Surgical Options in the Management of Heart Failure

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Congestive heart failure (CHF) is a pathophysiologic state of inadequate myocardial contraction and/or relaxation leading to decreased cardiac output and inadequate organ perfusion. CHF, a leading cause of morbidity and mortality, can result from a variety of insults to the myocardial tissue. According to American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the evaluation and management of chronic heart failure there are four classes based on stages of the syndrome (Table 1).[1] In the early stages of the disease, ventricular contractility is maintained by adrenergic stimulation, renin-angiotensin-aldosterone activation, and other neurohormonal and cytokine system responses.[2.3] However, as the disease progresses and these compensatory mechanisms cease to provide benefit, ventricular dilation and fibrosis occur and cardiac function deteriorates. This produces a chronic state of low perfusion, ACC/AHA Class D (Table 2). New York Heart Association (NYHA) functional classification is also used to assess the severity of functional limitations and correlates fairly well with prognosis (Table 2). Strategies for treating end-stage CHF aim to improve quality of life, limit disease progression, and prolong life. Medical therapies such as angiotensin-converting enzyme inhibitors (ACEI), β blockers, diuretics, inotropic agents, and antiarrhythmics represent the usual standard of care for CHF management. However, even multidrug regimens may not prevent progression toward Class D CHF; when this occurs, there is a greater than 75% two-year mortality risk, with surgical intervention being the only effective treatment. According to ACC/AHA guidelines, the only established surgical treatment option for advanced heart failure is transplantation.[1]

Cardiac Transplantation

In the United States, cardiac transplantation is performed in member centers of the United Network for Organ Sharing (UNOS), an umbrella organization responsible for coordinating organ procurement, organ allocation and statistical information. UNOS selection guidelines for cardiac transplantation include patients with end-stage heart failure with life expectancy less than 1 year, such as patients in cardiogenic shock or a low-output state requiring mechanical or inotropic support, patients with advanced symptomatic heart failure with peak oxygen uptake <10 ml/kg/min (with achievement of anaerobic threshold), patients with NYHA class IV heart failure due to advanced hypertrophic or restrictive cardiomyopathy, patients with refractory angina pectoris due to inoperable coronary artery disease, and patients with life-threatening, refractory ventricular arrhythmias uncontrolled by all appropriate medical and surgical modalities.[5,6]

UNOS allocates donor hearts based on patients' priority status, ABO-group compatibility, body size match, and distance from the donor center. Priority status is given to inpatients supported by mechanical circulatory assist devices for acute hemodynamic decompensation, patients on assist devices with significant device related complications, patients requiring continuous infusion of single or multiple high-dose intravenous inotropic medications, and patients with life expectancy

less than 7 days without transplantation. Certainly, cardiac transplantation represents the definitive therapy for terminal CHF; it is associated with excellent 1-year survival (>80%), 5-year survival (60%), and functional capacity.[6] However, whereas over 10,000 patients are on a heart transplant waiting list, fewer than 2200 donor hearts are available each year.[7] Also, these organs are usually reserved for patients younger than 65 years of age, even though older patients have the highest prevalence of CHF. Furthermore, patients with comorbidities are often ineligible for transplantation. It is this mismatch between the increasing number of potential candidates for cardiac transplantation and the relatively fixed number of donors, as well as the large number of acute CHF deaths that continues to stimulate the search for alternative surgical therapies.

Ventricular assist devices

Ventricular assist devices (VADs) are designed to connect to the heart or to be placed within the heart to assume some of the workload and to allow the ventricle to rest, undergo reverse remodeling, and recover some of its contractile function. It has been previously demonstrated that the myocardium has the capacity to repair itself during a period of unloading,[8,9] after which some patients are able to resume a normal lifestyle and no longer need cardiac transplantation. Some important factors need to be taken into consideration during *device selection* process, such as: the expected duration of support, type of support needed (right, left or biventricular assist), overall cost, device-related mobility, and FDA approval status. The latest *indications* for mechanical assistance include reversible ventricular dysfunction occurring after cardiac surgery, bridge to heart transplantation, destination therapy for nontransplant candidates. The use of mechanical assist devices as bridges to cardiac transplantation has been found to improve the survival rates and outcomes of patients with decompensated heart failure.[10] In addition, long-term left VAD support has proven to be superior to optimal medical treatment in patients with end-stage CHF who are not candidates for heart transplantation.[10] Thus, mechanical assistance has become an important tool in the surgical management of patients with failing hearts. Currently there are various cardiac assist devices available for both short- and long-term support. Based on the device related blood flow characteristics, VADs could be classified as *nonpulsatile* or *pulsatile* (Table 3). When the site of implantation is taken into account mechanical assist devices could be categorized as *extracorporeal* or *intracorporeal.* Most of the extacorporeal devices, nonpulsatile and pulsatile, are now used for short to medium-term support. Nonpulsatile devices were designed with either c*entrifugal* or *axial* flow patterns. Axial flow pumps present the advantage of being small, silent, with no valves, fully implantable; they work in concert with the heart and improve the position of the left ventricle on the Frank-Starling curve.

New VAD Systems in Clinical Trials

There are three new VAD systems that have recently been introduced into clinical trial. The HeartWare, Ventracor and Levacor devices are all third generation magnetically levitated devices. Currently, HeartWare LVAD has been implanted in 19 patients in Australia and Europe with excellent results, only few deaths and most of the remaining patients on continuous support. United States clinical trials for this device are anticipated to begin in that later part of 2007. The Ventracor LVAD clinical trials are also underway in Australia. Circulite pump is small, presents the potential of being implanted percutaneously, and has been recently used in 2 patients during the past few months. The Levacor LVAD should begin trials in the near future.

Expanding VAD Therapy

VAD therapy has been used in the most severely ill patients, which has resulted in complication and survival rates that are seemingly less than desirable. The current consensus among VAD developers is that this therapy is ready for use in a "less sick" population of patients, i.e. NYHA class IIIb. The major limitation of the use of VAD therapy is that referring cardiologist are not convinced that VAD support is better than medical therapy. The goal of new clinical trials must be able to demonstrate better survival and better quality of life than the current medical therapy used for end-stage heart failure. Clinicians and FDA agree to move to trials in less sick patients, but this will require new novel approaches to the trial design.

A key step toward more efficient clinical trials is center participation in the Intermacs VAD registry. Participation in this registry is mandated by CMS for all centers implantaing VADs for destination therapy. Intermacs only began during the past year and the number of patient data entered is small. Eventually, FDA would like to use the Intermacs registry for controls in clinical trials.

Recovery

The current focus of research on bridge to recovery is in two major areas, medical therapy and stem cell therapy. Recently, clenbuterol, a β_2 adrenergic-receptor agonist, has been studied in a number of centers in Europe and the US.[11]Reverse remodeling was reported with prolonged LV unloading with the use of LVAD in conjunction with administration of clenbuterol in order to prevent myocardial atrophy.[12] The second area of interest is the use of stem cells to enhance recovery during VAD support. There are a few groups that are conducting basic research to identify which cells can be used and how to prepare them. Another area of interest is the generation of myocardial cells for implantation in diseased areas of the heart. Researchers have cells contracting in-vitro, and are now developing techniques for implantation/transplantation. There are no active clinical protocols for this therapy, but this type of research should evolve soon.

Total Artificial Heart

SynCardia CardioWest TAH is a biventricular orthotopic pulsatile pump pneumatically driven. Each ventricle has a seamless blood-contacting diaphragm, two intermediate diaphragm and an air diaphragm made of polyurethane and separated by thin coatings of graphite. The inflow (27 mm) and outflow (25 mm) Medtronic-Hall valves are mounted on the housing. The ventricles fully fill and eject 70 ml/beat. Currently, CardioWest is the only total artificial heart device in use for bridging to heart transplantation.[13] Sixty eight percent of the transplant candidates patients treated with this device survived long-term.[14] Recently, CardioWest was successfully used in a restricted group of patients with irreversible cardiogenic shock. Patients recovered all dysfunctional organs and were successfully transplanted.[15]

OTHER SURGICAL TECHNIQUES

*Surgical ventricular remodeling p*rocedures meant to "remodel" the left ventricle through reversing left ventricular dilation have been investigated such as: *Posterior ventricular excision* with partial left ventriculectomy and *Dor procedure* with placement of endoventricular patch, mitral valve plasty and reduction of mitral regurgitation. Results have been variable, CHF has worsened in some patients, whereas other patients have shown stable improvement in cardiac function.[16,17,18]

Cardiomyoplasty involves an electrically stimulated flap of skeletal muscle, usually from the latissimus dorsi, which is wrapped around the heart in an attempt to augment systolic function.[18] The main benefit of the procedure may be the mechanical "girdling" effect of wrapping the heart to prevent further dilation of the left ventricle. At present, the clinical application of cardiomyoplasty remains limited.

Acorn CorCap^{TM} is a polyester-mesh cardiac support device that is surgically implanted to fit over the heart to produce passive ventricular reshaping. It has been shown to slow the progression of CHF, promote reverse remodeling, and improve functional status.[19]

Passive ventricular reshaping technique aims to preempt ventricular remodeling and address the mitral regurgitation that coexists with advanced CHF. A novel device, the Coapsys^{TM} (Myocor Inc., Maple Grove, MN) is used to draw the mitral valve leaflets together by means of two epicardial pads connected by a flexible cord that runs beneath the valve. Early clinical results with the Coapsys^{TM} have been promising in patients with moderate to severe functional mitral valve regurgitation.[20] Similarly, the use of polyester tension rods (Myosplint^{TM}; Myocor Inc., Maple Grove, MN) to draw the walls of the failing left ventricle together and thus alter its geometry has shown promise in patients with CHF.[21]

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Table 1
ACC/AHA Classification of Chronic Heart Failure[1]

Stage	Description
A-High risk for developing heart failure	Hypertension, diabetes mellitus, CAD, family history of cardiomyopathy
B-Asymptomatic heart failure	Previous MI, LV dysfunction, valvular heart disease
C-Symptomatic heart failure	Structural heart disease, dyspnea and fatigue, impaired exercise tolerance
D-Refractory end-stage heart failure	Marked symptoms at rest despite maximal medical therapy

Table 2:

New York Heart Association Heart Failure Symptom Classification System

NYHA Class	Level of Impairment
I	No symptom limitation with ordinary physical activity
II	Ordinary physical activity somewhat limited by dyspnea
III	Exercise limited by dyspnea at mild work load
IV	Dyspnea at rest or with very little exertion

Table 3. Types of ventricular assist devices (VADs)

Type	Device	Length of Support	Position	Ventricular Support	Drive Mechanism
Pulsatile	Abiomed BVS 5000	Short-term support	Extracorporeal	LV, RV, BV	Atrial and ventricular chambers pneumatically driven
	Thoratec VAD	Short- to medium-term support	Extracorporeal	LV, RV, BV	Pneumatically driven sac
	HeartMate IP and VE	Long-term as a bridge to transplantation, recovery or destination therapy (HeartMate VE)	Intracorporeal, abdominal (pre- or intra-peritoneal)	LV	Flexible textured polyurethane diaphragm pneumatically or electrically driven
	Novacor	Long-term as a bridge to transplantation, or recovery	Intracorporeal, abdominal (pre- or intra-peritoneal)	LV	Polyurethane pump sac compressed by electrically driven pusher plates
	AbioCor TAH	Long-term support	Intracorporeal	BV	Electric
Nonpulsatile	Levitronix CentiMag (centrifugal-flow)	Short-term	Extracorporeal	LV,RV,BV	Electric
	Tandem Heart (centrifugal-flow)	Sort-term	Extracorporeal	LV	Electric
	Impella (axial-flow)	Short term	Extracorporeal	LV	Electric
	Jarvik Flowmaker (axial-flow)	Long-term support	Intracorporeal	LV	Impeller electrically driven
	DeBakey LVAD (axial-flow)	Long-term support	Intracorporeal	LV	Electric
	HeartMate II (axial- flow)	Short-term	Intracorporeal	LV	Electric

IP-implantable pneumatic, VE-vented electric, LV-left ventricle, VAD ventricular assist device, TAH-total artificial heart