Cigna Medical Coverage Policy

Subject **Ventricular Assist Devices (VADs) and Percutaneous Cardiac Support Systems**

Effective Date **12/15/2013**
Next Review Date **12/15/2014**
Coverage Policy Number **0054**

Table of Contents

Hyperlink to Related Coverage Policies

External Counterpulsation
Heart Transplantation
Total Artificial Heart

INSTRUCTIONS FOR USE
*The following Coverage Policy applies to health benefit plans administered by Cigna companies. Coverage Policies are intended to provide guidance in interpreting certain **standard** Cigna benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supersedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2013 Cigna*

Coverage Policy

Cigna covers a U.S. Food and Drug Administration (FDA)-approved ventricular assist device (VAD) as medically necessary when used in accordance with device-specific, FDA-approved indications and contraindications when ANY of the following criteria is met:

- Individual in acute cardiogenic shock when recovery is expected
- Individual unable to be weaned from cardiopulmonary bypass following cardiac surgery when recovery is expected
- Individual in whom heart transplantation is anticipated and who is otherwise not expected to survive until transplantation
- Individual not expected to be considered a candidate for heart transplantation, when ALL of the following criteria are met
  - New York Heart Association (NYHA) Class IV end-stage left ventricular heart failure
  - left ventricular ejection fraction (LVEF) < 25%
  - demonstrated functional limitations, with a peak oxygen consumption of ≤14 milliliters per kilogram of body weight per minute
  - failure to respond to optimal medical therapy for 45 of the last 60 days, or dependence on intra-aortic balloon pump for a period of seven days, or inotropes for a period of at least fourteen days

Cigna covers the CentriMag® Right Ventricular Assist System (RVAS) as medically necessary for temporary circulatory support when used in accordance with the FDA's Humanitarian Device Exemption (HDE) requirements when BOTH of the following criteria are met:

- device is used for up to fourteen days for individuals in cardiogenic shock due to acute right ventricular failure
- individual is willing and able to be treated with heparin or an appropriate alternative anticoagulation

Cigna covers the HeartAssist 5® Pediatric VAD as medically necessary as a bridge to cardiac transplantation in a child when ALL of the following criteria are met, in accordance with the FDA's Humanitarian Device Exemption (HDE) requirements:

- age 5–16
- body surface area (BSA) ≥ 0.7 m^2 and < 1.5 m^2
- in NYHA Class IV end-stage (i.e., left ventricular) heart failure refractory to medical therapy
- listed candidate for cardiac transplantation
- none of the following contraindications:
  - primary coagulopathy or platelet disorders
  - anatomical anomalies that would prevent surgical connection of the outflow graft to the ascending aorta
  - right ventricular failure unresolved by medical therapy

Cigna covers the EXCOR® Pediatric Ventricular Assist Device as medically necessary as a bridge to cardiac transplantation in a child with severe isolated left ventricular or biventricular dysfunction who is a candidate for cardiac transplant and requires circulatory support, in accordance with the FDA's Humanitarian Device Exemption (HDE) requirements.

Cigna covers the TandemHeart® PTVA® System, the Impella Recover® LP 2.5 Percutaneous Cardiac Support System, Impella 5.0 Catheters, or Impella 2.5 Plus as medically necessary for the treatment of cardiogenic shock for up to six hours.

Cigna does not cover the TandemHeart® PTVA® System, the Impella Recover® LP 2.5 Percutaneous Cardiac Support System, Impella 5.0 Catheters, or Impella 2.5 Plus for any other indication because it is considered experimental, investigational or unproven.

General Background

Ventricular assist devices (VADs) function to reduce myocardial work by reducing ventricular preload while maintaining systemic circulation. VADs may be extracorporeal, paracorporeal, implantable with percutaneous power support, or fully implantable, and may provide continuous or pulsatile flow. VADs may be employed on a short-term or long-term basis, or as permanent (destination) therapy. VADs may provide left ventricular support (LVAD), right ventricular support (RVAD), or biventricular support (BiVAD).

Short-term VAD use may provide a bridge to recovery for patients in postcardiotomy shock or those with a potentially reversible condition (e.g., acute myocarditis). VADs are also used as a bridge to transplant for patients with heart failure. Heart failure is a complex syndrome that occurs secondary to inherited or acquired abnormalities of cardiac structure and/or function that impair the ability of the left ventricle to eject blood. More than five million people in the United States live with heart failure, and the incidence of heart failure continues to increase, due in part to the expanded aging population and advances in therapeutic management of cardiovascular disease. Transplantation has become the standard treatment for eligible patients with irreversible severe biventricular failure unresponsive to medical or surgical treatment. The supply of donor hearts has decreased in recent years, however, while the demand has increased. As patients become more hemodynamically compromised, there is an increased risk of death prior to transplantation, as well as a less favorable outcome following transplantation. Timely VAD use may restore hemodynamic stability and end-organ function, and allow nutritional support and rehabilitation prior to transplantation (Bonow: Braunnwald's Heart Disease, 2011; Hunt et al., 2009).

Throughout the 1990s, VADs underwent many modifications to improve reliability and reduce complications, as well as to improve utility and ease of use for patients living with these devices. Their improved reliability and

mobility has resulted in the use of VADs as destination therapy for selected patients who are not candidates for cardiac transplant.

Percutaneous VADs, also referred to as percutaneous circulatory support devices, have been proposed as an alternative to a traditional VAD or intra-aortic balloon pump (IABP) for short-term partial or total hemodynamic support. Unlike traditional VADs used for short-term support, percutaneous VADs are minimally invasive and do not require surgical implantation, and unlike IABP, percutaneous VADs provide hemodynamic support independent of left ventricular function. The IABP requires a residual level of left ventricular function to be effective. Percutaneous VADs have been proposed for use during emergent procedures for patients in acute heart failure caused by left ventricular dysfunction and/or cardiogenic shock. They have also been proposed as an alternative to IABP for use in high-risk percutaneous coronary intervention (PCI) procedures. Although there is no uniform definition of high-risk PCI, and the superiority of a device-based approach during high risk PCI has not been established in randomized controlled trials, the IABP had been in use for decades and has become widely accepted as a tool for hemodynamic support during these procedures.

The TandemHeart® PTVA® System (CardiacAssist, Inc., Pittsburgh, PA) can be placed using a percutaneous technique, inserting the inflow cannula in the left atrium through the femoral vein and right atrium, and across the interatrial septum. The outflow cannula is placed in the femoral artery. Both cannulae are connected to an extracorporeal miniaturized centrifugal pump. The system provides a flow up to four liters per minute. The Impella Recover® LP 2.5 Percutaneous Cardiac Support System (Abiomed, Inc., Danvers, MA), is a catheter-based pump that can be implanted percutaneously via a cutdown of the femoral or axillary artery or directly into the ascending aorta. The tip of the catheter contains a microaxial flow pump. The catheter is placed in the left ventricle through the aortic valve, and the pump at the tip of the catheter propels blood to the outflow portion of the device in the ascending aorta. The system includes a mobile console in addition to the implantable pump. Placement is performed under transesophageal echocardiography (TEE) or fluoroscopic guidance. The original Impella flows up to 2.5 liters per minute. The Impella 5.0 contains a larger pump, permitting a flow range up to 5 liters per minute. The Impella 5.0 LP is inserted through the femoral artery via cutdown, and the Impella 5.0 LD is inserted through the aorta Bonow: Braunwald's Heart Disease, 2011; Sarkar and Kini, 2010; ECRI, 2010).

The severity of heart failure is a key factor in assessing the need for VAD use. The New York Heart Association functional classification system, below, is the most frequently used measure of heart failure and is included in the FDA approval criteria for most VADs.

- Class I. Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.
- Class II. Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
- Class III. Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.
- Class IV. Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Many cardiologists further stratify Class III patients with a sub-classification of IIIA to indicate no dyspnea at rest, and IIIB to indicate recent dyspnea at rest.

U.S. Food and Drug Administration (FDA)
The VADs described below have been granted FDA approval through the premarket approval (PMA) process. Device selection is made based on specific FDA-labeled indications:

HeartWare^{R} Ventricular Assist System (HeartWare, Inc., Miami Lakes, FL): The HeartWare VAS received FDA approval through the PMA process on November 20, 2012. The device is intended for use as a bridge to cardiac transplantation in patients who are at risk of death from refractory end-state left ventricular heart failure, and is designed for in-hospital and out-of-hospital settings. The implanted components include the pump, which includes an integrated inflow cannula, an outflow conduit, and percutaneous driveline, and an apical sewing ring. The HeartWare VAS is a continuous flow blood pump which utilizes magnetic and hydrodynamic forces to elevate and rotate the impeller.

Abiomed BVS® 5000 Biventricular Support System/Abiomed AB 5000 Circulatory Support System (AbioMed Cardiovascular, Inc.): The Abiomed BVS 5000 system received FDA approval through the PMA process on April 6, 1990. On April 28, 2003, FDA approval was provided for the addition of the AB 5000 pneumatic drive console to the BVS 5000 system. The AB 5000 console can be used to drive one or two BVS 5000 blood pumps, and can be used either in the hospital or for transport between hospitals.

The modified device, marketed as Abiomed AB 5000 circulatory support system, received FDA approval through the PMA process on September 24, 2003. According to the approval order statement, it is indicated for use in patients with reversible ventricular dysfunction who have undergone successful cardiac surgery and subsequently develop low cardiac output, or patients with acute cardiac disorders leading to hemodynamic instability. The intent of AB 5000 system therapy is to provide circulatory support, restore normal hemodynamics, reduce ventricular work, and allow the heart time to recover adequate mechanical function.

Thoratec® Paracorporeal Ventricular Assist Device (PVAD™) System and TLC-II Portable VAD Driver: (Thoratec Corporation, Pleasanton, CA): On November 26, 2003 FDA approval was granted to expand the indications for use for the Thoratec VAD System. The modified device is marketed as the Thoratec PVAD System and TLC-II Portable VAD Driver. When used with the portable VAD driver, the device is intended for use for transportation of patients via ground ambulance, fixed wing aircraft or helicopter, and can also be used to allow suitably-qualified patients to take off-site excursions within a two-hour travel radius of the hospital in the company of a trained caregiver.

Thoratec Implantable Ventricular Assist Device (IVAD™) (Thoratec Corporation, Pleasanton, CA): On August 3, 2004, FDA approval was granted for the Thoratec IVAD as an alternative VAD blood pump for use in the approved Thoratec VAD System. The IVAD is designed to be compatible with both the dual driver console and the TLC-II portable VAD driver.

Thoratec HeartMate II® Left Ventricular Assist System (LVAS) (Thoratec Corporation, Pleasanton, CA): The HeartMate II LVAS received FDA approval through the PMA process on April 21, 2008. According to the approval letter, the device is indicated for use as a bridge to transplantation in cardiac transplant candidates at risk of imminent death from non-reversible left ventricular failure. It is intended for use both inside and outside the hospital, or for transportation of VAD patients via ground ambulance, fixed-wing aircraft, or helicopter.

The HeartMate II LVAS is an implanted continuous axial flow pump with external components. Electrical power to the implanted pump is delivered through a percutaneous lead that connects to an external system controller. The system controller is powered by a power base unit that connects to AC power, or by two batteries carried or worn by the patient. The HeartMate II LVAS, unlike previously approved VADs, is small in size and can be implanted in patients with a body surface area (BSA) less than 1.5 m^2. PMA approval was based in part on the HeartMate II Bridge to Transplantation Primary Study Cohort, a multi-center non-blinded non-randomized prospective study that demonstrated bridge to transplant rates comparable to currently approved devices.

On January 20, 2010, the HeartMate II indications for use were expanded to allow use in patients who meet the following criteria:

- New York Heart Association Class IIIB or IV end stage left ventricular failure
- received optimal medical therapy for at least 45 of the last 60 days
- life expectancy of less than two years
- not a candidate for cardiac transplantation

The expanded approval for the HeartMate II as destination therapy was based primarily on the results of the study by Slaughter et al., discussed below.

Thoratec CentriMag® Blood Pump (Thoratec Corporation, Pleasanton, CA): The CentriMag Blood Pump, originally marketed by Levitronix LLC as the CentriMag Right Ventricular Assist System {RVAS}) received FDA Humanitarian Device Exemption (HDE) approval on October 7, 2008. In order to receive HDE approval, a manufacturer must be granted a Humanitarian Use Device (HUD) exemption by demonstrating that the device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 people in the U.S. per year.

Although data demonstrating the safety and probable clinical benefit are required for HDE approval, clinical trials evaluating the effectiveness of the device are not required. Following HDE approval, the hospital or health care facility institutional review board (IRB) must also approve the use of the device at that institution before the device may be used in a patient.

The CentriMag RVAS is intended to provide temporary circulatory support for up to fourteen days for patients in cardiogenic shock due to acute right ventricular failure. The device is contraindicated in patients who are unable or unwilling to be treated with heparin or an appropriate alternative anticoagulation. Although right ventricular heart failure is infrequent, it may occur following cardiac surgery, myocardial infarction (MI), heart transplantation, or implantation of an LVAD. The device is intended to keep the patient alive until the heart recovers, the patient undergoes a heart transplant, or a long term VAD is implanted. The CentriMag is a continuous flow, centrifugal-type rotary blood pump. It is unique in that it is designed to operate without mechanical bearings or seals. This is possible because the motor levitates the rotor (i.e., the spinning component of the device) magnetically.

According to the FDA Summary of Safety and Probable Benefit, data from two unpublished U.S. pilot trials were considered in the HDE approval process. The Cardiogenic Shock Pilot trial (n=22) was a non-randomized multicenter pilot study to evaluate the CentriMag system for up to 14 days when used as either an LVAS or biventricular assist system (BVAS) to treat patients in cardiogenic shock. Two groups were evaluated: patients in cardiogenic shock following cardiotomy, and patients in cardiogenic shock following MI. Eight of the 22 patients were treated with a CentriMag for left-sided support only, and 14 patients were treated with a CentriMag RVAD as part of a biventricular configuration, with a CentriMag devices also serving as an LVAD. The RVAS Post-Commercial LVAD trial (n=10) was a nonrandomized, multicenter pilot trial to evaluate the use of the CentriMag System for up to 14 days as an RVAS following implantation of a commercially available LVAD. In both studies, success was defined as survival for 30 days after weaning, transplant, or being placed on a long-term VAD. The 30–day survival rate in the 24 patients who received RVAD support was 50%. The survival rate in the RVAS cohort treated solely for right-sided support was 60%. According to the FDA summary, the probable benefits of the CentriMag RVAS include adequate ventricular unloading, adequate circulatory support, ease of implantation, reliable device function, a low incidence of device-related complications, and support conditions conducive to postoperative recovery and weaning. The summary states that the positive outcome data combined with the low incidence of device related adverse events suggest the benefits associated with the use of the CentriMag RVAS VAD outweigh the risks.

John et al. (2011) conducted a multi-institutional study evaluate safety, effectiveness, and outcomes of the CentriMag in patients with cardiogenic shock following cardiotomy (n=12), myocardial infarction (14) or with right ventricular failure after left ventricular assist device placement (n=12). Devices were implanted in left (n=8), right (n=12), or biventricular (n=18) configurations. CentriMag support was continued until patients recovered, received a transplant, or received an implantable long-term VAD. The mean support duration for the entire cohort was 13 days (range 1–60 days), with 47% of patients surviving 30 days following removal Complications included bleeding (21%), infection (5%), respiratory failure (3%), hemolysis (5%), and neurologic dysfunction (11%). There were no device failures. The authors stated that in this preliminary study, the CentriMag VAS is capable of providing biventricular support for patients with medically refractory acute cardiogenic shock with an acceptable survival.

The HeartAssist 5® Pediatric VAD

The HeartAssist 5 Pediatric VAD (MicroMed Cardiovascular, Inc., Houston, TX), formerly called The DeBakey VAD Child, received FDA Humanitarian Device Exemption (HDE) approval on June 10, 2003. The DeBakey VAD HDE approval was based on a review of data from 190 adults who were implanted with the DeBakey VAD. According to the FDA Summary of Safety and Probable Benefit, he DeBakey VAD Child is expected to provide the same benefits for children that the adult version has provided for adults, with flow rates that will meet the level of output required to support pediatric patients. The HDE approval was also based on extensive mechanical testing performed by the manufacturer. The data showed that the miniaturized device has a reasonable probability of being safe and effective in children. The FDA Summary of Safety and Probable Benefit states that the DeBakey VAD Child is indicated to provide temporary left side mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients who meet all of the following criteria:

- age 5–16
- body surface area (BSA) ≥ 0.7 m^2 and < 1.5 m^2

- in NYHA Class IV end-stage heart failure
- refractory to medical therapy
- listed candidate for cardiac transplantation

The following contraindications are listed in the FDA Instructions for Use:

- patients under age five or with BSA < 0.7 m^2
- patients suffering from right ventricular failure unresolved by medical therapy
- patients with a primary coagulopathy or platelet disorders
- prior surgery where apical cannulation, pump replacement or graft anastomosis is not feasible

EXCOR® Pediatric Ventricular Assist Device (EXCOR) (Berlin Heart, Inc., Woodlands, TX): The EXCOR received FDA Humanitarian Device Exemption (HDE) approval on December 16, 2011. The device is intended to provide mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients. Pediatric candidates with severe isolated left ventricular or biventricular dysfunction who are candidates for cardiac transplantation and require circulatory support may be treated using the EXCOR.

According to the FDA Summary of Safety and Probable Benefit, the results of the Berlin Heart EXCOR Investigational Device Exemption (IIDE) study (Fraser et al., discussed below) demonstrated that a majority of primary study patients survived to successful weaning or cardiac transplantation with acceptable neurological status. The study also demonstrated, however, that use of the EXCOR device is accompanied by significant risks. A high rate of neurological events was seen in the EXCOR primary study patients; 30% experienced an ischemic neurological event. There also appeared to be a high incidence of pump thrombus. There was a higher failure rate in patients who did not meet the strict eligibility criteria and in patients implanted at non-study-centers.

According to the summary, data from the IDE trial demonstrate that the device is safe as defined by the safety endpoint, and in light of the other clinically available alternatives, the device provides probable benefit to this very limited patient population. The Circulatory System Devices Panel noted that survival rates were in favor of the EXCOR device compared to the control group treated with extracorporeal membrane oxygenation support (ECMO), and patients were able to remain on the device for longer periods of time compared to the patients on ECMO. The panel states that the device meets a critical need for patients with end stage heart failure who are awaiting a transplant. The panel agreed that the device provided a reasonable assurance of safety and that the probable benefit of the device outweighed the known risks. A post-approval study will include follow-up of current IDE study patients and enrollment of a new cohort with important baseline data and follow-up beyond explantation.

Percutaneous Ventricular Assist Devices
TandemHeart® PTVA® System (CardiacAssist, Inc., Pittsburgh, PA): The TandemHeart PTVA System consists of three components. The TandemHeart Transseptal Cannula Set-EF received FDA approval through the 510(k) process on January 17, 2006. The TandemHeart® Escort™ Controller received FDA approval through the 510(k) process on August 22, 2006. The Controller is a reusable, microprocessor-based pump motor drive and infusion system. The controller and cannula set are used with the TandemHeart PTVA Blood Pump. The controller generates the signals required to power the drive motor of the blood pump, which turns the impeller to propel blood through the pump.

According to the FDA 510(k) summary, the TandemHeart PTVA System is intended for extracorporeal circulatory support using an extracorporeal bypass circuit. The intended duration of use is for periods appropriate to cardiopulmonary bypass, up to six hours. It is also intended to be used as an extracorporeal circulatory support system (for periods up to six hours) for procedures not requiring complete cardiopulmonary bypass (e.g., valvuloplasty, mitral valve reoperation, surgery of the vena cava and/or aorta, liver transplant).

Impella Recover® LP 2.5 Percutaneous Cardiac Support System (Abiomed, Inc., Danvers, MA): The Impella Recover LP 2.5 Percutaneous Cardiac Support System received FDA 510(k) approval on May 30, 2008. The system provides circulatory support with the ability to deliver anticoagulant through an infusion system. It consists of a catheter which contains an integrated pump motor/infusate lumen; integrated intravascular pressure lumen and integral cannula; a controller/console; infusion system; and accessories. These

components are designed to work together. The Impella Recover is intended for partial circulatory support using an extracorporeal bypass control unit for periods up to six hours. It is also intended to be used to provide partial circulatory support (for periods up to six hours) during procedures not requiring cardiopulmonary bypass.

The Impella 5.0 Catheters received FDA approval through the 510(k) process on April 16, 2009. The Impella 5.0 catheter family is an extension of the Impella Percutaneous Cardiac Support line. There are two versions of Impella 5.0; the Impella 5.0 LP is inserted through the femoral artery via cutdown, and the Impella 5.0 LD is inserted through the aorta. The only difference between the two catheters is the shape of the inflow cannula. The characteristics of the Impella 5.0 are similar to the Impella 2.5, but the larger pump in the Impella 5.0 permits a higher flow range, up to 5 liters per minute.

A revised version of the Impella, the Impella 2.5 Plus, received 510(k) approval on September 5, 2012. The updated device includes a slight increase in the diameter of the inflow cannula, impeller and pump housing, allowing 30% higher flow. It is otherwise identical to the predicate device, the Impella 2.5. The Impella 2.5 Plus will be marketed as the Impella CP™ (Cardiac Power) in the U.S. Indications for use remain unchanged

Literature Review: VADs

Bridge to Recovery: VADs have been used since the 1970s as a bridge to recovery for patients with potentially reversible left ventricular dysfunction. Patients who undergo cardiac surgical procedures are at risk for myocardial injury because of myocardial stunning and ischemia, insufficient myocardial protection, reperfusion injury, and cardiac arrhythmias. Patients who have had persistent or significant dysfunction prior to the surgery are less likely to be weaned from device support, while those who had sufficient myocardial reserve prior to surgery may only require a few days of temporary support. In general, patients in profound shock with end-organ dysfunction and biventricular heart failure need early, effective support to avoid permanent end-organ damage and increase their chances of survival. Devices that provide full ventricular support can reestablish nearly normal hemodynamics, and have the potential to allow myocardial recovery. If prolonged support is anticipated, a longer term biventricular device may be implanted, or a longer term LVAD may be used in conjunction with a short-term RVAD device.

VADs have also been shown to be effective as a bridge to recovery in patients with acute myocarditis, particularly in young patients. It is difficult to determine which patients will recover after short-term support and which patients will need long-term device therapy. For this reason a long-term device may be inserted, and the device can be explanted if hemodynamic recovery is sufficient, or left in place as a bridge to transplantation.

Bridge to Transplantation: A number of published studies have evaluated LVADs as a bridge to transplantation. Frazier et al. (2001) conducted a prospective, multicenter, nonrandomized, controlled study (n=280) to evaluate LVAD as a bridge to transplantation. A total of 280 transplant candidates at 24 centers were treated with the HeartMate LVAD and compared to a historical control group of 48 patients not supported with LVADs. Outcome measures were defined as laboratory data (hemodynamic, hematologic and biochemical), New York Heart Association (NYHA) functional class, and survival. The mean duration of support was 112 days, with 54 patients supported for more than 180 days. A total of 188 patients (67%) were bridged to transplantation, and 10 patients (4%) elected to have the device removed. Of the LVAD patients, 82 patients (29%) died before transplantation, compared to 32 patients (67%) of the 48 control patients. Complications included bleeding, infection, neurological dysfunction and thromboembolic events. One-year post-transplant survival was significantly higher in patients in the LVAD group than in those in the control group: 158 patients (84%) vs. 10 patients (63%), respectively.

Pagani et al., for the HeartMate II Investigators (2009) conducted a prospective multi-site case series evaluating the use of the HeartMate II LVAD as a bridge to transplantation (n=281). Patients were required to have symptoms of NYHA functional class IV heart failure and be ill enough to have high priority for transplant. At 18 months, 222 patients (79%) received a transplant, 58 (20.6%) remained alive with ongoing LVAD support, 56 (19.9%) died, 7 (2.5%) recovered cardiac function, and 3 (1%) were withdrawn from the study and received another type of LVAD. There were significant improvements in functional status and six-minute walk test at three six months (from 0 to 83% of patients in NYHA Class I or II, and from 13% to 89% of patients completing the six-minute walk test). Significant improvements were also seen in quality of life as measured by the Minnesota Living with Heart Failure and Kansas City Cardiomyopathy questionnaires. Major adverse events included bleeding, stroke, right heart failure, percutaneous lead infection, and pump thrombosis.

Aaronson et al. (2012) conducted multicenter prospective study of an investigational device, the HeartWare VAD, as a bridge to transplantation in adults with heart failure who were eligible for transplantation and believed to be unable to survive without mechanical circulatory support. Outcomes in the study group (n=140) were compared to those of patients implanted contemporaneously with commercially available devices (n=499). The primary outcome, success, was defined as survival on the originally implanted device, transplant, or explant for ventricular recovery at 180 days, and was evaluated for both noninferiority and superiority. Secondary outcomes included an evaluation of survival between groups, and functional and quality of life outcomes and adverse events in the study group. Success occurred in 90.7% patients in the HeartWare group and 90.1% of those in the control group, establishing the non-inferiority of the device. At six months, median six-minute walk distance improved by 128.5 m, and both disease-specific and global quality-of-life scores improved significantly. Bleeding, infections, and perioperative right heart failure were the most frequent complications.

Slaughter et al. (2013) published additional results of the HeartWare bridge to transplant trial that included outcomes of the continued access protocol, which included 256 additional patients with the same enrollment criteria. A total of 332 patients in the pivotal bridge to transplant and continued access protocol trial completed the 180 day primary end-point assessment. Survival in patients treated with the HeartWare pump was 91% at 180 days and 84% at 360 days. Quality of life scores improved significantly and adverse event rates remained low.

Bridge to Transplantation in Children: Extracorporeal membrane oxygenation support (ECMO) has been routinely used in pediatric patients awaiting heart transplantation, but this treatment is limited to the inpatient setting. Waiting times for allografts frequently exceed the period of time a patient can be supported on ECMO. The use of long-term mechanical circulatory support has therefore increased over the past ten years as a bridge to transplantation for pediatric patients (Blume et al., 2006).

Blume et al. (2006) conducted a retrospective study to describe the clinical course and adverse events in 99 pediatric patients who underwent VAD implant as a bridge to heart transplantation, to define risk factors for death while waiting on support, and to compare post-transplantation survival between patients who did and did not receive a VAD. Data were analyzed from the Pediatric Heart Transplant Study database for the period of January 1993–December 2003. The database is a prospectively maintained database of patients younger than age 18 who are listed for heart transplantation at 23 North American centers. Four percent (n=99) of 2375 enrolled patients underwent VAD implantation prior to transplantation. Various VADs and combinations of VADs were used. None of these were pediatric-specific devices. The median age at VAD implantation was 13.3 years (range two days–17.9 years). The diagnosis was cardiomyopathy in 78% of patients, and congenital heart disease in 22% of patients. The mean duration of support was 57 days (range, 1–465 days). Seventy seven patients (77%) survived to transplantation, five patients were successfully weaned from support, and 17 patients (17%) died on support. The probability of successful bridge to transplantation was 85%, 80%, and 76% at one, three and six months, respectively. Risk factors for death while awaiting transplantation included earlier era of implantation (p=0.05), female gender (p=0.02), and congenital disease diagnosis (p=0.05). Evaluation of data from the more recent period of 2000–2003 demonstrated a success rate of 86% for the use of VAD as a bridge to transplantation. There were 17 deaths after VAD implantation due to stroke (11), infection/sepsis (3), multi-system organ failure (2), and dysrhythmia (1).There was no difference in five-year survival after transplantation for the 99 patients on VAD at the time of transplant compared to the 2293 who did not require VAD (77% vs. 73%, p=0.8).

A retrospective review by Morales et al. (2011) analyzed the initial Berlin Heart EXCOR pediatric experience as a bridge to transplantation prior to the approval of the FDA Investigational Device Exemption (IDE study). The device was implanted in 97 patients in North America under compassionate use regulations. The analysis was limited to 73 patients from 17 institutions for which retrospective data were available. Median age and weight at VAD implant were 2.1 years (range, 12 days–17.8 years) and 11 kg (range 3–87.6 kg). The primary diagnoses were dilated cardiomyopathy, congenital heart disease, myocarditis, and other cardiomyopathies. The EXCOR bridged 51 patients (70%) to transplant, and 5 (7%) to recovery. Of seventeen patients (23%) who died while on EXCOR. 35% were on BiVAD and 14% on LVAD. BiVAD support and younger age were significant risk factors for death while on EXCOR. The authors stated that this limited but large preliminary North American experience with the EXCOR VAD as a bridge to cardiac transplantation for children of all ages and sizes points to the feasibility of this approach.

Fraser et al. (2012) conducted a prospective, multicenter cohort study to compare children who underwent implantation of the EXCOR pediatric VAD as a bridge to transplantation (n=48) with a propensity-matched historical control group of children who received circulatory support with extracorporeal membrane oxygenation (ECMO) (n=48). Children were eligible for the study if they were age 16 or younger, weighed between 3 and 60 kg, had two-ventricle circulation, severe heart failure despite optimized medical treatment, and were on a waiting list for cardiac transplantation. The size of the device was based on age and body weight. VAD recipients were divided into two cohorts according to body surface area (cohort 1, $<0.7m^2$; median age one year, median weight 9 kg; cohort 2, 0.7–<1.5 m^2, median age 9 years, median weight 31 kg). Primary efficacy for the VAD group was defined as the time to death or weaning from the device with an unacceptable neurologic outcome. For the ECMO group, the primary endpoint was limited to time to death, since neurologic status data were not available in the database. The rate of survival to device explantation (either due to transplantation or recovery) was significantly higher with the VAD than with ECMO. The median survival time had not been reached at 174 days for patients in cohort 1, while in the matched ECMO group the median survival was 13 days ($p<0.001$). For patients in cohort 2 and the matched ECMO group, the median survival was 144 days and 10 days, respectively ($p<0.001$). Serious adverse events included major bleeding (42% in cohort 1, 50% in cohort 2), infection (63% in cohort 1, 50% in cohort 2), and stroke (29% in cohort 1 and 2).

A multicenter prospective cohort study conducted by Almond et al. (2013) analyzed outcomes for all U.S. children who received the Berlin Heart Excor pediatric VAD at 45 centers from May 2007 through December 2010. A total of 204 children were enrolled in the EXCOR database; 203 in the U.S. and 1 in Canada. Of these, 68 met investigational device exemption (IDE) trial criteria; 48 who were in the original FDA IDE trial cohort, and 10 additional patients who were implanted after trial enrollment was complete under a continued access protocol. One hundred thirty six patients were implanted under compassionate use; these patients were more likely to be smaller, younger, have congenital heart disease, be supported on ECMO, have worse end-organ function, and were more likely to receive the smallest 10 ml pump. The median duration of support was 40 days (range 1-435 days). Survival at 12 months was 75%, including 64% who achieved transplantation, 6% who recovered and 5% who were alive on the device. Lower weight, biventricular assist device support, and elevated bilirubin were identified as risk factors for early mortality, and bilirubin extremes, and renal dysfunction were identified as risk factors for late mortality. Neurological dysfunction occurred in 29% of patients and was the leading cause of death.

Although most studies are nonrandomized and many are retrospective, there is sufficient evidence that LVADs can improve functional and hemodynamic status and are associated with higher survival rates when compared to optimal medical therapy. In addition, improved post-transplant survival rates are seen in patients who received LVADs. This benefit of improved post-transplant survival is likely due to the efficient circulatory support provided by the device, as well as the fact that patients stabilized by LVAD implantation can wait for an optimal organ match. LVADs have therefore become an accepted tool to halt further deterioration, decrease the likelihood of death before transplantation, and improve long-term survival and quality of life in selected patients.

Destination Therapy: The REMATCH trial (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart failure) was a multicenter, randomized controlled trial comparing LVADs with medication (Rose, et al., 2001). Patients with chronic end-stage heart failure and contraindications to transplant (n=129) were randomly assigned in a 1:1 ratio to receive either an LVAD (n=68) or optimal medical therapy (n=61). The surgical risk associated with implantation of the device and the obviousness of the device precluded a double-blind study design. The risk of death by any cause was reduced by 48% in the LVAD group as compared to the medical therapy group. The rates of survival at one year were 52% in the LVAD group and 25% in the medical therapy group, and rates at two years were 34% and 8%, respectively. The frequency of serious adverse events in the LVAD group was 2.35 times that of the medical therapy group. Infection, bleeding, and malfunction of the device were the most frequent adverse events. Quality of life, as measured by physical-function and emotional-role subscales of the SF- (Standard Form) 36, was significantly improved at one year for the LVAD group.

Slaughter al., for the HeartMate II Investigators (2009) conducted a randomized controlled trial to evaluate the use of a continuous flow device vs. a pulsatile device in patients with advanced heart failure who were ineligible for transplantation. Enrolled patients met the following criteria: a left ventricular ejection fraction of less than 25%; a peak oxygen consumption of less than 14 ml per kilogram of body weight per minute, or less than 50% of the predicted value; and New York Heart Association (NYHA) class IIIB or IV symptoms for at least 45 of the 60 days before enrollment, or dependence on an intra-aortic balloon pump for a period of 7 days or inotropes for

a period of at least 14 days before enrollment. Patients were randomized on a 2:1 basis to undergo implantation of a continuous flow device (HeartMate II; n=134) or a pulsatile flow device (HeartMate XVE; n=66). The primary composite end point was survival free from disabling stroke and reoperation to repair or replace the device at two years. Secondary end points included survival, frequency of adverse events, quality of life, and functional capacity. The primary composite end point was achieved at two years in more patients with the continuous flow devices than with the pulsatile flow devices (62 of 134 [46%] vs. 7 of 66 [11%]; $p < 0.001$). Patients with the continuous flow devices had superior survival rates at two years (58% vs. 24%, p=0.008). Adverse events and device replacements were less frequent with continuous flow devices. Quality of life and functional capacity improved significantly in both groups.

Rogers et al. for the HeartMate II Investigators (2010) evaluated the impact of a continuous flow LVAD on functional capacity and heart failure-related quality of life. Data from advanced heart failure patients enrolled in the HeartMate II LVAD bridge to transplantation (BTT) (n=281) and destination therapy (DT) (n=374) trials. The authors assessed functional status as measured by NYHA functional class, six-minute walk distance, patient activity scores), and quality of life, as measured by the Minnesota Living With Heart Failure (MLWHF) and Kansas City Cardiomyopathy Questionnaires (KCCQ), prior to and after LVAD implantation. Patients demonstrated early and sustained improvements in functional status and quality of life compared to baseline. Most patients had NYHA functional class IV symptoms at baseline. Following implantation, 82% of bridge-to-transplant (BTT) patients and 80% of destination therapy (DT) patients improved to NYHA functional class I or II at six months. At 24 months, 79% of DT patients improved to NHYA functional class I or II at 24 months. The mean six-minute walk test in DT patients was 204 m in patients able to ambulate at baseline, improving to 350 and 360 m at 6 and 24 months, respectively. There were also significant and sustained improvements in BTT and DT patients in median MLWHF scores and KCCQ overall summary scores at 6 and 24 months.

There is adequate evidence in the published medical literature that LVAD therapy is effective as destination therapy for selected end-stage heart failure patients who are not eligible for heart transplantation. The Centers for Medicare & Medicaid (CMS) issued revised coverage for destination therapy on November 9, 2010. The revised coverage was based on data from the HeartMate II pivotal trial by Slaughter et al. and the Rogers et al. trial (discussed above), and other published evidence, reviews, and guidelines. VADs as destination therapy are covered for patients who have chronic end-stage heart failure (New York Heart Association Class IV end-stage left ventricular failure) who are not candidates for heart transplantation, and meet all of the following conditions:

- Have failed to respond to optimal medical management (including beta-blockers and ACE inhibitors if tolerated) for at least 45 of the last 60 days, or have been balloon pump-dependent for 7 days, or IV inotrope-dependent for 14 days; and,
- Have a left ventricular ejection fraction (LVEF) < 25%, and,
- Have demonstrated functional limitation with a peak oxygen consumption of $\leq$ 14 ml/kg/min unless balloon pump- or inotrope-dependent or physically unable to perform the test.

The coverage is aligned with the entry criteria for the Slaughter trial, but limits coverage to NYHA Class IV patients. The American College of Cardiology (ACC) and The Society of Thoracic Surgeons (STS) supported the CMS proposal not to extend coverage for VADs as destination therapy for NYHA class IIIB heart failure patients, stating, “Trial data does not provide any basis of evidence for mechanical circulatory support for Class III patients. The vague characterization of Class III has yet to be crystallized into clinical phenotypes as has begun for Class IV. There is no validated division into Class IIIA, IIIB, and most heart failure physicians would have difficulty finding a reference for this specific classification or to define the specifics of this population.”

VAD components vary, depending on the device and where it is to be used (inpatient vs. outpatient). In addition to the implanted device, components may include a system controller, system monitor, display module, power base, emergency power pack, power pack charger, rechargeable batteries, cannulae, and cables. The treating physician should contact CIGNA to discuss the need for associated equipment and supplies if discharge with an LVAD is being considered.

Literature Review: Percutaneous Ventricular Assist Devices (VADs)
Thiele, et al. (2005) conducted a randomized controlled trial to evaluate hemodynamic effects of the intra-aortic balloon pump (IABP) compared to the TandemHeart, and to assess mortality in patients with cardiogenic shock complicating acute myocardial infarction (MI). Patients were randomized to treatment with the IABP (n=20) or TandemHeart (n=21). Inclusion criteria were the presence of acute MI and cardiogenic shock with an intention to

revascularize the infarcted artery by percutaneous coronary intervention (PCI). Hemodynamic indices at baseline were similar for both groups, except for a higher pulmonary capillary wedge pressure in the IABP group. The primary endpoint, cardiac power index, was improved more effectively with the TandemHeart, ($p<0.001$) compared to the IABP ($p=0.02$) ($p=0.004$ for intergroup comparison). Weaning from the devices was completed using a stepwise approach over a period of four to eight hours. Complications occurred more frequently in the TandemHeart group compared to the IABP group, however. Severe bleeding occurred in 19 TandemHeart patients compared to 8 IABP patients ($p=0.002$), and limb ischemia occurred in 7 TandemHeart patients compared to 0 IABP patients. Thirty-day mortality was similar in both groups (IABP 45% vs. TandemHeart 43%, $p=0.86$). Although this trial did not have the power to detect differences in mortality, there was no trend in mortality benefit for the TandemHeart patients despite the improved hemodynamics.

Burkhoff et al. (2006) conducted a randomized controlled trial to determine whether the TandemHeart provided superior hemodynamic support compared to IABP in patients with cardiogenic shock (n=42).Patients from 12 centers presenting within 24 hours of developing cardiogenic shock were treated in an initial roll-in phase (n=9, or randomized to treatment with IABP (n=14) or TandemHeart (n=19).Of the 42 patients, 26 were diagnosed with acute MI. Most of the patients had an IABP in place before randomization. The mean duration of support was 2.5 days. Patients treated with the TandemHeart had significantly greater increases in cardiac index and greater decreases in pulmonary capillary wedge pressure compared to those treated with IABP. There was no significant difference in 30-day overall survival or incidence of adverse events between the two groups; serious adverse events occurred with a frequency of 1.3 per patient in the TandemHeart group and 1.2 per patient in the IABP group. The authors noted that larger scale studies are needed to assess the influence of improved hemodynamics on survival.

A randomized controlled trial by Seyfarth et al. (2008) was conducted to determine whether the Impella 2.5 percutaneous VAD provided superior hemodynamic support compared to the IABP (n=26). After an initial hemodynamic assessment, patients with acute MI and cardiogenic shock were randomized to Impella 2.5 (n=12) or IABP (n=13). One patient died prior to implantation. Patients were immediately transferred to the catheterization lab, and the assigned device was implanted after revascularization therapy. The primary endpoint was the change in cardiac index from baseline to thirty minutes after implantation. The cardiac index of patients in the Impella group was significantly increased after thirty minutes of support compared to the IABP group ($p=0.02$). The median duration of support was 25 hours in the Impella group and 23 hours in the IABP group. There was one case of acute limb ischemia in the Impella group. Transient hemolysis was significantly higher in the Impella group, with more packed red blood cells and fresh frozen plasma administered ($p=0.18$ and $p=0.39$, respectively) Overall thirty-day mortality was 46% in both groups.

The Europella Registry (Sjauw et al., 2009) evaluated the safety and feasibility of left ventricular support with the Impella 2.5 during high-risk PCI (n=144). Patients were older (62% > 70), and 54% had a left ventricular ejection fraction (LVEF) ≤ 30%. PCI was considered high risk due to left main disease, last remaining vessel disease, multivessel coronary artery disease, and low LV function in 53%, 17%, 81%, and 35% of cases, respectively. Rates of MI, stroke, bleeding requiring transfusion/surgery, and vascular complications at thirty days were 0%, 0.7%, 6.2%, and 4.0%, respectively. Thirty-day mortality was 5.5%.

A multicenter prospective case series conducted by Dixon et al. (2009) evaluated the safety and feasibility of the Impella 2.5 system in patients undergoing high-risk PCI (n=20) All patients had LVEF ≤ 35% and underwent PCI on an unprotected left main coronary artery or last patent coronary conduit. The primary safety end point was the incidence of major adverse cardiac events (MACE) at thirty days. The primary efficacy end point was freedom from hemodynamic compromise during PCI (defined as a decrease in mean arterial pressure below 60 mm Hg for more than ten minutes). The mean duration of support was 1.7 ± 0.6 hours (range 0.4–2.5 hours). The incidence of MACE at thirty days was 20%; two patients had a peri-procedural MI, and two died at days 12 and 14. The authors stated that, based on the results of this trial, a pivotal randomized trial is planned to compare the efficacy of prophylactic circulatory support during high-risk PCI with the Impella 2.5 vs. conventional IABP counterpulsation.

Cheng et al. (2009) conducted a meta-analysis of controlled trials to evaluate potential benefits of percutaneous LVADs on hemodynamics and thirty-day survival. Three trials met the inclusion criteria. Two of these evaluated the TandemHeart (Thiele et al. 2005; Burkhoff et al. 2006) and the third trial evaluated the Impella (Seyfarth et al. 2008). These trials are described above. Weighted mean differences were calculated for cardiac index (CI), mean arterial pressure (MAP), and pulmonary capillary wedge pressure (PCWP). Relative risks were calculated

for thirty-day mortality, leg ischemia, bleeding, and sepsis. After implantation, percutaneous LVAD patients had higher CI, higher MAP, and lower PCWP, compared with IABP patients. Similar thirty-day mortality was observed in both groups. No significant difference was seen in incidence of leg ischemia. Bleeding was significantly higher in TandemHeart patients compared to IABP patients. The authors stated that although percutaneous VADs provide superior hemodynamic support in patients with cardiogenic shock compared with IABP, the use of these devices did not improve early survival, and these results do not yet support percutaneous LVAD as a first-choice approach in the mechanical management of cardiogenic shock.

A retrospective case series (Alasnag et al., 2011) evaluated the safety and feasibility of prophylactic use of the Impella 2.5 during high-risk PCI (n=60). All patients were either considered inoperable by the cardiac surgeons or declined bypass surgery, and presented with multiple risk factors, including hypertension, diabetes, chronic pulmonary disease, prior MI, and prior bypass surgery, and 45% presented with acute coronary syndrome. The mean ejection fraction was 23% ± 15%. The majority of patients had multivessel disease, and 60% had left main disease. An angiographic success rate of 96% was achieved. The device was used for an average of 38 ± 15 minutes and provided a mean blood flow of 2.1 ± 0.2 liters/minute. Hemostasis was achieved in 56 of 60 patients; endovascular tamponade, manual compression, and vascular surgery were used for two, one, and one patient, respectively. The 30-day mortality rate was 5%, and rates of MI, stroke, target lesion revascularization and urgent bypass surgery were 0%. The authors concluded that use of the Impella 2..5 during high-risk PCI outside the controlled environment of a clinical trial is safe and feasible, but acknowledged study limitations, including the retrospective nature of the trial, and the fact that the determination that patients were sufficiently high risk to benefit from the use of the Impella was made by the cardiologist performing the procedure, and was not subject to rigid criteria. The authors stated that randomized controlled trial data is needed to quantify the benefit of Impella 2.5 support during high-risk PCI compared to that of the IABP.

Kar et al. (2011) evaluated the efficacy and safety of the TandemHeart percutaneous assist device (pVAD) in patients with refractory cardiogenic shock despite IABP and/or high-dose vasopressor support (n=117). Of the 117 patients, 56 (47.9%) underwent active cardiopulmonary resuscitation immediately prior to or at the time of implantation. The average duration of support was 5.8 ± 4.75 days. There was statistically significant improvement in the average cardiac index, systolic blood pressure and mixed oxygen saturation during the period of implantation. Urine output increased, and pulmonary capillary wedge pressure and lactic acid also improved significantly. The mortality rate was 40.2% at 30 days and 45.3% at six months. The authors concluded that the TandemHeart is an effective treatment option for rapidly reversing terminal circulatory collapse, and further prospective randomized controlled trials are warranted to evaluate the efficacy of early pVAD placement in severe refractory cardiogenic shock patients.

Shah et al. (2012) conducted a prospective observational study to evaluate the temporary use of a percutaneous left ventricular assist device (PLVAD) in 75 consecutive patients undergoing high-risk PCI or in cardiogenic shock. Patients undergoing high-risk PCI (n=57) and those in cardiogenic shock (n=17) were analyzed in separate cohorts. Patients undergoing PCI with intra-aortic balloon pump (IABP) (n=35) were compared to patients undergoing PCI with PLVAD (i.e., TandemHeart or Impella device) (n=22). Patients in cardiogenic shock treated with IABP (n=13) were compared to those treated with PLVAD (n=4). The primary endpoint was in-hospital major adverse cardiovascular events (MACE) and the secondary end point was in-hospital vascular complications. The primary and secondary endpoints were similar between groups for both high-risk PCI and cardiogenic shock. Patients presenting with ST elevated MI (STEMI) had IABP-assisted PCI more frequently, suggesting the speed of required support was important, and that infarct artery revascularization combined with IABP use adequately improved hemodynamics. The percentage of patients undergoing unprotected left main PCI and the number of lesions treated were higher in the PLVAD group. This suggests that the operator chose PLVAD support more frequently for elective, complex PCI when extensive revascularization was required. Although several risk scores were higher in the PLVAD group, other risk scores were similar between groups. The authors stated that these findings suggest overall similar baseline risk between the groups. It is possible, however, that more extensive revascularization was achieved despite impaired left ventricular function with PLVAD support.

Data from the USpella Registry regarding experience with the Impella 2.5 in complex high-risk PCI procedures was published by Maini et al. in 2012 (n=175). The primary endpoint was the incidence of major adverse cardiac events (MACE) at 30 days. Secondary endpoints included safety, efficacy, and patient outcomes at 12 months. PCI was elective in 53% of cases and urgent in 47%. A majority of patients (69%) had ejection fraction < 35%, and 66% were in NYHA Class III or IV heart failure. Multivessel disease was present in 89% of patients, and

56% had an unprotected left main or last patent coronary artery. Seven patients died within 30 days. Angiographic revascularization was successful in 99% of patients overall, and in 90% of those with multivessel revascularization. SYNTAX scores (a measure of the complexity of coronary artery disease), ejection fraction, and functional status all improved significantly The rate of overall MACE was 8%.at 30 days, and survival was 96%, 91%, and 88% at 30 days, six months, and 12 months, respectively. The authors cited limitations of the study, including the fact that the observational design of the registry cannot establish causality or efficacy compared to a no-device approach, and that patient selection may limit extrapolation of these findings to a more general patient population.

O'Neill et al. (2012) conducted a prospective multicenter randomized trial (the PROTECT II study) to assess whether a high-risk PCI strategy with the support of the Impella 2.5 device would result in better outcomes than a revascularization strategy with IABP support (n=452). Included patients were age 18 or older and scheduled to undergo a non-emergent PCI on an unprotected left main or last patent coronary vessel, with a left ventricular ejection fraction (LVEF) of ≤ 35%, or with 3-vessel disease and LVEF ≤ 30%. Patients were randomized to IABP (n=226) or Impella 2.5 (n=226) during nonemergent PCI. The primary endpoint was the composite rate of intra- and post-procedural major adverse events (MAE) at discharge or 30-day follow-up, whichever was longer. Between November 27, 2007 and December 6, 2010, 452 patients were enrolled; 69% of the planned enrollment. After review of the available interim data, the Data and Safety Monitoring Board (DSMB) recommended the early discontinuation of the study for futility based on the observed conditional power of the 30-day results of the first 327 patients and the assumed similar trend for the remaining patients to be included in the study. (When enrollment ceased, an additional 125 patients had been enrolled beyond the initial 327 patients). Based on an intent-to-treat analysis, there was no statistically significant difference in the primary endpoint, MAE at 30 days, between patients in the Impella arm (35.1%) and the IABP arm (40.1%) (p=0.277). A follow-up of the composite primary end point was also performed at 90 days, and showed a trend toward decreased MAE in the Impella arm (40.6%) compared to the IABP arm (49.3%) (p=0.066) in the intent-to-treat population, and 40.0% vs. 51.0% (p=0.023), in the per-protocol population, respectively. The authors acknowledged that because the difference in 30-day MAE did not reach statistically significance for the entire study, the analysis of 90-day events remains exploratory.

The Impella-EUROSHOCK-registry evaluated the safety and efficacy of the Impella 2.5 in 120 patients with cardiogenic shock after acute MI (Lauten et al., 2013). A total of 14 tertiary cardiovascular centers in five countries across Europe contributed data to the registry. The primary endpoint was mortality at 30 days; the secondary endpoints included change in plasma lactate following institution of hemodynamic support, rate of early major adverse cardiac and cerebrovascular events (MACCE), and long-term survival. Thirty-day mortality was 64.2%. After Impella implantation, lactate levels decreased from 5.8 ± 5.0 millimoles per liter (mmol/L) to 4.7 ± 5.4 mmol/L at 24 hours(p=0.28) and 2.5 ± 2.56 mmol/L (p=0.023) at 48 hours. Early MACCE were reported in 18 (15%) patients. Major bleeding at the vascular access site, hemolysis, and pericardial tamponade occurred in 34 (28.6%), 9 (7.5%), and 2 (1.7%) patients, respectively. Survival was 28.3% after 317 ± 526 days. The authors concluded that in patients with acute cardiogenic shock from acute MI, Impella 2.5 treatment is feasible and results in improved lactate levels, suggesting improved organ perfusion. Thirty-day mortality remained high, however, which likely reflected the last resort character of Impella application in patients with a poor hemodynamic profile and greater imminent risk of death. The authors further concluded that carefully conducted randomized controlled trials are necessary to evaluate the efficacy of Impella 2.5 support in this high-risk patient group.

An ECRI Evidence Report, Miniature Intracardiac Pump for Heart Failure, updated in 2012, evaluated the Impella when used as a bridge to recovery in patients at high risk of heart failure during or after PCI, or as a bridge to decision after cardiogenic shock from acute MI. The report considered evidence from two studies that compared the Impella to the IABP (Seyfarth et al., 2008; Sjauw et al., 2008) and nine single-group studies that included 308 patients. The report concluded that too few data are available to determine whether the use of the Impella reduces the time spent on support or reduces the length of hospitalization compared to an IABP. There is also insufficient data to determine whether the use of the Impella for cardiogenic shock or high-risk PCI decreases adverse events or increases survival compared to the IABP. The report concluded that the clinical utility of the intracardiac mini-pump and claims for its purported advantages during PCI cannot be established without comparison of the IABP in a randomized controlled trial.

Based on the available evidence, the Impella and TandemHeart may be indicated to provide short-term circulatory support for individuals in cardiogenic shock. Although the published evidence is limited, and does not

demonstrate improved outcomes compared to the intra-aortic balloon pump, these devices may provide improved hemodynamic support independent of left ventricular function in patients in cardiogenic shock. According to U.S. FDA clearance for these devices, use is limited to six hours.

Professional Societies/Organizations
Heart Failure: The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) 2013 Guidelines for the Management of Heart Failure (Yancy et al.) states that MCS has emerged as a viable therapeutic option for patients with advanced stage D heart failure (also referred to as refractory, or end-stage HF) with reduced ejection fraction refractory to optimal guideline-directed medical therapy and cardiac device interventions. The guideline includes the following recommendations for mechanical circulatory support (MCS):

Class IIa

- MCS is beneficial in carefully selected patients with stage D heart failure with reduced ejection fraction 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 ventricular assist devices (VADs), is reasonable as a “bridge to recovery” or “bridge to decision” for carefully selected patients with heart failure with reduced ejection fraction with acute, profound hemodynamic compromise (Level of Evidence: B)
- Durable MCS is reasonable to prolong survival for carefully selected patients with stage D heart failure with reduced ejection fraction (Level of Evidence: B)

Guideline recommendations are classified as Class I, Class IIa, Class IIb, and Class III. The classification system is described as follows:

- Class I: Benefit >>>Risk; Procedure/Treatment should be perfomed/administered
- Class IIa: Benefit >> Risk; Additional studies with focused objectives needed. It is reasonable to perform procedure/administer treatment
- Class IIb: Benefit ≥ Risk; Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/treatment may be considered.
- Class III: No Benefit. Procedure/Test not helpful/Treatment: no proven benefit
- Class III Harm. Procedure/Test: Excess cost without benefit, or harmful. Treatment: harmful to patients

The weight of evidence supporting each recommendation is classified as follows:

- Level A: Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.
- Level B: Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.
- Level C: Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care.

ST-Elevation MI (STEMI): The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) 2013 Guidelines for the Management of ST-Elevation Myocardial Infarction (O’Gara et al., 2013) include the following recommendations relevant to mechanical support in treatment of cardiogenic shock:

- Class IIa The use of intra-aortic balloon pump counterpulsation can be useful for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy. (*Level of Evidence: B*)
- Class IIb: Alternative left ventricular (LV) assist devices for circulatory support may be considered in patients with refractory cardiogenic shock. (*Level of Evidence: C*)

Mechanical Circulatory Support: An American Heart Association Scientific Statement: Recommendations for the Use of Mechanical Circulatory Support: Device Strategies and Patient Selection, was published in 2012 (Peura et al.). The statement is intended to provide an understanding of general considerations when determining the appropriateness of mechanical circulatory support (MCS). The document discusses management strategies for the MCS patient, including selection criteria, and underscores two principles that

have evolved over the past decade; some patients are too profoundly ill with multisystem organ failure to benefit from the best MCS and aggressive inotropic therapy; and that complex decisions about candidacy for transplantation or MCS are best made by an experienced multidisciplinary team. While it may become appropriate for smaller programs to implant elective destination therapy MCS in highly selected patients, more acutely ill patients should be referred to quaternary care hospitals that are accustomed to the management of such patients.

The statement makes reference to nondurable MCS that may be used as a first step when rapid support is necessary in patients with cardiogenic shock who are at too high a risk for implantation of a durable device, or as an alternative if recovery is possible. In the latter scenario, a bridge with a nondurable device provides stabilization and permits clarification and potential reversal of other medical issues they may interfere with a satisfactory outcome after transplantation or long-term device placement. The following are included in a list of nondurable devices that may be used as a bridge to recovery, and for temporary support until more definitive therapies can be used in patients in whom myocardial recovery does not occur: intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), BVS 5000, AB5000, Thoratec pVAD, CentriMag, TandemHeart, and Impella.

The scientific statement includes the following recommendations.

1. MCS for bridge to transplant (BTT) indication should be considered for transplant-eligible patients with end-stage heart failure (HF) 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).
2. Implantation of MCS in patients before the development of advanced HF (i.e., hyponatremia, hypotension, renal dysfunction, and recurrent hospitalizations) is associated with better outcomes. Therefore, early referral of advanced HF patients is reasonable (Class IIa; Level of Evidence B).
3. MCS with a durable, implantable device for permanent therapy or destination therapy (DT) is beneficial for patients with advanced HF, high 1-year mortality resulting from HF, and the absence of other life-limiting organ dysfunction; who are failing medical, surgical, and/or device therapies; and who are ineligible for heart transplantation (Class I; Level of Evidence B).
4. Elective rather than urgent implantation of destination therapy (DT) can be beneficial when performed after optimization of medical therapy in advanced HF patients who are failing medical, surgical, and/or device therapies (Class IIa; Level of Evidence C).
5. A. Urgent nondurable MCS is reasonable in hemodynamically compromised HF patients with end organ dysfunction and/or relative contraindications to heart transplantation/durable MCS that are expected to improve with time and restoration of an improved hemodynamic profile (Class IIa; Level of Evidence C).
   B. These patients should be referred to a center with expertise in the management of durable MCS and patients with advanced HF (Class I; Level of Evidence C).
6. Patients who are ineligible for heart transplantation because of pulmonary hypertension related to HF alone should be considered for bridge to potential transplant eligibility with durable, long-term MCS (Class IIa; Level of Evidence B).
7. Careful assessment of right ventricular (RV) function is recommended as part of the evaluation for patient selection for durable, long-term MCS (Class I; Level of Evidence C).
8. A. Long-term MCS is not recommended in patients with advanced kidney disease in whom renal function is unlikely to recover despite improved hemodynamics and who are therefore at high risk for progression to renal replacement therapy (Class III; Level of Evidence C).
   B. Long-term MCS as a bridge to heart–kidney transplantation might be considered on the basis of availability of outpatient hemodialysis (Class IIb; Level of Evidence C).
9. Assessment of nutritional status is recommended as part of the evaluation for patient selection for durable, long-term MCS (Class I; Level of Evidence B).
10. Patients with obesity (BMI >30 to <40 kg/ m2) derive benefit from MCS and may be considered for long term MCS (Class IIb; Level of Evidence B).
11. Assessment of psychosocial, behavioral, and environmental factors is beneficial as part of the evaluation for patient selection for durable, long-term MCS (Class I; Level of Evidence C).
12. Evaluation of potential candidates by a multidisciplinary team is recommended for the selection of patients for MCS (Class I; Level of Evidence C).

Percutaneous Coronary Intervention: The American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Intervention (ACCF/AHA/SCAI) Guideline for Percutaneous Coronary Intervention (Levine et al., 2011) updated the guideline published in 2005. The guideline includes a new section, percutaneous hemodynamic support devices, and includes the following as a Class IIb recommendation:

- Elective insertion of an appropriate hemodynamic support device as an adjunct to PCI may be reasonable in carefully selected high-risk patients (Level of evidence: C).

High risk patients may include those undergoing unprotected left main or last-remaining-conduit PCI, those with severely depressed ejection fraction patients undergoing PCI of a vessel supplying a large territory, and/or those with cardiogenic shock. The guideline summarizes the limited evidence available on the use of percutaneous VADs, and states that patient risk, hemodynamic support, ease of application/removal, and operator and laboratory expertise are all factors involved in consideration of use of these devices. With devices that require large cannula insertion, the risk of vascular injury and related complications are important considerations regarding necessity and choice of device.

A section on cardiogenic shock includes the following Class I recommendation:

- A hemodynamic support device is recommended for patients with cardiogenic shock after STEMI who do not quickly stabilize with pharmacological therapy. (Level of Evidence: B)

The guideline addresses procedural considerations for PCI in patients in cardiogenic shock, including pharmacological therapies, endotracheal intubation and mechanical ventilation with positive end-expiratory pressure for patients with respiratory failure, placement of a temporary pacemaker for patients with bradycardia or high-degree atrioventricular heart block, and use of a pulmonary artery catheter to provide information to dose and titrate inotropes and pressures. The authors also state, “Further hemodynamic support is available with IABP counterpulsation or percutaneous LV assist devices, although no data support a reduction in mortality rates.”

Use Outside of the U.S.
HeartWare: The HeartWare VAS received the CE mark in Europe for both bridge to transplantation and destination therapy. As noted above, the US FDA approval of the device is limited to use as a bridge to transplantation

Impella: The Impella Recover Pump System was awarded the CE mark for use in the European Union,, and also received a Class IV medical device license with conditions from Health Canada on June 28, 2007. The Recover LP 2.5 is intended for use in cardiology and cardiac surgery for up to 24 hours for various indications, including but not limited to patients with reduced left ventricular function, during coronary artery bypass surgery on the beating heart, to support during PCI and post PCI. The Recover LP5.0 and Recover LD System are intended for clinical use in cardiology and cardiac surgery for up to ten days for various indications, including but not limited to reduced left ventricular function and coronary bypass surgery on the beating heart.

The Impella 2.5 Plus **(**Abiomed, Inc., Danvers, MA) is referred to outside the U.S. as the Impella cVAD. The device received the CE mark on April 12, 2012. The Abiomed website states that according to the labeling under CE Mark in Europe and other countries, the Impella cVAD is intended for clinical use in cardiology and cardiac surgery for up to five days, Multiple indications for use of the device are listed, including post cardiectomy, low output syndrome, cardiogenic shock after acute MI, myocardial protection after acute MI, or for use as cardiovascular support during CABG or during high risk percutaneous coronary intervention (PCI), or post PCI.

As noted above, US FDA approval of the Impella 2.5 and 2.5 Plus is limited to provision of partial circulatory support for periods up to six hours during procedures not requiring cardiopulmonary bypass.

Excor Pediatric VAD (Berlin Heart): The Excor Pediatric VAD received the CE mark for use in the European Union in 1996, and was issued a Class IV License with conditions by Health Canada in 2009. According to the Health Canada Summary Basis of Decision, the Excor system is intended for use in pediatric patients to provide mechanical circulatory support as a bridge to cardiac transplantation or to recovery. Candidates include pediatric patients with acute or chronic cardiac insufficiency due to various medical conditions (e.g., myocarditis,

cardiomyopathy, congenital heart failure (NYHA class III or IV), who cannot be treated by conservative methods and who can be expected to require medium to long term support.

According to the U.S. FDA Humanitarian Device Exemption detailed above, use of the device in the U.S. is limited to treatment of a child with severe isolated left ventricular or biventricular dysfunction who is a candidate for cardiac transplant and requires circulatory support.

HeartAssist 5®: The HeartAssist 5 received the CE mark for use in Europe for both pediatric and adult patients. The device is currently available in the U.S. for children who meet the criteria in the Humanitarian Device Exemption detailed above.

National Institute for Health and Clinical Excellence (NICE) (United Kingdom)
In June 2006, NICE issued Interventional Procedure Guidance on short-term circulatory support with LVADs. The guidance states that limited evidence on the safety and efficacy of short-term circulatory support with LVADs as a bridge to cardiac transplantation or recovery appears adequate to support the use of this procedure, provided that the normal arrangements are in place for audit and clinical governance.

The published guidance states that management of patients with end-stage heart failure or acute heart failure from naturally reversible causes is challenging and may involve combination medical therapy (including inotropic support), intra-aortic balloon pumping and heart transplantation. Short-term circulatory support with an LVAD may be indicated for patients with end-stage heart failure of any etiology who are awaiting a donor heart for transplantation, and for patients with a severe acute heart failure syndrome from which myocardial recovery is anticipated (e.g., acute myocarditis). An LVAD is also sometimes used if weaning from cardiopulmonary bypass after cardiac surgery fails.

European Society of Cardiology (ESC): ESC guidelines for the diagnosis and treatment of acute and chronic heart failure McMurray et al., 2012) state that patients potentially eligible for implantation of a VAD include those with greater than two months of severe symptoms despite optimal medical and device therapy and more than one of the following:

- LVEF <25% and, if measured, peak VO2 < 12 mL/kg/min
- ≥3 heart failure (HF) hospitalizations in previous 12 months without an obvious precipitating cause
- Dependence on i.v. inotropic therapy
- Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mm Hg and SBP ≤80–90 mmHg or CI ≤2 L/min/m2)
- Deteriorating right ventricular function

Recommendations for surgical implantation of LVADs in patients with systolic heart failure include the following:

- An LVAD or BiVAD is recommended in selected patients with end-stage HF despite optimal pharmacological and device treatment and who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of HF hospitalization for worsening HF and to reduce the risk of premature death while awaiting transplantation. (Class I, level of evidence: B)
- An LVAD should be considered in highly selected patients who have end-stage HF despite optimal pharmacological and device therapy and who are not suitable for heart transplantation, but are expected to survive >1 year with good functional status, to improve symptoms, and reduce the risk of HF hospitalization and of premature death. (Class !!a, Level of evidence: B)

A Class I recommendation indicates evidence and/or general agreement that a given treatment or procedure is useful, effective, and the procedure is recommended/is indicated. Class IIa indicates conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the procedure, with the weight of evidence in favor of usefulness/efficacy. The procedure should be considered. Level of evidence B is defined as data derived from a single randomized clinical trial or large non-randomized studies.

The guideline states that, in addition to VADs, other forms of short-term temporary MCS may be used in selected patients with acute heart failure, including intra-aortic balloon counterpulsation, other percutaneous cardiac support, and ECMO. MCS, particularly ECMO, can be used as a ‘bridge to decision in patients with

acute and rapidly deteriorating heart failure where full evaluation has not been possible and in whom death will occur without MCS.

Summary
There is adequate evidence in the published medical literature to demonstrate that ventricular assist devices (VADs) can be effective when used on a short-term basis in the acute care setting as a bridge to recovery for patients in acute cardiogenic shock or acute myocarditis and for patients following cardiac surgery who cannot be weaned from cardiopulmonary bypass. There is also adequate evidence that VADs improve hemodynamic and functional status when used as a bridge to cardiac transplantation, and as destination therapy in selected patients who are not candidates for transplantation. Although VADs are associated with significant risks and complications, they are responsible for improved pre- and post-transplant survival rates and improved quality of life. For all indications, patients must, at a minimum, meet the United States Food and Drug Administration (FDA)-defined, device-specific inclusion and exclusion criteria.

Percutaneous VADs, including the TandemHeart and Impella, have been proposed as an alternative to a traditional VAD or intra-aortic balloon pump (IABP) for short-term partial or total hemodynamic support. Unlike traditional VADs used for short-term support, percutaneous VADs are minimally invasive and do not require surgical implantation, and unlike IABP, percutaneous VADs provide hemodynamic support independent of left ventricular function. Although the published evidence evaluating the Impella and TandemHeart is limited, and does not demonstrate improved outcomes compared to the intra-aortic balloon pump, these percutaneous devices may be indicated to provide short-term circulatory support for individuals in cardiogenic shock.. According to U.S. FDA clearance for these devices, use is limited to six hours.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement
3.) ICD-10 PCS Procedure Codes are for informational purposes only and are not effective until 10/01/2014

Covered when medically necessary:

CPT®* Codes	**Description**
33975	Insertion of ventricular assist device; extracorporeal, single ventricle
33976	Insertion of ventricular assist device; extracorporeal, biventricular
33979	Insertion 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

HCPCS Codes	**Description**
Q0478	Power adapter for use with electric or electric/pneumatic ventricular assist device, vehicle type
Q0479	Power module for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0480	Driver for use with pneumatic ventricular assist device, replacement only
Q0481	Microprocessor control unit for use with electric ventricular assist device, replacement only
Q0482	Microprocessor control unit for use with electric/pneumatic combination

	ventricular assist device, replacement only
Q0483	Monitor/display module for use with electric ventricular assist device, replacement only
Q0484	Monitor/display module for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0485	Monitor control cable for use with electric ventricular assist device, replacement only
Q0486	Monitor control cable for use with electric/pneumatic ventricular assist device, replacement only
Q0487	Leads (pneumatic/electrical) for use with any type electric/pneumatic ventricular assist device, replacement only
Q0488	Power pack base for use with electric ventricular assist device, replacement only
Q0489	Power pack base for use with electric/pneumatic ventricular assist device, replacement only
Q0490	Emergency power source for use with electric ventricular assist device, replacement only
Q0491	Emergency power source for use with electric/pneumatic ventricular assist device, replacement only
Q0492	Emergency power supply cable for use with electric ventricular assist device, replacement only
Q0493	Emergency power supply cable for use with electric/pneumatic ventricular assist device, replacement only
Q0494	Emergency hand pump for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0495	Battery/power pack charger for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0496	Battery, other than lithium-ion, for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0497	Battery clips for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0498	Holster for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0499	Belt/vest/bag for use to carry external peripheral components of any type ventricular assist device, replacement only
Q0500	Filters for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0501	Shower cover for use with electric or electric/pneumatic ventricular assist device, replacement only
Q0502	Mobility cart for pneumatic ventricular assist device, replacement only
Q0503	Battery for pneumatic ventricular assist device, replacement only, each
Q0504	Power adapter for pneumatic ventricular assist device, replacement only, vehicle type
Q0505	Miscellaneous supply or accessory for use with ventricular assist device
Q0606	Battery, lithium-ion, for use with electric or electric/pneumatic ventricular assist device, replacement only

Covered when medically necessary and used to report the TandemHeart® PVTA® System or the Impella Recover® LP 2.5 Percutaneous Cardiac Support System/Impella 5.0 Catheters, or Impella 2.5 Plus for the treatment of cardiogenic shock for up to six hours.

CPT®* Codes	Description
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

33993	Repositioning of percutaneous ventricular assist device with imaging guidance at separate and distinct session from insertion
33999	Unlisted procedure, cardiac surgery

ICD-9-CM Procedure Codes	Description
37.68	Insertion of percutaneous external heart assist device

ICD-10-PCS Procedure Codes (Effective 10/01/2014)	Description
02HA3QZ	Insertion of implantable heart assist system into heart, percutaneous approach

References

1. Aaronson KD, Slaughter MS, Miller LW, McGee EC, Cotts WG, Acker MA, et al. HeartWare Ventricular Assist Device (HVAD) Bridge to Transplant ADVANCE Trial Investigators. Use of an intrapericardial, continuous-flow, centrifugal pump in patients awaiting heart transplantation. Circulation. 2012 Jun 26;125(25):3191-200. doi: 10.1161/CIRCULATIONAHA.111.058412. Epub 2012 May 22.

2. Adams KF, Lindenfeld J, Arnold JMO, Baker DW, Barnard DH, Baughman KL, et al. HFSA 2006 Comprehensive Heart Failure Practice Guideline. J Card Fail. 2006 Feb;12(1):e86-e103.

3. Alasnag MA, Gardi DO, Elder M, Kannam H, Ali F, Petrina M, Kheterpal V, et al. Use of the Impella 2.5 for prophylactic circulatory support during elective high-risk percutaneous coronary intervention. Cardiovasc Revasc Med. 2011 Sep-Oct;12(5):299-303. Epub 2011 Mar 30.

4. Almond CS, Buchholz H, Massicotte P, Ichord R, Rosenthal DN, Uzark K, et al. Berlin Heart EXCOR Pediatric ventricular assist device Investigational Device Exemption study: study design and rationale. Am Heart J. 2011 Sep;162(3):425-35.e6. Epub 2011 Jul 30.

5. Almond CS, Morales DL, Blackstone EH, Turrentine MW, Imamura M, Massicotte MP, Jordan LC, et al. Berlin Heart EXCOR pediatric ventricular assist device for bridge to heart transplantation in US children.
6. Circulation. 2013 Apr 23;127(16):1702-11. doi: 10.1161/CIRCULATIONAHA.112.000685. Epub 2013 Mar 28.

7. American Heart Association. 1994 Revisions to Classification of Functional Capacity and Objective Assessment of Patients With Diseases of the Heart. Accessed Nov 5, 2010. Available at URL address: http://www.americanheart.org/presenter.jhtml?identifier=1712

8. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). J Am Coll Cardiol. 2004 Aug 4;44(3):E1-E211

9. Birks EJ, Tansley PD, Hardy J, George RS, Bowles CT, Burke M, et al. Left ventricular assist device and drug therapy for the reversal of heart failure. N Engl J Med. 2006 Nov 2;355(18):1873-84.

10. Blume ED, Nafterl DC, Bastardi HJ, Duncan BW, Kirklin JK, Webber SA, for the Pediatric Heart Transplant Sudy Investigators. Outcomes of children bridged to heart transplantation with ventricular assist devices: a multi-institutional study. Circulation. 2006 May 16;113(19):2313-9.

11. Boehmer JP. Device therapy for heart failure. Am J Cardiol. 2003 Mar 20;91(6A):53D-59D.

12. Bonow; Braunwald's heart disease: a textbook of cardiovascular medicine, 8th ed. Saunders, an imprint of Elsevier; 2011.

13. Burkhoff D, Cohen H, Brunckhorst C, O'Neill WW; TandemHeart Investigators Group. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. Am Heart J. 2006 Sep;152(3):469.e1-8.

14. Centers for Medicare & Medicaid Services. National Coverage Analysis (NCA) for Ventricular Assist Devices as Destination Therapy. (CAG-00119R2). Accessed Nov 2, 2012. Available at URL address: http://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=243&ver=5&NcaName=Ventricular+Assist+Devices+as+Destination+Therapy+(2nd+Recon)&bc=gEAAAAAAAAAA&

15. Chandra D, Kar B, Idelchik G, Simpson L, Loyalka P, Gregoric ID, et al. Usefulness of percutaneous left ventricular assist device as a bridge to recovery from myocarditis. Am J Cardiol. 2007 Jun 15;99(12):1755-6. Epub 2007 May 2.

16. Chavey WE 2nd, Blaum CS, Bleske BE, Harrison RV, Kesterson S, Nicklas JM. Guideline for the management of heart failure caused by systolic dysfunction: Part I. Guideline development, etiology and diagnosis. Am Fam Physician. 2001 Sep 1;64(5):769-74.

17. Cheng JM, den Uil CA, Hoeks SE, van der Ent M, Jewbali LS, van Domburg RT, Serruys PW. Percutaneous left ventricular assist devices vs. intra-aortic balloon pump counterpulsation for treatment of cardiogenic shock: a meta-analysis of controlled trials. Eur Heart J. 2009 Sep;30(17):2102-8. Epub 2009 Jul 18.

18. Dang NC, Topkara VK, Leacche M, John R, Byrne JG, Naka Yoshifumi. Left ventricular assist device implantation after acute anterior wall myocardial infarction and cardiogenic shock: a two-center study. J Thorac Cardiovasc Surg. 2005 Sep;130(3):693-8.

19. Dembitsky WP, Tecor AJ, Park S, Moskowitz AJ, Gelijns AC, Ronan NS, et al. Left ventricular assist device performance with long-term circulatory support: lessons from the REMATCH trial. Ann Thorac Surg. 2004 Dec;78(6):2123-9; discussion 2129-30.

20. Dixon SR, Henriques JP, Mauri L, Sjauw K, Civitello A, Kar B, et al. A prospective feasibility trial investigating the use of the Impella 2.5 system in patients undergoing high-risk percutaneous coronary intervention (The PROTECT I Trial): initial U.S. experience. JACC Cardiovasc Interv. 2009 Feb;2(2):91-6

21. ECRI Institute. Extracorporeal magnetically levitated ventricular assist device (VAD) as a bridge-to-decision. [Emerging Technology evidence report]. Plymouth Meeting (PA); ECRI Institute; 2009 May 8. Available at URL address: http://www.ecri.org

22. ECRI Institute. Impella 2.5 and 5.0 Ventricular Assist Devices (Abiomed, Inc.) for Treating Left Ventricular Heart Failure. Product Brief. Plymouth Meeting (PA); ECRI Institute;.2012 Nov. Available at URL address: http://www.ecri.org

23. ECRI Institute. Miniature intracardiac pump for acute heart failure. [Emerging Technology evidence report]. Plymouth Meeting (PA); ECRI Institute; Updated 2012 Jan 14. Available at URL address: http://www.ecri.org

24. ECRI Institute. Pediatric Ventricular Assist Device (Excor) as Bridge to Transplantation. [Emerging Technology Evidence Report]. Plymouth Meeting (PA): ECRI Institute; 2013 Apr. Available at URL address: http://www.ecri.org

25. el-Banayosy A, Korfer R. Long-term implantable left ventricular assist devices: out-of-hospital program. Cardiol Clin. 2003 Feb;21(1):57-65.

26. Fraser CD Jr, Jaquiss RD, Rosenthal DN, Humpl T, Canter CE, Blackstone EH, et al.; Berlin Heart Study Investigators. Prospective trial of a pediatric ventricular assist device. N Engl J Med. 2012 Aug 9;367(6):532-41. doi: 10.1056/NEJMoa1014164.

27. Frazier OH, Jacob LP. Small pumps for ventricular assistance: progress in mechanical circulatory support. Cardiol Clin. 2007 Nov;25(4):553-64; vi.

28. Frazier OH, Rose EA, Oz MC, Dembitsky W, McCarthy P, Radovancevic B, et al.; HeartMate LVAS Investigators. Left Ventricular Assist System. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. J Thorac Cardiovasc Surg. 2001 Dec;122(6):1186-95.

29. Greenberg B, Czerska B, Delgado RM, Bourge R, Zile MR, Silver M, et al.; MOMENTUM Investigators and Coordinators. Effects of continuous aortic flow augmentation in patients with exacerbation of heart failure inadequately responsive to medical therapy: results of the Multicenter Trial of the Orqis Medical Cancion System for the Enhanced Treatment of Heart Failure Unresponsive to Medical Therapy (MOMENTUM). Circulation. 2008 Sep 16;118(12):1241-9. doi: 10.1161/CIRCULATIONAHA.108.773275. Epub 2008 Sep 2

30. Heart Failure Society of America. 2010 Comprehensive Heart Failure Practice Guideline. Accessed Nov 3, 2010. Available at URL address: http://www.heartfailureguideline.org/

31. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. 2009 focused update incorporated into the ACC/AHA 2005 guideline for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Fouindation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2009;53. Article in press.

32. Jessup M, Brozena S. Heart failure. N Engl J Med. 2003 May 15;348(20):2007-18.

33. John R, Long JW, Massey HT, Griffith BP, Sun BC, Tector AJ, et al. Outcomes of a multicenter trial of the Levitronix CentriMag ventricular assist system for short-term circulatory support. J Thorac Cardiovasc Surg; 2011 Apr;141(4):932-9. Epub 2010 Jul 6.

34. Kar B, Gregoric ID, Basra SS, Idelchik GM, Loyalka P. The percutaneous ventricular assist device in severe refractory cardiogenic shock. J Am Coll Cardiol. 2011 Feb 8;57(6):688-96. Epub 2010 Oct 14.

35. Kherani AR, Oz MC. Ventricular assistance to bridge to transplantation. Surg Clin North Am. 2004 Feb;84(1):75-89, viii-ix.

36. King SB 3rd, Smith SC Jr, Hirshfeld JW Jr, Jacobs AK, Morrison DA, Williams DO. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. Circulation. 2008 Jan 15;117(2):261-95. Epub 2007 Dec 13.

37. Kirklin JK, Naftel DC, Pagani FD, Kormos RL, Stevenson L, Miller M, Young JB. Long-term mechanical circulatory support (destination therapy): on track to compete with heart transplantation? J Thorac Cardiovasc Surg. 2012 Sep;144(3):584-603; discussion 597-8. doi: 10.1016/j.jtcvs.2012.05.044. Epub 2012 Jul 15.

38. Kukuy EL, Oz MC, Rose EA, Naka Y. Devices as destination therapy. Cardiol Clin. 2003 Feb;21(1):67-73.

39. Lauten A, Engström AE, Jung C, Empen K, Erne P, Cook S, et al. Percutaneous left-ventricular support with the Impella-2.5-assist device in acute cardiogenic shock: results of the Impella-EUROSHOCK-registry. Circ Heart Fail. 2013 Jan;6(1):23-30. doi: 10.1161/CIRCHEARTFAILURE.112.967224. Epub 2012 Dec 4

40. Lazar RM, Shapiro PA, Jaski BE, Parides MK, Bourge RC, Watson JT, et al. Neurological events during long-term mechanical circulatory support for heart failure: the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) experience. Circulation. 2004 May 25;109(20):2423-7. Epub ahead of print 2004 May 3.

41. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; Society for Cardiovascular Angiography and Interventions. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. J Am Coll Cardiol. 2011 Oct 31. [Epub ahead of print

42. Lietz K, Long JW, Kfoury AG, Slaughter MS, Silver MA, Milano CA, et al. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. Circulation. 2007 Jul 31;116(5):497-505. Epub 2007 Jul 16.

43. Long JW, Kfoury AG, Slaughter MS, Silver M, Milano C, Rogers J, et al. Long-term destination therapy with the HeartMate XVE left ventricular assist device: improved outcomes since the REMATCH study. Congest Heart Fail. 2005 May-Jun;11(3):133-8.

44. Unverzagt S, Machemer MT, Solms A, Thiele H, Burkhoff D, Seyfarth M, et al. Intra-aortic balloon pump counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. Cochrane Database Syst Rev. 2011 Jul 6;(7):CD007398.\

45. Maini B, Naidu SS, Mulukutla S, Kleiman N, Schreiber T, Wohns D, et al. Real-world use of the Impella 2.5 circulatory support system in complex high-risk percutaneous coronary intervention: The USpella Registry. Catheter Cardiovasc Interv. 2012 Nov 1;80(5):717-25. doi: 10.1002/ccd.23403. Epub 2012 Apr 25.

46. Maybaum S, Mancini D, Xydas S, Starling RC, Aaronson K, Pagani FD, for the LVAD Working Group. Cardiac improvement during mechanical circulatory support: a prospective multicenter study of the LVAD Working Group. Circulation. 2007 May 15;115(19):2497-505. Epub 2007 May 7.

47. McMurray JJV, Pfeffer MA. Heart failure. Lancet. 2005 May 28-Jun 3;365(9474):1877-89.

48. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, Falk V, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2012 Aug;14(8):803-69. doi: 10.1093/eurjhf/hfs105.

49. Miller MA, Ulisney K, Baldwin JT. INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support): a new paradigm for translating registry data into clinical practice. J Am Coll Cardiol. 2010 Aug 24;56(9):738-40.

50. Morales DL, Almond CS, Jaquiss RD, Rosenthal DN, Naftel DC, Massicotte MP, et al. Bridging children of all sizes to cardiac transplantation: the initial multicenter North American experience with the Berlin Heart EXCOR ventricular assist device. J Heart Lung Transplant. 2011 Jan;30(1):1-8.

51. Moreno GE, Charroqui A, Pilán ML, Magliola RH, Krynski MP, Althabe M, et al. Clinical experience with Berlin Heart Excor in pediatric patients in Argentina: 1373 days of cardiac support. Pediatr Cardiol. 2011 Jun;32(5):652-8. Epub 2011 Mar 20.

52. Naidu SS. Novel percutaneous cardiac assist devices: the science of and indications for hemodynamic support. Circulation. 2011 Feb 8;123(5):533-43.

53. National Institute for Health and Clinical Excellence. Interventional procedure guidance 177. Short-term circulatory support with left ventricular assist devices as a bridge to cardiac transplantation or recovery. London, UK: NICE; 2006 Jun. Accessed Oct 26, 2010. Available at URL address: http://guidance.nice.org.uk/page.aspx?o=IPG177guidance

54. National Institute for Health and Clinical Excellence. Interventional procedure overview of short-term circulatory support with left ventricular assist devices as a bridge to transplant or to recovery. London, UK: NICE; 2005 Dec. Accessed Oct 26, 2010. Available at URL address: http://guidance.nice.org.uk/page.aspx?o=ip059overview\

55. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the American College of Emergency Physicians and Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv. 2013 Jul 1;82(1):E1-27. doi: 10.1002/ccd.24776. Epub 2013 Jan 8.

56. O'Neill WW, Kleiman NS, Moses J, Henriques JP, Dixon S, Massaro J, et al. A Prospective, Randomized Clinical Trial of Hemodynamic Support With Impella 2.5 Versus Intra-Aortic Balloon Pump in Patients Undergoing High-Risk Percutaneous Coronary Intervention: The PROTECT II Study. Circulation. 2012 Oct 2;126(14):1717-27. doi: 10.1161/CIRCULATIONAHA.112.098194. Epub 2012 Aug 30.

57. Pae WE, Connell JM, Adelowo A, Boehmer JP, Korfer R, El-Banayosy A, et al. Does total implantability reduce infection with the use of a left ventricular assist device? The LionHeart experience in Europe. J Heart Lung Transplant. 2007 Mar;26(3):219-29.

58. Pagani FD, Miller LW, Russell SD, Aaronson KD, John R, Boyle AJ, e t al.; HeartMate II Investigators. Extended mechanical circulatory support with a continuous-flow rotary left ventricular assist device. J Am Coll Cardiol. 2009 Jul 21;54(4):312-21.

59. Park SJ, Tector A, Piccioni W, Raines E, Gelijns A, Moskowitz A, et al. Left ventricular assist devices as destination therapy: a new look at survival. J Thorac Cardiovasc Surg. 2005 Jan;129(1):9-17.

60. Peura JL, Colvin-Adams M, Francis GS, Grady KL, Hoffman TM, Jessup M, et al.; on behalf of the American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Interventions, and Council on Cardiovascular Surgery and Anesthesia. Recommendations for the Use of Mechanical Circulatory Support: Device Strategies and Patient Selection: A Scientific Statement From the American Heart Association. Circulation. 2012 Oct 29. [Epub ahead of print]

61. Potapov EV, Stiller B, Hetzer R. Ventricular assist devices in children: current achievements and future perspectives. Pediatr Transplant. 2007 May;11(3):241-55.

62. Pulido JN, Park SJ, Rihal CS. Percutaneous left ventricular assist devices: clinical uses, future applications, and anesthetic considerations. J Cardiothorac Vasc Anesth. 2010 Jun;24(3):478-86. Epub 2010 Jan 6.

63. Renlund DG, Taylor DO, Smedira NG. Cardiac transplantation and mechanical circulatory support. In: Topol EJ, editor. Textbook of cardiovascular medicine, 3rd ed. Lippincott Williams & Wilkins, 2007.

64. Rogers JG, Aaronson KD, Boyle AJ, Russell SD, Milano CA, Pagani FD, et al.; HeartMate II Investigators. Continuous flow left ventricular assist device improves functional capacity and quality of life of advanced heart failure patients. J Am Coll Cardiol. 2010 Apr 27;55(17):1826-34.

65. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al; for the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med. 2001;345(20):1435-43.

66. Salzberg SP, Lachat ML, von Harbou K, Zund g, Turina MI. Normalization of high pulmonary vascular resistance with LVAD support in heart transplantation candidates. Eur J Cardiothorac Surg. 2005 Feb;27(2):222-5.

67. Sarker K, Kini AS. Percutaneous left ventricular support devices. Cardiol Clin. 2010 Feb;28(1):169-84

68. Seyfarth M, Sibbing D, Bauer I, Frohlich G, Bott-Flugel, Byrne R, et al. A randomized clinical trial to evaluate the safety and efficacy of a percutaneous left ventricular assist device versus intra-aortic balloon pumping for treatment of cardiogenic shock caused by myocardial infarction. J Am Coll Cardiol. 2008 Nov 4;52(19):1584-8.

69. Sharples LD, Cafferty F, Math M, Demitis N, Freeman C, Dyer M, et al. Evaluation of the clinical effectiveness of the Ventricular Assist Device Program in the United Kingdom (EVAD UK). J Heart Lung Transplant. 2007 Jan;26(1):9-15.

70. Shah R, Thomson A, Atianzar K, Somma K, Mehra A, Clavijo L, et al. Percutaneous left ventricular support for high-risk PCI and cardiogenic shock: who gets what? Cardiovasc Revasc Med. 2012 Mar-Apr;13(2):101-5. Epub 2012 Mar 7.

71. Sjauw KD, Engström AE, Vis MM, van der Schaaf RJ, Baan J Jr, Koch KT, et al. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? Eur Heart J. 2009 Feb;30(4):459-68. Epub 2009 Jan 23

72. Sjauw KD, Konorza T, Erbel R, Danna PL, Viecca M, Minden HH, et al. Supported high-risk percutaneous coronary intervention with the Impella 2.5 device the Europella registry. J Am Coll Cardiol. 2009 Dec 15;54(25):2430-4.

73. Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, et al.; HeartMate II Investigators. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med. 2009 Dec 3;361(23):2241-51. Epub 2009 Nov 17

74. Slaughter MS, Pagani FD, McGee EC, Birks EJ, Cotts WG, Gregoric I, et al.; HeartWare Bridge to Transplant ADVANCE Trial Investigators. HeartWare ventricular assist system for bridge to transplant: combined results of the bridge to transplant and continued access protocol trial. J Heart Lung Transplant. 2013 Jul;32(7):675-83. doi: 10.1016/j.healun.2013.04.004.

75. Slaughter M, Tsui SS, El-Banayosy A, Sun BC, Kormos RL, Mueller DK, at al., on behalf of the IVAD Study Group. Results of a multicenter clinical trial with the Thoratec Implantable Ventricular Assist Device. J Thorac Cardiovasc Surg. 2007 Jun;133(6):1573-80. Erratum in: J Thorac Cardiovasc Surg. 2007 Sep;134(3):A34.

76. Smart FW, Palanichamy N. Left ventricular assist device therapy for end-stage congestive heart failure: from REMATCH to the future. Congest Heart Fail. 2005 Jul-Aug;11(4):188-91.

77. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB 3rd, et al. American College of Cardiology/American Heart Association Task Force on Practice Guidelines; ACC/AHA/SCAI Writing

Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). Circulation. 2006 Feb 21;113(7):e166-286.

78. Stevenson LW, Kormos RL, Bourge RC, Gelijns A, Griffith BP, Hershberger RE, et al. Mechanical cardiac support 2000: current applications and future trial design: June 15-16, 2000 Bethesda, Maryland. Circulation. 2001 Jan 16;103(2):337-42.

79. Stevenson LW, Miller LW, Desvigne-Nickens P, Ascheim DD, Parides MK, Renlund DG, et al for the REMATCH Investigators. Left ventricular assist device as destination for patients undergoing intravenous inotropic therapy: a subset analysis from REMATCH (Randomized Evaluation of Mechanical Assistance in Treatment of Chronic Heart Failure). Circulation. 2004 Aug 24;110(8):975-81. Epub 2004 Aug 16.

80. Strüber M, Sander K, Lahpor J, Ahn H, Litzler PY, Drakos SG, et al. HeartMate II left ventricular assist device; early European experience. Eur J Cardiothorac Surg. 2008 Aug;34(2):289-94. Epub 2008 Jun 20.

81. Thiele H, Lauer B, Hambrecht R, Boudriot E, Cohen HA, Schuler G. Reversal of cardiogenic shock by percutaneous left atrial-to-femoral arterial bypass assistance. Circulation. 2001 Dec 11;104(24):2917-22.

82. Thiele H, Sick P, Boudriot E, Diederich KW, Hambrecht R, Niebauer J, Schuler G. Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. Eur Heart J. 2005 Jul;26(13):1276-83. Epub 2005 Feb 25.

83. Topol, EJ. Textbook of cardiovascular medicine. Lippincott Williams & Wilkins; 2007.

84. U.S. Department of Health and Human Services. CMS Centers for Medicare and Medicaid Services. NCD for Artificial Hearts and Related Devices. Publication no. 100.3. Version effective date, May 1, 2008. Accessed Nov 2, 2012. Available at URL address: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=246&ncdver=5&NCAId=211&ver=20&NcaName=Artificial+Hearts&bc=ACAAAAAAIAAA&

85. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health. Listing of Humanitarian Device Exemptions. Accessed Nov 2, 2012. Available at URL address: http://www.fda.gov/medicaldevices/productsandmedicalprocedures/deviceapprovalsandclearances/hdeapprovals/ucm161827.htm

86. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health. PMA-Premarket Approval database. Accessed Nov 2, 2012. Available at URL address: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm

87. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013 Oct 15;62(16):e147-239. doi: 10.1016/j.jacc.2013.05.019. Epub 2013 Jun 5

88. Zimpfer D, Zrunek P, Roethy W, Czerny M, Schima H, Huber L, et al. Left ventricular assist devices decrease fixed pulmonary hypertension in cardiac transplant candidates. J Thorac Cardiovasc Surg. 2007 Mar;133(3):689-95.