Surgical treatment concepts for heart failure

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Our present generation is seeing a continued increase in the incidence of heart failure worldwide. Fundamental advances in medical and surgical therapy for patients with heart failure has been laid out for over two decades, and a number of treatment options to prevent or delay its onset has, until now, been a main focus of experimental and clinical researches.

Much as has been said and done, heart failure remains a progressive disease, and if left untreated, 30-40% of patients die in end-stage heart failure (NYHA III-IV, AHA/ACC D) (1). And because of enormous strides made in medical treatment of chronic heart failure, more patients are reaching the end-stage of chronic heart failure, which may be refractory to medical therapy. Over these years, several surgical options in treatment for heart failure (Figure 1) have been clinically tried and results reported. We may categorize them into abandoned surgical options, surgical options with hitherto unfulfilled hopes and currently established surgical strategies.

Orthotopic heart transplantation is a fairly well established and standardized procedure with good long term results (2). Quality of life is determined by side-effects of life-long medication. The fate of the patients is determined by the side effects of immunosuppressive drugs, increased tumor incidence and chronic vascular transplant disease. Donor heart availability cannot be foreseen. The heart is obtained by complicated harvesting and transport logistics. It is subject to an unpleasant competition process, especially in Germany (2, 3). With the increasing number of patients eligible for heart transplantation, it is impossible to meet the demands for donor hearts, even if the potential for organ donations were fully exploited. This results in an
ever-longer waiting times, which is highly associated with poor prognosis, and 20% mortality during the waiting period. With ever decreasing numbers of donor hearts, heart transplantation nowadays becomes a rare procedure limited to a small highly-selected patient group and cannot be considered a readily-available treatment concept. Against the backdrop of a widening gap between demand for, and supply of, the donor hearts, what are the other treatment options?

**Abandoned surgical options**

*Dynamic cardiomyoplasty* involves wrapping the heart with the latissimus dorsi muscle and stimulating the muscle to assist contraction. The wrap itself may provide a constraint helping to limit progressive cardiac dilation and/or assist in reversing this process. It has been introduced by Carpentier and Chachques (4) on a human in 1985. They performed more than 1500 operations since then; however, symptomatic improvement was seen only in highly selected patients and no improvement of 1-year survival as well as in haemodynamics have been reported. Leier (5) stated that “it appears that those who can survive the operation do not need it, and those who need it, cannot survive it”.

*Passive cardiomyoplasty* aims to reduce ventricular enlargement due to ventricular remodeling with the help of an elastic net, called a cardiac support device, slipped over the myocardium, like an elastic girdle around the heart, to help reverse chamber remodeling. The reduction in ventricular radius by the device is meant to ease cardiac wall strain and thus prevent further ventricular dilatation by improving cardiac efficiency (6).

Data from clinical studies with the ACORN CorCap do not allow a definitive assessment of the technique of passive cardiomyoplasty. Hence, at the moment, the system cannot be
viewed as a proven therapeutic alternative for patients with end-stage heart failure, as no advantage has been determined in terms of survival rates and ejection fraction. *Partial left ventriculectomy*, which directly reverses remodeling by acute removal of a portion of the lateral wall, has been introduced by Batista (7) as an alternative surgical therapy to heart transplantation. It has emerged under keen attention in the past decade but then results are controversial if not intriguing, thus, it almost disappeared because of high operative mortality and frequent recurrence of heart failure (8).

**Surgical options with hitherto unfulfilled hopes**

*Cardiomyocyte restoration by stem cell therapy.* Utilizing stem cells to repair the damaged heart has seen an intense amount of activity over the last decade (9). Currently, there are multiple ongoing clinical studies to test the efficacy of various different cell therapy approaches to repair the damaged myocardium, both preclinical and clinical trials. With the plethora of trials and cell alternatives, there has come not only great enthusiasm for the therapeutic potential, but also great confusion about what has been achieved. Cell therapy has the potential to regenerate and replace damaged tissue with healthy tissue. Bone marrow cells appear to release biologically active factors that limit myocardial damage. Unfortunately, bone marrow cells from patients with chronic diseases propagate poorly and can die prematurely.

Substantial challenges must be addressed and resolved to advance the use of stem cells in cardiac repair including identifying the optimal stem cell(s) that permit transplantation without requirements for host immune suppression; timing of stem cell transplantation that maximizes chemotraction of stem cells to infarcts; and determining the optimal technique for injecting stem cells for cardiac repair. Techniques must be developed to enhance survival and propagation of stem cells in the myocardium. It is now becoming clear through a number of notable examples that progress to the clinic may have occurred too quickly, before adequate testing and independent verification of results could be completed. Broad reproducibility and transfer of results from one lab to another has been and always will be essential for the successful application of any cell therapy. So, what is the prognosis for cell therapy to repair heart damage? Will there be an approved cell therapy, or multiple ones, or will it require combinations of more than one cell type to be successful? These are questions often asked.

The answers are difficult to know and even more difficult to predict because there are so many variables associated with cell-based therapies. There is much about the biology of cell systems that we still do not understand. Despite the false starts so far, there is the strong likelihood one or possibly multiple cell therapies will succeed. Clearly, important information has been gained, which should better guide the field to achieving success. The coming years will no doubt bring some exciting developments.

**Cardiology treatment option**

*Cardiac resynchronization therapy* (CRT). Patients with advanced systolic heart failure often show interventricular or intraventricular conduction disturbances. Analysis from large clinical trials demonstrated a positive correlation of the width of the QRS complex with mortality in heart failure patients. In pathophysiologic terms, left bundle branch block results in asynchronous ventricular contraction, presystolic mitral insufficiency, and mechanical disturbance of pump function, which is accompanied by worsening symptoms. CRT can therefore be expected to improve left
ventricular systolic function and prognosis by preventing cardiac decompensation. Early studies investigating the short-term effect of biventricular pacing in patients with advanced heart failure (NYHA III-IV) who are in sinus rhythm showed a statistically significant mean reduction of one NYHA Functional Class improved quality of life, and a mean increase in walking distance of approximately 100 meters (10). In patients with advanced heart failure (NYHA Functional Class III-IV), reduced left ventricular function (EF < 35%) and wide QRS complexes with dyssynchrony and sinus rhythm CRT reduces symptoms and mortality. While several patients qualifying for CRT have less severe heart failure than patients suitable for heart transplantation, for those who are candidates for heart transplantation, CRT may improve symptoms and prognosis on the waiting list. For patients excluded from heart transplantation due to comorbidities or other reasons, CRT may be an alternative. In conclusion, the benefits of CRT appear remarkably durable. Delay in implanting a CRT device in a patient who has recent or persistent NYHA class III/IV heart failure appears to be associated with an irrevocable reduction in survival (10).

**Current surgical strategies**

Conventional heart surgery can be performed with acceptable risk and fairly good long-term results in well-selected patients (those with left ventricular failure, obstruction of coronary arteries, ischemic mitral incompetence and left ventricular aneurysm, which we termed LOCIMAN) with advanced heart failure. The results appear to depend mostly upon the quality and the amount of viable myocardium that can be improved by the procedure. Relatively, concerns arise as to the relative contribution of hibernating myocardium, ischemic mitral incompetence and left ventricular aneurysm or akinesia to left ventricular failure. It is anticipated that some patients will eventually need additional mechanical short or medium-term or even permanent mechanical support.

**Coronary revascularization**

In heart failure from ischemic cardiomyopathy, revascularization is most effective in hibernating myocardium without cell death and without scarring. A good left ventricular wall thickness on echo ( > 8 mm) in the absence of infarct is a reliable indicator of viability (11). A high grade proximal coronary obstruction and good peripheral recipient vessel represent optimal conditions for bypass grafting. Coronary artery disease with severely impaired left ventricular function is the main cause of heart failure in 27.5% of all patients considered for heart transplantation (12).

However, most patients with end-stage heart failure from ischemic cardiomyopathy are not suitable candidates for heart transplantation because of age limitation, concomitant diseases or elevated pulmonary vascular resistance; hence heart transplantation is not an option in this group. Coronary artery revascularization remains a mainstay approach.

The surgical risk associated with coronary artery bypass grafting (CABG) in patients with ischemic cardiomyopathy has been substantially reduced in recent years thanks to the developments in cardiac surgery. However, the role of CABG as a standard therapy in patients with advanced heart failure remains unclear, as Ennker (13) discussed.

To date few well-designed large-scale studies have investigated factors on which a decision in favor of surgical revascularization should be based.

Whether a patient with ischemic cardiomyopathy will ultimately benefit from CABG...
in terms of survival and recovery of left ventricular function depends primarily on the presence of vital, revascularizable myocardial tissue (hibernating or stunned myocardium) (14). Different diagnostic methods are currently performed to assess myocardial viability such as fluorodeoxyglucose positron emission tomography, magnetic resonance imaging, single-photon emission computed tomography or echocardiography, to differentiate between stunned (still adequately perfused and metabolized), hibernating (mismatch between perfusion and metabolism, which is intact) and an infarction scar (neither perfused nor metabolized). Therefore, the operative risk can be reduced with the help of preoperative patient screening and selection by myocardial viability assessment, and this selection process may extend the indication for CABG to those patients otherwise referred for heart transplantation.

**Ventricular restoration**

Left ventricular size is an important prognostic factor for long-term survival in patients with ischemic cardiomyopathy. Ventricular reconstruction is therefore an option for patients with ventricular dilatation and this could slow or present progressive heart failure in these patients. Perioperative mortality rates are at an acceptable level, and long-term survival rates are significantly better after surgical ventricular reconstruction than after coronary revascularization alone, as Beyersdorf (15) has discussed in the recent RHICS 4th Expert Forum-EACTS annual Meeting. He also pointed out that as in coronary revascularization, the decision as to whether perform ventricular reconstruction depends on the vitality of the remote myocardium and the size of the asynergistic area, since patients with large asynergistic areas of more than 35% of the total left ventricular volume are not suitable candidates for this procedure.

**Left ventricular aneurysmectomy**

This procedure is ideal when aneurysm is localized and thin-walled and when the other coronary artery systems are unaffected. Maximum improvement is obtained in patients with advanced heart failure. As with ventricular restoration, the value of ventricular volume reduction depends on the quality of the remaining myocardium. For assessment of indications for and dimensions of ventricular reduction, a combined view of computed tomography motion scans and echo strain rate has been helpful in our hands.

**Valve repair for ischemic mitral incompetence**

Ischemic mitral incompetence (IMI) is the most important mitral valve disease of the future. Ventricular dilatation due to ventricular remodeling processes in heart failure often leads to mitral insufficiency, which in turn causes additional left ventricular stain and further exacerbation of symptoms. This is an unfavorable combination. Mitral valve repair is a therapeutic alternative, to reduce elevated myocardial load and left ventricular oxygen demands due to mitral insufficiency and thus improve left ventricular function. One surgical technique available in ischemic or dilated cardiomyopathy is annuloplasty using an undersized annuloplasty ring.

Our technique differs in a way that no prosthetic ring is applied, since it distorts the ventricular geometry and may even cause left ventricular obstruction. We use untreated autologous pericardial strip to augment the posterior leaflet and bring it closer to the anterior mitral leaflet area by providing a wider coaptation surface area. However, mitral valve repair may not probably be suitable as a permanent alternative
to heart transplantation, as some patients again develop end-stage heart failure after three years.

**Mechanical circulatory assist devices**
The evolution of mechanical circulatory assist devices, aimed to bridge the heart to transplantation, or to myocardial recovery, has helped many of patients. Nowadays, these devices are even implanted for long-term support, particularly in elderly patients and in those with contraindications to heart transplantation. This may even be the best and the optimal solution to treat heart failure patients in the future. Mechanical circulatory support as a bridge to transplantation was successfully introduced by our group in 1987 (16, 17). The ensuing routine use of assist devices to keep patients alive until transplantation paved the way to their clinical use as an established treatment for end-stage heart failure by itself.

This has become essential in the face of the increasing donor organ shortage, with many patients receiving permanent assist devices and fewer receiving heart transplants. Various assist systems are now able to improve physical conditions and offer the patient good quality of life for several years. This is also true for patients with contraindications for heart transplantation. Moreover, now some patients prefer a mechanical device to a donor heart.

**Surgical options for end-stage congenital heart disease**
Great developments and progress in cardiac surgery and cardiology have resulted in pediatric patients with congenital heart disease (CHD) who previously would have died now reaching adulthood. Although long-term survival and quality of life in children and adults with complex congenital heart disease has remarkably improved due to advances in operative techniques and perioperative management, as well as the increasing experience of congenital heart surgeons, a growing number of patients with complex CHD eventually develop end-stage heart failure and will require another treatment. These may be the patients with single ventricle physiology and failed Fontan circulation, those with transposition of the great arteries, either palliated or corrected, and those with situs inversus. What do we have to offer them then? Two alternatives remain: heart transplantation or permanent mechanical circulatory support.

It is unlikely that there will be enough donor hearts for these patients if or when heart failure eventually ensues. Perhaps the best hope for this growing population lies in the developments in implantable devices (18), rather than in transplantation. For the patient with a single ventricle, mechanical support may be very difficult, although not impossible.

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