Surgical Therapy for Heart Failure

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After a meeting of the American College of Cardiology in 2003, the cover of *US News and World Report* boldly proclaimed: “The end of heart disease.”¹ The media frenzy after one of the national cardiology meetings is always interesting to observe. The late-breaking trials of pharmacology, drug-eluting coronary stents, and percutaneous heart valves conspire to make even the busiest cardiothoracic surgeon think of his or her own professional future. But amid our cardiology colleagues’ excitement over the “vanishing scalpel”¹ are some sobering statistics (Table 1). Cardiovascular disease remains the leading cause of death in the US. Ischemic heart disease accounts for a large portion of these deaths. Although the number of patients dying acutely from myocardial infarction has decreased nearly 30% in the last 2 decades, the number of patients dying from heart failure (HF) has doubled. Despite improving medical therapy, many of these patients continue to have functional decline and ultimately die. Management of HF, as such, has evolved into a steadily growing discipline. This review will discuss the role of surgical therapy for treating the enlarging population of patients with HF.

**HEART FAILURE—THE MODERN EPIDEMIC**

The American Heart Association’s latest update estimates that nearly 5,000,000 Americans suffer from HF. Over 500,000 patients are newly diagnosed each year. HF does not discriminate by gender, race, or age. It is increasingly prevalent in men and women, Caucasian and non-Caucasian, and young and old. At age 40, the lifetime risk of HF developing is 20%.² Importantly, because of an aging population and better medical therapy, patients with advanced HF are now much older, with more attendant comorbidities.³ HF is associated with staggering costs to society—estimated to be more than $30 billion last year—that are related to repeat hospitalizations, loss of work potential, and prescription medicines.³ Although medical therapy has greatly increased the quality and length of life for these patients, diagnosis of HF has traditionally carried a mortality rate of 20% within 1 year and 50% within 2 years.⁴

HF is the clinical end point for a number of diseases resulting in myocardial dysfunction. Ischemic cardiomyopathies (from coronary artery disease) and dilated cardiomyopathies (either idiopathic or familial) make up the majority of cases. Many other diseases can also lead to end-stage heart failure, including valvular, congenital, metabolic, and inflammatory disorders. Pathologically, cardiac remodeling is characterized by myocyte hypertrophy, chamber dilation, and changes in matrix composition. Ultimately, the fibrotic heart becomes more spherical and, subsequently, a less-efficient pump. An important goal is to identify and favorably intervene before onset of terminal myocardial remodeling.

Patients present with a variety of symptoms related to both systolic (poor antegrade pump function) and diastolic (poor ventricular relaxation and compliance) dysfunction. Descriptions of patients with HF have been noted as early as 1600 BC in the Ebers papyrus. Other references to “dropsy” (accumulation of lymph fluid) and cardiac cachexia were noted by Hippocrates. Typical symptoms of HF include dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, fatigue, and abdominal symptoms related to right heart congestion. These symptoms are often associated with several physical findings, including elevated jugular venous pressure, a third heart sound, pulmonary congestion, and peripheral edema.

Traditionally, the New York Heart Association (NYHA) Classification has been used to define the functional limitations of patients with HF. Recent guidelines have suggested a new classification system that emphasizes its evolution, progression, and structural deterioration (Table 2).⁵ This staging system encourages the same
levels of care of HF patients that we would use for cancer: identify and treat patients at risk for HF (ie, hypertension), with early disease (ie, diastolic dysfunction), with established disease (ie, medically managed HF), and with advanced disease (ie, medically refractory HF).4

A host of diagnostic studies are available to study these patients. Transthoracic echocardiography with or without pharmacologic stress is inexpensive and provides functional and anatomic information. Radiouclide scans can evaluate ejection fraction (EF), especially of the right ventricle. MRI has recently proved to be a valuable resource in assessment of myocardial function and viability. Right and left heart catheterization assesses presence of coronary artery disease and pulmonary vascular disease. Finally, measurement of peak oxygen consumption with exercise can help stratify the functional limitation of patients with HF.

HEART FAILURE—MEDICAL THERAPY
Medical therapy, including preventive measures, serves as the first-line strategy for treating patients with HF. In 1997, the Systolic Hypertension in the Elderly Program (SHEP) Cooperative Research Group followed over 5,000 patients with isolated systolic hypertension. HF occurred more than twice as often in the placebo group versus those treated with antihypertensive agents. Additionally, treated patients with an earlier myocardial infarction had an 80% risk reduction in HF development compared with those not treated.6 Control of other risk factors, including diabetes, coronary artery disease, and structural valve disease, similarly prevents pathologic ventricular remodeling and HF development.

Once diagnosis of HF is established, a number of pharmacologic strategies exist to limit and reverse manifestations of congestive heart failure (CHF). In particular, blocking the renin-angiotensin and β-adrenergic systems improves mortality among patients with HF. Angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers, increase survival and decrease repeat hospitalizations.7 These benefits are also found in several types of β-adrenergic blockers, including metoprolol and carvedilol.8,9

Patients often have difficulty tolerating either angiotensin-converting enzyme inhibitors or β-blockers. A number of additional medication regimens are also used in managing these patients, including loop and thiazide diuretics and aldosterone antagonists. Diuretic therapy decreases ventricular diastolic pressure, which reduces ventricular wall stress, and maximizes subendocardial perfusion. Digoxin, a cardiac glycoside, is used to help improve symptoms associated with CHF through improvement in cardiac contractility. Although use of digoxin does not confer a survival benefit, it has reduced the number of hospitalizations from worsening HF.10 Recently, there has been renewed enthusiasm for vasodilator therapy using a combination of hydralazine and isosorbide dinitrate.11 Finally, when patients are refractory to standard therapy, they often require hospitalization for IV diuretics, vasodilators, and inotropic agents.

SURGICAL ALTERNATIVES FOR ADVANCED HF
Despite considerable improvements in medical therapy, overall death rates for HF patients have failed to drop appreciably. And, with nearly 10% of the population over 75 years old diagnosed with HF, a more complicated set of patients is emerging and growing. Typically, patients over 65 years of age are not candidates for heart transplantation. Older patients can successfully receive traditional approaches to heart operation,12 but resource allocation and increased morbidity and mortality raise important societal issues.13 A number of innovative surgical approaches have evolved to serve these diverse, refrac-
tory medical patients, with aims of enhancing ventricular function, quality of life, and, ultimately, survival (Fig. 1).

Heart transplantation

With progressive end-stage HF despite maximal medical therapy, the “gold standard” therapy has been heart transplantation. Since the first orthotopic heart transplantation in 1967 by Christiaan Barnard, the world has seen tremendous progress and advancement in the field of cardiac transplantation. Compared with patients who receive only medical therapy, transplant recipients have fewer rehospitalizations, marked functional improvements, enhanced quality of life, more gainful employment, and longer lives, with 50% surviving to 10 years (Fig. 2). Careful selection of donors and recipients and efforts to minimize potential perioperative dangers (ischemic times, pulmonary hypertension, mechanical support, cardiogenic shock) are critical to ensure good outcomes. The single largest advancement in ensuring longterm allograft function is attributed to development of immunologic modulators. Pioneered by Dr Norman Shumway at Stanford University, steroids and antipurine metabolites, including azathioprine and mycophenolate mofetil, have been widely used. Central to current immunosuppressive regimens are the calcineurin inhibitors, cyclosporine, and tacrolimus. These drugs inhibit cellular pathways responsible for interleukin-2 production and subsequent T-cell activation. “Triple drug therapy,” consisting of steroids, calcineurin inhibitors, and mycophenolate mofetil, has become standard initial immunotherapy after heart transplantation. Additional agents, such as antithymocyte globulin, rapamycin, and interleukin-2 receptor antagonists, also have important roles in modern immunosuppression protocols.

Although heart transplantation is a viable solution for patients with end-stage HD, use is limited by inadequate donor supply. In the US, fewer than 2,500 heart transplantations are performed each year. Unfortunately, an estimated 10% to 20% of patients die annually on the heart transplant waiting list. Of the 5 million people diagnosed with HF, it is estimated that 30,000 to 100,000 patients suffer from such advanced disease that they would benefit from transplantation or mechanical circulatory support. This disparity between the numbers of patients needing transplants and the availability of heart donors has refocused efforts to find other ways to support the severely failing heart.

Coronary artery bypass

Historically, studies of medical versus surgical therapy for coronary artery disease focused on patients with normal left ventricle (LV) function. The Veterans Affairs Cooperative Study of Surgery demonstrated a substantially higher survival rate in a subset of patients with reduced left ventricular EFs (< 50%) after coronary bypass operation versus those who were randomized to medical therapy. This survival benefit was particularly evident at the 11-year followup period (50% versus 38%). The Coronary Artery Surgery Study (CASS) showed that in patients with left main equivalent disease, operative revascularization prolonged life in most clinical and angiographic subgroups versus those who received medical therapy. Importantly, this study demonstrated that surgical therapy markedly improved the 5-year cumulative survival in patients with EF < 50% (80% versus 47%).

These earlier randomized trials are limited by their inclusion of patients with what is currently considered “good” EF. That is, many patients referred for coronary revascularization live with EF < 35%. Both the Yale and University of Virginia groups, among many others, have published their results of coronary artery bypass operations in patients with extremely poor LF function who were on the transplant waiting list. Elefteriades and col-

Table 2. Heart Failure Classifications

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<th>New York Heart Association</th>
<th>ACC/AHA guidelines</th>
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<tr>
<td>I  No symptoms</td>
<td>A  No structural damage</td>
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<tr>
<td>II Symptoms with substantial activity</td>
<td>B  Structural abnormality</td>
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<td>IV Symptoms at rest</td>
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leagues demonstrated that coronary artery bypass operation in patients with EF < 30% had a survival rate of 80% at 4.5 years, which remarkably approaches that of cardiac transplantation. Likewise, Kron and colleagues reported a 3-year survival rate of 83% in patients who underwent coronary bypass with EF < 20%.

Pathophysiologically, patients who stand to gain the greatest benefit from surgical revascularization are those who possess hibernating myocardium. This term is used to describe regions of the heart that are dysfunctional under ischemic conditions but retain the capacity to regain normal function after blood flow is restored. A number of studies demonstrate that patients with ischemic HF and substantial areas of viable myocardium can reduce mortality, improve NYHA class, favorably alter LV geometry, and increase LV EF after surgical revascularization. MRI has become particularly useful for determining both wall motion abnormalities and viable myocardium and has been demonstrated to predict the success of low-EF revascularization.

Many surgeons have evolved their practices to meet the demands of higher-risk patients and adopt measures to strive for better graft patency. The former is highlighted by adoption of off-cardiopulmonary bypass and on-cardiopulmonary bypass, beating heart techniques for revascularization. The latter, “preventive” strategy is manifest by increased use of bilateral mammary and arterial grafting.

Although the Coronary Artery Surgery Study, European, and Veterans Affairs studies established many of the standards for treatment of coronary artery disease, no such large studies address similar questions in the modern medical era, especially in patients with ischemic cardiomyopathies. The Surgical Treatment of Ischemic Heart Failure (STICH) trial is a prospective, randomized trial currently underway to determine the role of coronary artery bypass in patients with HF. The first hypothesis will test whether coronary artery bypass grafting (CABG) with intensive medical therapy versus medical therapy alone confers an additional survival benefit in patients with EF < 35%. End points of interest will be morbidity and mortality rates, quality of life, and economic impact of the treatment strategies. Enrollment for this arm of the study is expected to reach its goal of 1,000 patients by the end of 2006.

Aortic valve replacement
Diseases of the aortic valve can frequently lead to onset and progression of CHF. Although the natural histories of both aortic stenosis and aortic regurgitation are well known, patients are frequently followed conservatively after presenting with considerable HF. Of the three classic symptoms of aortic stenosis—syncope, angina, and dyspnea—the latter is the most robust risk factor for death, with only 50% of patients alive within 2 years. Conversely, age-corrected survival of patients undergoing aortic valve replacement for aortic stenosis is similar to the normal population. Unfortunately, once severe LV dysfunction develops, results of aortic valve replacement are more guarded. Because of poor LV function, substantial transvalvular gradients (ie, low output, low gradient aortic stenosis) are not able to develop in these patients. Critical in the preoperative decision process is
determining if ventricular dysfunction is truly valvular (which would improve with replacement) versus other forms of cardiomyopathy, such as ischemia or restrictive processes (which would not improve with replacement). Precise measurement of aortic valve area is difficult because the calculated valve area is directly proportional to cardiac output. Also, the Gorlin constant varies at lower outputs. In this situation, the valve areas might be considered critically small when, at operation, the valve is only moderately diseased. Preoperative evaluation with dobutamine (increase contractile reserve) or vasodilator-induced stress echocardiography (using continuity equation rather than the Gorlin formula) can be helpful with this distinction and can guide candidacy for this relatively high-risk procedure.37 Nevertheless, because of the possibility of ventricular recovery and lengthened patient survival, most patients with HF and aortic stenosis are offered valve replacement.38

Timing of surgical intervention for aortic insufficiency is more challenging than with patients with aortic stenosis. Similarly, once symptoms occur and there is evidence of LV structural changes, morbidity and mortality for aortic insufficiency increases.39 In a retrospective review from the Mayo Clinic, 450 patients receiving aortic valve replacement for aortic insufficiency were compared by ranges of EF (< 35%, 35% to 50%, > 50%). Although the group with severe dysfunction carried an operative mortality of 14%, EF improved and 10-year survival was 41%.40 Earlier intervention, before onset of severe LV dysfunction, is crucial to improving survival of patients with this lesion,41 as seen with aortic stenosis.

**Mitral valve repair**

Mitral valve regurgitation can both cause and result from CHF. Its presence is an independent risk factor for cardiovascular morbidity and mortality.42 The pathophysiology of mitral regurgitation (MR) is generally a result of its etiology. In addition to frank papillary muscle rupture associated with acute myocardial infarction, chronic ischemic cardiomyopathies result in papillary muscle migration as the ventricle dilates, causing tenting of the mitral leaflets, restricting their coaptation (Fig. 3). Dilated cardiomyopathies can have similar issues and annular dilation. In addition to mitral MR, this alteration in the LV geometry contributes to volume overload, increases LV wall tension, and leaves patients susceptible to exacerbations of HF.43 Mitral valve operation in patients with HF has gained enthusiasm because it abolishes the regurgitant lesion and decreases symptoms. The pathophysiologic rationale for repair or replacement is to reverse the cycle of excessive ventricular volume, allow for ventricular unloading, and promote myocardial remodeling.

**Figure 3.** Pathophysiology of mitral regurgitation associated with heart failure. Ventricular and annular dilation impede the mitral leaflets from adequately meeting (ZC, zone of coaptation as the heart fails). Changes in ventricular geometry with papillary muscle displacement results in leaflet tenting, additionally restricting their motion. Reprinted from Badhar V, Bolling SF. Non-transplant surgical options for heart failure. In: Cohn LJ, Edmunds LH Jr, eds. Cardiac surgery in the adult. 2nd ed. New York: McGraw-Hill; 2003:1515–1526, with permission.94
Among others, the Michigan group has been an advocate for mitral repair in the HF population. Bolling and colleagues demonstrated that mitral valve repair was associated with an increased EF, an improvement in HF class from 3.9 to 2.0, and a decrease in the number of hospitalizations. Additional effects with repair in these patients is the increase in coronary blood flow reserve afforded by reduction in LV volume. Despite the potential benefits of mitral valve repair for patients with severe MR and considerable LV dysfunction. This most recent analysis is not overly surprising. HF in the majority of these patients is not because of flail leaflets, for example, but is secondary to ventricular dysfunction. Most commonly, repair for cardiomyopathy-associated MR involves insertion of either a complete or partial band attached to the annulus of the mitral valve. Mitral repair only deals with one aspect of the overall pathophysiologic condition, ie, annuloplasty rings can assist with tenting of the leaflets and the chordal attachments. This destruction of the subvalvular apparatus results in ventricular dysfunction. In many patients, the underlying problem continues unabated (ie, primary myopathy).

In evaluating studies of HF with MR, it will be important to separate causes (ie, ischemic versus dilated) and surgical approaches. Future trials must be designed to distinguish differences among various operative strategies, such as annuloplasty, papillary muscle resuspension, secondary chordal transection, ventricular reconstruction, passive restraints, and chordal-sparing valve replacement. Paramount in these procedures is to have little or no residual MR. If feasibility of repair is deemed improbable, mitral replacement should be performed. Traditional mitral valve replacement includes complete resection of the leaflets and the chordal attachments. This destruction of the subvalvular apparatus results in ventricular dysfunction. Preservation of the chordal attachments to the ventricle with valve replacement might provide similar or even better results than annuloplasty in patients with MR and HF. Although it might not portend an increased survival in these high-risk patients, the beneficial effects on quality of life (decreased HF) will likely keep low EF mitral valve interventions in the armamentarium of HF surgeons.

**Ventricular restoration**

After transmural myocardial infarction, the ventricle remodels pathologically from its normal elliptical shape to a spherical shape and this change in geometry is responsible, in part, for the constellation of symptoms associated with CHF and decreased survival. There are several ventricular restoration techniques, all aim to correct this pathologic alteration in geometry. Most approaches involve incising and excluding nonviable myocardium with either patch or primary reconstruction, decreasing ventricular volume. Although the initial enthusiasm of ventricular resection in nonischemic dilated cardiomyopathies (“the Batista procedure”) has faded, it has long been established that resection of dyskinetic segments associated with LV aneurysm can increase functional status and prolong life. Success of early lytic and percutaneous therapy for acute myocardial infarctions has decreased the incidence of true LV aneurysms. Ventricular restoration as such, now focuses on excluding more subtle regions of akinetic myocardium. The Reconstructive Endoventricular Surgery returning Torsion Original Radius Elliptical shape to the LV (RESTORE) group reported in 2004 that after ventricular restoration using the technique described by Dor, there was an increase in EF from 29.6% to 39.5%, a decrease in end-systolic volume index, and considerable improvement in NYHA function class (67% NYHA III/IV preoperatively versus 85% NYHA I/II postoperatively). Similarly, Yamaguchi and colleagues demonstrated a substantially improved 5-year survival in patients with ischemic cardiomyopathy who underwent ventricular restoration and CABG versus those who underwent CABG alone, 90% versus 53.5%, respectively.

Much enthusiasm currently exists to use ventricular remodeling operation for HF patients. Most studies outside of the Reconstructive Endoventricular Surgery returning Torsion Original Radius Elliptical investigators are single-institution, retrospective analyses. Although many believe that this therapy is warranted for dyskinetic and large akinetic segments of myocardium, some are beginning to perform this procedure even on hypokinetic regions. The major study of ventricular reconstruction is the NIH-funded Surgical Treatment of Ischemic Heart Failure trial. In its second hypothesis, the Surgical Treatment of Ischemic Heart Failure investigators are prospectively randomizing patients with akinetic, low EF ventricles to CABG versus CABG and ventricular reconstruction. Enrollment for this aim will
be met within the next year and, after prolonged followup, should shed light on the importance of both revascularization and ventricular geometry in these very ill patients.32

**Passive restraints**

Fundamental principles in hemodynamics (ie, Laplace’s law) hint as to the progression of structural deterioration associated with HF. A cycle exists with increasing ventricular volume resulting in increased wall tension, which is compensated with thickening of the ventricle and its dilation. Historically, dynamic cardiomyoplasty, ie, wrapping the latissimus dorsi muscle around the heart and entraining it to beat synchronously with the heart, was intended to augment systolic function. Although this technique was somewhat cumbersome and not overwhelmingly successful, investigators learned that this external fixation of the heart prevented its dilation and improved HF. Recent enthusiasm, as such, has focused on devices that restrain the heart.

The most studied product is the CorCap device (Acorn Cardiovascular), which is a mesh-like support that is sewn circumferentially around the ventricle. Animal studies have demonstrated its downregulation of stretch response proteins, attenuation of myocyte hypertrophy, and improvement of sarcoplasmic-reticulum calcium cycling. Early reports in humans have demonstrated a decrease in ventricular chamber dimensions and improvement in EF and NYHA class.60 The Acorn Pivotal Trial was completed recently. Patients with NYHA class III/IV disease were randomized to one of four groups: optimal medical therapy, optimal medical therapy with the cardiac support device, mitral valve repair/replacement alone, or mitral valve repair/replacement with cardiac support device. Results revealed that patients who received the cardiac support device required fewer major cardiac procedures (eg, transplantation, left ventricular assist device [LVAD]) compared with controls after implantation, a greater reduction in LV end diastolic and systolic volumes, and considerable improvement in quality of life.61 Wide-spread use is not available, but the FDA recently denied its approval, citing need for additional statistical evidence to demonstrate its efficacy.62

**Electrophysiology**

Patients with HF and interventricular conduction abnormalities (roughly defined as a QRS interval > 120 to 130 ms) are potential candidates for chronic resynchronization therapy by insertion of a biventricular pacemaker. Chronic resynchronization therapy aims to improve cardiac performance by restoring interventricular septal electrical and mechanical synchrony of the heart, reducing presystolic MR, and optimizing diastolic function by reducing mismatch between cardiac contractility and energy expenditure.63 Technically, three cardiac leads are placed transvenously: an atrial lead, a right ventricular lead, and a LV lead, which is threaded through the coronary sinus and out one of its lateral wall tributaries. Surgeons have assisted on difficult transvenous LV placements by epicardial insertion of LV leads by a number of techniques, including minithorocotomy, thorcoscopy, or robotically. Several prospective, randomized trials have been performed evaluating the efficacy of chronic resynchronization therapy. The Multicenter InSync Randomized Clinical Evaluation (MIRACLE) Study Group demonstrated an improvement in NYHA functional class, quality of life, and EF. In addition to augmenting functional capacity, chronic resynchronization therapy also appears to favorably affect mortality effect. Although the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial only demonstrated an increase in survival when biventricular pacing was placed with a defibrillator,65 the Cardiac Resynchronization in Heart Failure (CARE-HF) trial recently showed a 36% reduction in death with biventricular pacing alone.66 Mortality in both studies was usually sudden death. Indeed, the role of the implantable cardioverter defibrillator has expanded rapidly over the last decade. Patients with HF are 5 to 10 times more likely to die of sudden death than the general population. Sudden death from both ischemic and nonischemic sustained ventricular tachyarrhythmias has been remarkably reduced, such that current American Heart Association guidelines recommend an implantable cardioverter defibrillator in virtually all patients with EF < 35%.

Interestingly, prophylactic use of an implantable cardioverter defibrillator at the time of low-EF CABG failed to improve survival compared with those patients only revascularized.67 This study speaks to the importance of the independent influence of CABG on reduction of mortality in ischemic cardiomyopathies. We have recently adopted an approach of placing prophylactic LV epicardial leads on patients with conduction delays at the time of high-risk HF operation. These leads are tun-
neled for future connection to a traditional transvenous atrial and right ventricle biventricular pacer-defibrillator. The benefit of this strategy remains to be proved prospectively.

Atrial fibrillation (AF), with or without HF, is an independent risk factor for increased cardiovascular morbidity and mortality. In a large retrospective study of patients with LV dysfunction, patients with AF had greater all-cause mortality (34% versus 23%) and greater number of deaths attributed to pump failure (16.7% versus 9.4%). Aggressive management of AF in HF patients is receiving greater attention. Compared with controls, HF patients with concurrent AF who underwent catheter ablation demonstrated considerable improvement in LV function (increased EF by 21%), decrease in LV dimensions, and improvements in exercise capacity, symptoms, and quality of life as compared with controls.

The cardiac surgical community has increasingly adopted an aggressive approach to treatment of AF during concurrent operations. The Cox-Maze procedure, developed in the early 1990s, involves creation of multiple incisions to prevent atrial reentry and allow for propagation of normal sinus impulses. This technique proved successful in curing AF, but is technically challenging and time-intensive, lessening its widespread adoption. A number of variations from this original technique have evolved throughout the past decade. Most use a host of adjunct ablation devices to replace many of the “cut and sew” lesions, including cryothermy, radiofrequency, microwave, and high-intensity focused ultrasonography. The ease and efficacy of these technologies have allowed their adoption in combination with other procedures performed for HF. Indeed, some evidence exists that LV function can be improved with concomitant ablation of AF during operations for structural (usually valvular) heart disease. Although the conceptual advantages of restoring atrial function exist, no study has looked at the role of surgical AF ablation in impacting the natural history of these patients. To date, surgical ablation for lone AF in HF patients remains anecdotal.

MECHANICAL CIRCULATORY SUPPORT

Ventricular assist devices
In 1963, Dr Michael DeBakey reported the first clinical use of a ventricular assist device (VAD) in an individual who suffered a cardiac arrest after an aortic valve replacement. Unfortunately, the patient died. Three years later, DeBakey successfully implanted a newer device in an individual who was unable to be weaned from cardiopulmonary bypass. This patient was mechanically supported for 10 days, allowing for myocardial recovery, and was successfully discharged from the hospital. Since this early era, VAD development has progressed rapidly and is now an invaluable tool in treatment of HF (Fig. 4).

A number of devices are currently available to support both the acutely and chronically decompensated heart. In some cases of extreme cardiopulmonary failure, the only recourse is complete support with extracorporeal membrane oxygenation. Despite some encouraging results with extracorporeal membrane oxygenation for cardiogenic shock, most patients requiring circulatory assistance can be helped with ventricular support alone. Depending on the particular device used, both the right and LVs can be assisted (LVAD, right ventricular assist device [RVAD], and biVAD). Conceptually, they are all similar: blood is removed from the failing ventricle into a pump, which delivers blood to either the aorta (LVAD) or pulmonary artery (RVAD). Often these devices can be placed temporarily to allow myocardial recovery (ie, acute viral myocarditis, postcardiomyotomy). The most common use of these devices is to bridge the acutely failing heart to eventual heart transplantation. This method allows patients to recover end-organ damage, obtain rehabilitation, and possibly go home before definitive heart transplantation. Finally, there are a group
of patients with severe CHF who are not transplantation candidates and who otherwise would succumb. These patients are candidates for lifetime use or destination therapy. With this method, devices would be placed that would be intended for indefinite therapy.

Currently, nearly 30 different mechanical circulatory devices are either in use or in the preclinical phase. Conceptually, these pumps differ in their mode of function, including pneumatic, electric, pulsatile, and rotary pumps. In the US, several options exist (ie, FDA-approved) for bridge to recovery and transplantation, including the Abiomed BVS 5000 (typically used for short-term support), Abiomed AB5000, Thoratec paracorporeal and intracorporeal left and right ventricular assist, Novacor LVAD, and Heartmate LVAD. In addition, several smaller, axial flow devices are actively involved with clinical trials, including the Jarvik 2000 Flowmaker (Fig. 5). Although the Heartmate LVAD is the only device FDA-approved for destination therapy, several other devices are actively being studied in the US for use as destination therapy, including Novacor, Heartmate II, and DeBakey-Noon Micromed LVADs.

Each device used for bridge to transplantation has its good and bad points. For example, the Heartmate device does not require warfarin anticoagulation like the other well-known pulsatile pump (Novacor), but it does not carry the same durability as the Novacor. The newer axial flow pumps are much smaller, easier to insert, and have less morbidity, but the effect of longterm continuous flow has yet to be determined. Despite the presumed weaknesses of these therapies, the survival through heart transplantation for patients receiving VADs is roughly 70%—quite impressive in this desperately sick cohort of patients. The evolving technology allows for a host of clinical and physiologic questions that, when studied, will continue to advance the field.

Results of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) study have been widely discussed and offer the only prospective, randomized data comparing very sick, nontransplantation-eligible CHF patients on optimal medical therapy with those receiving an early generation Heartmate LVAD. In brief, survival of medical and LVAD patients at 1 year was 48% versus 26% and at 2 years was 26% and 8%, respectively. In addition to their survival advantage, LVAD patients had improvements in several measures of quality of life. Recent modifications of technique and perioperative care have decreased the high LVAD-related morbidity and mortality observed in Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure. Although Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure represents a single study in a very high-risk group of patients, these data serve as proof of concept for future development of these technologies.
Total artificial heart

The creation of a suitable total artificial heart (TAH) for orthotopic implantation has been the subject of intense investigation for the past 40 years. In 1969, Dr Denton Cooley implanted the Liotta TAH in a high-risk patient after failing to wean the patient off cardiopulmonary bypass after LV aneurysm repair. He was sustained for 3 days until a donor heart became available. Unfortunately, the patient died from pneumonia and multiple organ failure. The historic development of the TAH is rich with technologic genius, device failure, and personal intrigue. Compared with LVADs, the TAH has several potential advantages, including assisting the patient with severe biventricular failure, lack of device pocket and lessened risk of infection, and treating patients with systemic diseases who are not otherwise transplantation candidates (amyloidosis, malignancy).

To date, there are two TAHs receiving the most attention (Table 3). The Cardiowest (Syncardia Systems) is a structural cousin of the original Jarvik-7 TAH that was implanted in Barney Clark with great publicity in 1982. Investigators have recently reported data allowing it to become the only FDA-approved TAH for use as a bridge to transplantation. Nearly 80% of patients survived to transplantation versus only 46% in the control, medical arm. Survival rates at 1 and 5 years in device patients were 86% and 64%, respectively, compared with 69% and 34% in the control group. The Cardiowest’s main limitation is its external power source and large control consul. The Abiocor TAH (Abiomed) uses a novel method of transcutaneous transmission of energy, freeing the patient of any external drive lines. External battery packs are exchanged by the patient and can last for up to 4 hours. The first clinical implantation was performed in July 2001. Currently, only 14 patients have received the device, as part of a trial that includes only patients with less than 30 days to live. Although all have subsequently died, four patients were ambulatory after the operation, two patients were discharged from the hospital to a transitional care setting, and one of the discharged patients was discharged to home on postoperative day 209. The Abiocor is limited by its large size, allowing implantation in only 50% of men and 20% of women. The next TAH to emerge clinically will be the second-generation TAH from Abiomed. The Abiocor II is designed to be 35% smaller and durable to pump for over 5 years. Despite over 40 years of effort, the emergence of artificial heart technology into clinical practice is still immature. With approval of the Cardiowest device, and new efforts with smaller pumps, TAHs will ultimately be a routine component of HF operation for very sick HF patients with biventricular failure.

TRANSLATIONAL APPROACHES

Although many therapies are time-tested, such as bypass surgery and aortic valve replacement, others are maturing, waiting for longterm followup and well-designed prospective studies. The future is filled with advancements in mechanical devices and translational strategies. Indeed, biologic approaches to HF are actively being pursued, both experimentally and clinically.

Hottest on this list is use of stem cells to augment cardiac function. Cellular transplantation is based on the theory that a cardiac progenitor cell can progress into fully differentiated cardiac myocytes and subsequently replace damaged myocardium. Conversely, some believe that these cells play more of a supportive role, rather than a regenerative role, by optimizing conditions for the heart to recover from ischemia. Multiple cell types are currently being studied both experimentally and clinically; these include bone marrow stem cells (both mesenchymal and hematopoietic), dendritic cells, adipocytes, endothelial progenitor cells, and skeletal myoblasts.

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<td>60</td>
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<tr>
<td>Maximum cardiac output (L/min)</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Power source</td>
<td>External</td>
<td>Internal</td>
</tr>
<tr>
<td>Valves</td>
<td>Mechanical</td>
<td>Trileaflet plastic</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>160</td>
<td>900</td>
</tr>
<tr>
<td>FDA-approved</td>
<td>Yes (bridge to transplantation)</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 3. Comparison of Cardiowest and Abiocor Total Artificial Heart

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To date, clinical trials are performed mostly in single centers with limited patient numbers. Some intriguing results have been reported. Intracoronary infusion of cardiac progenitor cells in patients with acute myocardial infarctions have demonstrated improved LV EF and end-systolic volumes.\(^87\) In a recent phase I clinical trial using autologous skeletal myoblasts at the time of surgical revascularization, Menasché and colleagues\(^88\) demonstrated increased NYHA functional class (2.7 preoperatively to 1.6 postoperatively), EF (24% to 32%), and systolic thickening by echo at the site of implant in 63%. Unfortunately, ventricular arrhythmias developed in many of these patients. Recently, Patel and colleagues\(^89\) randomized 20 patients to receive off-cardiopulmonary bypass revascularization in HF patients (EF < 35%) with or without subepicardial injection of autologous bone marrow stem cells. Compared with the revascularization group, the stem cell-treated patients were observed to have increased EF at 6 months (46% versus 37%).\(^89\) Many variations on the stem cell theme exist, including angiogenic therapy to increase vascularity at the site of infarct and growth factors to increase native stem cell homing to injured myocardium.\(^90\) More questions than answers exist in this growing field, including optimal cell type, optimal cell density, identification of correct patients, frequency of administration, and adjuncts for revascularization. Most available clinical trials vary tremendously in many of these features and are nonrandomized, making interpretation of the results difficult. Although use of biologic therapy is in its infancy, these early results show its potential promise.

In conclusion, the modern paradigm of treating patients with HF is truly multidisciplinary, including cardiologists, cardiac surgeons, nurses, social workers, therapists, and basic scientists. Thematically, these patients uniformly have multiple comorbidities and are at high risk with any intervention. Their ultimate outcomes, as such, depend on the constellation of preoperative evaluation, intraoperative conduct, and postoperative care. These patients, as to the latter point, require meticulous multiorgan attention to ensure their success. Indeed, a solid working relationship among caregivers is essential to an effective HF surgery program.\(^92\)\(^93\)

Management of HF is truly multifaceted in nature and is constantly evolving. Clinically and scientifically, surgeons are uniquely positioned to have a considerable impact on treatment strategies for these sick patients. The number of options—ranging from bypass and valve operations to transplantation and mechanical assist—suggest that the so-called “vanishing scalpel” will be central to the longevity and quality of life for our aging HF population.

REFERENCES
myoblast transplantation for severe postinfarction left ventricular dysfunction. J Am Coll Cardiol 2003;41:1078–1083.


