MECHANICAL CIRCULATORY SUPPORT: RESPONSE OF THE FAILING HEART TO A NEW GENERATION OF PUMPS

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INTRODUCTION

Since the REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) clinical trial demonstrated the superiority of long-term mechanical support for end-stage heart failure2 patients have been offered ventricular assist devices (VAD) as a standard therapeutic bridge to cardiac transplantation.1.4 However, expanding indications and greater utilization of mechanical circulatory support has led to the development of smaller and technically varied VADs. As opposed to the currently approved VADs, newer systems provide continuous non-pulsatile circulatory support using impellers in an axial flow system (Figure 1). The purpose of this review is to present the current status and applications of axial flow pumps, as well as to discuss the response of the failing myocardium to continuous flow support.

CONTINUOUS VERSUS PULSATILE CIRCULATORY SUPPORT

Mechanical support devices move blood from the left ventricle into the ascending aorta bypassing the aortic valve (Figure 2). Pulsatile pumps powerfully unload the ventricle and essentially replace the work of the heart, while maintaining peripheral pulses. In fact, it has been suggested that, over time, che myocardium may undergo atrophy, and the aortic valve develop significant calcifications and stenosis due to being persistently closed. These pulsatile VAD can be placed intra- or extra-corporeally, despite limitations co patient mobility. However, only external pumps are currently approved for right ventricular support. These devices are indicated for inability to wean from cardiopulmonary by-pass, and as a bridge to cardiac transplantation.3 Patients supported **with** these devices typically remain hospitalized until definitive therapy is established.

Continuous flow systems may be technically easier to implant, are suitable for smaller patients and, while they are at an earlier stage of development, appear to be adequate alternatives to bridge patients to cardiac transplantation. When patients are fully supported with continuous flow devices, there is no variation in systolic-diastolic pressure and therefore, peripheral pulses are not detected. However, if the support of a continuous flow device is reduced co allow flow thorough che aortic valve, pulsatilicy can be maintained.

Long-term continuous flow pumps utilize turbine-like impellors aligned to receive blood in an axial fashion, and continuously eject blood into the aorta. At the present time, there are three implantable devices that provide continuous flow support. One of these devices, the MicroMed DeBakey VAD®, is currently approved in Europe as a bridge to cardiac transplantation, and in the United States for utilization in pediatric populations. le also is undergoing clinical evaluation in the United States in randomized clinical trials as a bridge for cardiac transplantation, as well as for destination therapy.

The primary advantage of continuous or axial flow pumps over pulsatile pumps is their smaller size, which makes them easier to implant, even in small patients. In addition, axial flow pumps are noiseless and may decrease the risk of device-associated infection.

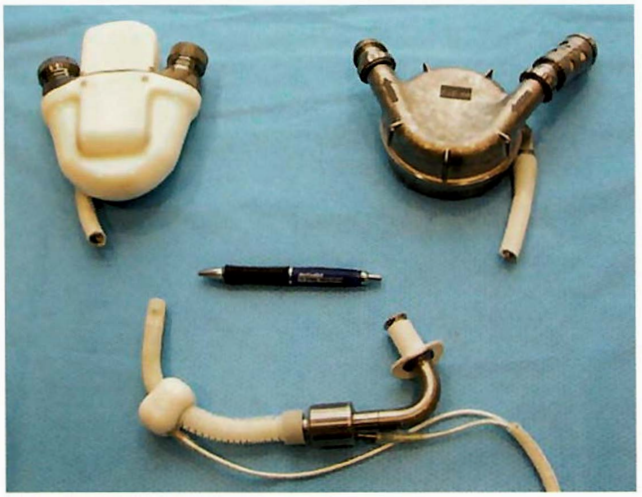

Figure 1.
Left Ventricular Assist Device. The devices in this figure illustrate pulsatile (top two) and continuous-axial flow (bottom) pumps.

In addition to being placed in the ventricles of the heart, continuous flow devices also can be placed extra-corporeally. The external continuous flow devices are generally used for a short lengrh of time, typically a few weeks, and are very helpful for patients who failed weaning from cardio-pulmonary bypass following cardiac surgery. These kinds of pumps can be placed to assist either the failing right or left ventricle.

One of the most recent and novel implantable axial flow pumps designed for short-term support is the Impella Recover System, which can be percutaneously placed via the femoral artery. This system offers full circulatory support to patients who are in cardiogenic shock without an open cardiac procedure. Physicians from the Methodist DeBak$_{ey}$ Heart Center recently implanted the first system of chis type in a patient in the United States. The effectiveness of its pumping ability was demonstrated by the dramatic decrease in left ventricular size that occurred following placement of the device. The Impella System is currently in clinical trials in five centers across the United States including the Methodist DeBakey Heart Center (Figure 3).

EFFECTS OF CONTINUOUS, AXIAL FLOW SUPPORT ON FAILING MYOCARDIUM

The use ofVADs to treat patients with refractory heart failure has permitted the study of human failing myocardium at two stages. Failing myocardial tissue can be obtained when the device is implanted, and at the time of removal for cardiac transplantation. The ability to obtain paired human myocardium at these two points has facilitated the detailed analysis of the effect of chronic mechanical unloading on the expression of various genes and proteins that rypify the failing phenotype.[6]

While much is known about the responses of failing myocardium to pulsatile-rype devices, there is little data available on the cellular and hemodynamic response of failing myocardium to continuous flow support. However, the Methodist DeBakey Heart Center has conducted a series of experimental studies that demonstrated that chronic mechanical support with the DeBakey VAD leads to decreases in cardiac myocyte size, collagen reduction and reduction of cardiac TNFcx expression as well as normalization of dystrophin expression.[5,7] Thus continuous-axial flow support with the DeBakey VAD supports the circulation in a manner similar to that which has been observed with the pulsatile-flow devices.

The underlying hypothesis that unites much of the research into YAO-mediated cardiac recovery is that hemodynamic unloading of the failing heart allows reversal of the compensatory and stress responses of the overloaded myocardium, and resulcs in structural and functional remodeling of the tissue, known as "reverse remodeling."[8]

CLINICAL BENEFITS OF MECHANICAL UNLOADING

The biological response of the failing heart to mechanical unloading includes the improvement of a large number of cellular markers that are abnormal in the failing phenotype. Furthermore, functional analysis, as shown by hemodynamics or electrical properties of the failing heart, may also improve. However, translation of these changes into improvements in function is a phenomenon that is difficult to study. Nevertheless, some patiencs regain cardiac function to the point that device removal is possible with some recovery of cardiac function. These improvements are ostensibly preceded by cellular, hemodynamic and electrophysiological alterations associated with reverse-remodeling.

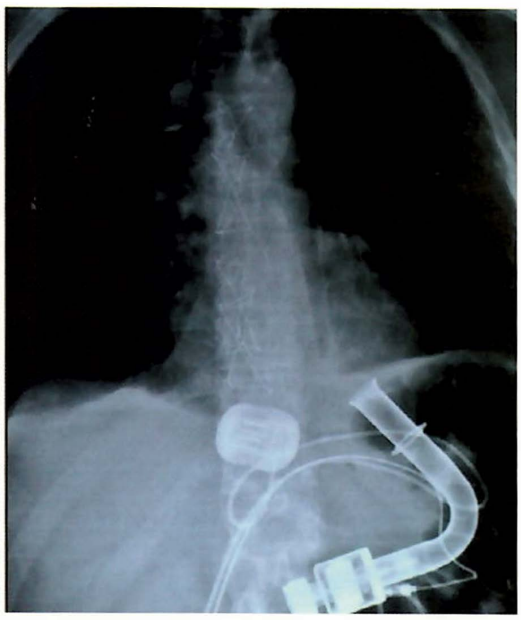

Figure 2.
Radiograph illustrating placement of the DeBakey-Noon pump. Left Ventricular Assist Devices (LVAD) are implanted in the left ventricle and deviate blood through the pump into the ascending aorta via an outflow graft.

CONCLUSIONS

Mechanical circulatory support via VADs has become a standard therapeutic option available to bridge patients with end-stage heart failure to cardiac transplantation, as well to provide some patients a definitive or destination therapy. Mechanical unloading of the myocardium may, in effect, re-set the progress of heart failure, and even potentiare device removal in some patients without rhe need for cardiac transplantation. Most of rhe work so far in this field has been developed with bigger, noisier pumps that are difficult to implant, and fully support the circulation via total lefi: ventricular cardiac replacement.

Newer pumps provide continuous

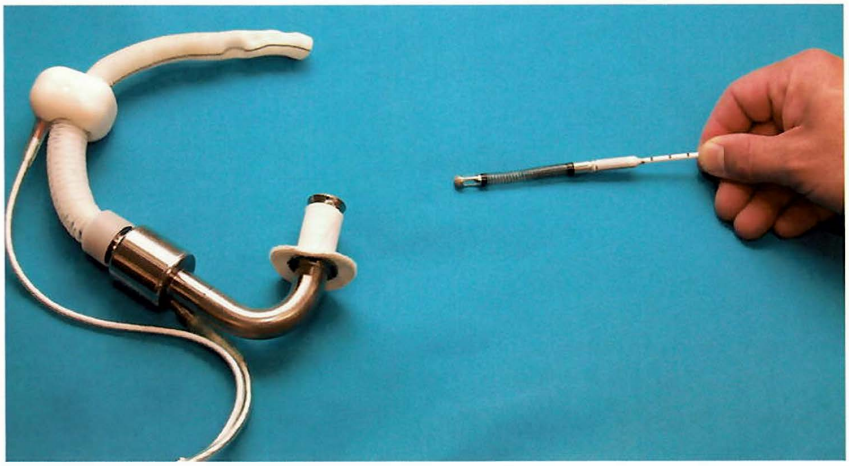

Figure 3.
The Impella Recover System. The figure illustrates the relative size difference between the DeBakey VAD (left) and the Impella system (right), which can be percutaneously placed via the femoral artery.

axial-flow, and permit pulsatility depending on the degree of support utilized. Initial scientific observations and clinical experience with continual flow VADs reveal that improvement of myocardial function is possible in some patients, and perhaps future emphasis should be aimed at determining signals needed to enhance recovery, or the design of better devices that permit optimal physiological recovery.

The DeBakey VAD is at the from-stage of development in the use of continuous-axial flow support for chronic therapy, having been implanted in over 200 patients worldwide, and evaluated worldwide as a bridge œ cardiac transplantation, as well as destination therapy. With regard to the effect of the DeBakey pump in failing myocardium, it appears continual support by chis device induces beneficial cellular changes and therefore, may provide a strategy for myocardial recovery. In addition, a short-term continuous-axial flow pump that can be placed via the femoral artery, the lmpella Recover System, is currently undergoing clinical trials. The first implant of this minimally invasive device was performed at the Methodist DeBakey Heart Center with functional success.

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