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Ventricular Assist Devices and Total Artificial Hearts

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Related Policies (if applicable)
None

Disclaimer

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Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

Post-Cardiotomy Setting/Bridge to Recovery
Implantable ventricular assist devices (VADs) with U.S. Food and Drug Administration (FDA) approval or clearance **may be considered medically necessary** in the post-cardiotomy setting in individuals who are unable to be weaned off cardiopulmonary bypass.

Bridge to Transplantation
Implantable ventricular assist devices with FDA approval or clearance **may be considered medically necessary** as a bridge to heart transplantation for adult individuals 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 humanitarian device exemption (HDE), **may be considered medically necessary** as a bridge to heart transplantation in children 16 years old 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.

Total artificial hearts (TAH) with FDA approved devices **may be considered medically necessary** as a bridge to heart transplantation for individuals with biventricular failure 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.

Destination Therapy

Implantable ventricular assist devices with FDA approval or clearance **may be considered medically necessary** as destination therapy for adult individuals with end-stage heart failure who meet the following criteria:

- New York Heart Association (NYHA) Class III heart failure with dyspnea upon mild physical activity or NYHA Class IV;
- Left ventricular ejection fraction ≤ 25%;
- Inotrope-dependent; OR cardiac index <2.2 liters/min/m^2 while not on inotropes AND also meeting one of the following:
    1. 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
    2. Advanced heart failure for at least 14 days and dependent on intra-aortic balloon pump for ≥7 days.

Other Indications

Other applications of implantable ventricular devices or total artificial hearts **are considered experimental, investigational and/or unproven**, including, but not limited to, the use of total artificial hearts as destination therapy.

The use of non-FDA approved or cleared implantable ventricular assist devices or total artificial hearts **is considered experimental, investigational and/or unproven**.

Percutaneous ventricular assist devices (pVADs) (e.g., TandemHeart® or the Impella®) approved by the U.S. Food and Drug Administration (FDA) and used according to their FDA-approved specifications **may be considered medically necessary** when:

- Providing short-term circulatory support in ongoing cardiogenic shock that occurs immediately (<48 hours) following acute myocardial infarction; OR
- Used as an adjunct to percutaneous coronary intervention (PCI) in the following high-risk individuals:

1. Individuals undergoing unprotected left main or last-remaining-conduit PCI with ejection fraction less than 35%;
   OR
2. Individuals with three vessel disease and ejection fraction less than 30%.

NOTE 1: See policy description for a more detailed list of FDA approved devices and the approved indications.

Xenotransplantion/heterotransplantation (a graft transplantation between different species) of a baboon heart OR porcine/swine (pig) heart **is considered experimental, investigational and/or unproven** as bridge to transplantation.

Policy Guidelines

The intent of treatment may evolve over the course of treatment; for example, there is not necessarily a strict delineation between bridge to transplant and destination therapy.

Only 2 ventricular assist devices (VADs) have approval from the U.S. Food and Drug Administration (FDA) for the pediatric population. The DeBakey VAD Child device and the Berlin Heart EXCOR Pediatric VAD have FDA approval through the humanitarian device exemption process. The DeBakey VAD is indicated for use in children ages 5 to 16 years who are awaiting a heart transplant (i.e., a bridge to transplant) while the Berlin Heart EXCOR VAD is indicated for children with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support.

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

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

Contraindications for bridge to transplant VADs and total artificial hearts include conditions that would generally exclude individuals for heart transplant. Such conditions are chronic irreversible hepatic, renal, or respiratory failure; systemic infection; coagulation disorders, and inadequate psychosocial support. Due to potential problems with adequate function of the VAD or total artificial heart, implantation is also contraindicated in individuals with uncorrected valvular disease.

The Centers for Medicare and Medicaid Services requires that "Beneficiaries receiving a VAD must be managed by an explicitly identified, cohesive, multidisciplinary team of medical professionals with 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 informed decision making. 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 1 physician with cardiothoracic surgery privileges and individual experience implanting at least 10 durable, intracorporeal, left ventricular assist devices over the course of the previous 36 months with activity in the last year.
- At least 1 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 placement of a VAD.
- A VAD program coordinator.
- A social worker.
- A palliative care specialist."

Description

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 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 about 91%, 85%, and 78%, respectively. (3) The number of candidates for transplants exceeds supply of donor organs; thus, the interest in the development of mechanical devices.

Regulatory Status

A number of implantable VADs and artificial heart systems have been FDA approved through a Humanitarian Device Exemption, 510(k), or premarket approval regulatory pathway. This section discusses currently marketed devices.

The FDA maintains a list of recent device recalls at <http://www.fda.gov>.

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.

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.

The intent of treatment may evolve over the course of treatment; for example, there is not necessarily a strict delineation between bridge to transplant and destination therapy, and transplant eligibility can change.

Table 1 lists the VADs currently available in the Unites States. 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 left ventricular assistive devices (LVADs).

Table 1. Available Ventricular Assist Devices

Device	Manufacturer	Approval Date	FDA Clearance	PMA, HDE, or 610(k) Number	Indication
Thoratec IVAD	Thoratec	Aug 2004	PMA Supp	P870072	Bridge to transplant and postcardiotomy
DeBakey VAD Child	MicroMed	Feb 2004	HDE	H030003	Bridge to transplant in children 5-16 years
HeartMate II	Thoratec	Apr 2008	PMA	P060040	Bridge to transplant and destination
CentriMag	Thoratec	Dec 2019	PMA	P160038	Postcardiotomy, bridge to decision
Berlin Heart EXCOR Pediatric VAD	Berlin	Jun 2017	PMA	P160035	Bridge to transplant
HeartMate 3 Left Ventricular Assist System	Thoratec	Aug 2017 Oct 2018	PMA PMA	P160054 P160054/S008	Bridge to transplant Destination

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

Total Artificial Heart

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 U.S. (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.

Table 2. Available Total Artificial Heart

Device	Manufacturer	Approval Date	FDA Clearance	PMA Number	Indication
SynCardia Temporary Total Artificial	SynCardia Systems	2004	510(k)	P030011	Bridge to transplant in cardiac transplant-eligible candidates at

Heart (Formerly CardioWest Total Artificial Heart and Jarvik Total Artificial Heart)					risk of imminent death from biventricular failure.

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

Percutaneous Ventricular Assist Devices

Some circulatory assist devices are placed percutaneously (i.e., are not implanted). They may be referred to as pVADs. Two different pVADs have been developed, the TandemHeart and the Impella device (Table 3). 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 placed into the left ventricle. Blood is pumped from the left ventricle, through the device, and into the ascending aorta. 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. Adverse events associated with pVAD include access site complications such as bleeding, aneurysms, or leg ischemia. Cardiovascular complications can also occur, such as perforation, myocardial infarction, stroke, and arrhythmias.

Table 3. Available Percutaneous Ventricular Assist Devices

Device	Manufacturer	Approval Date	FDA Clearance	PMA Number	Indication
TandemHeart	Cardiac Assist	Sep 2011	510(k)	K110493	Temporary left ventricular bypass of ≤6 h
Impella Recover LP 2.5	Abiomed	May 2008	510(k)	K063723	Partial circulatory support using extracorporeal bypass control unit for ≤6 h
Impella 2.5 System	Abiomed	Mar 2015	PMA	P140003	Temporary left ventricular bypass of ≤6 h

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

Other Devices

Implantable Counterpulsation Ventricular Assist System

The NuPulse CV iVAS (cardiovascular intravascular assist system) provides hemodynamic support in advanced heart failure and is intended for use as a bridge for transplantation or as a bridge to recovery. The system is placed through the left subclavian vein and connected to an external battery. (4)

The NuPulse CV iVAS system is currently recruiting for studies to assess the preliminary safety and clinical performance. It is intended to provide hemodynamic support in advanced heart failure and is intended for use as a bridge for transplantation or as a bridge to recovery. The implantable counterpulsation ventricular assist system from NuPulse named iVAS has not yet received U.S. FDA approval. (4)

Rationale

Medical policies assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and 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 technology, two domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical uses 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 (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs 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.

This literature review assesses 3 devices: 1) ventricular assist devices (VADs), 2) total artificial hearts (TAHs), and 3) percutaneous VADs (pVADs). This policy addresses short-term use of the devices as a bridge to recovery or transplantation. Left VADs (LVADs) and TAHs are also evaluated as longer-term destination therapies for patients who are not transplant candidates.

Ventricular Assist Devices (VAD)s

Clinical Context and Therapy Purpose

The purpose of VADs 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 policy.

Population

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 ventricular assist devices. 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 individuals 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 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 comparator of interest is optimal medical management, including use of an intra-aortic balloon pump when indicated.

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

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

When VAD is used as destination therapy, the time of interest ranges from 6 months to 2 years following implantation.

Study Selections Criteria

- To assess efficacy outcomes, we included comparative controlled prospective trials, with preference for randomized controlled trials.
- 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.
- Within each category of study design, studies with larger size studies and longer duration were prioritized.
- Studies with duplicative or overlapping population were excluded.

VADs as Bridge to Heart Transplant in Adults
The insertion of a VAD will categorize its recipient as a high-priority heart transplant candidate. The available evidence on the efficacy of VADs in bridging patients with refractory heart failure

to transplant includes single-arm series, which generally have reported high success rates in bridging to transplant.

Systematic Reviews
Older systematic reviews concluded that VADs can provide an effective bridge to transplantation. (5)

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; 2) 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 0.84; 95% confidence interval [CI], 0.78–0.91, 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. (9)

Nonrandomized Studies
Slaughter et al. (2013) reported combined outcomes for patients included in the HeartWare bridge to transplant study previously described and a continued-access protocol granted by the FDA. (10) The study included 322 patients with heart failure, eligible for heart transplant, who received the HeartWare (140 patients from the original study; 190 patients in the continue-access protocol who were monitored to outcome or had completed 180-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: three from sepsis, three from multiple organ failure, and three 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 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 IN High-Risk Cardiac Procedures 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, QOL, and adverse event outcomes in the HeartWare group. Success on the primary outcome occurred in 90.7% of the HeartWare group and 90.7% of controls ($p<0.001$, noninferiority with a 15% margin). Serious adverse events in the HeartWare group included, most commonly, bleeding, infections, and perioperative right heart failure. (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. (13-17) 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 and 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 include 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 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 ($p<0.001$).

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 4,195 patients who received implants, there were 117 (14.3%) deaths among 821 Heartmate 3 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.

<u>VADs as Destination Therapy for End-Stage Heart Failure in Adults</u>

Systematic Reviews

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. (24) 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 these appear to be outweighed by this group's better outcomes on function; New York Heart Association (NYHA) functional class was significantly improved, as was QOL among those living to 12 months. VAD patients spent a greater relative proportion of time inside the hospital than medical management patients do, but the survival advantage would mean a longer absolute time outside the hospital.

Park et al. (2005) published reports on extended 2-year follow-up of patients from the REMATCH trial, which found that survival and QOL benefits were still apparent. (25, 26) 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 (e.g., 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; 2) 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 (relative risk 0.84; 95% CI, 0.78–0.91, 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. (27) 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 LVAD 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 also reported superior survival and health-related QOL in LVAD-treated patients. (28) Twelve-month, as-treated, event-free actuarial survival was 80% in the LVAD group compared with 63% in the best medical therapy group (p=0.022). Two-year results from this study were reported by Starling et al. (2017). (29) At the end of 2 years, 35 (34%) medical therapy patients and 60 (62%) LVAD patients were alive on their original therapy; 23 medical management patients received LVADs during the 2 years.

The LVAD-treated patients continued to have higher as-treated, event-free actuarial survival (70% vs 41%, p<0.001) although there was no difference in intention-to-treat survival (70% vs 63%, p=0.31).

In an FDA-required post approval study of the HeartMate II device for destination therapy, (30) 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 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 heart transplant. (31) Fifty-five patients who had NYHA functional class IV symptoms and who failed weaning from inotropic support were offered a Novacor LVAD; 18 did not receive a device due to preference or device unavailability and acted as a control group. The LVAD-treated patients had superior survival rates at 6 months (46% vs 22%; p=0.03) and 12 months (27% vs 11%; p=0.02), along with fewer adverse events.

Arnold et al. (2016) analyzed 1638 patients receiving LVADs as destination therapy between May 2012 and September 2013. (32) 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. (33) 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 post cardiotomy setting.

Acharya et al. (2016) reported on patients who underwent VAD placement for acute myocardial infarction (AMI) who were enrolled in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) registry, a prospective national registry of Food and Drug Administration (FDA)-approved durable mechanical circulatory support (MCS) devices. (34) 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 were 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=15,631). (35) One hundred twenty-five of these patients had a prior bridge to recovery left ventricular assist device (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 13,454 INTERMACS adults with implants between June 2006 and June 2015 without TAH or pulsatile-flow LVAD or heart transplant. (36) 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 patient demonstrated partial cardiac recovery.

In a prospective multicenter study to assess myocardial recovery in patients with LVAD implantation as a bridge to transplant, Maybaum et al. (2007) evaluated 67 patients with heart failure who had undergone LVAD implantation for severe heart failure. (37) After 30 days, patients demonstrated significant improvements compared with their 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, $p<0.001$), respectively. However, only 9% of patients demonstrated sufficient 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. (38) 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. (39) 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 for dilated cardiomyopathy who were supported with an LVAD or vasoactive infusions alone at the time of transplant from the Organ Procurement and Transplant Network registry (n=701). (40) Functional status as measured by the median

Karnofsky Performance Scale score at heart transplant was higher for children receiving LVAD (six) compared with vasoactive infusion (five; p<0.001) and children receiving LVAD were more likely to be discharged from the hospital at the time of transplant. The percentage of children having stroke at the time of transplant was higher in those receiving LVAD (3% vs 1%, p=0.04).

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. (41) The study included 2777 pediatric patients who underwent heart transplant from 2005 to 2012 who were identified through the UNOS database, of whom 428 were bridged with VADs and 189 were bridged with ECMO. In unadjusted analysis, the actuarial 5-year survival was highest in the direct-to-transplant group (77%), followed by the VAD group (49%) and then the ECMO group (35%). In a proportional hazards model to predict time to death, restricted to the first 4 months posttransplant, ECMO bridging was significantly associated with higher risk of death (adjusted hazard ratio, 2.77 vs direct-to-transplant; 95% CI, 2.12 to 3.61; p<0.001). 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 heart transplant. (42) Patients were divided into 2 groups based on body surface area (BSA); 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 (BSA <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<0.001). For participants in cohort 2 (BSA range, 0.7 to <1.5 m^2), the median survival was 144 days compared with 10 days in the matched ECMO group (p<0.001). Rates of adverse events were high in both EXCOR device cohorts, including major bleeding (42% and 50% of cohort 1 and cohort 2, respectively), infection (63% and 50% of cohort 1 and cohort 2), 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 at the time of implant and includes those implanted with either durable or temporary VADs. (43) At analysis, the registry included 241 patients; of these, 41 were implanted with a temporary device only, leaving 200 patients implanted with VADs for the present study. Most patients (73%) had an underlying diagnosis of cardiomyopathy. At the time of implantation, 64% were listed for transplant, while 29% were implanted with a "bridge to candidacy" strategy. A total of 7% were implanted with a destination therapy strategy. Actuarial survival at both 6 months and 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. (44) This study

included a broader patient population than the Fraser 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 patient survived 30 days), and 5% who were alive with the device in place. In a 2015 follow-up study that evaluated 204 children from the same registry, Jordan et al. reported relatively high rates of neurologic events in pediatric patients treated with the EXCOR device (29% of patients), typically early in the course of device use. (45)

Chen et al. (2016) reported on a retrospective, single-center series of pediatric patients with continuous-flow VADs, with a focus on outpatient experiences. (46) 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, two were on ongoing support, and one 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. (47) From 2005 to 2014, 27 children were supported with one of these devices, most commonly for congenital heart disease (42%). The median duration of support was 12 days, and 67% of all short-term continuous-flow VAD runs (19 of 28 runs) led to hospital discharge.

Effects of Pretransplant VADs on Transplant Outcomes

Published studies continue to report that the use of a VAD does not compromise the success of a subsequent heart transplant and, in fact, may improve posttransplant survival, thus improving the use of donor hearts. (12, 48-50) A systematic review by Alba et al. (2011) examined the evidence on the effect of VADs on posttransplant outcomes. (51) 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 (relative risk [RR], 1.8; 95% confidence interval [CI], 1.53 to 2.13). For patients treated with an extracorporeal device, the likelihood of survival 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. (52) Data from the United Network for Organ Sharing (UNOS), 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. (53) Using the UNOS database, Davies et al. (2008)

reported on the use of VADs in pediatric patients undergoing heart transplantation. (54) Their analysis concluded that pediatric patients requiring a pretransplantation VAD have similar long-term survival similar to those not receiving MCS.

Section Summary: VADs

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 (TAH)

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 policy.

Population

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

Interventions

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

Study Selection Criteria

- To assess efficacy outcomes, we included comparative controlled prospective trials, with a preference for randomized controlled trials.
- 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.
- Within each category of study design, studies with larger sample size studies and longer duration were prioritized.
- Studies with duplicative or overlapping populations were excluded.

TAH as a Bridge to Transplant for End-Stage Heart Failure

Nonrandomized Trials

The FDA approval of the CardioWest TAH was based on the results of a nonrandomized, prospective study of 81 patients. (55) Patients had failed inotropic therapy, had 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. (56) All patients either met established criteria for mechanical circulatory support (MCS) or were failing medical therapy on multiple inotropic drugs. Mean support time was 87 days (range, 1-441 days). The rate of survival to transplant was 68.3% (69/101). Of the 32 deaths before 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%.

TAH as Destination Therapy for End-Stage Heart Failure

Case Series

Data on the artificial heart are available from FDA approval information (57) and from a published article describing results for the first 7 patients. (58) 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 for people with severe heart failure

whose death was imminent and for whom no alternative treatments were available. Of the 14 patients studied, 12 survived surgery. Mean duration of support for the patients was 5.3 months. In some cases, the device extended survival by several months (survival was 17 months in 1 patient). Six patients were ambulatory; 1 patient was discharged home. Complications included postoperative bleeding and neurologic events. No device-related infections were reported.

Torregrossa et al. (2014) reported on 47 patients who received a TAH at 10 worldwide centers and had the device implanted for more than 1 year. (59) Patients were implanted for dilated cardiomyopathy (n=23), ischemic cardiomyopathy (n=15), and "other" reasons (n=9). Over a median support time of 554 days (range, 365-1373 days), 34 (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 (i.e., case series reporting substantial survival rates in patients without other alternatives). Therefore, similar to LVADs, this evidence is sufficient to conclude that TAH improves outcomes for these patients and TAH is a reasonable alternative for patients who require a bridge to transplantation but who are ineligible for other types of life-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 (pVADs) 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 PICO was used to select literature to inform this policy.

Population

The relevant population of interest are individuals with cardiogenic shock.

Interventions

The therapy being considered is pVADs.

Comparators

The comparator of interest is intra-aortic balloon pump (IABP).

Outcomes
The general outcomes of interest are OS, 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.
- 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.
- Within each category of study design, studies with larger sample size studies and longer duration were prioritized.
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
Romeo et al. (2016) reported on a systematic review and meta-analysis that evaluated various percutaneous mechanical support methods, including pVADs, for patients with cardiogenic shock due to AMI who were undergoing revascularization. Tables 4 and 5. (60) Reviewers included the 3 RCTs (described below) comparing pVADs with intra-aortic balloon pumps (IABPs), along with 3 observational studies. Observational studies were included in meta-analyses, with subgroup analyses by study design reported (see Table 4). In the comparison of pVADs with IABP, reviewers found that in-hospital mortality (the primary outcome of the analysis) had a nonsignificant increase in the pVAD group. Subgroup analysis did not find significant differences in estimates from RCTs and observational studies, and CIs overlapped. There was no significant heterogeneity within RCTs or observational studies. The relative risk reduction was -17.23%, translating to 8 more deaths per every 100 patients treated with pVADs instead of IABP.

Table 4. Characteristics of a Systematic Review Evaluating pVADs versus IABPs for Cardiogenic Shock

Study	Dates	Trials	Participants	N	Design
Romeo et al. (2016) (60)	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 versus IABLs for Cardiogenetic Shock

Study	In Hospital Mortality

Romeo et al. (2016) (60)	
RCTs	
Total N	100
Risk ratio (95% CI)	1.06 [0.68, 1.66]
I^2 (p)	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 four RCTs have compared pVADs with IABPs for patients with cardiogenic shock; three were included in the Romeo et al. (2016) systematic reviews described above, (61-63) and one was published after Romeo et al. (2016). (64) The 4 RCTs enrolled a total of 148 patients, 77 treated with a pVAD and 71 treated with an IABP. All 4 trial populations included patients with AMI and cardiovascular shock; 1 trial restricted this 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 6 and 7. 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 percutaneous coronary intervention (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

Author (Year)	Study (Registration)	Countries	Sites	Dates	pVAD	Key Eligibility Criteria
Ouweneel et al. (2017) (64)	IMPRESS (NTR3450)	Netherlands Norway	2	2012-2015	Impella CP	AMI and severe CS in the setting of immediate PCI; receiving mechanical ventilation
Seyfarth et al.	ISAR-SHOCK (NCT00417378)	Germany	2	2004-2007	Impella LP 2.5	AMI <48 h and CS

(2008) (62)						
Burkhoff et al. (2006) (61)	TandemHeart (NR)	United States	12	2002-2004	TandemHeart	CS <24 h due to MI or heart failure
Thiele et al. (2005) (63)	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; ISAR-SHOCK: 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 Comparing pVADs and IABPs for Cardiogenic Shock

Study	30-Day Mortality	60-Day Mortality	Bleeding	Leg Ischemia	Other Outcomes
Ouweenel et al. (2017) (64) IMPRESS					*Rehospitalization*
N	48	48	48		48
pVAD	46%	50%	33%		21%
IABP	50%	50%	8%		4%
HR (95% CI)	0.96 (0.42 to 2.18)	1.04 (0.47 to 2.32)			
Seyfarth et al. (2008) (62) 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) (61) 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) (63)					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.

Long-term follow-up of the IMPRESS trial outcomes were published by Karami et al. (2021). (65) 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. (66) Using registry data, the researchers retrospectively identified 237 patients who had been treated with the Impella device and matched them to patients who had received IABP as part of an RCT. There was no significant difference between groups in 30-day all-cause mortality (48.5% vs 46.4%, p=.64). Severe or life-threatening bleeding (8.5% vs 3.0%, p<.01) and peripheral vascular complications (9.8% vs 3.8%, p=.01) occurred significantly more often in the Impella group.

Case series of patients treated with pVADs as an alternative to IABP in cardiogenic shock have reported high success rates as a bridge to alternative therapies. (67-72) However, given the availability of RCT evidence, these studies add little to the body of evidence on the efficacy of pVADs for the management of cardiogenic shock.

Section Summary: Percantaneous Ventricular Assist Devices (pVADs) for Cardiogenic Shock

Four RCTs comparing pVAD with IABP for patients with cardiogenic shock failed to demonstrate a mortality benefit for pVAD use and reported higher complication rates associated with pVAD use. Comparative observational studies and a long-term follow-up study were consistent with the RCT evidence.

PVADs 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 PICO was used to select literature to inform this policy.

Populations

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

Interventions
The therapy being considered is a pVADs.

Comparators
The comparator of interest is intra-aortic balloon pump (IABP).

Outcomes
The general outcomes of interest are OS, 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.
- Within each category of study design, studies with larger sample size studies and longer duration were prioritized.
- Studies with duplicative or overlapping populations were excluded.

Percutaneous Ventricular Assist Devices 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 8 shows a comparison of the RCTs included in each. Only 1 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 8 and 9). (73) 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	Ait Ichou et al. (2018) (71)	Briasoulis et al. (2016) (72)
O'Neill et al. (2012) (75) PROTECT II	●	●

Ouweneel et al. 2016 (64) IMPRESS	●	
Ouweeneel et al. (2016) IMPRESS in STEMI (72)	●	
Seyfarth et al. (2008) (62) 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 10. The RCTs found similar rates of all-cause mortality between the Impella device and IABP. One RCT reported higher rates among patients randomized to Impella (7.6% vs 5.9%) but the difference was not statistically significant (p=.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 1 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 3 of the 4 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 2 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. (74) Reviewers identified 18 nonrandomized observational studies and a single RCT (PROTECT II). (75) 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.	Inception-2016	20	High-risk patients	Impella	1287 (10-225)	4 RCT, 2 controlled	1-42 months

(2018) (73)			undergoing PCI			observational, 14 uncontrolled observational	
Briasoulis et al. (2016) (74)		Impella: 12 Tandem Heart:8	High-risk patients undergoing PCI	Impella and Tandem Heart	Impella: 1350 (10-637) Tandem Heart: 252 (7-68)	Impella: Tandem Heart:	Impella: Tandem Heart:

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

Table 10A. Results of SRs Evaluating pVAD as Ancillary Support for High-Risk Percutaneous Coronary Intervention

Study	All-Cause Mortalilty (30days)	All-Cause Mortality (3 months)	All-Cause Mortality (12 months)	Stroke (30 days)	Stroke (3 months)
Ait Ichou et al. (2018) (73)					
Range of effect (controlled studies)					
Impella	7.6%-46%	12.1%-50%	15.3%-26%	0%	0.9%-8%
IABP	0%-46%	8.7%-50%	11%-25.8%	0%-1.8%	0%-4%
Range of effect (uncontrolled studies)					
Impella	0%-74%	--	10%-45.5%	0%-2%	--
Briasoulis et al. (2016) (74)					
Impella	54/1346				
Pooled effect (95% CI)	0.35 (0.022, 0.048)				
I^2 (p)	20% (0.243)				
TandemHeart	22/212				
Pooled effect (95% CI)	0.080 (0.029, 0.131)				
I^2 (p)	55% (0.030)				

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

Table 10B. Results of SRs Evaluating pVAD as Ancillary Support for High-Risk Percutaneous Coronary Intervention

Study	Stroke (12 months)	Major Adverse Events (30days)	Major Adverse Events (3 months)	Major Adverse Events (12 months	Vascular Complications
Ait Ichou et al. (2018) (73)					
Range of effect (controlled studies)					
Impella	8%	15%-35.1%	26%-40.6%	37%	
IABP	0%	40%-40.1%	33%-49.3%	47%	
Range of effect (uncontrolled studies)					
Impella	--	0%-20%	--	30%	
Briasoulis et al. (2016) (74)		*Major bleeding*			
Impella		126/1346			89/1346
Pooled effect (95% CI)		0.71 (0.043, 0.99)			0.049 (0.023, 0.076)
I^2 (p)		63% (0.002)			78% (<0.001)
TandemHeart		11/205			15/205
Pooled effect (95% CI)		0.036 (0.011, 0.061)			0.065 (0.032, 0.099)
I^2 (p)		0% (0.581)			0% (0.865)

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

High-Risk Ventricular Tachycardia Ablation

Reddy et al. (2014) reported on outcomes for a series of 66 patients enrolled in a prospective, multicenter registry who underwent ventricular tachycardia (VT) ablation with a pVAD or IABP. (76) Twenty-two patients underwent ablation with IABP assistance, while 44 underwent ablation with either the TandemHeart or Impella pVAD device (non-IABP group). Compared with patients who received support with an IABP, those who received support with a pVAD had more unstable VTs that could be mapped and ablated (1.05 vs 0.32, p<0.001), more VTs that 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 period (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. (77) Thirty-four patients had hemodynamic support periprocedurally with a pVAD. Percutaneous VAD- and non-pVAD-supported patients were similar at baseline, with no differences in procedural success rates between groups. Compared with non-pVAD-supported patients, patients in the pVAD group had a longer maximum time in unstable VT (27.4 min vs 5.3 min, p<0.001), more VT ablations per procedure (1.2 vs 0.4, p<0.001), a 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 Ventricular Assist Devices for High-Risk Percutaneous Coronary Intervention

RCTs, controlled and uncontrolled observational studies, and systematic reviews of these studies have demonstrated a benefit of pVAD used as ancillary support for patients undergoing high-risk PCI. Major adverse events at 30 days were significantly less with Impella versus IABP (15%-40%).

Percutaneous Ventricular Assist Devices for Cardiogenic Shock Refractory to IABP Therapy

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 PICO was used to select literature to inform this policy.

Population

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

Interventions

The therapy being considered is the use of a pVADs.

Comparators

The comparator of interest is optimal medical therapy without IABP and other MCS.

Outcomes

The general outcomes of interest are OS, 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.
- Within each category of study design, studies with larger sample size studies and longer duration were prioritized.
- Studies with duplicative or overlapping populations were excluded.

Nonrandomized Studies

In a large series, Kar et al. (2011) treated 117 patients who had severe, refractory cardiogenic shock with the TandemHeart System. (78) 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 Ventricular Assist Devices for Cardiogenic Shock Refractory to Intra-Aortic Balloon Pump 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 VADs is associated with improvements in health outcomes for patients with cardiogenic shock refractory to IABP therapy.

Summary of Evidence

Ventricular Assist Device

For individuals who have end-stage heart failure who receive a ventricular assist device (VAD) as a bridge to transplant, the evidence includes a randomized controlled trial (RCT), single-arm trials and observational studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life (QOL), 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 improving mortality as well as QOL. 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 an 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 RCTs and multiple single-arm studies. Relevant outcomes are overall survival, symptoms, functional outcomes, QOL, 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 patient's ineligible for heart transplant. Despite an increase in adverse events, both mortality and QOL appear to be improved for these patients. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Total Artificial Heart

For individuals who have end-stage heart failure who receive a total artificial heart (TAH) as a bridge to transplant, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, QOL, and treatment-related mortality and morbidity. Compared with VADs, the evidence for TAHs in these settings is less robust. However, based on 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 an 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, QOL, 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 that the technology results in an improvement in the net health outcomes.

Percutaneous Ventricular Assist Device

For individuals with cardiogenic shock or who undergo high-risk cardiac procedures who receive a percutaneous Ventricular Assist Device (pVAD), the evidence includes randomized controlled trials and observational studies. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, QOL, and treatment-related mortality and morbidity. RCTs, controlled and uncontrolled observational studies, and systematic reviews of these studies have demonstrated a benefit of pVAD used as ancillary support for patients undergoing high-risk PCI. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cardiogenic shock refractory to intra-aortic balloon pump therapy who receive a pVAD, the evidence includes case series. Relevant outcomes are OS, symptoms, morbid events, functional outcomes, QOL, and treatment-related mortality and morbidity. Case series of patients with cardiogenic shock refractory to intra-aortic balloon pump have reported improved hemodynamic parameters following pVAD placement. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

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 11). (79) The guideline authors noted, "Compared with IABP, contemporary percutaneous circulatory support devices provide a significant increase in cardiac index and mean arterial pressure; however, reported 30-day outcomes are similar."

Table 11. 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.

American College of Cardiology Foundation et al.

In 2017, the American College of Cardiology Foundation, American Heart Association (AHA) and Heart Failure Society of American published a focused update of the 2013 recommendations released by the American College of Cardiology Foundation and AHA. (80) Left VAD was 1 of several treatment options recommended for patients with refractory NYHA class III or IV heart failure (stage D). If symptoms were not improved after guideline-directed management and therapy, which included pharmacologic therapy, surgical management and/or other devices, then left VAD 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. (81) The guidelines categorized pVADs and extracorporeal VADs as nondurable MCS devices. Since the 2017 update, these guidelines have been updated regularly, with the most recent update occurring in 2022. (82) Table 12 provides class IIA guidelines on MCS devices.

Table 12. AHA/ACC/HFSA Guidelines on Mechanical Circulatory Support (MCS)

Recommendation	COE[a]	LOE[b]
"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	IIA	B-NR

assist devices, are reasonable as a 'bridge to recovery' or 'bridge to decision'"		

ACC: American College of Cardiology; AHA: American Heart Association; COE: class of evidence; GDMT: guideline-directed medical therapy; HFrEF: heart failure with reduced ejection fraction; HFSA: Heart Failure Society of America; LOE: level of evidence; LVAD: left ventricular assist device; MCS: mechanical circulatory support; NYHA: New York Heart Association; QOL: quality of life; RCT: randomized controlled trial.

[a]I: Strong; IIa: Moderate.

[b]A: high quality evidence from more than 1 RCT; B-R: Moderate-quality evidence from 1 or more RCTs; B-NR: Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies.

American Heart Association (AHA)

In 2012, AHA published recommendations for the use of MCS. (83) These guidelines defined nondurable MCS as intraballoon pumps, extracorporeal membrane oxygenation, extracorporeal VADs, and pVADs. Table 13 lists recommendations made on indications for the use of MCS, including durable and nondurable devices.

Table 13. 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." "These patients should be referred to a center with expertise in the management of durable MCS and patients with advanced HF."	IIA I	C 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. (84) 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 14 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	B

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

Society for Cardiovascular Angiography and Interventions et al.

In 2015, the Society for Cardiovascular Angiography and Interventions, the Heart Failure Society of America, the Society of Thoracic Surgeons, and the American College of Cardiology published a joint clinical expert consensus statement on the use of percutaneous mechanical circulatory support (MCS) devices in cardiovascular care. (85) This statement addressed intra-aortic balloon pumps, left atrial-to-aorta assist device (e.g., TandemHeart), left ventricle-to-aorta assist devices (e.g., Impella), extracorporeal membrane oxygenation, and methods of right-sided support. Specific recommendations were not made, but the statement reviews the use of MCS in patients undergoing high-risk percutaneous intervention, those with cardiogenic shock, and those with acute decompensated heart failure**.**

Ongoing and Unpublished Clinical Trials

Some currently unpublished and ongoing trials that might influence this policy are listed in Table 15.

Table 15. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01633502	Effects of Advanced Mechanical Circulatory Support in Patients with ST Segment Elevation	360	Jan 2024

	Myocardial Infarction Complicated by Cardiogenic Shock. The Danish Cardiogenic Shock Trial		
NCT01627821[a]	Evaluation of the Jarvik 2000 Left Ventricular Assist System with Post-Auricular Connector - Destination Therapy Study	350	Dec 2023
NCT02326402[a]	THEME Registry: TandemHeart Experiences and Methods	450	Jun 2023
NCT01187368[a]	Prospective Multi-Center Randomized Study to Evaluate 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 2024
NCT04768322	Left Ventricular Assist Device (LVAD) Versus Guideline Recommended Medical Therapy in Ambulatory Advanced Heart Failure Patients (GDMT)	92	Feb 2027
Unpublished			
NCT02232659[a]	SynCardia 70cc Temporary Total Artificial Heart (TAH-t) for Destination Therapy (DT)	38	May 2022 (status unknown)

NCT: national clinical trial; [a] Denotes industry-sponsored or cosponsored trial; FDA: U.S. Food and Drug Administration; PCI: percutaneous coronary intervention.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	33927, 33928, 33929, 33975, 33976, 33977, 33978, 33979, 33980, 33981, 33982, 33983, 33990, 33991, 33992, 33993, 33995, 33997, 93750, [Deleted 1/1/2022: 0451T, 0452T, 0453T, 0454T, 0455T, 0456T, 0457T, 0458T, 0459T, 0460T, 0461T, 0462T, 0463T]
HCPCS Codes	L8698, Q0477, Q0478, Q0479, Q0480, Q0481, Q0482, Q0483, Q0484, Q0485, Q0486, Q0487, Q0488, Q0489, Q0490, Q0491, Q0492, Q0493, Q0494, Q0495, Q0496, Q0497, Q0498, Q0499, Q0500, Q0501, Q0502, Q0503, Q0504, Q0506, Q0507, Q0508, Q0509

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
11/15/2024	Reviewed. No changes.
02/01/2024	Document updated with literature review. Coverage unchanged. References 1, 2, 23, 33, 65, 82 and 84 added; others removed.
12/01/2022	Reviewed. No changes.
04/15/2022	Document updated with literature review. The following changes were made to Coverage: 1) Modified language specific to pediatric use of implantable ventricular assist devices as a bridge to transplantation to “children 16 years old or younger”, and 2) Modified conditional criteria for the use of implantable ventricular assist devices when used as destination therapy for end-stage heart failure patients. Added references 8, 21 and 64; others removed.
04/15/2021	Document updated with literature review. The following change was made to Coverage: Modified conditionally medically necessary language for percutaneous ventricular assist devices. References 4, 7-14, 19, 31-33, 70-71, 76, 78, 82-83 added.
08/01/2019	Reviewed. No changes.
12/15/2017	Document updated with literature review. Coverage unchanged.
04/15/2017	Document updated with literature review. Coverage has changed. The word Implantable has been added to the following statement: Implantable ventricular assist devices with FDA approval or clearance, including humanitarian device exemption (HDE), may be considered medically

	necessary as a bridge to heart transplantation for patients in the pediatric population who meet the criteria noted.
01/01/2017	Document updated with literature review. Coverage unchanged.
05/01/2015	Document updated with literature review. Coverage unchanged.
08/01/2013	Document updated with literature review. Additional criteria were added to the statements for "Implantable ventricular assist devices" and "Total artificial hearts" under the Bridge to Transplantation section of the coverage. The following coverage statements were added: 1) Ventricular assist devices with FDA approval or clearance, including humanitarian device exemptions, may be considered medically necessary as a bridge to heart transplantation for patients in the pediatric population who are not expected to survive until a donor heart can be obtained AND are currently listed as heart transplantation candidates or are undergoing evaluation to determine candidacy for heart transplantation. 2) The use of non-FDA approved or cleared implantable ventricular assist devices or total artificial hearts is considered experimental, investigational and unproven. 3) Percutaneous ventricular assist devices (pVADs) that are FDA approved may be considered medically necessary when following the FDA approved indications.
10/01/2010	Document updated with literature review. Coverage is changed to: Total artificial heart may be conditionally medically necessary as bridge to transplant; Total artificial hearts are considered experimental, investigational and unproven as destination therapy. Title is changed from Cardiac Mechanical Assist Device to Ventricular Assist Devices and Total Artificial Hearts.
10/01/2008	Revised/Updated Entire Document
09/01/2005	Revised/Updated Entire Document
01/25/2005	CPT/HCPCS code(s) updated
10/01/2003	CPT/HCPCS code(s) updated
02/01/2002	CPT/HCPCS code(s) updated
05/01/2000	Revised/Updated Entire Document
04/01/1999	Revised/Updated Entire Document
11/01/1997	Revised/Updated Entire Document
03/01/1991	New medical document