BlueCross BlueShield of Alabama

Name of Policy:

Total Artificial Hearts and Implantable Ventricular Assist Devices

~~**Ventricular Assist Devices and Total Artificial Hearts**~~

Policy #: 033 Latest Review Date: August 2018

Category: Surgery Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

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

Heart Failure

Heart failure may be the consequence of a number of differing etiologies, including ischemic heart disease, cardiomyopathy, congenital heart defects, or rejection of a heart transplant. The reduction of cardiac output is considered to be severe when systemic circulation cannot meet the body's needs under minimal exertion. Heart transplantation improves quality of life and has survival rates at 1-, 3-, and 5-years of 91%, 85%, and 78%, respectively. The number of candidates for transplants exceeds the supply of donor organs; thus the interest in the development of mechanical devices.

Treatment

Ventricular Assist Devices (VAD)

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

At least one VAD system has been developed that is miniaturized and generates an artificial pulse, the HeartMate III™ LVAD (St. Jude Medical, Pleasanton, California). The HeartMate® III™ was FDA approved August 23, 2017.

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

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

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

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

Policy:

Ventricular assist device (VAD) implantation meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage only when performed in a Medicare-approved heart transplant facility **OR** Medicare-approved VAD destination therapy facility **AND** follows individual criteria for specific indications listed below. A list of these facilities is maintained on the CMS web site and available at
www.cms.gov/CertificationandComplianc/Downloads/ApprovedTransplantPrograms.pdf
and
www.cms.gov/Medicare/Medicare-General-Information/MedicareApprovedFacilities/VAD-Destination-Therapy-Facilities-Aug2007.html.

Bridge to Recovery
Ventricular assist devices with FDA approval or clearance **meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage in **patients in the post-cardiotomy setting who are unable to be weaned off cardiopulmonary bypass.**

Percutaneous ventricular assist devices (pVAD) with FDA approval or clearance **meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage for use in patients **undergoing high risk percutaneous coronary intervention (PCI)** when **ALL** of the following are met:

- Patient has LVEF of less than 35% **AND;**
- Will undergo PCI on an unprotected left main coronary artery or last patent coronary conduit.

Bridge to Transplantation

TAH

Total artificial hearts with FDA-approved devices meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage when performed in a Medicare-approved heart transplant facility as a **bridge to heart transplantation** when **ALL** of the following criteria are met:

- Biventricular failure **AND**,
- No other reasonable medical or surgical treatment options; **AND**
- Are ineligible for other univentricular or biventricular support devices; **AND**
- Are currently listed as heart transplantation candidates

  OR

  Are undergoing evaluation to determine candidacy for heart transplantation; **AND**
- Are not expected to survive until a donor heart can be obtained.

VAD- Adult

Ventricular assist devices with FDA approval or clearance **meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a **bridge to transplantation** when **ALL** of the following criteria are met:

- Patient is diagnosed with severe congestive heart failure (CHF); **AND**
- Is an approved heart transplant candidate by an approved heart transplant center;

  OR

  Is undergoing evaluation to determine candidacy for heart transplantation; **AND**
- Is at risk of dying before a donor heart is available**; **AND**
- On optimal inotropic (influencing the contractility of muscular tissue) support; **AND**
- If possible, on an intra-aortic balloon pump.

**The criteria listed below may be used as hemodynamic selection criteria:

1. Either a left atrial pressure of 20m Hg or a cardiac index of less than 2.0L/min/m while on maximum medical support;
2. Patients who are usually being treated as inpatients and according to the American Heart Association or comparable, as Class IV CHF;
3. Classified as status I by the United Network for Organ Sharing (considered the highest priority for transplantation).

Pediatric- VAD

Ventricular assist devices with FDA approval or clearance, including humanitarian device exemptions **meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage in **children 16 years old and younger** as a **bridge to heart transplantation** 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 transplant.

Destination Therapy

Ventricular assist devices with FDA approval or clearance **meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage when used as a permanent alternative (**destination therapy**) **for patients with end-stage heart failure and who are not candidates for heart transplantation** when **ALL** of the following criteria are met:

- New York Heart Association (NYHA) Class IV heart failure not responding to optimal medical management for at least 60 days,

  OR

  NYHA Class III/IV for at least 28 days and received ≥ 14 days support with an intra-aortic balloon pump

  OR

  NYHA Class III/IV for at least 28 days and dependent on intravenous (IV) inotropic agents, with two failed weaning attempts; **AND**

- Left ventricular ejection fraction (LVEF) < 25%; **AND**
- Patients must **not** be candidates for human heart transplant for **one or more of the following reasons:**
  - Age > 65 years; **or**
  - Insulin-dependent diabetes mellitus with end-organ damage; **or**
  - Chronic renal failure with serum creatinine > 2.5 mg/dl for ≥ 90 days; **or**
  - Other clinically significant condition.

Other Indications

Total artificial hearts including, but not limited to, the use of total artificial hearts as destination therapy does not meet Blue Cross and Blue Shield of Alabama's medical criteria and is considered **investigational for all other indications**.

Ventricular assist devices and percutaneous ventricular assist devices do not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered **investigational for all other indications**.

Use of a non-FDA approved ventricular assist device does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical

judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The most recent literature search was performed for the period through June 21, 2018.

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

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

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

Ventricular Assist Devices as a Bridge to Heart Transplant for End-Stage Heart Failure

Clinical Context and Therapy Purpose

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

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

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

Patients

The relevant population of interest is individuals with end-stage heart failure. A subset of patients who receive a VAD as a bridge to transplantation have demonstrated improvements in

their cardiac function, sometimes to the point that they no longer require the VAD. This results in the use of VAD as a bridge to recovery.

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

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

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

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

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

VADs as Bridge to Recovery
Prospective Studies
VADs may have a role in bridging patients to recovery, particularly if there is reverse remodeling of the left ventricle. Several studies have investigated the role of VADs in bridging patients to decision for transplant eligibility. One clearly defined population in which the potential for myocardial recovery exists is in the postcardiotomy setting.

In 2016, Acharya et al (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. 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.

In 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). One hundred twenty-five of these patients had a prior bridge to recovery LVAD strategy. Cardiac recovery occurred in 192 (1.3%) of the LVAD patients overall and in 14 (11.2%) of the bridge to recovery patients. Topkara et al (2016) reported a similar analysis of 13,454 INTERMACS adults with implants between June 2006 and June 2015 without TAH or pulsatile-flow LVAD or heart transplant. Device explant rates for cardiac recovery were 0.9% at 1-year, 1.9% at 2-year, and 3.1% at 3-year follow-up. An additional 9% of patients demonstrated partial cardiac recovery.

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

Retrospective Studies

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

Takayama et al (2014) reported outcomes for a retrospectively defined cohort of 143 patients who received a CentriMag Right Ventricular Assist Device as a "bridge to decision" for refractory cardiogenic shock due to a variety of causes. Patients were managed with a bridge to decision algorithm. Causes of cardiogenic shock included failure of medical management (n=71), postcardiotomy shock (n=37), graft failure after heart transplantation (n=2), and right ventricular failure postimplantable LVAD (n=13). The device configuration was biventricular in 67%, isolated right VAD in 26%, and isolated LVAD in 8%. After a mean duration of support of 14 days (interquartile range, 8-26 days), 30% of patients had myocardial recovery, 15% had device exchange to an implantable VAD, and 18% had a heart transplant.

VADs as Bridge to Heart Transplant

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

Adult Patients

Systemic Reviews

Several older systematic reviews have that VADs can provide an effective bridge to transplantation.

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

Case Series
In 2011, Strueber et al published a case series of 50 patients awaiting heart transplantation treated with HeartWare® VAD (HVAD), which is a smaller continuous flow centrifugal device that is implanted in the pericardial space. Patients were followed until transplantation, myocardial recovery, device explant, or death. The median duration of time on the VAD was 322 days. Nine patients died, three from sepsis, three from multiple organ failure, and three from hemorrhagic stroke. At the end of follow-up, 20 patients had undergone transplant (40%), four had the pump explanted (8%), and the remaining 17 continued on pump support (34%). The most common complications were infection and bleeding. A total of 21 patients had infections (42%), and five patients had sepsis (10%). Bleeding complications occurred in 15 patients (30%), ten of whom (20%) required surgery.

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

In five reports published from 2007 to 2008, with samples ranging from 32 to 279 patients, most participants received the continuous-flow device as a bridge to transplantation. Survival rates at six months were between 67% and 87%, and between 50% and 80% at one year. These rates are similar to those reported by the INTERMACS Registry. A study by Patel and colleagues (2008) compared HeartMate® I and HeartMate® II recipients at a single center, finding the same one-year survival and similar rates of subsequent development of right heart failure. Serious adverse events occurring after HeartMate® II-implantation include bleeding episodes requiring reoperation, stroke, infection, and device failure.

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

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

Pediatric Patients

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

Registry Studies

Bulic et al (2017) identified all U.S. children between 1 and 21 years of age at heart transplant between 2006 and 2015 for dilated cardiomyopathy who were supported with an LVAD or vasoactive infusions alone at the time of transplant from the Organ Procurement and Transplant Network registry (n=701). Functional status as measured by the median Karnofsky Performance Scale score at heart transplant was higher for children receiving LVAD (6) compared with vasoactive infusion (5; p<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).

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

Fraser et al (2012) evaluated the EXCOR® device among 48 children, ages 16 or younger, with 2-ventricle circulation who had severe heart failure, despite optimized treatment, and were listed for heart transplant. Patients were divided into 2 groups based on body surface area; a historical control group of children, receiving circulatory support with ECMO from the Extracorporeal Life Support Organization registry, were matched in a 2:1 fashion with study participants based on propensity-score matching. For participants in cohort 1 (body surface area <0.7 m2), the median survival time had not been reached at 174 days, while in the matched ECMO comparison group, the median survival was 13 days (p<0.001). For participants in cohort 2 (body surface area range, 0.7 to <1.5 m2), the median survival was 144 days compared with 10 days in the matched ECMO group (p<0.001). Rates of adverse events were high in both EXCOR® device cohorts, including major bleeding (cohort 1, 42%; cohort 2, 50%), infection (cohort 1, 63%; cohort 2, 50%), and stroke (29% of both cohorts).

Non-comparative Studies

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

In 2013, Almond et al reported results from a prospective, multicenter registry to evaluate outcomes in children who received the Berlin Heart EXCOR® device as a bridge to transplant. This study included a broader patient population than the Fraser et al study. All patients were followed up from the time of EXCOR® implantation until transplantation, death, or recovery. The study included 204 children, 67% of whom received the device under compassionate use. Survival at 12 months on EXCOR® support was 75%, including 64% who survived to transplantation, 6% who recovered (device explanted and patient survived 30 days), and 5% alive with the device in place. In a follow-up study which evaluated 204 children from the same registry, Jordan et al (2012) 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.

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

In 2016, Conway et al conducted a retrospective, single-center series of pediatric patients treated with short-term continuous flow VADs, which included the Thoratec PediMag® or CentriMag®, and the Maquet RotaFlow®. From January 2005 and May 2014, 27 children were supported with one of these devices, most commonly for congenital heart disease (42%). The median duration of support was 12 days, and 67% of all short term continuous flow VAD runs (19 of 28 runs) lead to hospital discharge.

Effects of Pretransplant VADs on Transplant Outcomes

Published studies continue to report that the use of a VAD does not compromise the success of a subsequent heart transplant and, in fact, may improve posttransplant survival, thus improving the use of donor hearts. A systematic review published by Alba et al (2011) examined the evidence on the effect of VADs on post-transplant outcomes. This review included 31 observational studies that compared outcomes of transplant in patients who did and did not have

pre-transplant VAD. Survival at one year was more likely in patients who had VAD treatment, but this benefit was confined to patients who received an intra-corporeal device (relative risk [RR]: 1.8, 95% confidence interval [CI]: 1.53-2.13). For patients treated with an extracorporeal device, the likelihood of survival was not different from patients who were not treated with an LVAD (RR: 1.08, 95% CI: 0.95-1.22). There was no difference in the risk of rejection between patients who did and did not receive VAD treatment.

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

Section Summary: Ventricular Assist Devices as a Bridge to Heart Transplant for End-Stage Heart Failure

Questions remain about defining and identifying the population most likely to experience cardiac recovery with VAD placement. One clearly defined population in which the potential for myocardial recovery exists is in the 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.

In adults, the evidence on the efficacy of VADs as a bridge to transplant consists of uncontrolled trials, registry studies, and case series. In children, the evidence consists of several uncontrolled trials and a trial with historical controls. Collectively, these studies have reported that substantial numbers of patients have survived to transplant in situations in which survival is historically low. Despite the lack of high-quality controlled trials, this evidence supports a finding that outcomes are improved in patients because they have no other treatment options.

VADS as Destination Therapy for End-Stage Heart Failure

Clinical Context and Therapy Purpose

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

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

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

Patients

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

Interventions

The therapy being considered is a VAD as destination therapy.

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

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

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

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

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

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

Park et al (2005) published an extended two-year follow up of patients in the REMATCH trial, which found that survival and quality of life benefits were still apparent. In addition, this study and other case series suggest continuing improvement in outcomes related to ongoing improvements in the device and patient management. However, the durability of the HeartMate® device used in the REMATCH trial is a concern. For example, at one participating institution, all six long-term survivors required device change-outs.

Nonrandomized Comparative Studies
A subsequent prospective observational study called the Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients study 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 quality of life in LVAD-treated patients. 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). In 2017, Starling et al reported two-year results from this study. 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, which included the first 247 HeartMate® II patients identified as eligible for the device as destination therapy, outcomes and adverse events did not differ significantly from those treated in the original trial, which compared patients who received the HeartMate® II to earlier generation devices (Slaughter et al [2009], described below). Survival in the post approval cohort was 82% and 69% at one and two years postoperatively, respectively.

After publication of the REMATCH study results, Rogers et al (2007) published results from a prospective, nonrandomized clinical trial comparing LVAD as destination therapy with optimal medical therapy for patients with heart failure who were not candidates for heart transplant. Fifty-five patients who had NYHA functional class IV symptoms and who failed weaning from inotropic support were offered a Novacor LVAD; 18 of these did not receive a device due to preference or device unavailability and acted as a control group. The LVAD-treated patients had superior survival rates at six months (46% vs 22%; p=0.03) and 12 months (27% vs 11%; p=0.02), along with fewer adverse events.

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

Section Summary: VADs as Destination Therapy for End-Stage Heart Failure
The highest quality evidence on the efficacy of LVADs as destination therapy in patients who are not transplant candidates is from a multicenter randomized controlled trial (RCT), the REMATCH study. This trial reported that the use of LVADs led to improvements in survival, quality of life, and functional status. This evidence is sufficient to establish that health outcomes are improved for this patient population.

Total Artificial Heart as a Bridge to Transplant for End-Stage Heart Failure
Clinical Context and Therapy Purpose
The purpose of a total artificial heart (TAH) as a bridge to heart transplant in patients who have end-stage heart failure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

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

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

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

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

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

Timing
Time-to-transplant is of interest, as are short-term outcomes ranging from 30 days to 1 year.

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

Nonrandomized Trials
The FDA approval of the CardioWest™ TAH was based on the results of a nonrandomized, prospective study of 81 patients. Patients had failed inotropic therapy and had biventricular failure and thus were not considered appropriate candidates for an LVAD. The rate of survival to transplant was 79%, which was considered comparable to the experience with LVAD in patients with left ventricular failure. The mean time from entry into the study until transplantation or death was 79.1 days.

Case Series
Other case series have been reported on outcomes of the TAH as a bridge to transplant. For example, Copeland et al (2012) reported on 101 patients treated with the SynCardia artificial heart as a bridge to transplant. All patients either met established criteria for mechanically assisted circulatory support, or were failing medical therapy on multiple inotropic drugs. The mean support time was 87 days, (with a range of 1-441 days). Survival to transplant was 68.3% (69/101). Of the 32 deaths prior to transplant, 13 were due to multiple organ failure, six were due to pulmonary failure, and four were due to neurologic injury. Survival after transplant at one, five and ten years, respectively, was 76.8%, 60.5%, and 41.2%.

Section Summary: Total Artificial Heart as a Bridge to Transplant for End-Stage Heart Failure
There is a smaller amount of evidence on the use of TAH as a bridge to transplantation, or as destination therapy, compared to the use of LVADs. The type of evidence on bridge to transplant is similar to that for LVADs, (i.e., case series reporting substantial survival rates in patients without other alternatives). Therefore, similar to LVADs, this evidence is sufficient to conclude that TAH improves outcomes for these patients and TAH is a reasonable alternative for patients who require a bridge to transplantation but who are ineligible for other types of life-sustaining support devices.

Total Artificial Heart (TAH) as Destination Therapy for End-Stage Heart Failure

Clinical Context and Therapy Purpose

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

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

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

Patients

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

Interventions

The therapy being considered is a TAH as destination therapy.

Comparators

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

Outcomes

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

Timing

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

Setting

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

Case Series

Data on the artificial heart are available from information concerning the FDA approval and from a published article describing results for the first seven patients. 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.

The patients with a one-month survival prognosis of not more than 30%, were not eligible for cardiac transplants, and were felt to not benefit from VAD therapy. The study was reported to show that the device is safe and has likely benefit for people with severe heart failure whose death is imminent and for whom no alternative treatments are available. Of the 14 patients in the study, 12 survived surgery. Mean duration of support for the patients was 5.3 months. In some cases, the device extended survival by several months; (survival was 17 months in one patient). Six patients were ambulatory; one patient was discharged home. Complications included postoperative bleeding and neurological events. Device-related infection was "non-existent."

In 2014, Torregrossa et al reported on 47 patients who received a TAH at ten worldwide centers and had the device implanted for more than one year. Patients were implanted for dilated cardiomyopathy (n=23), ischemic cardiomyopathy (n=15), and "other" reasons (n=9). Over a median support time of 554 days (range, 365-1373 days), 34 patients (72%) were successfully transplanted, 12 patients (24%) died while on device support, and one patient (2%) was still supported. Device failure occurred in five patients (10%). Major complications were common, including systemic infection in 25 patients (53%), driveline infections in 13 patients (27%), thromboembolic events in nine patients (19%) and hemorrhagic events in seven patients (14%). Two of the deaths occurred secondary to device failure.

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

Percutaneous VADS for Cardiogenic Shock
Clinical Context and Therapy Purpose
The purpose of pVADs in patients who have cardiogenic shock is to provide a treatment option that is an alternative to or an improvement on existing therapies.

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

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

Patients
The relevant population of interest is individuals with cardiogenic shock.

Interventions
The therapy being considered is a pVADs.

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

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

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

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

Systematic Reviews
Romeo et al (2016) reported on a systematic review and meta-analysis which evaluated a variety of percutaneous mechanical support methods, including pVADs, for patients with cardiogenic shock due to acute myocardial infarction who were undergoing revascularization. This review included 3 RCTs, comparing pVADs with intra-aortic balloon pump (IABP), along with 3 observational studies. In the analysis of the comparison of pVADs with IABP, the authors found that in-hospital mortality, the primary outcome of the analysis, was nonsignificantly increased in the pVAD group.

A 2009 meta-analysis by Cheng et al included the same 3 trials as Romeo (2016).None of the three trials reported an improvement in mortality associated with pVAD use. The combined analysis estimated the relative risk for death in pVAD patients as 1.06 (95% CI, 0.68 to 1.66; p=0.80). All three trials reported an improvement in LV hemodynamics in the pVAD group. On combined analysis, there was a mean increase in cardiac index of 0.35 L/min/m2 for the pVAD group, an increase in mean arterial pressure of 12.8 mm Hg (95% CI, 3.6 to 22.0; p<0.001), and a decrease in pulmonary capillary wedge pressure of 5.3 mm Hg (95% CI, 1.2 to 9.4; p<0.05). Complications were more common in the pVAD group. On combined analysis, patients in the pVAD group had a significantly increased likelihood of bleeding events with a relative risk of 2.35 (95% CI, 1.40 to 3.93). Leg ischemia was also more common in the pVAD group, but this difference did not meet statistical significance (RR=2.59; 95% CI, 0.75 to 8.97; p=0.13).

Table 1 provides a crosswalk of studies in the systematic reviews. Tables 2 and 3 summarize the characteristics and results of the systematic reviews.

Table 1. Comparison of Systematic Reviews Evaluating pVADs and IABPs for Cardiogenic Shock

Studies	Romeo et al (2016)	Cheng et al (2016)
Burkhoff et al (2006)	●	●
Seyfarth et al (2008)	●	●
Thiele et al (2005)	●	●
Schwartz et al (2012)	●	
Shah et al (2012)	●	
Manzo-Silberman (2013)	●	

IABP: intra-aortic balloon pump; pVAD: percutaneous ventricular assist device.

Table 2. Characteristics of Systematic Reviews Evaluating pVADs and IABPs for Cardiogenic Shock

Study	Dates	Trials	Participants	N	Design
Romeo et al (2016)	2000-2010	6	Patients receiving IABP or pVADs	271	RCT and observational
Cheng et al (2016)	2000-2015	3	Patients receiving IABP or pVADs	100	RCT

IABP: intra-aortic balloon pump; pVAD: percutaneous ventricular assist device.

Table 3. Results of Systematic Reviews Evaluating pVADs and IABPs for Cardiogenic Shock

Study	Overall In-Hospital Mortality Events		Incidence of Bleeding Events	Incidence of Leg Ischemia
	RCTs	**OBS Studies**		
Romeo et al (2016)				
pVAD	24	42		
IABP	20	53		
p	0.80	0.20		
Cheng et al (2016)				
pVAD	24		Increased likelihood	Increased likelihood
IABP	20			
RR (95% CI)	1.06 (0.68 to 1.66)		2.35 (1.40 to 3.93)	2.59 (0.75 to 8.97)

CI: confidence interval; IABP: intra-aortic balloon pump; OBS: observational; pVAD: percutaneous ventricular assist device; RR:
relative risk.

Randomized Controlled Trials

Four RCTs have compared pVADs with IABPs for patients with cardiogenic shock; three were included in the systematic reviews described above, and one was published after the reviews. 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 4 and 5. Some trials reported improvements in hemodynamic and metabolic parameters, but none found any improvement in 30-day mortality. The 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 4. Characteristics of RCTs Evaluating pVADs and IABPs for Cardiogenic Shock

Study	Trial (Registration)	Countries	Sites	Dates	pVAD	Key Eligibility Criteria
Ouweneel et al (2017)	IMPRESS (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	Germany	2	2004-2007	Impella LP 2.5	AMI <48 h and CS

(2008)	(NCT00417378)					
Burkhoff et al (2006)	TandemHeart (NR)	U.S.	12	2002-2004	TandemHeart	CS <24 h due to MI or heart failure
Thiele et al (2005)	NR	Germany	1	2000-2003	TandemHeart	AMI with CS and intent to revascularize with PCI

AMI: acute myocardial infarction; CS: cardiogenic shock; IABP: intra-aortic balloon counterpulsation; IMPRESS: Impella versus IABP Reduces mortality in STEMI patients treated with primary PCI in Severe cardiogenic SHOCK; 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 5. Results of RCTs Evaluating pVADs and IABPs for Cardiogenic Shock

Study	**Numbers Randomized**		**PVAD vs IABP**			**Other Outcomes**
	PVAD	**IABP**	**30- Day Mortality**	**Bleeding**	**Leg Ischemia**	
IMPRESS	24	24	• 46% vs 50% • HR=0.96 (042 to 2.18)[a] • 50% vs 50% HR=1.04 (0.47 to 2.32)[a]	33% vs 8%	NR	Rehospitalization: 21%vs 4%
ISAR-SHOCK	13	13	46 vs 46%	NR	8% vs 0%	Increase in cardiac index (L/min/m$^{2)}$: 0.49 vs 0.11
TandemHeart®	19	14	47% vs 36%	42% vs 14%	21% vs 14%	At least 1 adverse event: 95% vs 71%
Thiele et al (2005)	21	20	43% vs 45%	90% vs 40%	33% vs 0%	Final cardiac index (W/m^2): 0.37 vs 0.28

AMI: acute myocardial infarction; 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; NR: not reported; pVAD: percutaneous ventricular assist devices; RCT: randomized controlled trial. a Values are hazard ratio (95% confidence interval). b Major bleeding.

Registry Studies

In 2014, O'Neill et al compared outcomes for patients with acute MI complicated by cardiogenic shock; who received pVAD support before percutaneous coronary intervention (PCI) with those who received pVAD support after PCI using data from 154 consecutive patients enrolled in a multicenter registry. Patients who received pVAD support pre-PCI had a higher survival to discharge rate (65.1%) than those who received pVAD support post-PCI (40.7%; p=0.003). In multivariable analysis, receiving pVAD support pre-PCI was associated with in-hospital survival (odds ratio [OR], 0.37; 95% CI, 0.17 to 0.79; p=0.01). However, the potential for underlying differences in patient groups other than the use of pVAD support makes the study's implications uncertain.

Basir et al (2017) compared survival in patients with AMI complicated by cardiogenic shock and undergoing coronary angioplasty who received an Impella® device. Exactly 287 consecutive patients from the global catheter-based VAD (cVAD) Registry were analyzed. Impella®

implantation before and after PCI and before initiation of inotropes or vasopressors was independently associated with survival in multivariate analysis. Survival rates were 66% in patients who received the Impella® device less than 1.25 hours from shock onset, 37% in those receiving the device within 1.25 to 4.25 hours, and 26% after 4.25 hours (p=0.017).

Case Series

Case series of patients treated with pVADs as an alternative to intra-aortic balloon pumps (IABPs) in cardiogenic shock have been published, and report high success rates as a bridge to alternative therapies. However, given the availability of RCT evidence, these studies add a limited amount to do not add much to the body of evidence on the efficacy of pVADs for the management of cardiogenic shock.

Section Summary: Percutaneous VADs for Cardiogenic Shock

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

Percutaneous VADS for High-Risk Cardiac Procedures

Clinical Context and Therapy Purpose

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

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

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

Patients

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

Interventions

The therapy being considered is a pVAD.

Comparators

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

Outcomes

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

Timing

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

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

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

Systematic Reviews

In 2016, Briasoulis et al reported on a meta-analysis of pVAD devices as an adjunct to high-risk PCI. The authors included RCTs and cohort studies, and identified 18 nonrandomized observational studies and 1 RCT. The single RCT identified was the PROTECT II trial described in more detail below. In the observational studies, the sample sizes ranged from 7 to 637. In pooled analysis, the 30-day mortality rate following Impella®-assisted high-risk PCI was 3.5% (95% CI 2.2 to 4.8%; I2 20%), while that for TandemHeart®-assisted high-risk PCI was 8% (95% CI 2.9 to 13.1%; I2 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.

Randomized Controlled Trials

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

In a prespecified subgroup analysis of the PROTECT II trial, Kovacic et al (2015) compared outcomes for the Impella® system compared with IABP among 325 patients with three vessel disease with LVEF less than or equal to 30%. In the three vessel disease subgroup, 167 subjects were randomized to PCI with Impella® support and 158 to PCI with IABP support. PCI characteristics differed in that rotational atherectomy was more aggressively used in the Impella®-support group, with more passes per patient (5.6 vs 2.8, p=0.002) and more passes per coronary lesion (3.4 vs 1.7, p=0.001). Acute procedural revascularization results did not differ between groups. At 30 days, the major adverse event rate did not differ significantly between groups (32.9% of Impella® patients vs 42.4% of IABP patients, p=0.078). At 90 days, Impella® patients had a significantly lower major adverse event rate compared with IABP patients (39.5% vs 51.0%, p=0.039). The 90-day event rates for the individual components of the composite major adverse event score differed only for severe hypotension requiring treatment, which was more common in patients treated with IABP (7.6% vs 2.4%, p=0.029).

In a post-hoc analysis, results of the PROTECT II trial were reanalyzed by Dangas et al (2014), using a revised definition of MI in the determination of patients with major adverse events and major adverse cardiac and cerebral events. In contrast to the original trial, which used a cutoff of three times the upper limit of normal for biomarker elevation to define periprocedural MI, the authors used a cutoff of eight times the upper limit of normal for biomarker elevation or the presence of Q waves to define periprocedural MI. In multivariable analysis, compared with IABP, treatment with the Impella® system was associated with freedom from 90-day major adverse events (OR=0.75; 95% CI 0.1 to 0.92; p=0.007) and major adverse cardiac and cerebral events (OR=0.76; 95% CI 0.61 to 0.96; p=0.020).

Nonrandomized Studies

In 2013, Kovacic et al retrospectively compared outcomes for the TandemHeart® and Impella® devices in 68 patients undergoing high-risk PCI from 2005 to 2010 from a single-center database. There were no reported in-hospital deaths or strokes. There was one periprocedural MI in the TandemHeart® group and 2 in the Impella® group. For 63 patients with available intermediate- and long-term data, there was no statistically significant difference in time to death.

The PROTECT trial evaluated whether the Impella® 2.5 system would improve outcomes for patients undergoing high-risk PCI procedures. PROTECT I was a feasibility study of 20 patients who had left main disease or last patent coronary conduit that required revascularization but who were not candidates for coronary artery bypass graft surgery. High-risk PCI was performed using the Impella® system for circulatory support. All procedures were successfully completed without any hemodynamic compromise in-procedure. Two (10%) patient died within 30 days, and 2 (10%) patients had a periprocedural MI. Two other patients had evidence of hemolysis, which was transient and resolved without sequelae.

Registry Studies

Schreiber et al (2017) reported outcomes for 127 consecutive patients from the USpella Registry not in cardiogenic shock who underwent unprotected left main PCI supported with an Impella® LV device between 2008 and 2015. The in-hospital and 30-day mortality rates were 1.6% and 2.4%, respectively. The 30-day major adverse cardiovascular event rate was 2.4%. One patient had vascular complications requiring surgery. Three (2.4%) patients had a hematoma, and 5 (3.9%) patients had bleeding requiring transfusion.

Maini et al (2012) retrospectively analyzed 175 patients with data in the USpella Registry undergoing high-risk PCI with pVAD support using the Impella® 2.5 circulatory support system. The primary safety end point was the incidence of major adverse cardiac events at 30 days. Secondary end points included device safety and efficacy and patient outcomes at 30 days and 12 months. Angiographic revascularization was successful in 99% of patients. At 30-day follow-up, the major adverse cardiac event rate was 8%; survival rates were 96%, 91%, and 88% at 30 days, 6 months, and 12 months, respectively. Secondary safety end points included acute renal dysfunction (2.8%), hypotension on support (3.4%), ventricular tachycardia (VT), or cardiopulmonary resuscitation (2.8%); other vascular complications included vessel dissection and arteriovenous fistula (3.4%), hematomas ipsi- or contralateral to the device insertion site (8.6%), infection (5.1%), and blood transfusion (9.7%).

In 2009, Sjauw et al retrospectively analyzed 144 consecutive patients undergoing high-risk PCI with pVAD support (Impella®) from a European registry. End points included successful device function and incidence of adverse events at 30 days. The device was successfully implanted in all 144 patients. There were a periprocedural death and 8 deaths at 30 days for a mortality rate of 5.5%. Bleeding requiring transfusion or surgery occurred in 6.2% of patients, and vascular access site complications occurred in 4.0%. There was 1 (0.7%) stroke, and no MIs were reported.

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

Percutaneous VADs for High-Risk Ventricular Tachycardia (VT) Ablation
Reddy et al (2014) reported outcomes for a series of 66 patients enrolled in a prospective, multicenter registry who underwent ventricular tachycardia ablation with a pVAD or IABP. Twenty-two patients underwent ablation with IABP assistance, while 44 underwent ablation with either the TandemHeart® or Impella® pVAD device (non-IABP group). Compared with patients who received support with an IABP, those who received support with a pVAD had greater numbers of unstable ventricular tachycardia's that could be mapped an ablated (1.05 vs 0.32, $p<0.001$), greater numbers of ventricular tachycardia's that could be terminated by ablation (1.59 vs 0.91, $p=0.001$), and fewer numbers of ventricular tachycardia's that were terminated with rescue shocks (1.9 vs 3.0, $p=0.049$). More pVAD-supported patients could undergo entrainment/activation mapping (82% vs 59%, $p=0.046$). Mortality and ventricular tachycardia 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 ventricular tachycardia who underwent ablation with or without pVAD support. Thirty-four patients had hemodynamic support peri-procedurally with a pVAD. pVAD- and non-pVAD-supported patients were similar at baseline, with no differences in procedural success rates between groups. Compared with non-pVAD-supported patients, patients in the pVAD group had a longer maximum time in unstable ventricular tachycardia (27.4 vs 5.3 minutes, $p<0.001$), a greater number of ventricular tachycardia ablations per procedure (1.2 vs 0.4, $p<0.001$), a shorter radiofrequency ablation time (53 vs 68 seconds, $p=0.022$), and a shorter hospital length of stay (4.1 vs 5.4 days, $p=0.013$). Over a follow up period of 19 months, rates of ventricular tachycardia recurrence did not differ between groups.

Section Summary: Percutaneous VADs for High-Risk VT Ablation
Two nonrandomized studies have compared VT ablation with pVAD or IABP. In both studies, patients who had pVAD support spent less time in unstable VT than patients without pVAD

support. Rates of recurrence of VT was comparable between groups for both studies. The current evidence based does not support conclusions about the use of pVAD for VT ablation.

Percutaneous VADS for Cardiogenic Shock Refractory to IABP Therapy

Clinical Context and Therapy Purpose

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

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

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

Patients

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

Interventions

The therapy being considered is the use of a pVAD.

Comparators

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

Outcomes

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

Timing

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

Setting

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

Case Series

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

(5.1%); limb ischemia in four patients (3.4%); femoral artery dissection or perforation in two patients (1.7%); stroke in eight patients (6.8%); coagulopathy in 13 patients (11.0%).

Section Summary: Percutaneous VADs for Cardiogenic Shock Refractory to IABP Therapy
Percutaneous VADs have been tested in RCTs and uncontrolled studies of patients with cardiogenic shock, including those refractory to IABP, and in patients undergoing high-risk cardiac interventions such as PCI and VT ablation. The RCTs have not consistently reported a benefit for the use of pVADs, except for use with high risk PCI.

Summary of Evidence

Ventricular Assist Device

For individuals who have end stage heart failure who receive VADs as bridge to transplant, the evidence includes single arm clinical trials and observational studies. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, treatment-related mortality, and treatment-related morbidity. There is a substantial body of evidence from clinical trials and observational studies supporting implantable ventricular assist devices as a bridge to transplant in patients with end-stage heart failure, possibly improving mortality as well as quality of life. These studies report that substantial numbers of patients survive to transplant in situations in which survival would not be otherwise expected. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

Total Artificial Heart

For individuals who have end stage heart failure who receive total artificial hearts (TAHs) as bridge to transplant, the evidence includes case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, treatment-related mortality, and treatment-related morbidity. Compared with VADs, the evidence for total artificial heart in these settings is less robust. However, given the limited evidence from case series and the lack of medical or surgical options for these patients, TAH is likely to improve outcomes for a carefully selected population with end-stage biventricular heart failure awaiting transplant who are not appropriate candidates for an LVAD. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

For individuals who have end stage heart failure who receive TAHs as destination therapy, the evidence includes 2 case series. Relevant outcomes are overall survival, symptoms, functional outcomes, quality of life, treatment-related mortality, and treatment-related morbidity. The

body of evidence for TAHs as destination therapy is very limited. The evidence is insufficient to determine the effects of the technology on health outcomes.

Percutaneous Ventricular Assist Device

For individuals undergoing high- risk percutaneous coronary intervention receiving a pVAD, the evidence includes RCTs, registry studies, systematic reviews and comparative studies. Relevant outcomes are overall survival, symptoms, morbid events, functional outcomes, quality of life, treatment-related mortality, and treatment-related morbidity. Based on available evidence, the use of pVADs may be indicated in patients who are undergoing high risk PCI; however, the evidence does not support improvement of health outcomes for any other indication. Complications have been reported when using pVADs with high risk PCI procedures, but several studies have shown that the major adverse event rate at 30 and 90+ days post pVADs are favorable.

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

Practice Guidelines and Position Statements

Society for Cardiovascular Angiography and Interventions et al

In 2015, the Society for Cardiovascular Angiography and Interventions (SCAI), the Heart Failure Society of America (HFSA), the Society of Thoracic Surgeons (STS), the American Heart Association (AHA), and the American College of Cardiology (ACC) published a clinical expert consensus statement on the use of percutaneous mechanical circulatory support (MCS) devices in cardiovascular care. This statement addressed intra-aortic balloon pumps (IABPs), left atrial (LA)-to-aorta assist device (e.g., TandemHeart®), left ventricle (LV)-to-aorta assist devices (e.g., Impella®), extracorporeal membrane oxygenation (ECMO), and methods of right-sided support. Specific recommendations 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:

1. "Percutaneous MCS provides superior hemodynamic support compared to pharmacologic therapy. This is particularly apparent for the Impella® and TandemHeart® devices. These devices should remain available clinically and be appropriately reimbursed.
2. Patients in cardiogenic shock represent an extremely high risk group in whom mortality has remained high despite revascularization and pharmacologic therapies. Early placement of an appropriate MCS may be considered in those who fail to stabilize or show signs of improvement quickly after initial interventions.
3. MCS may be considered for patients undergoing high-risk PCI, such as those requiring multivessel, left main, or last patent conduit interventions, particularly if the patient is

inoperable or has severely decreased ejection fraction or elevated cardiac filling pressures."

American College of Cardiology Foundation et al

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

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

American College of Cardiology and American Heart Association

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

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

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

In 2012, AHA published recommendations for the use of MCS. These guidelines define nondurable MCS as intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation, extracorporeal VADs, and pVADs. The following recommendations were made regarding indications for use of MCS, including durable and nondurable devices:

- MCS for bridge-to-transplant indication should be considered for transplant-eligible patients with end-stage heart failure who are failing optimal medical, surgical, and/or device therapies and at high risk of dying before receiving a heart transplantation. (Class I; Level of Evidence B).
- Implantation of MCS in patients before the development of advanced heart failure… is associated with better outcomes. Therefore, early referral of heart failure patients is reasonable. (Class IIa; Level of Evidence B).
- MCS with a durable, implantable device for permanent therapy or destination therapy is beneficial for patients with advanced heart failure, high one year mortality resulting from heart failure, and the absence of other life-limiting organ dysfunction; who are failing medical, surgical, and/or device therapies; and who are ineligible for heart transplantation. (Class I; Level of Evidence B).
- Elective rather than urgent implantation of destination therapy can be beneficial when performed after optimization of medical therapy in advanced heart failure patients who are failing medical, surgical, and/or device therapies. (Class IIa; Level of Evidence C).
    - Urgent nondurable MCS is reasonable in hemodynamically compromised heart failure patients with end-organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with time and restoration of an improved hemodynamic profile. (Class IIa; Level of Evidence C).
    - These patients should be referred to a center with expertise in the management of durable MCS and patients with advanced heart failure. (Class I; Level of Evidence C).
- Patients who are ineligible for heart transplantation because of pulmonary hypertension related to heart failure alone should be considered for bridge to potential transplant eligibility with durable, long-term MCS. (Class IIa; Level of Evidence B).

<u>Heart Failure Society of America</u>

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

- Patients awaiting heart transplantation who have become refractory to all means of medical circulatory support should be considered for a mechanical support device as a bridge to transplant. (Strength of Evidence = B)
- Permanent mechanical assistance using an implantable assist device may be considered in highly selected patients with severe HF [heart failure] refractory to conventional therapy who are not candidates for heart transplantation, particularly those who cannot be weaned from intravenous inotropic support at an experienced HF center. (Strength of Evidence = B)
- Patients with refractory HF and hemodynamic instability, and/or compromised end-organ function, with relative contraindications to cardiac transplantation or permanent

mechanical circulatory assistance expected to improve with time or restoration of an improved hemodynamic profile should be considered for urgent mechanical circulatory support as a "bridge to decision." These patients should be referred to a center with expertise in the management of patients with advanced HF. (Strength of Evidence = C)

U.S. Preventive Services Task Force Recommendations
Not applicable

Key Words:

Ventricular assist device, biventricular support, BIVAD, cardiac support, heart transplantation (transplant), LVAD, VAD, destination therapy, HeartWare®, Impella LV®, Impella 2.5, Impella 2.5 circulatory assist device, DeBakey, percutaneous ventricular assist device, pVAD, TandemHeart®, Berlin Heart EXCOR®, Impella RP, Carmat, bioprosthetic artificial heart, HeartMate III™, Total Artificial Heart, TAH, CardioWest™ Total Artificial Heart, HeartMate II®, SynCardia artificial heart, Right Ventricular Assist Device, RVAD, PediMag®, short-term continuous flow ventricular assist devices, STCF-VADs, intraluminal axial support

Approved by Governing Bodies:

A number of mechanical circulatory support devices have received approval or clearance for marketing by FDA. These devices are summarized in Table 1, and described further in the sections below.

Table 1: Available Mechanical Circulatory Support Devices

Device	Manufacturer	Approval Date	FDA Clearance	PMA, HDE, or 510(k) No.	Indication
Thoratec® IVAD	Thoratec	Aug 2004	PMA supplement	P870072	Bridge to transplant and postcardiotomy
DeBakey VAD® Child	MicroMed	Feb 2004	HDE	H030003	Bridge to transplant in children 5-16 years of age
HeartMate II®	Thoratec	Apr 2008	PMA	P060040	Bridge to transplant and destination therapy
Centrimag®	Levitronix	Oct 2008	HDE	H070004	Postcardiotomy
Berlin Heart EXCOR® Pediatric VAD	Berlin	Dec 2011	HDE	H100004	Bridge to transplant
HeartWare® Ventricular Assist System	HeartWare	Dec 2012	PMA	P100047	Bridge to transplant, and destination therapy
HeartMate	Thoratec	Aug 2017	PMA	P160054	Bridge to transplant, and

III™ Left Ventricular Assist System					destination therapy

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

Ventricular Assist Devices

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

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

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

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

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

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

In December 2011, the Berlin Heart EXCOR® Pediatric VAD was approved via HDE. The indications for this device are pediatric patients with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplant and require circulatory support.

In December 2012, device HeartWare® Ventricular Assist System (HeartWare, Inc., Framingham, Mass.) was approved by the FDA using the INTERMACS registry as a control. INTERMACS registry was established in 2005 as a joint effort involving the FDA, National Heart, Lung and Blood Institute (NHLBI), Centers for Medicare and Medicaid Services (CMS), clinicians, scientists, and industry. This was the first time the FDA approved an LVAD using registry data as a control. INTERMACS is managed by the University of Alabama at Birmingham.

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

In September 2017, HeartWare® Ventricular Assist System (HeartWare, Inc., Framingham, Mass.) was approved by the FDA for providing long-term hemodynamic support (e.g., destination therapy) in patients with advanced heart failure.

In August 2017, the HeartMate™ 3 Left Ventricular Assist System (Thoratec Corp., Pleasanton, CA) was approved by the FDA for providing short-term hemodynamic support (e.g., bridge to transplant or bridge to myocardial recovery) in patients with advanced refractory left ventricular heart failure.

In October 2018, the HeartMate™ 3 Left Ventricular Assist System (Thoratec Corp., Pleasanton, CA) was approved by the FDA for providing long-term hemodynamic support (e.g., destination therapy) in patients with advanced heart failure.

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

Total Artificial Heart

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

In 2006, the AbioCor® Implantable Replacement Heart System (Abiomed) was approved by FDA through the humanitarian device exemption (H040006) process in severe biventricular end-stage heart disease patients who are not cardiac transplant candidates and who:

- are younger than 75 years of age;
- require multiple inotropic support;
- are not treatable by left VAD destination therapy; and
- are not weanable from biventricular support if on such support.

In addition to meeting other criteria, patients who are candidates for the AbioCor® TAH must undergo a screening process to determine if their chest volume is large enough to hold the device. The device is too large for about 90% of women and for many men.

NOTE: The Carmat bioprosthetic total artificial heart has **not been FDA approved.

Percutaneous VADs (Circulatory Assist Devices)

Table 2. Available Mechanical Circulatory Support Devices

Device	Manufacturer	Approval Date	FDA Clearance	PMA, 510(k) No.	Indication
TandemHeart ®	Cardiac Assist	Sep 2005	510(k)	K110493	Temporary left ventricular bypass of ≤6 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 ventricular support for ≤6 h

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

Comparative Efficacy of Left VAD Devices

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

The evidence of the comparative efficacy of centrifugal continuous-flow vs axial continuous-flow devices consists of 2 randomized controlled trials of 2 different centrifugal continuous-flow devices.4,5 The MOMENTUM 3 trial compared HeartMate III™ centrifugal continuous-flow device with the HeartMate II® axial continuous-flow device in patients indicated for circulatory support as a bridge to transplant or destination therapy. HeartMate III™ received PMA approval in August 2017 but was recalled in April 2018. The ENDURANCE trial compared HeartWare® centrifugal continuous-flow device with the HeartMate II® axial continuous-flow device in patients indicated for circulatory support as destination therapy. HeartWare® is FDA-approved as a bridge to transplantation device. Both trials found the centrifugal device to be noninferior to the axial device for the primary, composite outcome including measures of survival, freedom from disabling stroke, and freedom from device failure. While there are fewer device failures with the centrifugal devices without a significant increase in disabling stroke, the HeartWare® device was associated with increased risk of any stroke over a period of 2 years.

The evidence on the comparative efficacy of continuous-flow vs pulsatile-flow devices consists of a randomized controlled trial and several nonrandomized comparative studies.6-10 The randomized controlled trial reported fairly large differences in a composite outcome measure favoring the continuous-flow devices, with increases in revision and reoperation rates for the pulsatile device group being the largest factor driving the difference in outcomes. Other nonrandomized comparative studies, including a database study with large numbers of patients, have not reported important differences in clinical outcomes between devices.

Percutaneous Ventricular Assist Devices (circulatory assist devices)
The Impella® Recover LP 2.5 Percutaneous Cardiac Support System (Abiomed, Aachen, Germany) received FDA 510(k) approval in May 2008 for short-term (less than six hours) use in patients requiring circulatory support.

In March 2015, the Impella® 2.5 System received approval through the PMA process for temporary ventricular support during high-risk percutaneous coronary interventions.

The TandemHeart® (Cardiac Assist, Pittsburgh) received a similar 510(k) approval for short-term circulatory support in September 2005.

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

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP contracts: Special benefit consideration may apply. Refer to member's benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

CPT codes:

33927	Implantation of a total replacement heart system (artificial heart) with recipient cardiectomy **(Effective 01/01/18)**
33928	Removal and replacement of total replacement heart system (artificial heart) **(Effective 01/01/18)**
33929	Removal of a total replacement heart system (artificial heart) for heart transplantation (List separately in addition to code for primary procedure) **(Effective 01/01/18)**
33975	Implantation of ventricular assist device; extracorporeal, single ventricle
33976	Implantation of ventricular assist device; extracorporeal, biventricular
33977	Removal of ventricular assist device; extracorporeal single ventricle
33978	Removal of ventricular assist device; extracorporeal, biventricular
33979	Insertion of ventricular assist device, implantable intracorporeal, single ventricle
33980	Removal of ventricular assist device, implantable intracorporeal, single ventricle
33981	Replacement of extracorporeal ventricular assist device, single or biventricular, pump(s), single or each pump

33982	Replacement of ventricular assist device pump(s); implantable intracorporeal, single ventricle, without cardiopulmonary bypass
33983	Replacement of ventricular assist device pump(s); implantable intracorporeal, single ventricle, with cardiopulmonary bypass
33990	Insertion of ventricular assist device, percutaneous including radiological supervision and interpretation; arterial access only
33991	Insertion of ventricular assist device, percutaneous including radiological supervision and interpretation; both arterial and venous access, with transseptal puncture
33992	Removal of percutaneous ventricular assist device at separate and distinct session from insertion
33993	Repositioning of percutaneous ventricular assist device with imaging guidance at separate and distinct session from insertion
93750	Interrogation of ventricular assist device (VAD), in person, with physician or other qualified health care professional analysis of device parameters (e.g., drivelines, alarms, power surges), review of device function (e.g., flow and volume status, septum status, recovery), with programming, if performed, and report

ICD-9 codes:

398.91	Rheumatic heart failure (congestive)
402.01	Malignant hypertensive heart disease with congestive heart failure
402.11	Benign hypertensive heart disease with congestive heart failure
404.01	Hypertensive heart and chronic kidney disease, malignant, with congestive heart failure and with chronic kidney disease stage I through IV, or unspecified
404.03	Hypertensive heart and chronic kidney disease, malignant, with congestive heart failure and with chronic kidney disease stage V or end stage renal disease
404.11	Hypertensive heart and chronic kidney disease, benign, with congestive heart failure and with chronic kidney disease stage I through stage IV, or unspecified
428.0	Congestive heart failure

ICD-10-CM

I09.81	Rheumatic heart failure
I11.0	Hypertensive heart disease with heart failure
I13.0	Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease
I13.2	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease
I50.1-I50.9	Heart failure code range
I97.0	Postcardiotomy syndrome

Previous Codes

0051T	Implantation of a total replacement heart system (artificial heart) with recipient cardiectomy **(Deleted 12/31/17)**
0052T	Replacement or repair of thoracic unit of a total replacement heart system (artificial heart) **(Deleted 12/31/17)**
0053T	Replacement or repair of implantable component or components of total replacement heart system (artificial heart) excluding thoracic unit **(Deleted 12/31/17)**

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Policy History:

TEC, March 1999
Medical Policy Administration Committee, February 2002
Medical Review Committee, March 2004
Medical Policy Group, May 2004 **(1)**
Medical Review Committee, May 2004
Medical Policy Administration Committee, June 2004
Available for comment June 28-August 11, 2004
Medical Policy Group, March 2006 **(1)**
Medical Policy Group, April 2008 **(2)**
Medical Policy Group, August 2009 **(1)**
Medical Policy Administration Committee, September 2009
Available for comment September 4-October 19, 2009
Medical Policy Group, October 2010 **(1):** Description, Key Points and Governing Body Approval updated
Medical Policy Group, November 2010 Reference Update
Medical Policy Administration Committee November 2010
Available for comment November 4 – December 20, 2010
Medical Policy Group, September 2011 **(1):** Update to Description, Key Points and References; Entire policy reformatted, no changes to policy statements
Medical Policy Group, December 2011 **(3)**: Update to Approved by Governing Bodies & References (FDA Approval of EXCORE)

Medical Policy Group, March 2012 (**3**): Updated coverage for total artificial heart for bridge to transplant. Added other specialty recommendations and references.
Medical Policy Administration Committee March 2012
Available for comment March 15 – April 30, 2012
Medical Policy Group, November 2012 **(3)**: 2012 Update to Key Points, Governing Bodies, and References
Medical Policy Group, November 2012: 2013 Coding Update-Added Codes 33990 - 33993; deleted Codes 0048T & 0050T effective 1/1/2013
Medical Policy Group, December 2012 **(3)**: Update to Approved by Governing Bodies & References (FDA Approval of HeartWare)
Medical Policy Group, December 2012 **(3)**: 2013 Coding update – Verbiage change to Code 93750-added "or other qualified health care professional"
Medical Policy Panel, February 2013
Medical Policy Group, February 2013 **(3)**: Updated policy statement on children – amended age range from 5-16 years to 0-16 reflecting approval of the BERLIN heart EXCOR device for pediatric patients age 0-16; and clarified info on Medicare-approved heart transplant facility requirement for total artificial hearts; and Medicare-approved heart transplant facility OR Medicare-approved VAD destination facility requirement for VADs
Medical Policy Administration Committee March 2013
Available for comment March 12 through April 25, 2013
Medical Policy Group, August 2013 **(4):** Added verbiage to BTT policy section "Or a patient who is undergoing evaluation to determine candidacy for heart transplantation.
Medical Policy Administration Committee August 2013.
Available for comment August 22 through October 5, 2013
Medical Policy Group, February 2014 **(5):** Added ICD-9 and ICD-10-CM diagnosis under Coding; no change to policy statement.
Medical Policy Panel, February 2014
Medical Policy Group, February 2014 (**4**): Updated description. NO changes to the policy statement.
Medical Policy Group, March 2015 **(4):** Added Impella RP to Key Words and Approved Governing Bodies.
Medical Policy Panel, May 2015
Medical Policy Group, May 2015 **(4):** Updates to Key Points, Approved Governing Bodies, and References. Added policy statements to include total artificial hearts and pVADs are considered investigational for all other indications. Also, rearranged policy statements for ease of reading. Policy statement intents unchanged.
Medical Policy Panel, August 2016
Medical Policy Group, August 2016 **(4):** Updates to Description, Key Points, Key Words, Approved Governing Bodies and References. No change to current policy statement. Removed policy statement section for "effective dates prior to February 2012".
Medical Policy Panel, August 2017
Medical Policy Group, September 2017 **(4)**: Updates to Description, Key Points, Approved by Governing Bodies, and References. No change to policy statement.
Medical Policy Group, December 2017: Annual Coding Update 2018. Added new codes 33927 – 33929 effective 01/01/18 to Current Coding. Moved deleted codes 0051T – 0053T to Previous Coding.

Medical Policy Group, April 2018 **(4):** corrected typo.
Medical Policy Panel, August 2018
Medical Policy Group, August 2018 (**3**): Updates to Title, Description, Key Points, References, Approved By Governing Bodies, and Key Words; added: AbioCor® Total Artificial Heart, CardioWest™ Total Artificial Heart, HeartMate II®, SynCardia® Artificial Heart, Right Ventricular Assist Device, RVAD, PediMag®, Short-Term Continuous Flow Ventricular Assist Devices, STCF-VADs, intraluminal axial support, Impella® LV, and BIVAD. No changes to policy statement or intent.
Medical Policy Group, October 2018 (**3**): Updated to reflect the FDA approval of the HeartMate III™ device and the HeartWare® Ventricular Assist System for providing long-term hemodynamic support (e.g., destination therapy) in patients with advanced heart failure.
