J. of Cardiovasc. Trans. Res. (2014) 7:292–300
DOI 10.1007/s12265-014-9548-6

Aortic Counterpulsation: C-Pulse and Other Devices for Cardiac Support

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Received: 7 November 2013 / Accepted: 4 February 2014 / Published online: 20 February 2014

Abstract Heart failure is the leading cause of hospitalization in the USA. Despite major advances in the medical and device-related therapy including chronic resynchronization therapy for management of heart failure, significant number of patients eventually require advanced cardiac therapy including mechanical circulatory support or heart transplant. Heart transplant is a gold standard for end-stage heart failure but is limited by the donor heart shortage creating a definite need for alternative effective therapies. The earliest and most common form of mechanical circulatory support is counterpulsation therapy. Annually, more than 150,000 patients worldwide receive counterpulsation therapy for various indications including cardiogenic shock or severe left ventricular dysfunction (Nanas and Moulopoulos in *Cardiology*, *84*:156–167, 1994) and many thousands of lives are saved each year (65 % survival) (Torchiana et al. in *Journal of Thoracic and Cardiovascular Surgery*, *113*(4):758–764, 1997). There are different types of aortic counterpulsation devices. Here, we will give an overview of different counterpulsation devices with focus on C-Pulse device. Extra-aortic balloon counterpulsation, C-Pulse (Sunshine Heart Inc., Eden Prairie, MN), is an important and novel approach in the management of patients with advanced heart failure who remain symptomatic despite optimum medical and device-based therapy. C-Pulse is designed to provide permanent, long-term, continuous partial circulatory support for New York Heart Association class III and ambulatory class IV heart failure patients. C-Pulse is a nonblood-contacting counterpulsation using an inflatable cuff around the ascending aorta, extra-aortic balloon (EAB) counterpulsation device. A pivotal, multicenter US study to assess the safety and efficacy of C- Pulse in patient with Stage C and NYHA Class III or ambulatory Class IV heart failure is in progress.

Keywords Counterpulsation · Aortic · Extra-aortic · Assist devices · Heart failure · Balloon

Associate Editor Craig Stolen oversaw the review of this article

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Introduction

Heart failure (HF) is a complex clinical syndrome characterized by impairment of either filling or ejection of blood by ventricles due to array of cardiac disorders [3]. Heart Failure is the leading cause of hospitalization affecting approximately 5.8 million patients in the USA [3–5] with approximately 670,000 new cases diagnosed each year [6]. With the recent advances in the management of cardiac disorders, more patients are living longer and there is a trend towards increased prevalence of heart failure. Treatment with ACE inhibitors, β-blockers, and aldosterone antagonists is associated with improved morbidity and mortality in patients with NYHA class II–IV heart failure [7–10]. Patients with class III and ambulatory class IV heart failure are typically unable to engage in normal activities, compromising their quality of life. Despite major advances in the medical and device-related therapy including chronic resynchronization therapy (CRT) for management of HF, significant number of patients eventually require advanced cardiac therapy including mechanical circulatory support or heart transplant. Heart transplant is a gold standard for end-stage heart failure but is limited by the donor heart shortage creating a need for effective therapy with short- or long-term, partial or complete mechanical circulatory support (MCS) that can improve quality of life, functional capacity, and survival of these patients.

Mechanical circulatory support devices can function by direct systolic augmentation of the heart, mechanically

diverting blood from the left ventricle directly into the aorta or via counterpulsation therapy with diastolic augmentation [11]. The earliest and most common form of mechanical circulatory support is counterpulsation therapy. Each year, more than 150,000 patients receive counterpulsation therapy, often in severe left ventricular dysfunction following acute myocardial infarction or cardiac surgery or cardiogenic shock and significant lives are saved [2]. Intra-aortic balloon pump (IABP) was the first used mechanical circulatory support device with counterpulsation technique, which worked with the principle of diastolic augmentation. Extra-aortic balloon counterpulsation, C-Pulse (Sunshine Heart Inc., Eden Prairie, MN), is an important and novel extra-aortic implantable counterpulsation, long-term partial support device designed to create similar physiological effects as IABP counterpulsation and provides relief of symptoms in moderate to severe heart failure patients who remain symptomatic despite optimum medical and device-based therapy.

Counterpulsation technique was first introduced in 1953 when Kantrowitz et al. demonstrated augmentation of coronary blood flow via increase in diastolic aortic pressure [12]. In 1959, Kantrowitz et al. further showed that contraction of a diaphragm wrapped around the descending thoracic aorta during diastole led to reduction of left ventricular stress [13]. Other long-term counterpulsation approaches attempted included using intra-aortic balloon pumping through a synthetic graft attached to the left subclavian artery [14], a descending aortic patch sewn into the descending thoracic aorta [15], and by wrapping the pedicle latissimus dorsi muscle around the ascending aorta (i.e., aortomyoplasty) [16]. However, each of these approaches has its limitations.

The hemodynamic benefits of counterpulsation therapy in patients with acute cardiac dysfunction have led to the use of IABP as an effective temporary circulatory assist device. IABP was first used in 1968 [17] and since then has been widely used in patients with cardiogenic shock, those waiting for advanced cardiac care, and those undergoing coronary artery bypass surgery [18]. With the recent quest for smaller and more effective long-term cardiac assist devices, a number of other counterpulsation devices have been under investigation, including C-Pulse, Symphony, etc.

Counterpulsation is effective in various positions in aorta including in the descending aorta (IABP), on descending aorta (Kantrowitz CardioVAD^{TM}), around the ascending aorta (C-Pulse), axillary artery (Symphony), and lower extremity (enhanced external counterpulsation). In this review, hemodynamic effects of counterpulsation, types of counterpulsation devices, the evolving concepts, and current update on extra-aortic counterpulsation device, C-Pulse is discussed.

Hemodynamic Effects of Counterpulsation

Counterpulsation technique increases aortic pressure during early diastole which augments coronary/distal end organ perfusion and myocardial performance as well as decreases aortic pressure during early systole which reduces ventricular afterload and workload [17]. The device inflation and deflation is triggered by precise timing to the ECG or aortic pressure waveform. Counterpulsation therapy increases the diastolic aortic pressure by 30–70 % and improves coronary perfusion [1, 19, 20]. The peak systolic pressure is reduced by 5–15 % [1]. It improves the myocardial oxygen supply through increased coronary perfusion [21, 22], and it reduces myocardial oxygen consumption by decreasing afterload and left ventricular work [23]. Cardiac output and stroke volume increases up to 20 % [19, 24] and the native heart rate is reduced by 10 % [23]. This form of therapy has been shown to augment cerebral, renal, mesenteric, and pulmonary blood flow [25–28] and improves end organ function [23].

Types of Counterpulsation Devices

Extracorporeal Counterpulsation Devices

Extracorporeal counterpulsation therapy is provided noninvasively by enhanced external counterpulsation (ECP). Enhanced external counterpulsation device is a series of pneumatically actuated cuffs placed on the patient's lower extremities. The inflation and deflation of these cuffs are timed and sequenced to reduce afterload and increase cardiac output. Usually, three cuffs are placed on the lower extremities, including on upper thigh, lower thigh, and calf. Inflation and deflation is triggered by patient's ECG (R wave detection). The sequence of inflation is first calf, then lower thigh, and finally upper thigh cuff. This order is reversed during deflation. Cuffs are inflated to approximately 300 mmHg and are controlled by a pressure monitor. ECP has been shown to relieve angina, decrease the degree of ischemia in a cardiac stress test, improve exercise tolerance, and improve cardiac output in patients with heart failure [29–31]. ECP is indicated for patients with symptoms of ischemic cardiomyopathy who are not amenable to percutaneous coronary intervention or coronary artery bypass graft surgery. Contraindications of ECP include severe peripheral vascular disease, aortic insufficiency, atrial fibrillation, significant left main coronary artery disease, overt congestive heart failure, uncontrolled hypertension, phlebitis, deep vein thrombosis, stasis ulcers, and bleeding diathesis. Limitations of ECP include that patients are nonambulatory during the therapy and there can be discomfort

associated with cuff inflation. The ECP therapy does not require surgical implantation or anticoagulation regimen.

Percutaneous Counterpulsation Devices

Intra-aortic Balloon Pump

IABP is a widely used short-term counterpulsation circulatory assist device. The IABP is a cylindrical polyethylene balloon that is placed in the aorta, approximately 2 cm from the left subclavian artery. The IABP is inflated and deflated by shuttling helium. Intra-aortic balloon pump (IABP) is inserted through the femoral artery by modified Seldinger's technique and positioned in the proximal descending thoracic aorta. IABP is inflated during diastole and deflated during systole. The IABP has to be significantly and rapidly deflated (−100 ms) before the onset of ventricular ejection to ensure that the balloon does not obstruct aortic flow [32]. This rapid deflation causes brief retrograde cerebral, myocardial, and systemic flows limiting the positive hemodynamic and metabolic benefits of IABP counterpulsation.

The IABP is indicated but not limited to Cardiogenic shock, reversible cardiac complications following myocardial infarction (acute mitral regurgitation and septal perforation), unstable angina pectoris, postcardiotomy failure, perioperative injury to myocardial tissue, high risk coronary artery bypass graft surgery, thrombolytic therapy of acute myocardial infarction, preoperative use for high-risk patients e.g., those with unstable angina with stenosis greater than 70 % of main coronary artery, in ventricular dysfunction with an ejection fraction less than 35 %, and percutaneous coronary angioplasty [18]. Absolute contraindications for IABP therapy are: severe aortic valve insufficiency, aortic dissection, and severe aortoilliac occlusive disease. Relative contraindications are prosthetic vascular aortic grafts, aortic aneurysm, and aortofemoral grafts. The IABP therapy requires anticoagulation with Heparin.

However, due to the location of an IABP in descending thoracic aorta and access through femoral artery, IABP can only be used for short durations (less than 14 days) [33, 34]. IABP requires patient to remain supine, patient cannot be discharged, and with prolonged IABP support (>20 days), there is significant increase in vascular complications, infections, and bleeding [34]. Recent advances in IABP technology include sheathless insertion technique, smaller balloon catheter sizes, and fiber-optic pressure sensors. The sheathless insertion technique and the removal of a fluid-filled pressure sensor (fiber-optic) improve distal limb perfusion by reducing the IABP catheter outer diameter lumen.

Given the above limitations of temporary percutaneous IABP and the proven benefits of counterpulsation therapy, a number of new chronic counterpulsation devices are being developed, including Sunshine Heart (C-Pulse) [35], Kantrowitz CardioVAD™ (KCV) [36], and others. All these devices reduce ventricular work and improve systemic and coronary artery perfusion, have less invasive implantation system, and are anticipated to be used chronically for advanced heart failure.

Implantable Counterpulsation Devices

The Kantrowitz CardioVAD™ (KCV) (LVAD Technology, Detroit, MI)

KCV is an implantable long-term aortic counterpulsation partial support device designed to provide chronic mechanical assistance. It is an electrically powered, pneumatically driven counterpulsation circulatory assist device. It provides diastolic augmentation and systolic unloading to the failing heart. The pumping chamber is surgically implanted in the descending thoracic aorta with the patient on cardiopulmonary bypass. KCV system consists of a 60-cc pumping chamber, a percutaneous access device (PAD), and an external controller. Its physiologic function is similar to that of the intra-aortic balloon pump (IABP). It has been reported that there is documented hemodynamic and functional improvement in patients with heart failure [36]. It is a nonobligatory device and can be turned on/off as needed without increasing risk of thromboembolism and does not require any anticoagulation. It depends upon native heart activity to function and cannot be placed in patients with severe biventricular dysfunction and uncontrolled tachyarrhythmias [36].

Abiomed (Danvers, MA) and SCR (Louisville, KY)

The Symphony device (ClinicalTrials.gov identifier: NCT01543022) is developed for superficial implantation via infraclavicular incision without the need to enter chest. The Symphony device is a 30-ml stroke volume polyurethane-lined pumping chamber, which is designed to fit comfortably in a pacemaker-like pocket on the right side of a patient [37, 38]. The pumping chamber is implanted into a pocket below the pectoralis muscle on the anterior chest and attached to the graft. The pumping chamber is connected to the systemic circulation by a short vascular graft anastomosed to the subclavian artery using a simple surgical procedure. The driveline is tunneled out through the skin and attached to the drive console. During systole, the driver evacuates air from the pumping chamber, thus removing blood from the circulation and reducing cardiac work. During diastole, the Symphony ejects the blood into the circulation providing diastolic augmentation and improving coronary perfusion. Symphony filling and ejection are triggered by the patient's ECG. Preclinical studies have demonstrated equivalent or better metabolic and

hemodynamic benefits compared to IABP [37, 38]. Symphony device is indicated in patients with NYHA class IIIB and IV heart failure with chronic angina or recovering from acute myocardial infarction (AMI). Contraindications include end-stage heart failure, aortic insufficiency, severe hypertension, infection, severe vascular disease, and small or obstructed axillary or brachiocephalic arteries. The Symphony requires surface surgical implantation (equivalent to ICD pocket and vascular anastomosis) with an anticoagulation regimen of initial heparin in the immediate postoperative period which transitions to chronic warfarin and antiplatelet therapy with Plavix.

Extra-aortic Balloon Counterpulsation, C-Pulse Device

C-Pulse (Sunshine Heart Inc., Eden Prairie, MN) is a mechanical, implantable, extra-aortic counterpulsation system [39]. C-Pulse is designed to provide permanent, long-term, continuous or on-demand partial circulatory support for Class III and ambulatory Class IV HF patients. C-Pulse is a nonblood-contacting counterpulsation using an inflatable cuff around the ascending aorta, extra-aortic balloon counterpulsation (EAB) device.

The C-Pulse (Sunshine Heart Inc., Eden Prairie, MN) [40] heart assist system includes a nonblood-contacting, ECG-gated, pneumatically driven, implantable cuff; a sensing lead that transmits electrical signals from the heart to the controller; and an extracorporeal wearable battery-powered or mobile AC-powered controller/drive unit [40]. The C-Pulse cuff consists of a polyurethane balloon and polyester wrap designed to conform to the ascending aorta (Fig. 1). The device is implanted through a median sternotomy [40]. The ascending aorta is circumferentially mobilized up to the brachiocephalic artery and the C-Pulse pneumatic polyurethane cuff is wrapped around the patient's ascending aorta just above the heart with no aortic perforation and no contact to the aortic blood. The cuff is linked by an air tube. A bipolar epicardial ECG-sensing lead is attached to the right ventricular outflow tract that transmits electrical signals from the heart to the controller. The sense lead and air tube passes subcutaneously through the abdominal wall and is linked to the controller/drive unit, which pumps air into the balloon, inflating and deflating in time with the heart's pumping cycle. The extracorporeal wearable controller/drive unit is programmable, and adjustments can be made in both inflation volume and the rate of inflation/deflation. The cuff inflates inwardly causing a "thumb-printing" deflection of the outer curvature of the ascending aorta (Fig. 1). Approximately 20–30 ml of ascending aortic blood volume can be displaced per beat, depending on the cuff size (small, medium, or large) and aortic diameter. The cuff accommodates a range of ascending aortic diameters (28 to 40 mm). Timing of the balloon inflation occurs at the dicrotic notch of the aortic blood pressure waveform, which represents closure of the aortic valve; and deflation occurs on the R wave on the ECG, which is before the aortic valve opens and ventricle ejects [40].

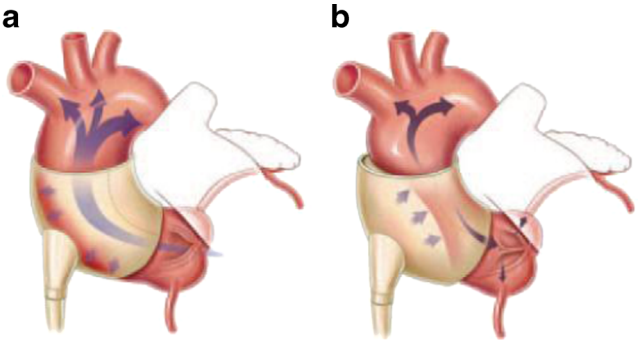

Fig. 1 Scheme of the extra-aortic balloon wrapped around the ascending aorta (**a** deflated, **b** inflated), showing "thumb printing" effect on the greater curve of the ascending aorta (reprinted from Legget et al. [35], with permission from Wolters Kluwer Health)

Studies on Extra-aortic Balloon Counterpulsation, C-Pulse Device

In 2005, Davies et al. compared the circulatory effects of counterpulsation using the EAB with IABP in an acute pig model [41]. This study compared the effects of extra-aortic balloon counterpulsation with a balloon volume of 17 ml secured around the ascending aorta to a standard IABP with a balloon volume of 25 ml positioned in the descending aorta. In this study, authors measured arterial and central venous pressures, flow in the coronary circulation and descending thoracic aorta at baseline and after an EAB or an IABP using 1:1 (one inflation every heart beat) and 1:2 (one inflation every second heart beat) counterpulsation modes. Baseline data was compared to EAB and IAB data in 1:1 mode. Assisted beat data compared to unassisted beat data was also analyzed in 1:2 mode. This study reported that both devices augmented peak diastolic arterial pressure and decreased afterload. EAB counterpulsation increased diastolic coronary flow in both the 1:1 mode by 69 % ($P<0.05$) and in the 1:2 mode by 63 % (assisted versus unassisted beat, $P<0.05$). The IAB significantly increased diastolic coronary flow only in the 1:2 mode by 28 % $P<0.01$). Both devices augmented total coronary flow and some augmentation of aortic flow was observed. This study showed comparable hemodynamic effects of EAB and IABP (Fig. 2.) and suggested that the EAB could be used as a nonblood-contacting heart assist device in patients suffering from moderate to severe heart failure.

The study by Davies et al. leads to a feasibility study of EAB in humans [35]. The aim of this feasibility study by Legget et al. was to determine the safety and performance of EAB in six patients with normal ventricular function undergoing first time

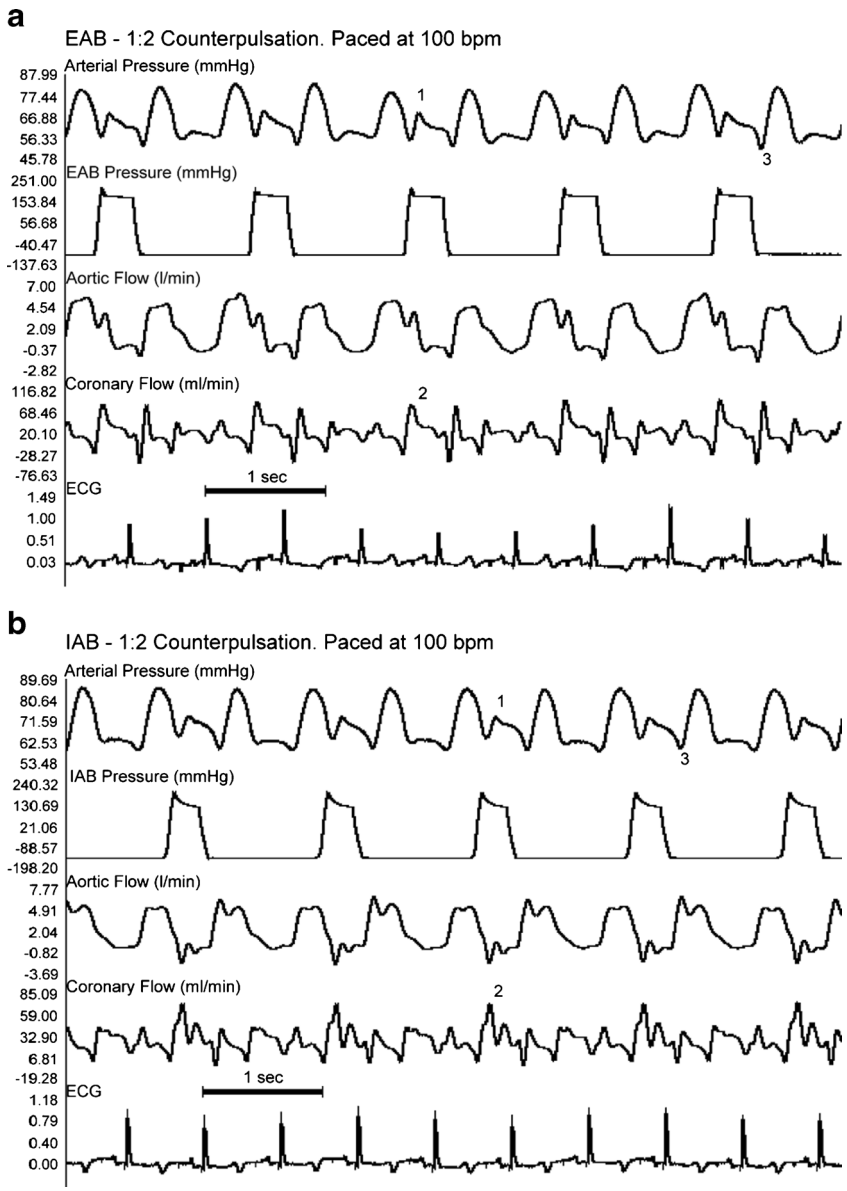

Fig. 2 Arterial pressure, EAB pressure or IAB pressure, descending aortic flow, coronary flow, and ECG recording during operation of EAB and IAB in 1:2 counterpulsation mode—heart rate paced at 100 bpm. An illustration of augmentation of diastolic pressure, aortic flow, and coronary blood flow by both devices. **a** EAB—1:2 counterpulsation. *Point 1* indicates augmentation of arterial pressure and *point 2* indicates the change in coronary blood flow during counterpulsation in diastole. *Point 3* indicates a reduction in preload due to deflation of the EAB. **b** IAB—1:2 counterpulsation. Point 1 indicates augmentation of arterial pressure and point 2 indicates the change in coronary blood flow during counterpulsation in diastole (reprinted from Davies et al. [41])

off-pump coronary bypass surgery via sternotomy. EAB was secured around the ascending aorta and attached to a standard counterpulsation console. At baseline and with 1:2 (one inflation every second heartbeat) and 1:1 (one inflation every heartbeat) augmentation, hemodynamic and echocardiographic parameters of ventricular function and coronary flow were measured. High-intensity transient signals were measured using transcutaneous Doppler over the right common carotid artery. Systolic, diastolic, and mean arterial or central venous pressures were comparable at baseline and during counterpulsation; heart rate tended to be lower during 1:1 counterpulsation than at baseline (72 ±1.1 versus 76±1.2, P=0.055). There was no significant change in heart rate or blood pressure, and no increase in high-intensity transient signals with EAB. There was a 67 % increase in diastolic coronary blood flow (mean left-main diastolic velocity time integral 15.3 cm unassisted versus 25.1 cm assisted, P<0.05). Transesophageal echocardiography showed a 6 % reduction in end-diastolic area (P=NS), a 16 % reduction in end-systolic area (P<0.01), a 31 % reduction in left ventricular wall stress (P<0.05), and a 13 % improvement in fractional area change (P<0.005) with EAB during 1:1 mode compared to baseline. The EAB counterpulsation demonstrated a 26 % increase in velocity of fiber shortening (P<0.005). There was a significant inverse correlation between wall stress and fiber shortening with EAB device in 1:1 augmentation mode (Fig. 3.), indicating that EAB improves ventricular function by decreasing left ventricular afterload. This study concluded that EAB counterpulsation augments coronary flow and reduces left ventricular afterload, and there were no complications observed during the short-term use of EAB [35].

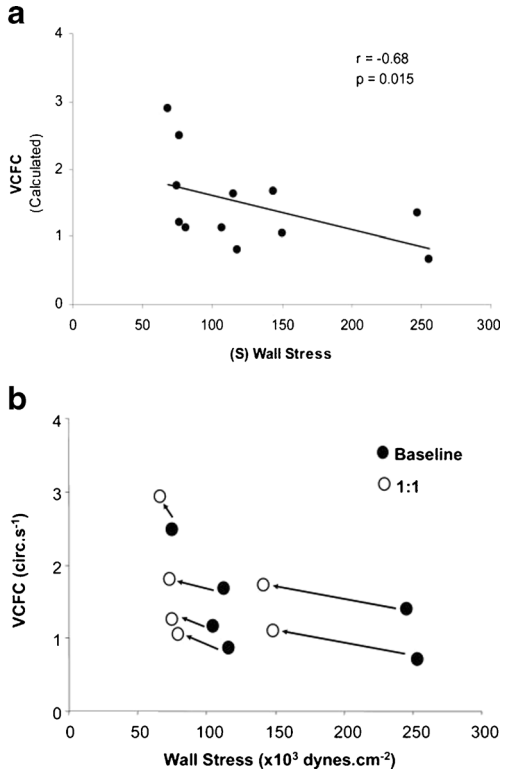

Fig. 3 Plots of wall stress versus rate-corrected velocity of fiber shortening. **a** All nonaugmented and augmented beats showing the inverse relationship between wall stress and fiber shortening. **b** The effect of counterpulsation in each patient, demonstrating the consistent reduction in afterload and increase in contractility in each individual (reprinted from Legget et al.[35], with permission from Wolters Kluwer Health)

Subsequently, Hayward CS et al. described a first-in-human experience with C-Pulse to explore the device feasibility, hemodynamic effects, and safety in five severe heart failure (NYHA class III or IV symptoms) patients, aged 54 to 73 years [40]. All patients improved by one NYHA class, and improvements in invasive hemodynamics were documented in three patients. However, 60 % patients developed infectious complications. One patient was successfully transplanted at 1 month. One patient remained hemodynamically improved on the device at 6 months but suffered infectious complications [40].

Currently, a prospective, multicenter, randomized trial to assess the safety and efficacy of C-Pulse (A Heart Assist Device Pivotal IDE study) (ClinicalTrials.gov identifier: NCT01740596) in patients with Stage C and NYHA class III or ambulatory class IV heart failure is in progress. The estimated enrolment in this study is 388 subjects and patients will be randomized to C-Pulse arm or control arm, and estimated completion of study is in 2017. The purpose of the study is to determine whether the use of the C-Pulse as a treatment for patients in moderate to severe heart failure has demonstrated safety and efficacy, such that the C-Pulse system merits Food and Drug Administration approval to market the device in the USA. The primary outcome of the study is to evaluate the efficacy of the C-Pulse therapy by measuring freedom from worsening heart failure resulting in hospitalization, left ventricular assist device (LVAD) implantation, cardiac transplantation, or death as compared to optimal medical therapy (OMT). The primary safety endpoint is all serious procedure and device-related adverse events.

Hemodynamic Effects of Extra-aortic Balloon Counterpulsation Device

The EAB pump causes aortic blood flow augmentation during inflation phase with increased coronary blood flow during ventricular diastole and ventricular unloading during the deflation phase immediately before the ventricular sytole. Presystolic ventricular unloading leads to reduced end systolic wall stress, left ventricular pressure and volume, and myocardial oxygen consumption which helps with improved cardiac output and myocardial contractility [41]. Afterload reduction causes a decrease in left ventricular end-systolic and end-diastolic volume and pressure, with further reduction in systolic wall tension and oxygen consumption. In brief, EAB counterpulsation pump increases myocardial contractility and cardiac output as a consequence of improved diastolic coronary blood flow and presystolic afterload reduction.

Candidates for Extra-aortic Balloon Counterpulsation Device

C-Pulse system is an implantable, nonblood contacting, nonobligatory, heart assist device. Based on the studies reported above, patient with LEVF <35 % with ACC/AHA stage C and NYHA class III or ambulatory Class IV symptoms despite optimum medical and device-based therapy can be considered candidates for C-Pulse device. Ascending aortic outside diameter should be greater than 28 mm and less than 42 mm. Prior to establishing candidacy, appropriate investigative studies (echocardiography, CT chest, etc.) are performed to exclude any comorbidities that can preclude patients from getting EAB device. Appropriate timing of candidate selection and implantation is important; once patients develop nonambulatory NYHA class IV heart failure, it might be too late for EAB counterpulsation device. Contraindications include any degree of ascending aortic calcification, ascending aortocoronary bypass grafts, history of aortic dissection, Marfan's disease or other connective tissue disorder or repaired aortic coarctation or ascending aortic composite graft or root replacement, inotropic dependent patients, ACC/AHA stage D heart failure or nonambulatory NYHA class IV patients, moderate to severe aortic insufficiency

(≥2+), prior LVAD or heart transplant, and high degree of carotid stenosis. It can be acceptable if patients have mild degree of aortic atheroma (intimal thickening, grade I) and mild aortic regurgitation. It is possible that approximately 60–70 % of the heart failure patients screened for C-Pulse device might qualify for the device. There is no published data yet to exactly predict this number.

Pros and Cons of Extra-aortic Balloon Counterpulsation, C-Pulse

C-Pulse is an easily implantable device that is wrapped around the ascending aorta and pneumatically driven by an external console. Advantages of this device are that it does not require anticoagulation as it is nonblood contacting device, thereby reducing the risk of embolism or hemorrhage. C-Pulse system may be implanted via a small pacemaker like incision through the ribs (minithoracotomy) and sternum (ministernotomy) or through a traditional full sternotomy (Sunshine Heart Inc.). The C-Pulse is designed to be implanted without the need for cardiopulmonary bypass or extensive dissection, and is able to be activated immediately and allowing the patient to ambulate. There are no clinically significant embolic events, nor postoperative neurologic complications related to C-Pulse device. Since C-Pulse device is a nonobligatory counterpulsation device in moderate to severe heart failure patients, it can be disconnected for few hours. Diastolic counterpulsation is more effective at the level of ascending aorta than at the descending aorta [42]. The "thumb print" deflection by the C-pulse cuff on the anterior ascending aortic wall reduces strain and produces no mechanical injury to the endothelium and hence less risk of possible trauma to the aortic wall unlike intra-aortic balloon pump in which there is risk for mechanical injury to the endothelium due to placement in the lumen of aorta [41].

Extra-aortic counterpulsation does have some limitations. C -Pulse is contraindicated in patients with prior heart surgeries, severe atherosclerosis of the ascending aorta, significant vascular disease, aortic insufficiency, and presence of patent coronary artery bypass grafts. The C-Pulse requires surgical implantation (sternotomy). Device or drive-line infection remains the most common adverse event in the C-Pulse device [40]. The long-term effect of the C-Pulse device on the aortic wall is not established. In an acute pig model, C-Pulse cuff compression showed only mild hemorrhagic inflammatory changes of the adventitia and normal media and intima of the ascending aorta [41]. In a human study, Legget et al. [35] reported absence of any acute adverse effects due to external aortic compression of the C-Pulse cuff. The degree of improvement in cardiac output may be insufficient in patients with New York Heart Association class IV heart failure.

Conclusion

Despite major advances in the medical and device-related therapy including chronic resynchronization therapy (CRT) for management of HF, significant number of patients eventually require advanced cardiac therapy including mechanical circulatory support or heart transplant. Heart transplant is a gold standard for end-stage heart failure, but is limited by the donor heart shortage. Although mechanical circulatory support devices including left ventricular assist devices (LVAD) have been effective as a bridge to transplant and destination therapy, there have been complications. Patients with class III and ambulatory class IV heart failure are typically unable to engage in normal activities, compromising their quality of life creating a need for effective therapy with long-term, partial or complete mechanical circulatory support that can improve quality of life, functional capacity, and survival of these patients. Annually, more than 150,000 patients worldwide receive counterpulsation therapy for various indications including cardiogenic shock or severe left ventricular dysfunction, and many thousands of lives are saved each year.

It is important to point out that a counterpulsation device is intended to augment native heart function and is fundamentally different from total artificial hearts, left ventricular assist devices, and heart transplants which are meant to be a total replacement or an alternative to the native heart. Thus, the counterpulsation device is considered nonobligatory and not life-supporting.

The current need is for a counterpulsation device or method that is effective enough to make its application appealing as a long-term implant to a large number of patients and physicians. It must be simple and safe, with a straightforward implant procedure, and with long-term measurable patient benefits. Further, it would be advantageous for the counterpulsation device to be smaller, easier to insert, allow for ambulation and disconnection, and not be in the bloodstream. Such a device may be more readily adopted by a wider group of cardiologists and surgeons, and be suitable for a wider group of patients in NYHA class III to ambulatory class IV heart failure.

Extra-aortic counterpulsation, C-Pulse device for the management of advanced heart failure is a novel management approach for patients with moderate to severe heart failure. The long-term effect of extra-aortic counterpulsation on the human aortic wall is not established. The degree of improvement in cardiac output may be insufficient in patients with New York Heart Association class IV heart failure. Its role as a destination therapy device, bridge to transplantation, or recovery will be studied in future trials. Although feasibility of this device is demonstrated by the pilot study, safety and efficacy is being tested in a multicenter US study with larger cohort and longer follow-up. The success of the proposed systems on quality of life and activities of daily life are currently under

evaluation in prospective clinical trials. In summary, devices like C-Pulse could be considered early on in the treatment of advanced heart failure and this may potentially reduce the number of patients requiring advanced cardiac therapy like heart transplantation or left ventricular assist device.

Clinical Relevance

This article reviews different types of aortic counterpulsation devices that can be considered for management of patients with heart failure who are symptomatic despite optimum medical and device-based therapy. It seems tempting to suggest that devices like C-Pulse should be considered early on in the treatment of moderate to severe heart failure and this may potentially reduce the number of patients progressing towards cardiac replacement therapy with transplantation or more invasive left ventricular assist devices.

Conflict of Interest I am an advanced heart failure cardiologist and manage patients with different types of mechanical circulatory support devices.

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