Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 5/1/24**
(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
According to a 2022 report from the American Heart Association and based on data collected from 2015 to 2018, roughly 6 million Americans ages 20 years or older had heart failure during that time frame.[1] Prevalence of heart failure is projected to affect more than 8 million people 18 years of age and older by the year 2030. Between 2015 and 2018, the prevalence of heart failure was highest in non-Hispanic Black males. Based on data from the Multi-Ethnic Study of Atherosclerosis (MESA), in those without baseline cardiovascular disease, Black individuals had the highest risk of developing heart failure (4.6 per 1000 person-years), followed by Hispanic (3.5 per 1000 person-years), White (2.4 per 1000 person-years), and Chinese individuals (1.0 per 1000 person-years).[2] Similar findings were demonstrated in the Atherosclerosis Risk in Communities (ARIC) Community Surveillance data, in which Black men and women had the highest burden of new-onset heart failure cases and the highest-age adjusted 30-day case fatality rate in comparison to White men and women. Higher risk reflected differential prevalence of hypertension, diabetes, and low socio-economic status.

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.[3] 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 cardiotomy affecting the ventricular wall may preclude VAD use.

Total Artificial Hearts

The total artificial heart (TAH) is a biventricular device that completely replaces the function of the diseased heart. An internal battery requires frequent recharging from an external power source. Many systems use a percutaneous power line, but a transcutaneous power-transfer coil allows for a system without lines traversing the skin, possibly reducing the risk of infection. Because the native heart must be removed, failure of the device is synonymous with cardiac death.

Currently the Syncardia Temporary Total Artificial Heart (Syncardia Systems) is the only Total Artificial Heart available in the US (Table 2). The AbioCor Total Artificial Heart was FDA approved under the Humanitarian Device Exemption program in 2006, but is no longer being marketed or in development.

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 Discontinued August 2021, no longer available
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	Temporatry ventricular support for <=6 h
Total Artificial Heart				
SynCardia Temporary Total Artificial Heart (Formerly CardioWest Total Artificial Heart and Jarvik Total Artificial	SynCardia Systems	2004	510(k)	Bridge to transplant in cardiac transplant-eligible candidates at risk of imminent death from biventricular failure.

Heart)				

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. HeartWare® is no longer available.

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.

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 2017and 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 2 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

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 Class III heart failure with dyspnea upon mild physical activity or NYHA Class IV;
  - Left ventricular ejection fraction $\leq$ 25%
  - Inotrope-dependent, or cardiac index <2.2 liters/min/m^2, while not on inotropes and also meeting one of the following:
    - On optimal medical management, based on current heart failure practice guidelines for at least 45 of the last 60 days and are failing to respond or
    - Advanced heart failure for at least 14 days and dependent on intra-aortic balloon pump for $\geq$7 days

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*
Have no other reasonable medical or surgical treatment options, who are ineligible for other univentricular or biventricular support devices, and are currently listed as heart transplantation candidates; or Have no other reasonable medical or surgical treatment options, are ineligible for other univentricular or biventricular support devices, are 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

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

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

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

Interventions
The therapy being considered is a VAD.

There are 4 categories of use for VADs. However, these categories may overlap, as the intent of using a VAD may evolve over the course of treatment. Recently the concept of short and long term mechanical circulatory support has been used to describe the overlap across these indications.

- Bridge to transplant: Use of a VAD to sustain life until a donor heart becomes available.
- Destination therapy: Permanent use of the device, typically for patients ineligible for transplantation.
- Bridge to recovery: Use of a VAD results in restoration of myocardial function, sufficient that heart transplant is not needed.

- Bridge to decision: Use of a VAD in an attempt to reverse secondary organ dysfunction that is a contraindication to transplant. However, these cases are often characterized as destination therapy rather than bridge to decision.

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 Heart Transplant in Adults

Randomized Controlled Trial
The Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (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; inclusion criteria included: 1) New York Heart Association (NYHA) Class III heart failure with dyspnea upon mild physical activity or NYHA Class IV; 1) left ventricular ejection fraction ≤ 25%; 3) inotrope-dependent OR cardiac index <2.2 liters/min/m^2 while not on inotropes plus on optimal medical management for at least 45 of the last 60 days and failing to respond or with advanced heart failure for at least 14 days and dependent on intra-aortic balloon pump for ≥7 days. HeartMate 3 received premarket approval (PMA) 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 [RR], 0.84; 95% confidence interval [CI], 0.78 to 0.91, p<.001).[6.] Prevalence of stroke at 2 years was lower in the HeartMate 3 than the HeartMate II 2 group (10.1% vs 19.2%; p=.02).[7.] Measures of functional capacity and Health-Related QOL did not differ between the 2 devices at 6 months.[8.]

A prespecified subgroup analysis of MOMENTUM 3 published in 2020 did not find differences in outcomes based on preoperative categories of bridge to transplant, bridge to transplant candidacy, or destination therapy. [9.]

Nonrandomized Studies

Slaughter et al (2013) reported combined outcomes for patients included in the HeartWare bridge to transplant study and a continued-access protocol granted by the U.S. Food and Drug Administration (FDA). FDA.[10,] The study included 322 patients with heart failure, eligible for a heart transplant, who received the HeartWare (140 patients from the original study; 190 patients in the continue-access protocol who were monitored to the outcome or had completed 180-day follow-up at the time of analysis). Survival rates at 60, 180, and 360 days were 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 QOL measures. (Note: The HeartWare VAD System was discontinued in June 2021 due to evidence from observational studies demonstrating a higher frequency of neurological adverse events and mortality with the system compared to other commercially available LVADs.)

Strueber et al (2011) published a case series of 50 patients awaiting heart transplantation treated with HeartWare Ventricular Assist System, which is a smaller, continuous-flow centrifugal device implanted in the pericardial space.[11,] 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 4 from hemorrhagic stroke. At the end of follow-up, 20 (40%) patients had undergone transplant, 4 (8%) had had the pump explanted, and the remaining 17 (34%) continued on pump support. The most common complications were infection and bleeding: 21 (42%) patients had infections, 5 (10%) had sepsis, while 15 (30%) patients had bleeding complications, 10 (20%) of whom required surgery. (Note: The HeartWare VAD System was discontinued in June 2021 due to evidence from observational studies demonstrating a higher frequency of neurological adverse events and mortality with the system compared to other commercially available LVADs.)

Aaronson et al (2012) reported on results of a multicenter, prospective study of the HeartWare device.[12,] The study enrolled 140 patients awaiting heart transplantation who underwent HeartWare implantation. A control group of 499 subjects comprised patients drawn from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database, which collects data on patients who receive FDA approved durable mechanical circulatory support (MCS) 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 status, QOL, and adverse event outcomes in the HeartWare group. Success on the primary outcome occurred in 90.7% of the HeartWare group and 90.1% of controls ($p<.001$, noninferiority with a 15% margin). Serious adverse events in the HeartWare group included, most commonly, bleeding, infections, and perioperative right heart failure. (Note: The HeartWare VAD System was discontinued in June 2021 due to evidence from observational studies demonstrating a higher frequency of neurological adverse events and mortality with the system compared to other commercially available LVADs.)

In 5 reports published from 2007 to 2008, with sample sizes ranging from 32 to 279 patients, most participants received the continuous-flow device as a bridge to transplantation.[13,14,15,16,17,] Survival rates at 6 months ranged between 67% and 87%, and between 50% and 80% at 1 year. These rates were similar to those reported from the INTERMACS registry.[18,] A study by Patel et al (2008) compared HeartMate I with HeartMate II recipients at a single-center, finding similar rates of 1 year survival and subsequent

development of right heart failure.[16] Serious adverse events occurring after HeartMate II implantation included bleeding episodes requiring reoperation, stroke, infection, and device failure.

Aissaoui et al (2018) published an observational study comparing 224 patients in Germany and France with end-stage heart failure who received a VAD (group I, n=83) or heart transplantation or medical therapy as first treatment options (group II, n=141).[19] The estimated 2-year survival was 44% for group I and 70% for group II (p<.001).

Reports from registries of patients who received the HeartMate 3 device have been published recently. Schmitto et al (2019) reported 2-year outcomes in 50 patients who received the device as a bridge to transplant.[20] Survival rates at 6 months, 1 year, and 2 years were 92%, 81%, and 74%, respectively, and the total stroke rate over 2 years was 24%. Gustafsson et al (2018) reported 6-month outcomes of 482 patients; 66% of patients received the VAD as a bridge to transplant, 26% as destination therapy, 2% as a bridge to recovery, and 6% as a bridge to transplant candidacy or decision. Results were not separately reported by indication.[21] The 6-month survival rate was 82% (95% CI, 79% to 85%). Three patients received a transplant. The incidence of stroke was 6.1%. Pagani et al (2021) used Medicare claims data to analyze survival outcomes in patients who received different LVADs between January 2014 and December 2018, with follow-up through December 2019.[22] Of 4195 patients who received implants, there were 117 (14.3%) deaths among 821 Heartmate3 patients, 375 (20.4%) deaths among 1840 Heartmate II patients, and 375 (24.5%) deaths among 1534 patients with other VADs. The adjusted hazard ratio for mortality at 1-year (confirmed in a propensity score matched analysis) for the HeartMate 3 versus HeartMate II was 0.64 (95% CI, 0.52 to 0.79; p<.0001) and for the HeartMate 3 versus other-VADs was 0.51 (95% CI, 0.42 to 0.63; p<.0001).

Additionally, after the randomized trial phase of MOMENTUM 3 was completed, a post-pivotal trial continuous access protocol was initiated as a single-arm prospective study to assess the reproducibility of HeartMate 3 LVAD outcomes across centers.[23] Full results are described below.

Ventricular Assist Devices as Destination Therapy for End-Stage Heart Failure in Adults

Systematic Reviews

The evaluation of VADs as destination therapy was informed by a TEC Assessment (2002) that offered the following observations and conclusions[24]:

- The available evidence comes from a single, well-designed and rigorously conducted randomized trial, Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure, known as the REMATCH study.[25] The trial was a cooperative effort of Thoratec, Columbia University, and the National Institutes of Health.
- The trial found that patients with end-stage heart failure who are not candidates for cardiac transplantation had 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 they appear to be outweighed by this group's better outcomes on function; New York Heart Association functional class was significantly improved, as was the QOL among those living to 12 months.

- VAD patients spent a greater relative proportion of time inside the hospital than medical management patients did but the survival advantage would mean a longer absolute time outside the hospital.

Park et al (2005) published reports on the extended 2-year follow-up of patients from the REMATCH trial, which found that survival and QOL benefits were still apparent.[26,27,] In addition, their reports and other case series have suggested continuing improvement in outcomes related to ongoing improvements in the device and patient management. However, the durability of the HeartMate device used in the REMATCH trial was a concern (eg, at a participating institution, all 6 long-term survivors required device change-outs).

Randomized Controlled Trials

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; inclusion criteria included 1) NYHA Class III heart failure with dyspnea upon mild physical activity or NYHA Class IV; 1) left ventricular ejection fraction ≤ 25%; 3) inotrope-dependent OR cardiac index <2.2 liters/min/m^2 while not on inotropes plus on optimal medical management for at least 45 of the last 60 days and failing to respond or with advanced heart failure for at least 14 days and dependent on intra-aortic balloon pump for ≥7 days. 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 (RR, 0.84; 95% CI, 0.78 to 0.91, p<.001).[6,] Prevalence of stroke at 2 years was lower in the HeartMate 3 than the HeartMate 2 group (10.1% vs 19.2%; p=.02).[7,] Measures of functional capacity and Health-Related QOL did not differ between the 2 devices at 6 months.[8,]

A prespecified subgroup analysis of MOMENTUM 3 published in 2020 did not find differences in outcomes based on preoperative categories of bridge to transplant, bridge to transplant candidacy, or destination therapy. Additionally, nearly 15% of those initially deemed transplant ineligible were eventually transplanted within 2 years of follow-up, supporting that clinical categorizations based on transplant eligibility should no longer be used.[9,]

The ENDURANCE trial compared the HeartWare centrifugal continuous-flow device with the HeartMate II axial continuous-flow device in patients indicated for circulatory support as destination therapy.[28,] 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 2 years. (Note: The HeartWare VAD System was discontinued in June 2021 due to evidence from observational studies demonstrating a higher frequency of neurological adverse events and mortality with the system compared to other commercially available LVADs.)

Nonrandomized Studies

A prospective observational study called the Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients (ROADMAP) study, reported by Estep et al (2015), compared LVAD support (n=97)

with optimal medical therapy (n=103) for patients with heart failure not requiring inotropes and found superior survival and health-related QOL in LVAD-treated patients.[29,] Twelve-month, as-treated, event-free actutimes actutimes survival was 80% in the LVAD group and 63% in the best medical therapy group (p=.022). Two-year results were reported by Starling et al (2017).[30,] 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 actutimes actutimes survival (70% vs 41%, p<.001), although there was no statistical difference in intention-to-treat survival (70% vs 63%, p=.31).

In an FDA required, post-approval study of the HeartMate II device for destination therapy,[31,] 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 the release of the REMATCH trial results, Rogers et al (2007) published results from a prospective, nonrandomized trial comparing LVAD as destination therapy with optimal medical therapy for patients with heart failure who were not candidates for a heart transplant.[32,] Fifty-five patients who had NYHA functional class IV symptoms and who failed to wean from inotropic support were offered a Novacor LVAD; 18 did not receive a device due to preference or device unavailability and served as a control group. The LVAD-treated patients had superior survival rates at 6 months (46% vs 22%; p=.03) and 12 months (27% vs 11%; p=.02), along with fewer adverse events.

Arnold et al (2016) analyzed 1638 patients receiving LVADs as destination therapy between May 2012 and September 2013.[33,] Results were selected from the INTERMACS registry and assessed for poor outcomes. Poor outcome was defined as death or mean Kansas City Cardiomyopathy Questionnaire overall score less than 45 throughout the year after implantation. Analyses included inverse probability weighting to adjust for missing data. About 22.4% of patients died within the first year after implantation, and an additional 7.3% had persistently poor QOL; 29.7% met the definition of poor outcome. Poor outcomes were more common in those patients having higher body mass indices, lower hemoglobin levels, previous cardiac surgery, history of cancer, severe diabetes, and poorer QOL preimplant.

After the randomized trial phase of MOMENTUM 3 was completed, a post-pivotal trial continuous access protocol was initiated as a single-arm prospective study to assess the reproducibility of HeartMate 3 LVAD outcomes across centers.[23,] Of the 516 patients initially randomized to HeartMate 3 in the MOMENTUM 3 pivotal trial, 515 comprised the pivotal cohort. Starting in October 2017, bridge to transplant patients were excluded from continuous access phase enrollment. In the continuous access phase cohort, 1685 patients were ultimately included. The primary outcomes for this extended study were survival to transplant, recovery, or ongoing LVAD support, free of disabling stroke or reoperation to replace or remove a malfunctioning pump, at 2 years post-implant. At 2 years post-implant, a similar proportion of patients in the continuous access group versus the pivotal cohort achieved the composite endpoint (76.7% vs 74.8%; adjusted HR, 0.87; 95% CI, 0.71 to 1.08; p=.21). Pump exchange rates were low in both cohorts with 98.4% of the continuous access cohort and 96.9% of the pivotal cohort being free of pump replacement at 2 years. Overall survival at 2

years was 81.2% in the continuous access cohort compared to 79% in the pivotal cohort. After controlling for baseline demographics between cohorts, the adjusted HR for continuous access versus pivotal cohort was 0.84 (95% CI, 0.67 to 1.06; p=.15). Survival based on whether the HeartMate was used a bridge to transplant or as destination therapy was also similar between the continuous access and pivotal trial cohorts (bridge to transplant adjusted HR, 0.70; 95% CI, 0.43 to 1.14; p=.15; destination therapy adjusted HR, 0.89; 95% CI, 0.68 to 1.16; p=.38). This additional trial in a larger cohort reproduced similar results to the initial MOMENTUM 3 study, especially in individuals using VADs as destination therapy.

Mehra et al (2022) reported 5-year observational outcomes from the MOMENTUM 3 study comparing the HeartMate 3 centrifugal continuous-flow device with the HeartMate II axial continuous-flow device.[34,] The per-protocol population initially included in the MOMENTUM 3 RCT was 1020 patients. A total of 477 patients of 536 patients still receiving LVAD support at 2 years contributed to the extended-phase analysis. At 5 years, 141 patients in the HeartMate 3 group and 85 in the HeartMate II group had completed follow-up. The composite of 5-year survival to transplant, recovery, or LVAD support free of debilitating stroke or reoperation to replace the pump occurred in 336/515 patients (65.2%) in the HeartMate 3 group versus 240/505 patients (47.5%) in the HeartMate II group. The Kaplan-Meier estimates of event-free survival at 5 years were 54% in the HeartMate 3 group and 29.7% in the HeartMate II group (HR, 0.55; 95% CI, 0.45 to 0.67; p<.001). The overall survival rates were 58.4% in the HeartMate 3 group and 43.7% in the HeartMate II group (HR, 0.72; 95% CI, 0.58 to 0.89; p=.003). In a post-hoc analysis, there were consistent survival findings in the destination therapy-specific subgroup, with a 5-year survival rate of 54.8% in the HeartMate 3 group and 39.4% in the HeartMate II group (HR, 0.70; 95% CI, 0.55 to 0.90; p=.005). Rates for device thrombosis (0.010 vs 0.108 events/patient-years), stroke (0.050 vs 0.136 events/patient-years), and bleeding (0.430 vs 0.765 events/patient-years) were significantly lower in the HeartMate 3 group compared to the HeartMate II group over 5 years, respectively. Infection, cardiac arrhythmias, and right ventricular failure were similar between groups. These 5-year outcomes demonstrate that the HeartMate 3 was associated with a better composite outcome and a higher likelihood of survival at 5 years.

Ventricular Assist Devices as Bridge to Recovery in Adults

Nonrandomized Studies

VADs may have a role in bridging patients to recovery, particularly if there is reverse remodeling of the left ventricle. 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 postcardiotomy 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.[35] 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).[36] 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.[37]

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.[38] 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.

Agrawal et al (2018) conducted a retrospective cohort study evaluating the 30-day readmissions of 2510 patients undergoing LVAD implantation.[39.] 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.

Ventricular Assist Devices in Pediatric Patients

The FDA-approved EXCOR Pediatric VAD is available for use as a bridge to cardiac transplant in children. The FDA approval was based on data from children who were part of the initial clinical studies of this device.[40] Publications have reported positive outcomes for children using VADs as a bridge to transplantation.

Comparative Studies

Bulic et al (2017) identified all U.S. children between 1 and 21 years of age at heart transplant between 2006 and 2015 who had dilated cardiomyopathy and were supported with an LVAD or vasoactive infusions alone at the time of transplant from the Organ Procurement and Transplant Network registry (N=701).[41.] Functional status as measured by the median Karnofsky Performance Scale score at heart transplant was higher for children receiving LVAD (6) compared with vasoactive infusion (5; p<.001) and children receiving LVAD were more likely to be discharged from the hospital at the time of transplant. The percentage of children having a stroke at the time of transplant was higher in those receiving LVAD (3% vs 1%, p=.04).

Wehman et al (2016) reported on posttransplant survival outcomes for pediatric patients who received a VAD, extracorporeal membrane oxygenation (ECMO), or no MCS, in the

pretransplant period.[42,] 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 actutimes actutimes 5-year survival rate 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 posttransplant, ECMO bridging was significantly associated with a higher risk of death (adjusted hazard ratio, 2.77 vs direct-to-transplant; 95% CI , 2.12 to 3.61; p<.001). However, a model to predict time to death excluding deaths in the first 4 months posttransplant, the bridging group was not significantly associated with risk of death.

Fraser et al (2012) evaluated the EXCOR device among 48 children, ages 16 or younger, with 2-ventricle circulation who had severe heart failure, despite optimized treatment, and were listed for a heart transplant.[43,] Patients were divided into 2 groups based on body surface area; a historical control group of children receiving circulatory support with ECMO from the Extracorporeal Life Support Organization registry were matched in a 2:1 fashion with study participants based on propensity-score matching. For participants in cohort 1 (body surface area <0.7 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<.001). For participants in cohort 2 (body surface area range, 0.7 to <1.5 m^2), the median survival was 144 days compared with 10 days in the matched ECMO group (p<.001). Rates of adverse events were high in both EXCOR device cohorts, including major bleeding (cohort 1, 42%; cohort 2, 50%), infection (cohort 1, 63%; cohort 2, 50%), and stroke (29% of both cohorts).

Noncomparative Studies

Blume et al (2016) published the first analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support, which is a prospective, multicenter registry that collects data on patients who are under age 19 years at the time of implant, and includes those implanted with either durable or temporary VADs.[44,] At analysis, the registry included 241 patients; of them, 41 were implanted with a temporary device only, leaving 200 patients implanted with VADs for this study. Most patients (73%) had an underlying diagnosis of cardiomyopathy. At the time of implantation, 64% were listed for transplant, while 29% were implanted with a "bridge to candidacy" strategy. A total of 7% were implanted with a destination therapy strategy. Actutimes Actutimes survival at both 6 months and 1 year was 81%. By 6 months, 58% of patients had received transplants.

Almond et al (2013) reported results from a prospective, multicenter registry to evaluate outcomes in children who received the EXCOR device as a bridge to transplant.[45,] This study included a broader patient population than the Fraser et al (2012) study (discussed above). All patients were followed 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 the patient survived 30 days), and 5% who were alive with the device in place. In a follow-up study that evaluated 204 children from the same registry, Jordan et al (2015) 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.[46,]

Chen et al (2016) reported on a retrospective, single-center series of pediatric patients with continuous-flow VADs, with a focus on outpatient experiences.[47] The series included 17 children implanted with an intracorporeal device from 2010 to 2014. Eight (47%) patients were discharged after a median postimplant hospitalization duration 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 had been transferred or died.

Another retrospective, single-center series of pediatric patients, conducted by Conway et al (2016), reported on outcomes with short-term continuous-flow VADs, including the Thoratec, PediMag, or CentriMag, or the Maquet RotaFlow.[48] From 2005 to 2014, 27 children were supported with 1 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) led to hospital discharge.

Effects of Pretransplant Ventricular Assist Devices 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 posttransplant survival, thus improving the use of donor hearts.[12, 49,50,51] A systematic review by Alba et al (2011) examined the evidence on the effect of VADs on posttransplant outcomes.[52] Reviewers included 31 observational studies that compared transplant outcomes 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 specific to patients who received an intracorporeal device (RR, 1.8; 95% CI, 1.53 to 2.13). For patients treated with an extracorporeal device, the likelihood of survival did not differ from patients not treated with a VAD (RR, 1.08; 95% CI, 0.95 to 1.22). There was no difference in the risk of rejection rates between patients who did and did not receive LVAD treatment.

Deo et al (2014) reported no significant differences in outcomes for 37 bridge to transplant patients with a VAD and 70 patients who underwent a heart transplant directly.[53] Data from the United Network for Organ Sharing Network, reported by Grimm et al (2016), suggested that patients bridged to transplant with an LVAD have better outcomes than those bridged with TAHs or biventricular assist devices.[54] Using the United Network for Organ Sharing database, Davies et al (2008) reported on the use of VADs in pediatric patients undergoing heart transplantation.[55] Their analysis concluded that pediatric patients requiring a pretransplantation VAD have long-term survival similar to those not receiving MCS.

Section Summary: Ventricular Assist Devices

In adults, the evidence on the efficacy of VADs as a bridge to transplant consists of controlled trials comparing different VADs, uncontrolled trials, registry studies, and case series.

The highest-quality evidence on the efficacy of LVADs as destination therapy in patients who are not transplant candidates is the REMATCH trial. This multicenter RCT reported that the use of LVADs led to improvements in survival, QOL, and functional status. A more recent trial comparing VADs has broader inclusion criteria and supports that criteria move away from use of transplant ineligibility, as treatment may evolve over the course of treatment. This evidence supports that health outcomes are improved with LVADs in this patient population.

Questions remain about defining and identifying the population most likely to experience cardiac recovery with VAD placement. One clearly defined population in which the potential for myocardial recovery exists is in the postcardiotomy setting. The current evidence is insufficient to identify other heart failure patient populations that might benefit from the use of an LVAD as a specific bridge to recovery treatment strategy.

The evidence in children, mainly from registry studies, demonstrates the effectiveness of pediatric devices as a bridge to heart transplant.

Total Artificial Heart

Clinical Context and Therapy Purpose
The purpose of a TAH in individuals who have end-stage heart failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following **PICO** was used to select literature to inform this review.

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

Interventions
The therapy being considered is a TAH used as a bridge to heart transplant or as destination therapy.

Comparators
The comparator of interest is optimal medical therapy without a TAH.

Outcomes
The general outcomes of interest are OS, survival to transplant, transplant outcomes, device malfunction or replacement, infection, and quality of life.

Time-to-transplant is of interest, as the short-term outcome ranging from 30 days to 1 year. When TAH is used as destination therapy, the time of interest ranges from 6 months to 2 years following implantation.

Total Artificial Heart as a Bridge to Transplant for End-Stage Heart Failure
Nonrandomized Studies
The FDA approval of the CardioWest TAH was based on the results of a nonrandomized, prospective study of 81 patients.[46.] Patients had failed inotropic therapy, had a biventricular failure, and thus were not considered appropriate candidates for an LVAD. Of the patients included, 88% were male. Race and ethnicity were not described. The rate of survival to transplant was 79%, which was considered comparable with the experience with LVAD in patients with left ventricular failure. The mean time from entry into the study until transplantation or death was 79.1 days.

Case series have been reported on outcomes for 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 MCS or were failing medical therapy on multiple inotropic drugs. Mean support time was 87 days (range,

1 to 441 days). The rate of survival to transplant was 68.3% (69/101). Of the 32 deaths before the transplant, 13 were due to multiorgan failure, 6 were due to pulmonary failure, and 4 were due to neurologic injury. Survival rates after transplant at 1, 5, and 10 years, respectively, were 76.8%, 60.5%, and 41.2%.

Total Artificial Heart as Destination Therapy for End-Stage Heart Failure

Case Series

Data on the artificial heart are available from the FDA approval information[58,] and from a published article describing results for the first 7 patients.[59,] The FDA indicated that its decision on the AbioCor implantable heart was based on the manufacturer's (Abiomed) laboratory and animal testing and on a small clinical study of 14 patients conducted by Abiomed. Study participants had a 1-month survival prognosis of not more than 30%, were ineligible for cardiac transplants, and were not projected to benefit from VAD therapy. The study showed that the device was safe and likely to benefit people with severe heart failure whose death was imminent and for whom no alternative treatments were available. Of the 14 patients studied, 12 survived the 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 to 1373 days), 34 (72%) patients were successfully transplanted, 12 (24%) patients died while on device support, and 1 (2%) patient was still supported. Device failure occurred in 5 (10%) patients. Major complications were common, including systemic infection in 25 (53%) patients, driveline infections in 13 (27%) patients, thromboembolic events in 9 (19%) patients, and hemorrhagic events in 7 (14%) patients. Two of the deaths occurred secondary to device failure.

Section Summary: Total Artificial Heart

There is less evidence on the use of TAH as a bridge to transplant compared with the use of LVADs. The type of evidence on a bridge to transplant is similar to that for LVADs (ie, 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-prolonging support devices.

There is 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 individuals who have cardiogenic shock is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations
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 4. Characteristics of a Systematic Review Evaluating pVADs vs. IABPs for Cardiogenic Shock

Study	Dates	Trials	Participants	N	Design
Romeo et al (2016)	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 5. Results of a Systematic Review Evaluating pVADs vs. IABP for Cardiogenic Shock

Study	In Hospital Mortality
Romeo et al (2016)	
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[62-64] and 1 was published after Romeo et al (2016).[65] 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 6. Characteristics of RCTs Evaluating pVADs and IABPs for Cardiogenic Shock

Study	Trial (Registration)	Countries	Sites	Dates	pVAD	Key Eligibility Criteria
Ouweneel et al (2017)	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)	ISAR-SHOCK (NCT00417378)	Germany	2	2004-2007	Impella LP 2.5	AMI <48h and CS
Burkhoff et al (2006)	TandemHeart (NR)	U.S.	12	2002-2004	TandemHeart	CS<24 h due to MI or heart failure
Thiele et al (2005)	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 7. Results of RCTs Evaluating pVADs and IABPs for Cardiogenic Shock

Study	30-Day Mortality	60-Day Mortality	Bleeding	Leg Ischemia	Other Outcomes
Ouweenel et al (2017) 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) 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) TandemHeart					*At least 1 adverse event:*
N	33		33	33	33
pVAD	47%		42%	21%	95%
IABP	36%		14%	14%	71%
Thiele et al (2005)					*Final cardiac index* (W/m^2)
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.

Long-term follow-up of the IMPRESS trial outcomes were published by Karami et al (2021).[66.] For this 5-year assessment, all-cause mortality, functional status, and occurrence of major adverse cardiac and cerebrovascular events were studied. Ultimately, there was no difference between groups in terms of 5-year mortality; in patients who received pVADs, 5-year mortality was 50% (12/24) and 63% (15/24) in patients who received IABP (RR, 0.87; 95% CI, 0.47 to 1.59; p=.65). Major adverse cardiac and cerebrovascular events, including death, myocardial re-infarction, repeat PCI, coronary artery bypass grafting, and stroke, occurred in 50% of the patients who received pVAD versus 79% of the IABP patients (p=.07). All survivors except for 1 were NYHA class I or II (pVAD n=10 [91%] and IABP n=7 [100%]; p=1.0) and no patients had residual angina. There were no differences in left ventricular ejection fraction between the 2 groups, supporting previously published data from the original IMPRESS trial.

Nonrandomized 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.[67] 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.[68-73]

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 individuals who undergo high-risk cardiac procedures is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

Populations
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).[74] 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 8. 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) PROTECT II	•	•
Ouweneel et al 2016 IMPRESS	•	
Ouweeneel et al (2016) IMPRESS in STEMI	•	
Seyfarth et al (2008) ISAR-SHOCK	•	

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 IBP. 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.[75] Reviewers identified 18 nonrandomized observational studies and a single RCT (PROTECT II).[76] 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 9. 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)	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 10. 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)							*Major bleeding*			
Impellla	54/1346						126/1346			89/1346
Pooled effect (95% CI)	0.35 (0.022,						0.71 (0.043,			0.049 (0.023, 0.076)

	0.048)						0.99)			
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.

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.[77] 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.[78] 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 individuals 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 following **PICOTS** were used to select literature to inform this review.

Populations

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.

Nonrandomized Studies
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.[79] 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/m^2 to 3.0 L/min/m^2 ($p<0.001$), 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 11.

Table 11. 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 2024
NCT01627821[a]	Evaluation of the Jarvik 2000 Left Ventricular Assist System With Post-Auricular Connector--Destination Therapy Study	350	Dec 2023
NCT02232659[a]	SynCardia 70cc Temporary Total Artificial Heart (TAH-t) for Destination Therapy (DT)	38	May 2022
NCT02326402[a]	THEME Registry: TandemHeart Experiences and Methods	450	Jun 2023
NCT01187368[a]	Prospective Multi-Center Randomized Study for Evaluating the EVAHEART®2 Left Ventricular Assist System: the COMPETENCE Trial	399	Mar 2024
NCT02387112	Early Versus Emergency Left Ventricular Assist Device Implantation in Patients Awaiting Cardiac Transplantation	200	Dec 2022
NCT04768322	Left Ventricular Assist Device (LVAD) Versus Guideline Recommended Medical Therapy in Ambulatory Advanced Heart Failure Patients (GDMT)	92	Feb 2027

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 sufficient 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 sufficient 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 12).[80] 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 12. 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.[86] 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.[81] 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.[82] The guidelines categorized pVADs and extracorporeal VADs as nondurable MCS devices. Table 10 provides class IIA guidelines on MCS devices. Since the 2017 update, these guidelines have been updated regularly, with the most recent update occurring in 2022.[83]

Table 13. 2017 Guidelines on MCS

Recommendations	COE	LOE
“In select patients with advanced HFrEF with NYHA class IV symptoms who are deemed to be dependent on continuous intravenous inotropes or temporary MCS, durable LVAD implantation is effective to improve functional status, QOL, and survival.”	I	A
"In select patients with advanced HFrEF who have NYHA class IV symptoms despite GDMT, durable MCS can be beneficial to improve symptoms, improve functional class, and reduce mortality."	IIA	B-R
"In patients with advanced HFrEF and hemodynamic compromise and shock, temporary MCS, including percutaneous and extracorporeal ventricular assist devices, are reasonable as a 'bridge to recovery' or 'bridge to decision'"	IIA	B-NR

COE: class of evidence; HF*r*EF: heart failure with reduced ejection fraction; LOE: level of evidence; MCS: mechanical circulatory support.

American Heart Association

The AHA (2012) published recommendations for the use of MCS.[84] 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 14. 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.

International Society for Heart and Lung Transplantation

The International Society for Heart and Lung Transplantation and the Heart Failure Society of America released a guideline on acute MCS in 2023.[85] The guideline focuses on timing, patient and device selection of acute MCS, and periprocedural and postprocedural care for cardiogenic and pulmonary shock. They provide specific recommendations depending on which MCS device is chosen. Table 15 summarizes relevant recommendations for timing of acute MCS made in the guidelines. Additional recommendations related to specific devices is related to procedural considerations.

Table 14. ISHLT/HFSA Guideline on Acute MCS

Recommendation	COR	LOE
"Acute MCS should be initiated as soon as possible in patients with CS who fail to stabilize or continue to deteriorate despite initial interventions."	I	B
"The use of acute MCS should be considered in patients with multiorgan failure to allow successful optimization of clinical status and neurologic assessment before placement of durable MCS or organ transplantation."	II	C

COR: class of recommendation; CS: cardiogenic shock; HFSA: Heart Failure Society of America; ISHLT: International Society for Heart and Lung Transplantation; LOE: level of evidence; MCS: mechanical circulatory support

Government Regulations
National:

National Coverage Determination (NCD) for Artificial Hearts and Related Devices (20.9)[87]

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

References

1. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. Circulation. Feb 22 2022; 145(8): e153-e639. PMID 35078371
2. Lewsey SC, Breathett K. Racial and ethnic disparities in heart failure: current state and future directions. Curr Opin Cardiol. May 01 2021; 36(3): 320-328. PMID 33741769
3. Organ Procurement and Transplantation Network. Heart Kaplan-Meier Patient Survival Rates For Transplants Performed : 2008 - 2015. 2018; https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#. Accessed January 2024.
4. TEC Assessment Program. Ventricular assist devices in bridging to heart transplantation. 1996;Volume 11;Tab 26.
5. Goldstein DJ, Oz MC, Rose EA. Implantable left ventricular assist devices. N Engl J Med. Nov 19 1998; 339(21): 1522-33. PMID 9819452
6. Mehra MR, Uriel N, Naka Y, et al. A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. N Engl J Med. Apr 25 2019; 380(17): 1618-1627. PMID 30883052

7. Colombo PC, Mehra MR, Goldstein DJ, et al. Comprehensive Analysis of Stroke in the Long-Term Cohort of the MOMENTUM 3 Study. Circulation. Jan 08 2019; 139(2): 155-168. PMID 30586698
8. Cowger JA, Naka Y, Aaronson KD, et al. Quality of life and functional capacity outcomes in the MOMENTUM 3 trial at 6 months: A call for new metrics for left ventricular assist device patients. J Heart Lung Transplant. Jan 2018; 37(1): 15-24. PMID 29153637
9. Goldstein DJ, Naka Y, Horstmanshof D, et al. Association of Clinical Outcomes With Left Ventricular Assist Device Use by Bridge to Transplant or Destination Therapy Intent: The Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3 (MOMENTUM 3) Randomized Clinical Trial. JAMA Cardiol. Apr 01 2020; 5(4): 411-419. PMID 31939996
10. Slaughter MS, Pagani FD, McGee EC, et al. HeartWare ventricular assist system for bridge to transplant: combined results of the bridge to transplant and continued access protocol trial. J Heart Lung Transplant. Jul 2013; 32(7): 675-83. PMID 23796152
11. Strueber M, O'Driscoll G, Jansz P, et al. Multicenter evaluation of an intrapericardial left ventricular assist system. J Am Coll Cardiol. Mar 22 2011; 57(12): 1375-82. PMID 21414534
12. Aaronson KD, Eppinger MJ, Dyke DB, et al. Left ventricular assist device therapy improves utilization of donor hearts. J Am Coll Cardiol. Apr 17 2002; 39(8): 1247-54. PMID 11955839
13. Frazier OH, Gemmato C, Myers TJ, et al. Initial clinical experience with the HeartMate II axial-flow left ventricular assist device. Tex Heart Inst J. 2007; 34(3): 275-81. PMID 17948075
14. John R, Kamdar F, Liao K, et al. Improved survival and decreasing incidence of adverse events with the HeartMate II left ventricular assist device as bridge-to-transplant therapy. Ann Thorac Surg. Oct 2008; 86(4): 1227-34; discussion 1234-5. PMID 18805167
15. Miller LW, Pagani FD, Russell SD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med. Aug 30 2007; 357(9): 885-96. PMID 17761592
16. Patel ND, Weiss ES, Schaffer J, et al. Right heart dysfunction after left ventricular assist device implantation: a comparison of the pulsatile HeartMate I and axial-flow HeartMate II devices. Ann Thorac Surg. Sep 2008; 86(3): 832-40; discussion 832-40. PMID 18721570
17. Strüber M, Sander K, Lahpor J, et al. HeartMate II left ventricular assist device; early European experience. Eur J Cardiothorac Surg. Aug 2008; 34(2): 289-94. PMID 18571932
18. Kirklin JK, Naftel DC, Stevenson LW, et al. INTERMACS database for durable devices for circulatory support: first annual report. J Heart Lung Transplant. Oct 2008; 27(10): 1065-72. PMID 18926395
19. Aissaoui N, Morshuis M, Maoulida H, et al. Management of end-stage heart failure patients with or without ventricular assist device: an observational comparison of clinical and economic outcomes. Eur J Cardiothorac Surg. Jan 01 2018; 53(1): 170-177. PMID 28950304
20. Schmitto JD, Pya Y, Zimpfer D, et al. Long-term evaluation of a fully magnetically levitated circulatory support device for advanced heart failure-two-year results from the HeartMate 3 CE Mark Study. Eur J Heart Fail. Jan 2019; 21(1): 90-97. PMID 30052304

21. Gustafsson F, Shaw S, Lavee J, et al. Six-month outcomes after treatment of advanced heart failure with a full magnetically levitated continuous flow left ventricular assist device: report from the ELEVATE registry. Eur Heart J. Oct 01 2018; 39(37): 3454-3460. PMID 30165521
22. Pagani FD, Mehra MR, Cowger JA, et al. Clinical outcomes and healthcare expenditures in the real world with left ventricular assist devices - The CLEAR-LVAD study. J Heart Lung Transplant. May 2021; 40(5): 323-333. PMID 33744086
23. Mehra MR, Cleveland JC, Uriel N, et al. Primary results of long-term outcomes in the MOMENTUM 3 pivotal trial and continued access protocol study phase: a study of 2200 HeartMate 3 left ventricular assist device implants. Eur J Heart Fail. Aug 2021; 23(8): 1392-1400. PMID 33932272
24. TEC Assessment Program. Left ventricular assist devices as destination therapy for end-stage heart failure. 2002;Volume 17;Tab 19.
25. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med. Nov 15 2001; 345(20): 1435-43. PMID 11794191
26. Park SJ, Tector A, Piccioni W, et al. Left ventricular assist devices as destination therapy: a new look at survival. J Thorac Cardiovasc Surg. Jan 2005; 129(1): 9-17. PMID 15632819
27. Long JW, Kfoury AG, Slaughter MS, et al. Long-term destination therapy with the HeartMate XVE left ventricular assist device: improved outcomes since the REMATCH study. Congest Heart Fail. 2005; 11(3): 133-8. PMID 15947534
28. Rogers JG, Pagani FD, Tatooles AJ, et al. Intrapericardial Left Ventricular Assist Device for Advanced Heart Failure. N Engl J Med. Feb 02 2017; 376(5): 451-460. PMID 28146651
29. Estep JD, Starling RC, Horstmanshof DA, et al. Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: Results From the ROADMAP Study. J Am Coll Cardiol. Oct 20 2015; 66(16): 1747-1761. PMID 26483097
30. Starling RC, Estep JD, Horstmanshof DA, et al. Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients: The ROADMAP Study 2-Year Results. JACC Heart Fail. Jul 2017; 5(7): 518-527. PMID 28396040
31. Jorde UP, Kushwaha SS, Tatooles AJ, et al. Results of the destination therapy post-food and drug administration approval study with a continuous flow left ventricular assist device: a prospective study using the INTERMACS registry (Interagency Registry for Mechanically Assisted Circulatory Support). J Am Coll Cardiol. May 06 2014; 63(17): 1751-7. PMID 24613333
32. Rogers JG, Butler J, Lansman SL, et al. Chronic mechanical circulatory support for inotrope-dependent heart failure patients who are not transplant candidates: results of the INTrEPID Trial. J Am Coll Cardiol. Aug 21 2007; 50(8): 741-7. PMID 17707178
33. Arnold SV, Jones PG, Allen LA, et al. Frequency of Poor Outcome (Death or Poor Quality of Life) After Left Ventricular Assist Device for Destination Therapy: Results From the INTERMACS Registry. Circ Heart Fail. Aug 2016; 9(8). PMID 27507111
34. Mehra MR, Goldstein DJ, Cleveland JC, et al. Five-Year Outcomes in Patients With Fully Magnetically Levitated vs Axial-Flow Left Ventricular Assist Devices in the MOMENTUM 3 Randomized Trial. JAMA. Sep 27 2022; 328(12): 1233-1242. PMID 36074476

35. Acharya D, Loyaga-Rendon RY, Pamboukian SV, et al. Ventricular Assist Device in Acute Myocardial Infarction. J Am Coll Cardiol. Apr 26 2016; 67(16): 1871-80. PMID 27102502
36. Wever-Pinzon O, Drakos SG, McKellar SH, et al. Cardiac Recovery During Long-Term Left Ventricular Assist Device Support. J Am Coll Cardiol. Oct 04 2016; 68(14): 1540-53. PMID 27687196
37. Topkara VK, Garan AR, Fine B, et al. Myocardial Recovery in Patients Receiving Contemporary Left Ventricular Assist Devices: Results From the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). Circ Heart Fail. Jul 2016; 9(7). PMID 27402861
38. Maybaum S, Mancini D, Xydas S, et al. Cardiac improvement during mechanical circulatory support: a prospective multicenter study of the LVAD Working Group. Circulation. May 15 2007; 115(19): 2497-505. PMID 17485581
39. Agrawal S, Garg L, Shah M, et al. Thirty-Day Readmissions After Left Ventricular Assist Device Implantation in the United States: Insights From the Nationwide Readmissions Database. Circ Heart Fail. Mar 2018; 11(3): e004628. PMID 29519902
40. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). Eur Heart J. Oct 2008; 29(19): 2388-442. PMID 18799522
41. Bulic A, Maeda K, Zhang Y, et al. Functional status of United States children supported with a left ventricular assist device at heart transplantation. J Heart Lung Transplant. Aug 2017; 36(8): 890-896. PMID 28363739
42. Wehman B, Stafford KA, Bittle GJ, et al. Modern Outcomes of Mechanical Circulatory Support as a Bridge to Pediatric Heart Transplantation. Ann Thorac Surg. Jun 2016; 101(6): 2321-7. PMID 26912304
43. Fraser CD, Jaquiss RD, Rosenthal DN, et al. Prospective trial of a pediatric ventricular assist device. N Engl J Med. Aug 09 2012; 367(6): 532-41. PMID 22873533
44. Blume ED, Rosenthal DN, Rossano JW, et al. Outcomes of children implanted with ventricular assist devices in the United States: First analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS). J Heart Lung Transplant. May 2016; 35(5): 578-84. PMID 27009673
45. Almond CS, Morales DL, Blackstone EH, et al. Berlin Heart EXCOR pediatric ventricular assist device for bridge to heart transplantation in US children. Circulation. Apr 23 2013; 127(16): 1702-11. PMID 23538380
46. Jordan LC, Ichord RN, Reinhartz O, et al. Neurological complications and outcomes in the Berlin Heart EXCOR® pediatric investigational device exemption trial. J Am Heart Assoc. Jan 22 2015; 4(1): e001429. PMID 25613996
47. Chen S, Lin A, Liu E, et al. Outpatient Outcomes of Pediatric Patients with Left Ventricular Assist Devices. ASAIO J. 2016; 62(2): 163-8. PMID 26720740
48. Conway J, Al-Aklabi M, Granoski D, et al. Supporting pediatric patients with short-term continuous-flow devices. J Heart Lung Transplant. May 2016; 35(5): 603-9. PMID 27009672
49. Frazier OH, Rose EA, McCarthy P, et al. Improved mortality and rehabilitation of transplant candidates treated with a long-term implantable left ventricular assist system. Ann Surg. Sep 1995; 222(3): 327-36; discussion 336-8. PMID 7677462

50. Bank AJ, Mir SH, Nguyen DQ, et al. Effects of left ventricular assist devices on outcomes in patients undergoing heart transplantation. Ann Thorac Surg. May 2000; 69(5): 1369-74; discussion 1375. PMID 10881807
51. Shuhaiber JH, Hur K, Gibbons R. The influence of preoperative use of ventricular assist devices on survival after heart transplantation: propensity score matched analysis. BMJ. Feb 10 2010; 340: c392. PMID 20147346
52. Alba AC, McDonald M, Rao V, et al. The effect of ventricular assist devices on long-term post-transplant outcomes: a systematic review of observational studies. Eur J Heart Fail. Jul 2011; 13(7): 785-95. PMID 21551162
53. Deo SV, Sung K, Daly RC, et al. Cardiac transplantation after bridged therapy with continuous flow left ventricular assist devices. Heart Lung Circ. Mar 2014; 23(3): 224-8. PMID 23954004
54. Grimm JC, Sciortino CM, Magruder JT, et al. Outcomes in Patients Bridged With Univentricular and Biventricular Devices in the Modern Era of Heart Transplantation. Ann Thorac Surg. Jul 2016; 102(1): 102-8. PMID 27068177
55. Davies RR, Russo MJ, Hong KN, et al. The use of mechanical circulatory support as a bridge to transplantation in pediatric patients: an analysis of the United Network for Organ Sharing database. J Thorac Cardiovasc Surg. Feb 2008; 135(2): 421-7, 427.e1. PMID 18242279
56. Copeland JG, Smith RG, Arabia FA, et al. Cardiac replacement with a total artificial heart as a bridge to transplantation. N Engl J Med. Aug 26 2004; 351(9): 859-67. PMID 15329423
57. Copeland JG, Copeland H, Gustafson M, et al. Experience with more than 100 total artificial heart implants. J Thorac Cardiovasc Surg. Mar 2012; 143(3): 727-34. PMID 22245242
58. Food and Drug Administration. Summary of Safety and Probable Benefit - H040006: AbioCor Implantable Replacement Heart. 2006; https://www.accessdata.fda.gov/cdrh_docs/pdf4/H040006b.pdf. Accessed June 20, 2023.
59. Dowling RD, Gray LA, Etoch SW, et al. Initial experience with the AbioCor implantable replacement heart system. J Thorac Cardiovasc Surg. Jan 2004; 127(1): 131-41. PMID 14752423
60. Torregrossa G, Morshuis M, Varghese R, et al. Results with SynCardia total artificial heart beyond 1 year. ASAIO J. 2014; 60(6): 626-34. PMID 25158888
61. Romeo F, Acconcia MC, Sergi D, et al. Percutaneous assist devices in acute myocardial infarction with cardiogenic shock: Review, meta-analysis. World J Cardiol. Jan 26 2016; 8(1): 98-111. PMID 26839661
62. Burkhoff D, Cohen H, Brunckhorst C, et al. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. Am Heart J. Sep 2006; 152(3): 469.e1-8. PMID 16923414
63. Seyfarth M, Sibbing D, Bauer I, et al. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol. Nov 04 2008; 52(19): 1584-8. PMID 19007597
64. Thiele H, Sick P, Boudriot E, et al. Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J. Jul 2005; 26(13): 1276-83. PMID 15734771

65. Ouweneel DM, Eriksen E, Sjauw KD, et al. Percutaneous Mechanical Circulatory Support Versus Intra-Aortic Balloon Pump in Cardiogenic Shock After Acute Myocardial Infarction. J Am Coll Cardiol. Jan 24 2017; 69(3): 278-287. PMID 27810347
66. Karami M, Eriksen E, Ouweneel DM, et al. Long-term 5-year outcome of the randomized IMPRESS in severe shock trial: percutaneous mechanical circulatory support vs. intra-aortic balloon pump in cardiogenic shock after acute myocardial infarction. Eur Heart J Acute Cardiovasc Care. Dec 06 2021; 10(9): 1009-1015. PMID 34327527
67. Schrage B, Ibrahim K, Loehn T, et al. Impella Support for Acute Myocardial Infarction Complicated by Cardiogenic Shock. Circulation. Mar 05 2019; 139(10): 1249-1258. PMID 30586755
68. Sieweke JT, Berliner D, Tongers J, et al. Mortality in patients with cardiogenic shock treated with the Impella CP microaxial pump for isolated left ventricular failure. Eur Heart J Acute Cardiovasc Care. Mar 2020; 9(2): 138-148. PMID 29405734
69. Schäfer A, Werner N, Burkhoff D, et al. Influence of Timing and Predicted Risk on Mortality in Impella-Treated Infarct-Related Cardiogenic Shock Patients. Front Cardiovasc Med. 2020; 7: 74. PMID 32478095
70. Griffith BP, Anderson MB, Samuels LE, et al. The RECOVER I: a multicenter prospective study of Impella 5.0/LD for postcardiotomy circulatory support. J Thorac Cardiovasc Surg. Feb 2013; 145(2): 548-54. PMID 22405676
71. Lemaire A, Anderson MB, Lee LY, et al. The Impella device for acute mechanical circulatory support in patients in cardiogenic shock. Ann Thorac Surg. Jan 2014; 97(1): 133-8. PMID 24090575
72. Lauten A, Engström AE, Jung C, et al. Percutaneous left-ventricular support with the Impella-2.5-assist device in acute cardiogenic shock: results of the Impella-EUROSHOCK-registry. Circ Heart Fail. Jan 2013; 6(1): 23-30. PMID 23212552
73. Ouweneel DM, de Brabander J, Karami M, et al. Real-life use of left ventricular circulatory support with Impella in cardiogenic shock after acute myocardial infarction: 12 years AMC experience. Eur Heart J Acute Cardiovasc Care. Jun 2019; 8(4): 338-349. PMID 30403366
74. Ait Ichou J, Larivée N, Eisenberg MJ, et al. The effectiveness and safety of the Impella ventricular assist device for high-risk percutaneous coronary interventions: A systematic review. Catheter Cardiovasc Interv. Jun 2018; 91(7): 1250-1260. PMID 28941078
75. Briasoulis A, Telila T, Palla M, et al. Meta-Analysis of Usefulness of Percutaneous Left Ventricular Assist Devices for High-Risk Percutaneous Coronary Interventions. Am J Cardiol. Aug 01 2016; 118(3): 369-75. PMID 27265673
76. O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. Circulation. Oct 02 2012; 126(14): 1717-27. PMID 22935569
77. Reddy YM, Chinitz L, Mansour M, et al. Percutaneous left ventricular assist devices in ventricular tachycardia ablation: multicenter experience. Circ Arrhythm Electrophysiol. Apr 2014; 7(2): 244-50. PMID 24532564
78. Aryana A, Gearoid O'Neill P, Gregory D, et al. Procedural and clinical outcomes after catheter ablation of unstable ventricular tachycardia supported by a percutaneous left ventricular assist device. Heart Rhythm. Jul 2014; 11(7): 1122-30. PMID 24732372
79. Kar B, Gregoric ID, Basra SS, et al. The percutaneous ventricular assist device in severe refractory cardiogenic shock. J Am Coll Cardiol. Feb 08 2011; 57(6): 688-96. PMID 20950980

80. Kirklin JK, Pagani FD, Goldstein DJ, et al. American Association for Thoracic Surgery/International Society for Heart and Lung Transplantation guidelines on selected topics in mechanical circulatory support. J Heart Lung Transplant. Mar 2020; 39(3): 187-219. PMID 31983666
81. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. Aug 08 2017; 136(6): e137-e161. PMID 28455343
82. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. Oct 15 2013; 62(16): e147-239. PMID 23747642
83. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. May 03 2022; 145(18): e876-e894. PMID 35363500
84. Peura JL, Colvin-Adams M, Francis GS, et al. Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. Circulation. Nov 27 2012; 126(22): 2648-67. PMID 23109468
85. Bernhardt AM, Copeland H, Deswal A, et al. The International Society for Heart and Lung Transplantation/Heart Failure Society of America Guideline on Acute Mechanical Circulatory Support. J Heart Lung Transplant. Apr 2023; 42(4): e1-e64. PMID 36805198
86. Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Assocation, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. J Am Coll Cardiol. May 19 2015; 65(19): e7-e26. PMID 25861963
87. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Ventricular Assist Devices (20.9.1). 2020; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?ncdid=360&ncdver=2&keyword=ventricular%20assist&keywordType=starts&areaId=all&docType=NCD&contractOption=all&sortBy=relevance&bc=AAAAAAQAAAAA&KeyWordLookUp=Doc&KeyWordSearchType=Exact. Accessed January 2024.
83. HAYES Directory Assessment. Ventricular Assist Devices (VADs) in Children and Adolescents with Chronic, End-Stage Heart Failure. Lansdale, PA: HAYES, October 19, 2010, last updated September 2015. Archived November 2015; outdated
84. HAYES Directory Assessment. Left Ventricular Assist Devices (LVADs) in Adult Patients with Chronic, End-Stage Heart Failure. Lansdale, PA: HAYES, Inc. August 18, 2010, last updated February 2014. Archived September 2015; outdated
85. HAYES Health Technology Brief. Impella Recover LP 2.5 Percutaneous Cardiac Support System (Abiomed Inc.) for Patients Undergoing High-Risk Percutaneous Coronary Intervention (PCI). Lansdale, PA: HAYES, Inc. March 15, 2013, updated June 2017.

86. HAYES Health Technology Brief. Impella 2.5 System (Abiomed Inc.) for Emergent Hemodynamic Support in Patients with Cardiogenic Shock. Lansdale, PA: HAYES, Inc. updated July 2016..
87. HAYES Health Technology Brief. Impella Recover LP 2.5 Percutaneous Cardiac Support System (Abiomed Inc.) for Emergent Hemodynamic Support in Patients with Cardiogenic Shock. Lansdale, PA: HAYES, Inc. April 2, 2013, updated March13, 2014.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 2024, 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)
5/1/22	2/15/22		Routine policy maintenance, no change in policy status.
5/1/23	2/21/23		Rationale reorganized per BCBSA review, references added. No change in policy status. (ds)
5/1/24	2/20/24		Language under bridge to transplant reworded, no change in intent. Routine policy maintenance, no change in status. Vendor managed: N/A (ds)

Next Review Date: 1st Qtr. 2025

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.