

Mechanical Alternatives to the Human Heart: Paracorporeal Assist Systems

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“So Oz brought a pair of thinsmith’s shears and cut a small, square hole in the left side of the Tin Woodman’s breast. Then, going to a chest of drawers, he took out a pretty heart, made entirely of silk and stuffed with some sawdust.

Isn’t it a beauty? He asked.”

L. Frank Baum, *The Wizard of Oz*

In the United States, heart failure afflicts close to 1% of the adult population. It is a contributing factor in over 250,000 deaths annually, the primary diagnosis for more than 900,000 hospitalizations per year, and commands total treatment costs that approach \$38 billion annually or nearly 4% of total healthcare costs. Despite the availability of heart transplantation as the preferred surgical treatment for end-stage heart disease, this mode of therapy is limited and clearly insufficient to meet the increasing demand for donor organs. The most recent figures available from the United Network for Organ Sharing for 1999 suggest that while 4,152 patients were listed for heart transplantation, only 2,180 received a donor organ – a situation that is mirrored all over the world. Even if the availability of donor hearts increases, it is unlikely that donor availability will keep pace with the escalating prevalence of end-stage heart failure, underscoring the crucial need for alternatives to cardiac allotransplantation. This review will attempt to summarize the current status of the available mechanical alternatives to the human heart, focusing on their indications for use, their performance and results. To complete the picture, future devices, which are currently under investigation, will be described.

Indications

There are currently three major indications for mechanical assistance to the failing heart: a) as a bridge to myocardial or hemodynamic recovery; b) as a bridge to cardiac transplantation; and c) as destination therapy, namely, permanent devices as an alternative to transplantation.

Severe cardiogenic shock from a potentially reversible cardiac insult can be successfully bridged to myocardial recovery by the use of an assist device. The goals of the implanted assist system are decompression of the injured myocardium, allowing cardiac recovery and remodelling while providing physiologic support for the patient. Studies have shown that an assist device support may result in decreased myocyte necrosis and apoptosis, decreased myocytolysis, and improved myocyte contractility [1]. Moreover, these beneficial changes in the biology of the failing myocardium have been accompanied by favorable changes in the left ventricle geometry, left ventricular wall thickness and volume. Normalization of ventricular structure does not necessarily mean that ventricular function is normalized. Specific diagnoses for this category include acute viral cardiomyopathy, postpartum cardiomyopathy, postcardiotomy syndromes, anterior wall myocardial infarction (with revascularization), and reperfusion injury in cardiac allografts. Following successful recovery of the heart, the assist device may be weaned and subsequently explanted, although to date there are still no reproducible guidelines as to the right timing and clinical features for a successful recovery.

Bridging cardiac transplant candidates to heart transplantation is currently the most common indication for implantation of assist device. Candidates for transplant who continue to deteriorate despite aggressive pharmacologic support for whom no immediate donor organ is available can benefit from implantation of an assist device. The device can sustain them – sometimes for months or even years until a donor heart becomes available – and will be explanted at the time of transplantation.

The third, and currently still investigational, indication for assist system is as an alternative to cardiac transplantation. The recently published multicenter REMATCH trial (**R**andomized **E**valuation of **M**echanical **A**ssist **T**reatment for **C**ongestive **H**eart failure) compared the outcomes of 68 non-transplant candidates in New York Heart Association class IV heart failure supported with the Thoratec Corporation’s (formerly Thermo

Cardiosystems Inc., USA) HeartMate vented electric left ventricular assist system (VE LVAS) with those of 61 similar patients who received optimal medical management [2]. The rates of survival at one year were 52% in the device group and 25% in the medical therapy group ($P=0.002$), and the rates at 2 years were 23% and 8% ($P=0.09$), respectively. Although the frequency of serious adverse events in the device group was 2.35 times that in the medical therapy group, the quality of life was significantly improved at one year in the device group. Based on the REMATCH trial results, the Thoratec Corporation has filed a PreMarket Approval Supplement with the Food and Drug Administration, seeking approval to expand the intended use of its HeartMate VE LVAS to include long-term support for heart failure patients on optimal medical management who are not eligible for heart transplants.

The currently approved mechanical alternatives to the human heart can be assigned to three categories: paracorporeal assist systems, intracorporeal assist systems, and total artificial heart. This part of the review will summarize the paracorporeal assist systems.

Paracorporeal assist systems

At present there are four paracorporeal assist systems approved for use:

- Centrifugal pumps
- ABMIOMED BVS 5000 (Abiomed, Danvers, MA, USA)
- Thoratec Ventricular Assist Device (Thoratec Corporation, Pleasanton, CA, USA)
- The Berlin Heart (Berlin Heart AG, Berlin, Germany)

Centrifugal pumps

Of the various cardiac assist devices presently available, centrifugal pumps are most commonly used [3] because they are relatively simple to operate with no special training required and are inexpensive compared with other devices. In centrifugal pumps, blood enters the pump axially from an inlet tube and is caught up between vanes or stages and whirled outward. Rotation of the impellers or stages causes the velocity of the blood to change while it moves toward the periphery of the pump. As the blood exits through the outlet tube, pressure is increased. Centrifugal pumps can provide high flow rates with low pressure rises. Since most centrifugal pumps have only one moving part, disposable blood pumps can be manufactured inexpensively.

Several centrifugal pumps are currently available for use: the Bio-Medicus BIO-PUMP (Medtronic Bio-Medicus, Inc., Eden Prairie, MN, USA), the Sarns Centrifugal System (Terumo Cardiovascular Systems, Ann Arbor, MI, USA), the Lifestream centrifugal pump (Lifestream International, Haverhill, MA, USA), and the Nikkiso centrifugal pump (Nikkiso Co. Ltd., Shizuoka, Japan). All but the Medtronic Bio-pump, which consists of two concentric cones designed to impart a circular motion to incoming blood by viscous drag and constrained vortex principles, utilize the impellers technique, varying only in

the number of impellers. Each of these systems consists of a disposable pump coupled to a motorized pump drive unit containing monitors and controls of blood flow. *In vitro* and *in vivo* testing that compared mechanical function, hematologic effects (specifically hemolysis) and incidence of thromboembolism, revealed no compelling features that would dictate clear superiority of one centrifugal pump over another [4].

Implantation techniques for centrifugal pumps are simple but require great attention to details; otherwise bleeding, which is the most frequent complication, will ensue. Various cannulation sites have been used both for left and right heart support. For left heart bypass, the left atrium can be cannulated at the junction of the superior pulmonary vein, between the superior and inferior pulmonary veins, at the left atrial appendage or dome, or at the left ventricular apex. Blood from the centrifugal pump can be returned via the ascending aorta, the aortic arch, the subclavian artery, or the femoral artery. For right heart bypass, the right atrium can be cannulated at the appendage or at the junction of the inferior vena cava. Blood can be returned directly to the pulmonary artery or via the right ventricular outflow tract [Figure 1]. Whichever site is selected, it is important to avoid movement at the cannulation site post-

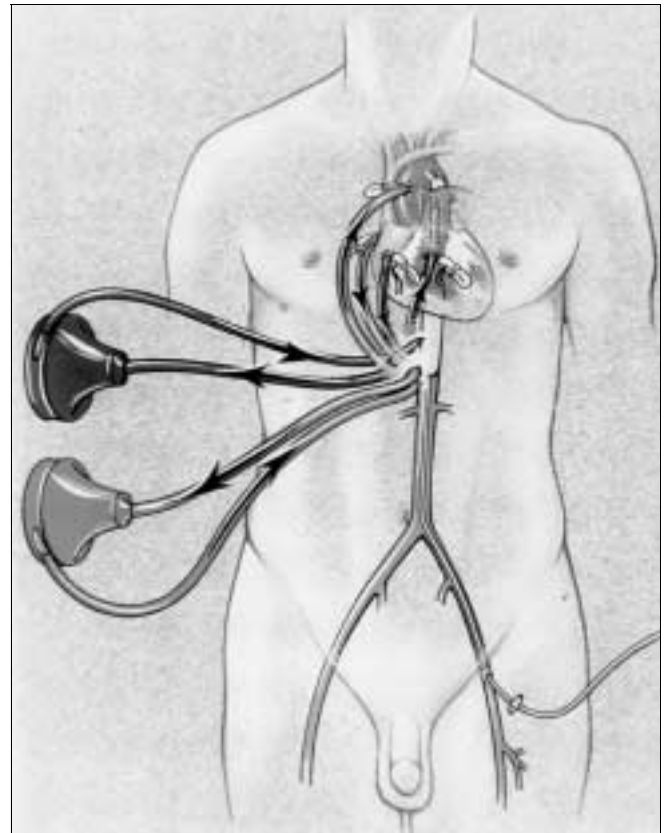


Figure 1. Patient with a BioMedicus centrifugal biventricular assist device and intraaortic balloon pump. (Reproduced with permission from Noon GP, Lafuente JA, Irwin S. Acute and temporary ventricular support with bioMedicus centrifugal pump. *Ann Thorac Surg* 1999;68:650–4)

operatively in order to prevent bleeding. Therefore, cannulae are usually exited from the median sternotomy incision or inferior to the left or right costal margin, and are secured to the skin with heavy silk sutures. The sternum is usually left open, and if the skin cannot be closed, a transparent silicone sheeting is sutured to the edges and an iodophor adhesive drape is placed over it.

All centrifugal pumps require anticoagulation medication for prevention of thromboembolism, one of the major hazards of these devices. If used for postcardiotomy failure, following complete reversal of heparin with protamine in the operating room, a heparin drip is begun to maintain the partial thromboplastin time in the range of 40 to 60 seconds.

The current centrifugal pumps were designed for short-term support. Although as long as 18 days without malfunction has been reported [5], usually seal disruption within the pump head, allowing fluid to accumulate in the magnet chamber, occurs within a median of 48 hours with left ventricular assist and 83 hours with right ventricular assist [5], necessitating pump replacement. Patients supported with centrifugal pumps remain fully bedridden and most of them are kept sedated and ventilated.

The most common indication for current use of centrifugal pumps is postcardiotomy ventricular failure [3,6]. They have also been successfully used as a bridge to heart transplantation [7], however due to scarcity of donors and predicted long waiting times they are rarely chosen for this purpose if other mechanical assist devices are available. An additional indication for their use is as a short-term bridge device to one of the long-term pulsatile electric or air-driven mechanical assist devices – the so-called bridge-to-bridge indication. Application of centrifugal pumps in this setting may allow for time to assess the patient's neurologic status and the function of other organ systems to determine if the patient is a candidate for cardiac transplantation. In case the long-term device is not available, the patient can be transferred to a referral hospital while being maintained on the centrifugal pump support.

A comparison of clinical outcomes of centrifugal pump assistance for postcardiotomy ventricular failure from different institutions is flawed due to varying hemodynamic indications and timing of the device application. In general, 20–25% of patients who would have been perioperative fatalities can be salvaged with the centrifugal mechanical assistance [6–8]. Patients who survive postcardiotomy mechanical assist ultimately do reasonably well, with 82% of hospital survivors alive at 2 years, 86% of them in NYHA class I or II [3].

The ABIOMED BVS 5000

The ABIOMED BVS 5000 is a paracorporeal pulsatile ventricular assist device that is capable of providing short-term left, right or biventricular support.

The device is a dual-chamber pump contained in a hard polycarbonate housing. The upper (atrial) chamber is a passive,

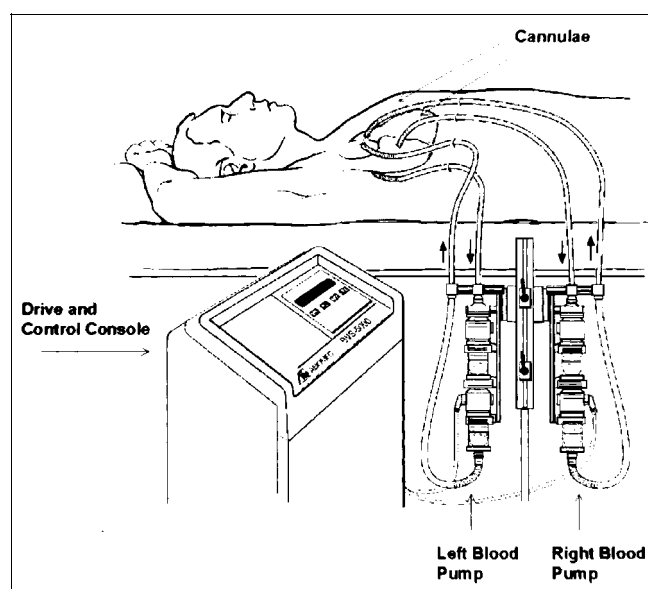


Figure 2. ABIOMED BVS 5000 system. (With permission from ABIOMED Inc., Danvers, MA, USA).

gravity-filled reservoir and the lower (ventricular) chamber is the pumping chamber. Each chamber contains a smooth-surface polyurethane bladder. The lower pumping chamber is isolated by two polyurethane trileaflet valves that ensure unidirectional blood flow. A compressed air drive line connects the console with the ventricular chamber. Blood drains from the atria by gravity into the upper chamber of the device, which is located on the side of the bed [Figure 2]. During pump systole, compressed air enters the device's ventricular chamber, causing the bladder to collapse and thus returning its blood volume to the patient. During diastole, air is vented through the console allowing ventricular bladder filling. The BVS 5000 console is an automated, self-regulating, pulsatile support device that operates asynchronously relative to the native heart rhythm. The console adjusts external pump beat rate as well as the duration of the pump diastole and systole to compensate for changes in preload and afterload. The console senses bladder filling and returns blood to the patient whenever the ventricular chamber is full. The BVS maintains a constant stroke volume (80 ml) and can provide a maximal output of 6 L/min. A single console can operate and adjust one or two blood pumps independently.

Left heart assistance by the BVS 5000 is achieved by cannulating the left atrium, or preferably the left ventricular apex, for inflow, and anastomosing the Dacron graft of the outflow cannula to the anterior aspect of the ascending aorta. Right heart assistance is achieved by cannulating the right atrium through the mid-right atrial wall for inflow, and anastomosing the Dacron graft of the outflow cannula to the main pulmonary artery. All cannulae are externalized subcostally. Once the BVS support has been initiated the patient is fully heparinized to prevent thromboembolism.

Postcardiotomy low cardiac output is the most common indication for the BVS 5000 support, comprising approximately

NYHA = New York Heart Association

63% in the Worldwide registry, maintained by ABIOMED, that currently includes more than 3,000 cases. In addition, other forms of heart failure have been successfully supported to recovery, such as acute myocardial infarction with cardiogenic shock [9] and acute myocarditis [10]. If recovery has not occurred, the BVS 5000 may be used to bridge to another device for long-term support or to bridge to transplant. It is currently the most commonly used device for temporary right heart assistance when right heart failure follows insertion of an intracorporeal left ventricular assist device or a donor heart transplantation. The ABIOMED BVS 5000 is a short-term support, with most patients being supported for 5 to 8 days. Patients' mobility is very limited and most of them remain bedridden.

According to the Worldwide voluntary registry maintained by ABIOMED, survival is related to the indication and the type of support. Postcardiotomy patients have a 31% discharge rate compared to 40% for cardiomyopathy patients. The acute myocardial infarction discharge rate is close to 33%. Recipients of univentricular support have generally fared better than patients requiring biventricular support. As with all other devices, the best determinant of survival was early insertion of the device. When the device was inserted within 3 hours of the decision to implant, the survival was 60%, versus 20% when device insertion was delayed. In addition, if the decision is made within 3 hours, the likelihood that a left ventricular assist device will be sufficient is greater than when the decision is delayed. Complications have been most common in postcardiotomy patients. This is due to the prolonged cardiopulmonary bypass time before the insertion of the device. Cardiomyopathy patients have experienced much less bleeding and other complications than have postcardiotomy patients.

The Thoratec ventricular assist device

The Thoratec ventricular assist device is currently the only system capable of providing long-term biventricular support, with more than 1,300 patients being supported so far.

The Thoratec VAD blood pump is positioned paracorporeally on the patient's abdomen, with cannulae piercing the skin below the costal margin, crossing the diaphragm, and going into the mediastinum where they are connected to the heart and great vessels [Figure 3]. The pump connects via a pneumatic drive line to a dual-drive console that controls and monitors pump operation. The pump is made of a flexible blood

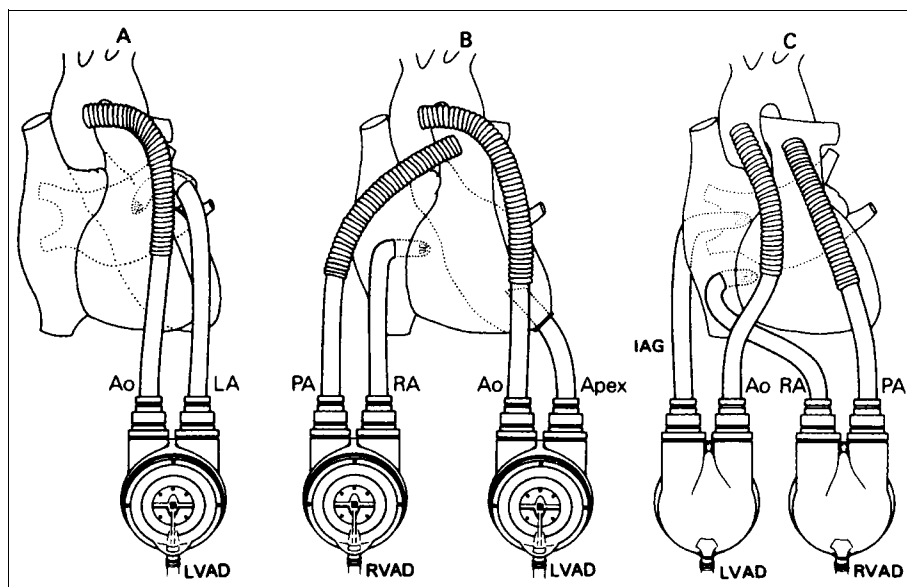


Figure 3. Schematic illustration of the Thoratec biventricular assist device connections. (With permission from Thoratec Laboratories, Pleasanton, CA, USA).

sac contained within a rigid outer casing. The console provides alternating positive and negative air pressures that actuate the blood sac. Monostrut tilting Delrin disc mechanical valves located in the inflow and outflow ports ensure unidirectional blood flow through the device. Left and/or right heart support is possible with the Thoratec VAD. The console is usually run in the "volume" (or "fill-to-empty") mode in which the pump operates on a fixed stroke volume with a variable pump rate, producing a variable pump output. Increased pump filling causes an increase in pump rate, which results in a higher pump output.

Left heart support with the Thoratec VAD is achieved by anastomosing the outflow cannula Dacron graft to the ascending aorta and cannulating the left atrium (dome, appendage or inter-atrial groove) or left ventricular apex for inflow [Figure 3]. Right heart support is achieved by anastomosing the outflow cannula Dacron graft to the main pulmonary artery and cannulating the right atrium for inflow [Figure 3]. After all cannulae have been brought out through the skin in the anterior abdominal wall, the blood pumps are connected to them and, following de-airing maneuvers, operation of the console is begun gradually as the patient is being weaned off the cardiopulmonary bypass. Careful management of the drive console is required to adjust diastolic vacuum, systolic duration, and drive line pressure so that optimal pump output can be achieved. Patients on the Thoratec VAD require anticoagulation therapy with warfarin.

Although the Thoratec VAD is presently the only device capable of providing long-term biventricular support, its major limitation lies in the restricted mobility and independence afforded to the patient. Patients supported with the Thoratec VAD can ambulate throughout the hospital but they usually

VAD = ventricular assist device

cannot leave it because of the size of the console. Thoratec has recently developed a compact and lightweight (9.1 kg) battery or line-operated biventricular pneumatic drive unit designed to promote greater mobility and self-care. It is intended to allow the patient to exercise more easily and move freely around the hospital grounds, and eventually away from the medical facility [11]. This device provides several portability options, either by hand-carrying the driver or by using a shoulder strap or a small custom trolley.

The Thoratec VAD, like all other currently available VAD systems, carries the risk of infection due to the need for transcatheter connection of the device. Compared to the intracorporeal electric devices, which are precluded in patients with small body habitus due to their size, the Thoratec VAD has been used in adult as well as in some adolescent patients with a body surface area as low as 0.73 m². An intracorporeal version of the device is now being developed [12].

The current indications for use of the Thoratec VAD are as a bridge to cardiac transplantation or as a temporary support for native heart recovery. Most patients can be successfully bridged to transplantation with an LVAD and pharmacologic support of the right ventricle. It is often not possible to predict preoperatively which patients will require biventricular assist device insertion. However, patients with clinically severe right heart failure, cardiogenic shock with end-organ failure [13,14], elevated pulmonary vascular resistance, and intractable ventricular arrhythmias should be considered for biventricular support. The final decision of whether to use biventricular support can be made intraoperatively after insertion of the LVAD. In that regard, the Thoratec VAD is sometimes used as a hybrid system when inserted as an RVAD following right ventricular failure, which follows implantation of one of the intracorporeal LVADs.

In a multicenter review [15], the most common complications following Thoratec VAD insertion were bleeding (42%), renal failure (36%), infection (36%), hepatic failure (24%), hemolysis (19%), respiratory failure (17%), multiorgan failure (16%), non-thromboembolic neurologic events (14%), and embolic neurologic events (8%). Another large multicenter study [16] showed survival to transplantation in 74% of LVAD patients and 58% of biventricular patients, with a hospital discharge rate of 89% and 81%, respectively. The Thoratec voluntary registry indicates that, as of May 2000, 60% of the 828 patients bridged to transplant were transplanted, with a post-transplant survival rate of 86% [17]. Survival rates following implantation of the Thoratec VAD for postcardiotomy cardiogenic shock or other forms of cardiogenic shock are lower, ranging between 30% and 47% [14,17]. The longest duration of support with a Thoratec LVAD was 515 days [17].

The Berlin Heart

The Berlin Heart assist device solves the problem of the Thoratec VAD, which is precluded in small children due to cannulae and blood pump size. Built very similarly to the Thoratec VAD, the Berlin Heart is available in various small

sizes, making it a particularly suitable paracorporeal device for the pediatric population. This device is not available for use in the United States.

Similar to the Thoratec VAD, the Berlin Heart is a univentricular or biventricular air-driven device, with a unique three-layered flexible polyurethane blood pump membrane encased within semi-rigid transparent polyurethane housing [Figure 4]. The three membranes are separated from one another with a graphite powder lubricant to minimize friction, while the innermost membrane, which is the only one that comes in contact with blood, is smooth-surfaced and heparin-coated. The Berlin Heart blood pumps are available in 80, 60, 30, 25, and 12 ml sizes. The adult size pumps are supplied with mono-leaflet tilting disc valves (Sorin Biomedica, Turin, Italy) in the inflow and outflow sides, while the pediatric size pumps are supplied with heparin-coated polyurethane trileaflet valves, marked by their flat construction that provides optimal washout behind the leaflets. A variety of steel-reinforced silicone cannulae, available also in small diameters, enables connection of the paracorporeal blood pump to the heart and great vessels [Figure 4]. The blood pump is operated by a variety of stationary or wearable electropneumatic drive units, each containing redundant drive units for safety. All drive units are equipped with rechargeable batteries in order to provide for patients' mobility.

The Berlin Heart implantation techniques are identical to those of the Thoratec VAD. Recently, when a left ventricular

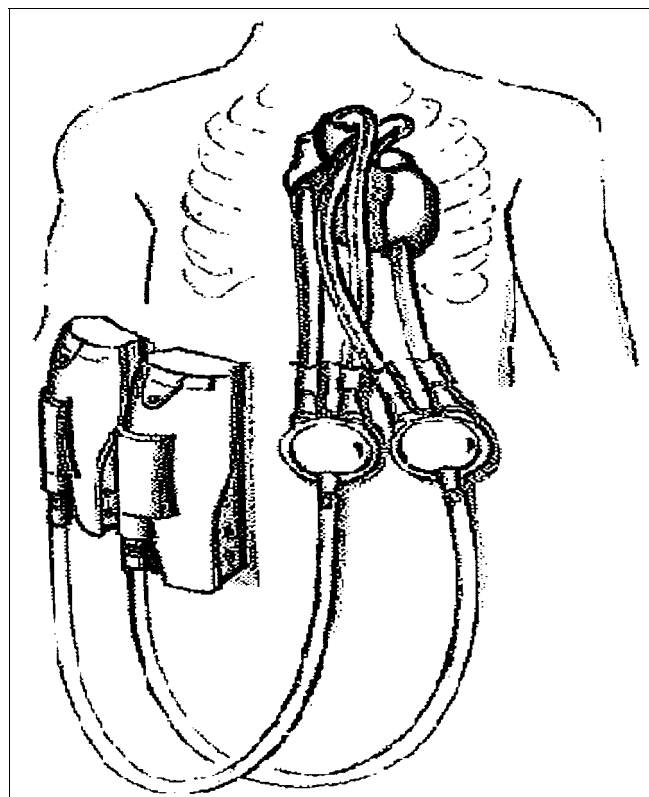


Figure 4. The Berlin Heart biventricular assist device.

apical cannula became available, the device was implanted in several patients who had undergone previous cardiac surgery by the left lateral thoracotomy approach, utilizing femorofemoral bypass, with the outflow graft anastomosed to the descending aorta, thereby avoiding repeat sternotomy [18]. Adult patients assisted by the Berlin Heart are kept on warfarin, aspirin and dipyridamole, while pediatric patients are kept on intravenous heparin.

The largest experience with the Berlin Heart VAD has been accumulated at the Deutsches Herzzentrum Berlin [19]. By February 1999, the device had been implanted in 346 patients, including 34 children under the age of 16. A biventricular support mode was chosen for 81%, isolated left ventricular support for 17%, and isolated right ventricular support for 2%. The main indication for support was bridge to transplant (59%), in addition to postcardiotomy heart failure (15%) and post-transplantation cardiac dysfunction (9%). The overall mean duration of support has been 63 days, with the current longest support being 525 days on biventricular assistance. Of the adult patients bridged to transplant, 52% have undergone transplantation and 74% of those were discharged after transplantation. Of the 34 children assisted with the Berlin Heart (aged between 6 days and 16 years, mean 7.5 years), 19 (56%) were taken off the device either after complete cardiac recovery or at the time of transplantation. Of the 14 transplanted children 10 were discharged.

Summary

The currently available paracorporeal assist systems provide reliable short or long-term mechanical assistance to the failing heart, albeit necessitating continuous hospitalization. The intracorporeal assist systems, which provide out of hospital assistance, will be described in the next part of this review.

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I find the medicine worse than the malady.

Beaumont and Fletcher, 1600. Elizabethan dramatists