better than other alternatives, such as an IABP but are associated with more complications. Some reviewers noted that, despite a lack of evidence to

indicate that pVADs improve overall outcomes, there might be cases when pVADs may be considered to support an intervention or treatment for a life-threatening condition.

PRACTICE GUIDELINES AND POSITION STATEMENTS

American Association for Thoracic Surgery/International Society for Heart and Lung Transplantation

In 2020, the American Association for Thoracic Surgery and the International Society for Heart and Lung Transplantation published guidelines on selected topics in mechanical circulatory support, including recommendations on the use of pVADs (Table 10).⁷⁹ The guideline authors noted, "Compared with IABP, contemporary percutaneous circulatory support devices provide a significant increase in cardiac index and mean arterial pressure; however, reported 30-day outcomes are similar."

Table 10. 2020 Guidelines on Mechanical Circulatory Support

Recommendation	COE	LOE
"Percutaneous LV to aorta pumps of appropriate size should be considered for cardiogenic shock from primary LV failure."	IIA	B

COE: class of evidence; LOE: level of evidence; LV: left ventricular.

Society for Cardiovascular Angiography and Interventions et al

In 2015, the Society for Cardiovascular Angiography and Interventions (SCAI), the Heart Failure Society of America (HFSA), the Society of Thoracic Surgeons (STS), the American Heart Association (AHA), and the American College of Cardiology (ACC) published a clinical expert consensus statement on the use of percutaneous mechanical circulatory support (MCS) devices in cardiovascular care.⁷⁷ This statement addressed intra-aortic balloon pumps (IABPs), left atrial (LA)-to-aorta assist device (e.g., TandemHeart), left ventricle (LV)-to-aorta assist devices (e.g., Impella), extracorporeal membrane oxygenation (ECMO), and methods of right-sided support. Specific recommendations are not made, but the statement reviews the use of MCS in patients undergoing high-risk percutaneous intervention (PCI), those with cardiogenic shock, and those with acute decompensated heart failure.

American College of Cardiology Foundation and American Heart Association

The American College of Cardiology Foundation, American Heart Association (AHA), and Heart Failure Society of American (2017) published a focused update of the 2013 recommendations released by the American College of Cardiology Foundation and AHA.⁷⁸ Left ventricular assist device was one of several treatment options recommended for patients with refractory New York Heart Association class III or IV heart failure (stage D). If symptoms were not improved after guidelines-directed management and therapy, which included pharmacologic therapy, surgical management and/or other devices, then left ventricular assist device would be an additional treatment option.

The 2017 update focused on changes in sections regarding biomarkers, comorbidities, and prevention of heart failure, while many of the previous recommendations remained unchanged. The American College of Cardiology Foundation and AHA (2013) released guidelines for the management of heart failure that included recommendations related to the use of MCS, including both durable and nondurable MCS devices.⁷⁹ The guidelines categorized pVADs and

extracorporeal VADs as nondurable MCS devices. Table 10 provides class IIA guidelines on MCS devices.

Table 11. 2013 Guidelines on MCS

Recommendations	COE	LOE
"MCS is beneficial in carefully selected patients with stage D HF _r EF in whom definitive management (e.g., cardiac transplantation) or cardiac recovery is anticipated or planned."	IIA	B
"Nondurable MCS, including the use of percutaneous and extracorporeal ventricular assist devices (VADs), is reasonable as a "bridge to recovery" or "bridge to decision" for carefully selected patients with HF _r EF with acute, profound hemodynamic compromise."	IIA	B
"Durable MCS is reasonable to prolong survival for carefully selected patients with stage D HF _r EF."	IIA	B

COE: class of evidence; HF_rEF: heart failure with reduced ejection fraction; LOE: level of evidence; MCS: mechanical circulatory support.

These 2013 guidelines also noted:

"Although optimal patient selection for MCS remains an active area of investigation, general indications for referral for MCS therapy include patients with LVEF [left ventricular ejection fraction] <25% and NYHA [New York Heart Association] class III-IV functional status despite GDMT [guideline-directed medical therapy], including, when indicated, CRT [cardiac resynchronization therapy], 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 [heart failure] and transplantation cardiologists, cardiothoracic surgeons, nurses, and ideally, social workers and palliative care clinicians."

American Heart Association

The AHA (2012) published recommendations for the use of MCS.⁸⁰ These guidelines defined nondurable MCS as intraballoon pumps, extracorporeal membrane oxygenation, extracorporeal VADs, and pVADs. Table 11 lists recommendations made on indications for the use of MCS, including durable and nondurable devices.

Table 12. 2012 Guidelines on MCS

Recommendation	COE	LOE
"MCS for BTT indication should be considered for transplant-eligible patients with end-stage HF who are failing optimal medical, surgical, and/or device therapies and at high risk of dying before receiving a heart transplantation."	I	B
"Implantation of MCS in patients before the development of advanced HF ... is associated with better outcomes. Therefore, early referral of HF patients is reasonable."	IIA	B
"MCS with a durable, implantable device for permanent therapy or DT is beneficial for patients with advanced HF, high 1-year mortality resulting from HF, 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."	I	B
"Elective rather than urgent implantation of DT can be beneficial when performed after optimization of medical therapy in advanced HF patients who are failing medical, surgical, and/or device therapies."	IIA	C
"Urgent nondurable MCS is reasonable in hemodynamically compromised HF 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."	IIA	C
"These patients should be referred to a center with expertise in the management of durable MCS and patients with advanced HF."	I	C

"Patients who are ineligible for heart transplantation because of pulmonary hypertension related to HF alone should be considered for bridge to potential transplant eligibility with durable, long-term MCS." IIA B

BTT: bridge to transplant; COE: class of evidence; DT: destination therapy; HF: heart failure; LOE: level of evidence; MCS: mechanical circulatory support.

Heart Failure Society of America

Heart Failure Society of America (2010) published guidelines on surgical approaches to the treatment of heart failure.⁸¹ Table 12 lists recommendations on left VADs.

Table 13. Guidelines on Left Ventricular Assist Devices

Recommendation	SOE
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."	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."	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."	C

HF: heart failure; SOE: strength of evidence.

Government Regulations National:

National Coverage Determination (NCD) for Artificial Hearts and Related Devices (20.9)⁸⁴
Implementation date: 9/30/14.

An artificial heart is a biventricular replacement device which requires removal of a substantial part of the native heart, including both ventricles. Removal of this device is not compatible with life, unless the patient has a heart transplant.

Indications and Limitations of Coverage

1. Bridge-to-transplant (BTT) (effective for services performed on or after May 1, 2008)
An artificial heart for bridge-to-transplantation (BTT) is covered when performed under coverage with evidence development (CED) when a clinical study meets all of the criteria listed below. The clinical study must address at least 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?

The clinical study must meet all of the criteria stated in Section D of this policy. The above information should be mailed to: Director, Coverage and Analysis Group, Centers for

Medicare & Medicaid Services (CMS), Re: Artificial Heart, Mailstop S3-02-01, 7500 Security Blvd, Baltimore, MD 21244-1850.

Clinical studies that are determined by CMS to meet the above requirements will be listed on the CMS Web site at: <http://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/Artificial-Hearts.html>.

2. Destination therapy (DT) (effective for services performed on or after May 1, 2008)
An artificial heart for destination therapy (DT) is covered when performed under CED when a clinical study meets all of the criteria listed below. The clinical study must address at least 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?

The clinical study must meet all of the criteria stated in Section D of this policy. The above information should be mailed to: Director, Coverage and Analysis Group, Centers for Medicare & Medicaid Services, Re: Artificial Heart, Mailstop S3-02-01, 7500 Security Blvd, Baltimore, MD 21244-1850.

Clinical studies that are determined by CMS to meet the above requirements will be listed on the CMS Web site at: <http://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/Artificial-Hearts.html>.

3. **Nationally Non-Covered Indications:** All other indications for the use of VADs or artificial hearts not otherwise listed remain non-covered, except in the context of Category B investigational device exemption clinical trials (42 CFR 405) or as a routine cost in clinical trials defined under section 310.1 of the NCD Manual.

National Coverage Determination (NCD) for Ventricular Assist Devices (VADs)

Implementation date: 9/30/14. (20.9.1)

A ventricular assist device (VAD) is surgically attached to one or both intact ventricles and is used to assist or augment the ability of a damaged or weakened native heart to pump blood. Improvement in the performance of the native heart may allow the device to be removed.

Indications and Limitations of Coverage

1. Post-cardiotomy (effective for services performed on or after October 18, 1993) Post-cardiotomy is the period following open-heart surgery. VADs used for support of blood circulation post-cardiotomy are covered only if they have received approval from the Food and Drug Administration (FDA) for that purpose, and the VADs are used according to the FDA-approved labeling instructions.
2. Bridge-to-Transplant (effective for services performed on or after January 22, 1996)
The VADs used for bridge to transplant are covered only if they have received approval from the FDA for that purpose, and the VADs are used according to FDA-approved

labeling instructions. All of the following criteria must be fulfilled in order for Medicare coverage to be provided for a VAD used as a bridge to transplant:

- The patient is approved for heart transplantation by a Medicare-approved heart transplant center and is active on the Organ Procurement and Transplantation Network (OPTN) heart transplant waitlist.
 - The implanting site, if different than the Medicare-approved transplant center, must receive written permission from the Medicare-approved transplant center under which the patient is listed prior to implantation of the VAD.
3. Destination Therapy (DT) (effective for services performed on or after October 1, 2003) Destination therapy (DT) is for patients that require mechanical cardiac support. The VADs used for DT are covered only if they have received approval from the FDA for that purpose.

Patient Selection (effective November 9, 2010):

The 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 at the time of VAD implant, and meet the following conditions:

- Have failed to respond to optimal medical management (including beta-blockers and ACE inhibitors if tolerated) for 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 (effective October 30, 2013):

Facilities currently credentialed by the Joint Commission for placement of VADs as DT 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 as DT under section 1862(a)(1)(A) of the Social Security Act (the Act):

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:

- At least one physician with cardiothoracic surgery privileges and individual experience implanting at least 10 durable, intracorporeal, left VADs as BTT 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 the Centers for Medicare & Medicaid Services.

NOTE: Medicare does not specifically address percutaneous LVAD insertions. The codes relating to pVADs (33990, 33991 and 33992) all have assigned fees.

Local:

There is no LCD on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Cardiac Support Devices
- Cardiac Rehabilitation
- Heart Transplant
- Surgical Ventricular Restoration

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through December 2019, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
9/1/13	6/18/13	6/26/13	Joint combined policy on Total Artificial Hearts and Ventricular Assist Devices established mirroring the BCBSA policy. It replaces the current JUMP policy on Total Artificial Heart as a Bridge to Transplant. The JUMP policy diverges from BCBSA in that percutaneous VADs are covered for select patients who are unable to tolerate or are not responding to IABP. The original JUMP policy on Ventricular Assist Devices was retired 7/1/08.
11/1/14	8/19/14	8/28/14	Routine maintenance. pVAD coverage expanded to cover their use during high-risk PCI (see inclusionary guidelines) and as first-line therapy for cardiogenic shock in carefully selected patients.
1/1/16	10/13/15	10/27/15	Routine maintenance
1/1/17	10/11/16	10/11/16	Routine policy maintenance. Updated rationale and references. Added Medicare information on VADs.
1/1/18	10/19/17	10/19/17	Routine policy maintenance. No change in policy status.
5/1/18	2/20/18	2/20/18	Code update, added codes 33927, 33928 and 33929 as established.
5/1/19	2/19/19		Routine policy maintenance, added code L8698. No change in policy status.
5/1/20	2/18/20		Updated rationale, added references 6, 7, 29, 30, 66, 70. No change in policy status.

5/1/21	2/16/21		Routine policy maintenance. No change in policy status. Added new codes 33995 and 33997 (EFD 1/1/21)
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Next Review Date: 1st Qtr. 2022

BLUE CARE NETWORK BENEFIT COVERAGE

POLICY: TOTAL ARTIFICIAL HEARTS AND IMPLANTABLE VENTRICULAR ASSIST DEVICES

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.