Published in final edited form as:

Curr Opin Cardiol. 2008 May ; 23(3): 249–253. doi:10.1097/HCO.0b013e3282f54fea.

Advances in the surgical treatment of heart failure

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Abstract

Purpose of review—Despite advancements in medical therapy, morbidity and mortality remain high. Surgical treatment of heart failure has been the subject of renewed focus, with a particular emphasis on applying the principles of evidence-based medicine to the evaluation of surgical therapies. The purpose of this review is to discuss emerging surgical therapies in heart failure, in particular, mechanical cardiac support and mitral valve repair.

Recent findings—The most widely established surgical therapy for heart failure is cardiac transplantation, but its impact is limited due to the limited number of donors. The Surgical Treatment for Ischemic Heart Failure study, a landmark evaluation of the role of coronary artery bypass grafting and surgical ventricular restoration in patients with ischemic heart disease and heart failure, has recently completed enrollment. Improvements in device design and patient selection appear likely to continue to improve outcomes with mechanical cardiac support in patients who are not deemed transplant candidates (destination therapy). Surgical repair of secondary mitral regurgitation is undergoing evaluation in the soon to be launched Surgery vs. Medical Treatment Alone for Patients with Mitral Regurgitation and Nonischemic study.

Summary—A variety of surgical therapies for heart failure are currently undergoing evaluation in randomized controlled trials. Data from these landmark studies will guide the application of surgical therapy in heart failure for the foreseeable future.

Keywords

heart failure; mitral valve; surgery; ventricular assist device

Introduction

Surgical therapies to address the morbidity and mortality of heart failure have recently been a focus of renewed interest. In this review, we will briefly outline the established surgical approaches to heart failure, and focus in greater detail on two emerging surgical approaches – mechanical cardiac support and mitral valve repair. Throughout this review, we will emphasize the strength of evidence supporting the various surgical approaches in heart failure patients.

Surgical therapy in the context of heart failure care

Chronic heart failure continues to increase in incidence and prevalence, with over 500 000 new cases diagnosed each year in the United States. The past two decades have seen dramatic improvements in medical and device-based therapy, with the successive

introduction of angiotensin-converting enzyme inhibitors, β -blockers, aldosterone antagonists, implantable cardiac defibrillators, and cardiac resynchronization therapy. Despite these advances, overall morbidity and mortality from this clinical syndrome remain high, with a 5-year survival of approximately 50%, which remains notably worse than that for many types of cancer [1]. Increasing survival with chronic heart failure and the aging of the overall population have led to a dramatic increase in the overall prevalence of heart failure, in particular more advanced disease. In addition to medical and device-based approaches, a variety of surgical techniques have been employed to treat heart failure, most notably cardiac transplantation and coronary artery bypass grafting (CABG). Notably, these therapies have generally not been subjected to the same scrutiny as medical therapy with regard to the level of evidence necessary to become a standard part of heart failure care. A summary of current guidelines and the strength of the evidence supporting them is provided in Table 1 [2].

Established surgical therapies for heart failure

CABG and cardiac transplantation are the most established forms of surgical therapy for heart failure. Although a complete review of these approaches is beyond the scope of this review, we will briefly describe recent developments as they relate to the rigorous scientific assessment of these therapies.

Coronary artery bypass grafting and surgical ventricular restoration

Surgical revascularization of patients with coronary artery disease and heart failure with CABG has become the standard of care, based on the logical belief that revascularization of ischemic but viable myocardium would lead to improved ventricular function and better clinical outcomes. Despite the logic of this approach and the long clinical history of CABG in this patient population, relatively little high-quality evidence exists to validate the efficacy of this strategy, and the data that does exist is primarily from an era that predated modern surgical techniques or contemporary medical and device therapy [3]. In this context, the Surgical Treatment for Ischemic Heart Failure (STICH) trial was funded by the National Institutes of Health in 2002 to evaluate the safety and efficacy of contemporary surgical revascularization versus contemporary medical/device therapy alone in patients with ventricular dysfunction and advanced coronary disease [4•]. The STICH trial has completed enrollment and is now in long-term follow-up.

Surgical ventricular restoration (SVR) is a group of related surgical procedures designed to remodel the failing ventricle by decreasing left ventricular volume and restoring a more elliptical ventricular shape. Although no randomized data from large studies are yet available, data from the Reconstructive Endoventricular Surgery returning Torsion Original Radius Elliptical shape to the left ventricle (RESTORE) registry demonstrated improvements in ventricular function and favorable long-term outcomes with this approach [5]. Subsequent reports have, however, suggested that this procedure may be more morbid when used in wider surgical practice [6]. In addition to evaluating the impact of revascularization, the STICH study will test the safety and efficacy of SVR as an adjunct to CABG in eligible patients. Overall, the STICH study will consist of three strata depending on patient eligibility for a given treatment – stratum A that will randomize to medical therapy versus CABG, stratum B that will randomize to medical therapy versus CABG versus CABG+SVR, and stratum C that will randomize to CABG versus CABG+SVR. The overall design of STICH is summarized in Fig. 1 [4•]. Overall, data from STICH is likely to dramatically inform the surgical approach to patients with heart failure and ischemic heart disease for the foreseeable future.

Cardiac transplantation

In selected patients with end-stage heart failure despite optimal medical and device-based therapy, cardiac transplantation remains the best option for long-term survival, with a median survival of more than 10 years [7]. Notably, the concept of cardiac transplantation has never been subjected to a randomized controlled trial, but observed outcomes with transplantation are so dramatically improved compared with the natural history of end-stage heart failure that it has been accepted as the standard of care despite the absence of randomized trial data [8]. Despite the excellent outcomes that have been obtained with cardiac transplant, its impact on the heart failure epidemic is modest, primarily due to the supply of donor organs, which has limited the number of transplants to approximately 2000 annually in the United States. Although a variety of strategies to increase the number of available donor organs have been proposed or attempted [9,10], the number of cardiac transplants performed annually appears unlikely to change dramatically.

Emerging surgical therapies for heart failure

In addition to the established surgical approaches described above, mechanical cardiac support and mitral valve repair are emerging surgical approaches to heart failure.

Mechanical cardiac support devices as destination therapy

The use of ventricular assist devices (VADs) to provide relatively short-term hemodynamic support to patients awaiting heart transplant has been a major therapeutic advance in advanced heart failure, and it has led to improvements in survival to transplant and post-transplant outcomes [11]. The favorable experience with these devices when used for this indication led to the concept of mechanical support as a long-term therapy in patients who were not transplant candidates, so-called 'destination therapy'. The safety and efficacy of this concept was tested in the landmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, which evaluated the use of VAD support as long-term therapy in patients with end-stage heart failure deemed ineligible for heart transplant [12]. In view of the favorable results of REMATCH, the HeartMate XVE device was approved for use as destination therapy in selected patients not eligible for cardiac transplant and who met REMATCH entry criteria. Subsequent experience in the nonrandomized Investigation of Nontransplant-Eligible Patients Who Are Inotrope Dependent (INTREPID) study with the Novacor device demonstrated similar efficacy compared with medical therapy alone [13•]. Notably, in both the REMATCH and the INTREPID, morbidity and mortality in the patients treated with device therapy remained very high, with 1-year survival of 52% in REMATCH and 27% in INTREPID. In general, morbidity during device therapy involved both device-related and patient-related factors. Thus, attempts to improve outcomes for destination therapy have focused on both improved device design and better patient selection. With regard to devices, a variety of novel pump designs including axial-flow and centrifugal-flow pumps are currently in development and appear to provide more durable support with lower complication rates in preliminary experience [14•,15]. Additional efforts have focused on improved patient selection. Clearly, the population of potential candidates for destination VAD ranges from patients who are on the verge of death (who may be too sick to benefit from the device) to those who are too well, in whom the risks of the device may outweigh the potential benefits. In the REMATCH study, patients who were inotrope-dependent gained the most benefit with the use of destination device therapy compared with optimal medical therapy [16]. Risk models to aid in patient selection for destination therapy are being developed [17•]. Data from the experience with HeartMate XVE pump in the 'post-REMATCH' era have identified a variety of patient characteristics that portend higher risk, including thrombocytopenia, poor nutritional status, and markers of other organ (liver and kidney) dysfunction [17•]. 'Clinical

profiles' of various patient populations are being developed to aid in better understanding the optimal selection of patients and timing of device implantation [18]. The development of a national registry to collect detailed data on patients receiving mechanical support devices for permanent support, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), will facilitate the continued refinement of patient selection and hopefully continue to lead to improved outcomes in this challenging population.

Mitral valve repair for secondary mitral regurgitation

Patients with left ventricular systolic dysfunction frequently develop mitral regurgitation (MR) as consequence of left ventricular remodeling [19]. As MR occurs in the absence of a primary abnormality of the mitral valve apparatus, it is referred to as 'secondary' or 'functional' MR. Left ventricular cavity enlargement with chordal tethering, increased ventricular sphericity, annular dilation, decreased annular contraction, and reduced trans-mitral pressure gradient have all been implicated in the pathogenesis on secondary MR [20–22]. Moderate-to-severe MR is found in 38–50% of patients with dilated cardiomyopathy, and the presence and severity of MR are a negative prognostic marker in patients with heart failure [23,24]. Whether the development of functional mitral MR significantly worsens left ventricular remodeling through volume overload and whether correction of the regurgitation favorably affects the clinical course of the disease remains controversial. Vasodilators, β -blockers and cardiac resynchronization therapies appear to lead to progressive decrease in the severity of MR over time with favorable clinical results [25–28]. It is unknown whether these improved clinical outcomes are mediated through a reduction in MR, or whether decreased MR merely reflects favorable ventricular remodeling.

Surgical correction of secondary MR via mitral valve repair typically consists of placement of a prosthetic annular ring that is 1–2 sizes smaller than predicted by measuring the fibrous intertrigonal annulus. These rings serve to normalize the annular size and reduce the antero-posterior dimension of the annulus, thereby improving leaflet coaptation.

In patients with nonischemic cardiomyopathy and secondary MR, small nonrandomized prospective studies have consistently demonstrated that mitral valve repair is associated with decreased left ventricular size and reduced symptoms among survivors. In a cohort of 48 patients with symptomatic heart failure and refractory 4+ severe mitral regurgitation treated with undersized flexible annuloplasty rings, the New York Heart Association function class improved from 3.9 ± 0.3 before surgery to 2.0 ± 0.6 at an average follow-up of 22 months after surgery, with a 2-year survival of 72% [28]. The frequency of hospitalization decreased, as did mean left ventricular end-diastolic volume (change at 24 months -75 ± 33 ml). The largest controlled experience with mitral repair in nonischemic cardiomyopathy took place in the Acorn Clinical Trial, which randomized 193 patients with symptomatic heart failure and MR (88% nonischemic) to mitral repair alone versus mitral repair with concomitant implantation of the CorCap cardiac support device [29]. In this study, mitral repair was associated with progressive reductions in left ventricular volumes over 2 years of follow-up, and improvements in quality-of-life measures, exercise performance, and the New York Heart Association function class after censoring patients lost to death or follow-up. Reductions in left ventricular dimensions were more pronounced in the CorCap-treated patients than in those treated with mitral valve surgery alone. Both groups saw an early decrease in ejection fraction at 3 months followed by progressive improvements in ejection fraction from 3 to 18 months after surgery (Fig. 2) [30••].

Secondary MR in patients with ischemic heart disease and heart failure results from more complicated pathophysiology. In particular, isolated changes in lateral ventricular wall geometry and papillary muscle function seem to play an important role in the development of ischemic MR. Consequently, repairs are more likely to include ring placement with

additional corrections to the mitral apparatus [31]. Surgical reconstruction of the submitral apparatus through chordae tendinae elongation or release can reduce leaflet tethering and enable improved leaflet coaptation [32].

Surgery for correction of secondary MR appears to be relatively safe, despite the increased risk of valvular surgery in patients with impaired left ventricular systolic function [33]. Of 101 patients with left ventricular ejection fraction, fewer than 45% undergoing isolated mitral valve repair at Duke University Medical Center, in-hospital mortality was 2.9% with 1-year survival 93% [34]. The heart failure patients receiving mitral valve surgery within the Acorn study had mortality rates of 1.6% at 30 days [30••]. These two case series suggest that mitral valve surgery can be performed with low surgical mortality and good intermediate-term clinical outcomes at experienced centers. Long-term durability of mitral valve repair is less uncertain. In the 101 Acorn study patients undergoing mitral valve repair without CorCap placement at 6 months after surgery, 14.5% of patients had 2+ or greater mitral regurgitation, indicating relatively good short-term durability of repair [30••]. Longer-term failure may be higher (30% or more), particularly in the ischemic population [35]. Overall, the balance of efficacy and safety of mitral valve repair in patients with heart failure and secondary MR remains uncertain. A rigorously controlled randomized clinical trial, the Surgery vs. Medical Treatment Alone for Patients with Mitral Regurgitation and Nonischemic Heart Failure (SMMART-HF) is currently being launched by the National Institutes of Health Heart Failure Clinical Research Network to address this question in patients with nonischemic heart failure.

Conclusion

Heart failure remains a highly morbid syndrome despite improvements in therapy. A variety of epidemiologic trends, including the aging of the population and greater survival after acute myocardial infarction, will lead to an increased prevalence of heart failure for the foreseeable future. Led by the landmark STICH trial, surgical therapies are entering an era of evidence-based medicine, and CABG in left ventricular dysfunction, SVR, and mitral valve repair are all currently being tested in randomized clinical trials against optimal medical and device therapy alone. The completion of these extremely challenging but critically important trials will inform the optimal utilization of surgical therapies in combating the heart failure epidemic moving forward.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 284–285).

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Figure 1. Design of the Surgical Treatment for Ischemic Heart Failure (STICH) study
 CABG, coronary artery bypass grafting; CAD, coronary artery disease; EF, ejection fraction; MED, medical therapy; SVR, surgical ventricular restoration. (Data from Velazquez *et al.* [4•].)

Figure 2. Change in ejection fraction over time after mitral valve repair in patients enrolled in the Acorn Clinical Trial
Data from Acker *et al.* [30••].

Table 1**Surgical therapies for heart failure**

Therapy	Current guideline recommendation^a	Level of evidence^a	Randomized trial
Revascularization for ischemic CM (left main disease or functional equivalent)	I	B	No
Revascularization for ischemic CM (absent left main disease or equivalent)	IIA	B	Ongoing
SVR	IIB	C	Ongoing
Cardiac transplant	I	B	No
Destination LVAD	IIA	B	Yes
Mitral valve repair	IIB	C	Ongoing

CM, cardiomyopathy; LVAD, left ventricular assist device; SVR, surgical ventricular restoration.

^aBased on ACC/AHA 2005 Guidelines for the Diagnosis and Management of Chronic Heart Failure [1] or the ACC/AHA 2004 Guidelines for Coronary Artery Bypass Surgery [2].