

Continuous internal counterpulsation as a bridge to recovery in acute and chronic heart failure

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Abstract

Cardiac recovery from cardiogenic shock (CS) and end-stage chronic heart failure (HF) remains an

often insurmountable therapeutic challenge. The counterpulsation technique exerts numerous beneficial effects on systemic hemodynamics and left ventricular mechanoenergetics, rendering it attractive for promoting myocardial recovery in both acute and chronic HF. Although a recent clinical trial has questioned the clinical effectiveness of short-term hemodynamic support with intra-aortic balloon pump (IABP, the main representative of the counterpulsation technique) in CS complicating myocardial infarction, the issue remains open to further investigation. Moreover, preliminary data suggest that long-term IABP support in patients with end-stage HF is safe and may mediate recovery of left- or/and right-sided cardiac function, facilitating long-term weaning from mechanical support or enabling the application of other permanent, life-saving solutions. The potential of long-term counterpulsation could possibly be enhanced by implementation of novel, fully implantable counterpulsation devices.

Key words: Counterpulsation; Recovery; Intra-aortic balloon pump; Heart failure; Cardiac remodeling; Reverse remodeling

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Core tip: The counterpulsation technique induces beneficial effects on systemic hemodynamics and left ventricular mechanoenergetics. In this manner, it may facilitate myocardial recovery in acute and chronic heart failure (HF). The intra-aortic balloon pump (IABP) remains the main representative of the counterpulsation technique. Although recent data have questioned the effectiveness of short-term hemodynamic support with IABP in cardiogenic shock complicating myocardial infarction, the issue remains open to further investigation. Preliminary data suggest that long-term IABP support in patients with end-stage HF is safe and may mediate recovery of left- or/and right-sided cardiac function. Novel, fully implantable counterpulsation devices, which enable long-term counterpulsation, are described in this manuscript.

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INTRODUCTION

Heart failure (HF) is a true pandemic, responsible for 5% of hospitalizations globally^[1]. HF, in its most severe forms, can manifest as two lethal clinical entities: (1) acute HF with cardiogenic shock (CS), with post-myocardial infarction (MI) CS mortality rates approaching 50%^[2]; and (2) end-stage chronic HF, with 1-year mortality of approximately 80% (worse than most types of cancer)^[3]. Despite significant advances in development of drug and device-based therapies, cardiac recovery from these two destructive forms of HF remains an often insurmountable therapeutic challenge. As we will see, the meaning of "recovery" and the remedial goal differ between acute and chronic HF.

RECOVERY IN ACUTE HF

Any cause of acute, severe left ventricular (LV) or right ventricular (RV) dysfunction may lead to CS. The most important cause of CS is severe LV dysfunction following a large acute MI^[4]. Despite the fact that the vast majority of these patients suffer from acute ST elevation MI, CS also occurs in approximately 2.5% of non-ST elevation MIs^[5]. Moreover, mechanical complications, such as ventricular septal rupture, acute severe mitral regurgitation and contained free wall rupture may lead to CS and must be suspected in patients with CS complicating non-anterior MI^[6]. Other less frequent causes include acute myopericarditis, isolated RV failure, Takotsubo cardiomyopathy, hypertrophic cardiomyopathy, acute valvular regurgitation (typically caused by endocarditis or chordal rupture), cardiac tamponade, excess beta or calcium channel blockade, dilated cardiomyopathy, peri-operative low output syndrome, and CS associated with cardiac catheterization complications^[7].

The meaning of "recovery" in the setting of acute HF and, thus, the treatment goal, is hemodynamic support during acute cardiac decompensation, including measures that allow the injured myocardium to recuperate and overcome the need for acute support^[8]. The therapeutic means to achieve this goal varies significantly depending on the cause of CS.

RECOVERY IN CHRONIC HF

Cardiac remodeling is a deleterious component of HF progression associated with poor prognosis^[9,10]. It

comprises molecular, cellular and interstitial changes, manifested clinically as changes in size, shape and function of the heart following cardiac overload or injury^[11]. Adverse changes at the organ level include alteration of LV geometry (less elliptical and more spherical LV shape)^[12,13], wall thinning^[14], LV dilatation (increase in LV end diastolic and end-systolic volumes) and decline in LV ejection fraction (EF)^[15]. Cellular and molecular changes include myocyte hypertrophy, loss of myocytes due to apoptosis^[16] or necrosis^[17], fibroblast proliferation^[18] and fibrosis^[19].

The therapeutic goal in chronic HF is to improve symptoms and life expectancy. That can be achieved by prevention of the adverse components of LV remodeling and reversal of already completed LV remodeling. Today we know that any level of reverse LV remodeling is associated with an analogous increase of survival in the patients suffering from HF^[20].

The term "bridge to transplantation" (BTT) for patients with chronic HF by use of mechanical assistance with an LVAD was introduced by the cardiac surgeons who were surprised to find a normal or almost normal recipient heart at the time of transplantation. Subsequently, "recovery" in chronic HF refers to sustained reversal of the aforementioned alterations, a process known as reverse remodeling with near normalization of LV function in patients on an LVAD as a BTT followed by a "safe" LVAD explantation. So, the definition of LV recovery presupposes that the patient can tolerate a large cardiac operation for LVAD explantation and remain clinically and hemodynamically stable thereafter.

This presupposition does not apply to patients assisted by a device easily explantable, like the percutaneous intra-aortic balloon pump (IABP). An example is one of our patient with chronic HF due to IDC complicated by CS requiring mechanical assistance by IABP. After 3 mo of continuous IABP support, he was successfully weaned from mechanical assistance and 5 years later he remains asymptomatic. He did not have to be subjected to a major cardiac surgical procedure to remove his bridging device, which may be the reason he did so well.

The patient mentioned above is now a 25-year-old man. He had had a history of progressively worsening HF when he presented at age 21 with CS, an LVEF of 17%, a BNP of 2800 pg/dL and a myocardial biopsy showed dilated cardiomyopathy. The patient was placed on intravenous infusion of inotropes and furosemide but further deteriorated. The patient was placed on IABP mechanical assistance and, although he was offered biventricular mechanical assistance (BiVAD), he preferred protracted IABP assistance. Initially he did not tolerate any anti-remodeling drug treatment. At the end of the 3 mo period on IABP his clinical and hemodynamic improvement permitted weaning from the IABP with a LVEF = 25% and a BNP = 207 pg/dL and 5 years later he remains asymptomatic with a LVEF = 30%, and VO_{2peak} =

Table 1 Criteria of sufficiency of recovery with easily-explantable counterpulsation devices and continuous flow left ventricular assist devices

Counterpulsation devices	
EF	↑ 5%
BNP	< 500 pg/mL
Continuous flow LVADs	
LVEDD	< 60 mm
LV end-systolic diameter	< 50 mm
EF	> 45%
LV end-diastolic pressure/PCWP	< 12 mmHg
Cardiac Index (resting)	> 2.8 L/min per square

EF: Ejection fraction; LV: Left ventricular; LVAD: Left ventricular assist device; PCWP: Pulmonary capillary wedge pressure; LVEDD: Left ventricular end-diastolic dimension.

29 mL/kg per minute. Thus, recovery no longer must presume a patient's ability to withstand an arduous LVAD explantation procedure.

In our experience, in patients who undergo mechanical assistance by a device that is easy and safe to explant (like the IABP), myocardial recovery can be considered adequate for termination of mechanical assistance when all of the following criteria are met (Table 1): (1) absolute increase in LVEF \geq 5% (measured by echo at the end of a 24-h reduced (1/4) pump function test) compared to baseline; and (2) BNP \leq 500 pg/mL (measured at the end of a 24-h reduced pump function test).

However, for the continuous flow LVADs which require a large and high risk operation for explantation, the recovery can only be considered adequate if the very demanding established criteria are met (Table 1): LVEDD < 60 mm, LV end-systolic diameter < 50 mm, and EF > 45%; LV end-diastolic pressure or PCWP < 12 mmHg, resting cardiac index > 2.8 L/min per square; and maximal oxygen consumption with exercise (mVO_2) > 16 mL/kg per square^[21].

COUNTERPULSATION

Counterpulsation was first conceived by Kantrowitz^[22] in the early 1950s, who managed to augment coronary blood flow by delaying arterial pulse in canine experimental models. In 1962, Mouloupoulos *et al.*^[23] developed the IABP, which was applied in human subjects 6 years later for the management of post-MI CS^[24]. Nowadays, IABP remains the single most widely-used short-term circulatory assist device in acute cardiac decompensation^[25]. However, the application of long-term IABP counterpulsation in the setting of chronic HF remains limited; the potential of long-term counterpulsation could possibly be enhanced by implementation of novel, fully implantable counterpulsation devices. These include the para-aortic counterpulsation device (PACD)^[26], representing the initial version of the pressure unloading LVAD (PULVAD) described below, the Kantrowitz CardioVAD (KCV)^[27], the

Table 2 Effects of counterpulsation on systemic hemodynamics and left ventricular mechanoenergetics

Decrease
Systolic aortic pressure
End-diastolic aortic pressure
LV systolic wall stress (afterload)
Myocardial oxygen/LV energy consumption
End-diastolic ventricular volume (preload)
Mean pulmonary capillary wedge pressure
Increase
Diastolic aortic pressure (augmentation)
LV mechanical performance (ejection fraction, stroke volume, cardiac output)
LV contractility and active relaxation (in the reperfused failing heart)
Coronary blood flow (post-ischemia, when coronary autoregulation is impaired and flow is pressure-dependent) ^[33]
Cerebral, renal, mesenteric and pulmonary blood flow
Mean arterial pressure (in patients with shock)

LV: Left ventricular.

Symphony counterpulsation device^[28,29] and C-pulse^[30].

How does counterpulsation promote recovery? Insights from experimental studies

Several experimental studies have demonstrated that counterpulsation exerts numerous beneficial effects on systemic hemodynamics and LV mechanoenergetics (Table 2), rendering it attractive for induction of recovery in both acute and chronic HF^[31-35]. In brief, counterpulsation unloads the LV (decreases LV afterload), decreases LV energy consumption and concurrently improves LV mechanical performance (EF, stroke volume, cardiac output). In addition, counterpulsation improves LV contractility and active relaxation of the reperfused failing heart, possibly through augmentation of coronary blood flow^[34]. However, it should be highlighted that the magnitude of the aforementioned beneficial effects varies widely, depending on several factors, such as the volume of counter-pulsated blood, the position of the device in the aorta, aortic compliance, heart rate/rhythm and systemic pressures and resistances^[36,37].

Counterpulsation in acute HF

IABP remains the most widely-used circulatory assist device in patients with CS complicating acute MI^[38]. Until 2012 IABP support was considered to be a class I treatment in the setting of post-MI CS^[39,40]. However, the clinical effectiveness of short-term IABP support in patients with CS post-MI has recently been called into question, mainly on the basis of the results of the IABP-SHOCK II trial, the largest randomized IABP trial to-date, which demonstrated no benefit of IABP support on either 30-d or 1-year all-cause mortality^[41,42]. Criticism of IABP SHOCK II study design and methodology have arisen^[43,44], mainly focusing on: (1) the late timing of IABP insertion (once revascularization had been completed), which could undermine the effectiveness of IABP support^[45];

and (2) the lower than expected mortality rate, which raises concerns about the severity of CS in the enrolled patient population. The interpretation of the trial's results is also complicated by methodological difficulties inherent to the design and execution of randomized trials in gravely ill patients with CS (e.g., need for rescue LVAD implantation, need for rescue IABP insertion in patients randomized to the non-IABP group). Overall 17% of the patients randomized to conventional treatment received mechanical assistance by IABP or LVAD. Furthermore, in everyday clinical practice only 22% of patients with post-MI CS undergo IABP assistance^[46], most likely only those with the most severe CS. So, the strong message of that study is that not all patients with post-MI CS need mechanical assistance by the IABP. Nevertheless, the lack of hard evidence regarding clinical effectiveness of IABP support resulted in reconsideration of American and European guidelines, which have downgraded the routine use of IABP support in post-MI CS to class II a and III treatments, respectively^[47,48]. It should be noted, though, that the absence of evidence should not necessarily be interpreted as evidence of absence of clinical effectiveness; given that mortality in CS remains unacceptably high^[41,42], new, appropriately-powered and carefully-designed, clinical studies are needed to clarify the role of IABP support in promoting cardiac recovery in this setting.

Counterpulsation in chronic HF

Patients with advanced chronic HF face a grim prognosis, with 1-year mortality rates approaching 80%. These vulnerable patients have limited access to donor hearts for cardiac transplantation and chronic mechanical circulatory support is often used as a last resort. Intriguingly, clinical observation shows that chronic mechanical unloading can occasionally reverse the complex process of myocardial remodeling to the point that a subset of patients can be weaned from the device after restoration of basic cardiac function^[9]. Yet, myocardial recovery induced by conventional left ventricular assist devices (LVADs) is disappointingly rare^[49]. A prominent reason for the low rate of recovery is the physiologic mechanism through which conventional LVADs provide salutary hemodynamic effects. These LVADs bypass the LV and unload the failing LV independently of its systolic reserve. As a consequence, the LV is rendered ineffective to generate adequate pressure to surpass the mean arterial pressure generated by the LVAD itself. Thus, clinically available LVADs assist the LV at the cost of severely suppressing native LV function, rendering the LV incapable of sustaining its conditioning and therefore compromising recovery. In addition, pulsatility of flow seems to play an important role for cardiac reverse remodeling; recovery in patients with IDC may be as low as 3% for currently-used continuous flow LVADs, yet 25% with older-generation pulsatile alternatives^[50].

Chronic counterpulsation can overcome the aforementioned limitations of conventional LVADs and therefore appears attractive, at least from a theoretical standpoint, for promoting cardiac reverse remodeling and recovery, as it: (1) unloads the LV and decreases its energy consumption; (2) utilizes the LV systolic reserve; (3) enhances native LV functional performance (unlike clinically-used LVADs which suppress it); (4) retains pulsatility of flow and; and (5) preserves heart integrity.

The aforementioned reasons theoretically rationalize the expansion of the indications of counterpulsation implementation, beyond that of short-term hemodynamic stabilization. New potential indications could include use of long-term counterpulsation as a bridge to decision making (cardiac surgery, LV assist device implantation or transplantation), bridge to transplantation and bridge to myocardial recovery. However, long-term IABP support is not risk-free; major complications include acute limb ischemia, severe bleeding, embolic events, infection and sepsis^[51]. However, sheathless implantation technique in combination with thinner catheters application significantly minimized the rate of complications from 20.7% for 12 French catheters to 8.4% for 9.5 French catheters. Though more recent data are not available, it is reasonable to assume that the contemporary complication rate with the use of 6 and 7 French IABP catheters is significantly lower. In addition, several recent studies (described later in this review) have demonstrated that long-term IABP support appears to be associated with a favorable safety profile^[52-58]. The potential of long-term counterpulsation could possibly be enhanced by implementation of novel, fully implantable counterpulsation devices (described later) and mobilization of the patient.

IABP FOR CHRONIC LV HF

Converging data suggest safety and possibly efficacy of long-term circulatory support with IABP in patients with end-stage LV HF. In the study by Gjesdal *et al.*^[52], 32 patients were successfully bridged to transplantation *via* IABP, after a mean IABP support of 21 d (range: 3-66 d), with few IABP-related complications. Importantly, mortality and hemodynamic indices at 1 year post-transplantation were similar in patients bridged to transplantation *via* IABP and in a control group, comprising 135 electively transplanted patients not needing circulatory support in the pre-transplant period. In the study by Cochran *et al.*^[53], 4 patients with end-stage ischemic HF were successfully bridged to transplantation *via* IABP, after a mean duration of IABP support of 31 d (range: 12-70 d). Long-term IABP resulted in a 10 to 50-fold decrease in cost compared to the cost associated with the use of LV assist devices as a bridge to transplantation. In the study by Russo *et al.*^[54], 14/17 patients with end-stage HF were successfully bridged

Table 3 Potential roles of long-term intra-aortic balloon pump support in chronic heart failure

Improves patients' clinical status and their hemodynamic indices, rendering them suitable candidates for heart transplantation (BTT)
Improves RV functionality and peripheral organ function, increasing the candidacy rates of patients who are ineligible for additional mechanical interventions (BTC)
Enhances native LV functional performance and unloads LV while maintaining its integrity, promoting reverse remodeling and cardiac recovery (BTR)

BTT: Bridge to transplantation; LV: Left ventricular; RV: Right ventricular.

to transplantation and 3/3 patients were successfully bridged to recovery *via* IABP after a mean support of 17 d (range: 3-48 d). In the study by Estep *et al*^[55], 50 patients received IABP support for a median of 18 d (range: 4-152 d) as a bridge to transplantation. Prolonged IABP support was associated with remarkable improvements in mean pulmonary artery pressure (MPAP) as well as in creatinine and total bilirubin concentrations. Forty-two patients (84%) were successfully bridged to transplantation and 38 of them (90%) were alive 90 d after transplantation. Additionally, in the study by Terrovitis *et al*^[56], 7 patients with end-stage HF (INTERMACS 2) due to idiopathic dilated cardiomyopathy underwent long-term circulatory support with IABP. One patient was successfully bridged to cardiac surgery, 4 patients were successfully bridged to assist device implantation, while the remaining 2 patients were successfully bridged to recovery and remained asymptomatic (NYHA class I) for at least 6 and 20 mo post-IABP removal^[56]. Finally, Tanaka *et al*^[57] investigated 88 patients with decompensated advanced HF who were implanted with IABP either as BTT and mechanical support ($n = 82$) or as bridge to recovery ($n = 6$). More than 90% of the patients succeeded the therapeutic goal with minimal rates of morbidity and mortality, while 3 out of 6 BTR patients experienced cardiac recovery.

IABP FOR CHRONIC RV HF

RV dysfunction is both a cause and an effect of HF progression, often leading to treatment dead-ends. On the one hand, patients with RV dysfunction are considered to be bad candidates for LVAD implantation^[59], as LVAD support aggravates pre-existing RV dysfunction through an increase in RV preload^[60]. On the other hand, the use of biventricular assist devices (often viewed as the only treatment option for these patients) is complicated and associated with poor long-term survival^[61]. We recently investigated the effects of long-term IABP support in a cohort of 15 patients suffering from biventricular end-stage HF (all classified as NYHA class IV, INTERMACS profiles 1 or 2), who were ineligible for any alternative LV interventional procedure^[58]. Long-term IABP support (median 72 d,

range: 13-115 d) resulted in substantial RV reverse remodeling, decreasing RV end-diastolic diameter and mean right atrial pressure. In addition, long-term IABP support increased cardiac index, increased RV stroke work index, and improved peripheral organ function. Clinical outcomes were encouraging, as 3 patients experienced complete clinical recovery and remained alive in NYHA class I at least 6 mo after IABP removal. Six patients exhibited partial clinical recovery, as long-term IABP support induced reversal of contraindications rendering them eligible for LVAD implantation. Four patients (all in INTERMACS profile 1) continued to deteriorate clinically and eventually died, while 1 patient died from septic shock on the 155th day of support and 1 from systemic inflammatory response syndrome on the 90th day. Putative mechanisms underlying the counterpulsation-induced recovery of RV function include an increase in RV myocardial blood flow and restoration of an optimal interventricular septal geometry, by relieving the septal shift induced by overload of the left ventricle. Regardless of the precise mechanism, these findings suggest that long-term counterpulsation may have a role in promoting recovery of the failing RV and could be used as a therapeutic strategy to increase the candidacy rates of patients who don't qualify for additional mechanical interventions.

The potential roles of long-term IABP support in chronic LV and RF HF are summarized in Table 3. Converging data suggest safety and efficacy of long-term IABP support as a bridge to transplantation or bridge to LVAD implantation. In addition, limited clinical data suggest that long-term IABP support may promote myocardial recovery. However, additional studies are warranted in order to clarify whether IABP-induced myocardial recovery can be consistently achieved or represents an anecdotal experience. The potential for myocardial recovery would undoubtedly be enhanced by prospective identification of patients who are more likely to undergo cardiac recovery^[62].

KCV FOR CHRONIC HF

KCV is a pneumatically-driven counterpulsation circulatory assist device, surgically implanted in the descending thoracic aorta by thoracotomy under cardiopulmonary bypass^[27]. The KCV system consists of a 60-cc pumping chamber (sutured to the descending aorta), a percutaneous access device (PAD, implanted in a subcutaneous pocket), and an external controller. With regard to clinical application, the device was implanted in 5 patients with end-stage HF refractory to pharmacological medical treatment, but responsive to IABP support. The first patient died intra-operatively due to technical complications, whereas the following 4 patients demonstrated improvements in cardiac index, pulmonary capillary wedge pressure,

right atrial pressure, and NYHA class.

C-PULSE FOR CHRONIC HF

C-Pulse is an implantable extra-aortic balloon (EAB) counterpulsation device, consisting of an inflatable cuff positioned around the ascending aorta^[63]. The polyurethane cuff is implanted through thoracotomy and is wrapped around the patient's ascending aorta without any contact with the aortic blood^[64]. The cuff is synchronized to inflate inwardly during the diastolic notch, producing a stroke volume between 20 and 30 mL, depending on the cuff size and the aortic diameter.

Hayward *et al.*^[63] investigated the feasibility and safety of C-Pulse support in 5 patients with advanced HF (NYHA class III or IV). All patients improved by 1 NYHA class, however, infectious complications were observed in 3/5 patients (with 2 patients suffering mediastinal infection necessitating device explantation). Recently, Abraham *et al.*^[64] performed a multicenter study to investigate the feasibility, safety and preliminary efficacy of C-Pulse support in 20 patients with advanced HF (NYHA class III or ambulatory class IV). No 30-d mortality was observed and no neurological events or myocardial infarctions were recorded during the 1 year of follow-up. However, one patient suffered a device-related death (due to mediastinal infection) and 40% of patients experienced drive line exit site infections. In terms of efficacy, C-Pulse support produced significant improvements in NYHA functional class, quality of life and 6-min walk distance. Currently, a prospective, multicenter, randomized trial investigating the safety and efficacy of C-Pulse support in moderate to severe HF is underway (NCT01740596); 388 patients will be randomized to undergo C-Pulse implantation of optimal medical treatment (1 year follow up)^[36]. The primary efficacy point of the trial is freedom from worsening HF resulting in hospitalization, LVAD implantation, cardiac transplantation or death during 1 year of follow-up.

THE SYMPHONY DEVICE FOR CHRONIC HF

The Symphony device (Symphony) is an implantable counterpulsation device designed to be implanted *via* a minimally-invasive superficial technique, without the need to open the thoracic cavity. Symphony comprises a valveless, single chamber 40-mL polyurethane-lined pumping sac, which is designed to fit in a pacemaker-like pocket on the right side of the thorax, in the subclavian fossa^[29]. The pumping sac is connected to the systemic circulation by a short vascular graft, which is anastomosed to the subclavian artery. The driveline is tunneled out through the skin and attached to the driving console.

An anatomical cadaver-fit study suggested that a 40-mL Symphony might not be suitable for a large

number of patients, including women and small-sized men and that a smaller-sized device (32 mL) should be examined^[29]. An experimental study in 8 calves with toxin-induced cardiomyopathy demonstrated that the 32 mL-Symphony device was superior to the 40 mL-IABP in decreasing LV myocardial oxygen consumption and increasing the ratio of diastolic coronary artery flow to left LV external work, and inferior to the IABP in decreasing aortic end-diastolic pressure. Giridharan *et al.*^[65] compared the effects of Symphony and IABP on aortic, carotid and coronary flows in a bovine experimental model of monensin-induced heart dysfunction. Compared to IABP, Symphony eliminated retrograde systolic blood flow (observed during IABP support) and increased total blood flow (despite producing less diastolic flow augmentation compared to IABP).

The first clinical application of Symphony was performed in a 64-year-old man with ischemic HF (NYHA III b)^[66]. Within 72 h of implantation, Symphony support increased cardiac index, and decreased right atrial pressure, pulmonary capillary wedge pressure and serum creatinine. However, following the patient's ambulation and increased activity, low flow to the pump and loss of right radial pulse were observed with cephalad movement of the right arm. This was attributed to compression of the subclavian artery due to device movement and the Symphony was explanted on the 10th postoperative day.

PULVAD

The PACD^[67,68], consists of a round valveless pumping chamber driven by an IABP console. The PACD is implanted in the thoracic cavity and is connected to the ascending aorta *via* a Dacron vascular graft. The PACD is superior to IABP in unloading the failing heart and increasing cardiac output^[69]. The PACD was implanted in 3 patients suffering from CS refractory to conventional treatment, including IABP; one patient died 4 h after the device implantation due to anesthesia-induced peripheral vasoparalysis, while the other two died due to septic shock 8 and 54 d after implantation, respectively^[26].

The PULVAD is the improved version of the PACD (Figure 1). It is smaller than PACD and can be driven by any conventional IABP console. In pigs weighing 80-100 kg and calves weighing approximately 100 kg it proved to be 3 times more effective than an IABP in reducing the systolic and end diastolic aortic pressure^[70,71].

The PULVAD'S ease of implantation (not requiring extracorporeal circulation), low cost of manufacture, wide availability of driving consoles and the fact that it provides only pressure unloading of the LV (which should prevent myocyte atrophy^[72,73] and cardiac fibrosis^[74], and promote myocardial recovery) make the PULVAD an attractive long-term alternative to the more expensive and complex LV assist devices currently used

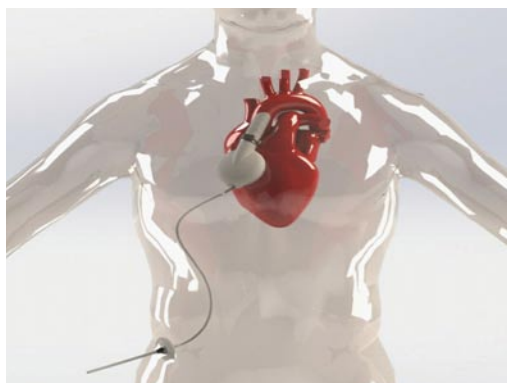


Figure 1 Pressure-unload left ventricle assist device.

in patients with end-stage decompensated HF.

DISCUSSION

Modern LVADs rely on continuous flow, and, while successful at prolonging life, LVAD-induced myocardial recovery is disappointingly rare. Clinically available LVADs bypass the LV and unload the failing LV independently of its systolic reserve. As a consequence, the dilated LV is rendered unable to generate at a basal pressure and LVEF is severely reduced because of the non-coupling of preload/afterload to LV systolic reserve. In other words, the continuous flow LVADs decrease LV preload but increase or maintain excessive afterload, driving LV function towards the bottom left of the Frank-Starling curve, reducing its functional performance. In general, we know that the lower the functional performance of the LV (*i.e.*, the lower the LVEF), the more vigorous is the process of adverse LV remodeling. In contrast to continuous flow LVADs the counterpulsation devices decrease LV afterload, thereby enhancing LV functional performance, and utilizing the LV systolic reserve to meet the peripheral metabolic demands. At the same time, the LV, based on the Frank-Starling curve, physiologically adjusts (decreases) its preload.

The IABP has been safely and effectively used for bridging chronic HF patients to transplantation^[52-56], to LVAD implantation and to recovery^[57,58]. Today, there are 4 counterpulsation devices (KardioVAD, C-Pulse, Symphony, and PULVAD) suitable for chronic mechanical assistance. These devices preserve heart integrity, unload the LV, decrease its energy consumption, enhance native LV functional performance and retain pulsatility of flow. In addition, the C-Pulse, Symphony and PULVAD counterpulsation devices do not require extracorporeal circulation for their implantation or explantation procedures. Knowing that recovery appears usually within the first 3-6 mo on mechanical assistance^[75], we propose that counterpulsation devices could be used temporarily (3-6 mo) as a bridge to recovery.

These devices appear suitable as a bridge to re-

covery not only for patients with acute HF but also for those with chronic HF, especially the ones with non-ischemic cardiomyopathy. We propose that when these patients become candidates for mechanical assistance the following practical rule can be followed: First assist them with IABP up to 2 wk and if the patients are hemodynamically stabilized (no need for IV inotropes/diuretics, no indication of peripheral organ malfunction, tolerance of HF medications, CVP ≤ 10 mmHg, HR ≤ 80 bpm, mean BP ≥ 65 mmHg) then proceed to implantation of a counterpulsation device suitable for chronic mechanical assistance as a BTR. However, in the case of non-stabilization or further deterioration on IABP, proceed with implantation of a continuous flow LVAD or a BiVAD.

In conclusion, counterpulsation devices appear attractive for cardiac recovery not only for acute but also for chronic HF. Their simplicity of design and ease of implantation/explantation may allow much more widespread use compared to that of the currently-used continuous flow LVADs. To that end, further experimental and clinical studies are urgently needed to better define the role of counterpulsation devices in HF.

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