SURGERY FOR HEART FAILURE

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The failing heart creates a huge health care problem. It is common and becomes more so with age. Recognising our aging population, it is understandable that the prevalence of heart failure is increasing¹ in the UK and is the most common diagnostic related group at hospital discharge. It is the primary or secondary diagnosis in about 1% of the population and consumes a similar proportion of the country's gross domestic product every year. So how do we recognise this monster? The 2005 American College of Cardiology/American Heart Association (ACC/AHA) guideline update for the diagnosis and management of chronic heart failure in the adult² defines heart failure as: "a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood".

CLASSIFICATION OF HEART FAILURE

It is a progressive disorder and to capture this the ACC/AHA has proposed a new approach to the classification of heart failure² (table 1).

Although this classification implies a progressive clinical picture for heart failure, it has an unpredictable course. It is difficult to characterise and especially so in its early stages. This probably follows from there being no diagnostic test for heart failure because it is "largely a clinical diagnosis that is based on a careful history and physical examination".² When symptoms present they are predominantly fatigue, breathlessness and limited exercise tolerance. Fluid accumulation is apparent on the right side as dependent oedema and on the left as pulmonary oedema. The condition is fickle and patients describe variation in symptoms. Thus sequential clinical assessment finds patients moving up and down the New York Heart Association (NYHA) functional classification (table 2).

A series of drug trials has firmly established the current pharmacological management of heart failure. These are summarised in the ACC/AHA guidelines with awarded levels of evidence.² As we consider a surgical approach to heart failure it is helpful to distil physiological themes that support pharmacologic treatment such as reduction of afterload to the heart or increased force of contraction. Let us express these in the following relationships:

The first:

$$\text{Cardiac output (CO)} = \frac{\text{perfusion pressure (arterial BP - venous P)}}{\text{peripheral resistance}(\Omega)}$$

This first relationship demonstrates that inadequate cardiac output can be improved either by increasing perfusion pressure (reducing venous pressure by diuresis or venodilatation) or reducing peripheral resistance (using arteriolar dilators or strategies to uncouple the augmented angiotensin-renin axis that characterises heart failure).

The second:

$$\text{Cardiac output (CO)} = \text{stroke volume (SV)} \times \text{heart rate (HR)}$$

The second relationship indicates that an increase in stroke volume or a raised heart rate (to an upper limit dictated by adequate diastolic filling of the ventricle or both) will improve the heart failure patient's lot.

The third:

$$\text{Ejection fraction} = \frac{(\text{end diastolic volume} - \text{end systolic volume}) \times 100\%}{\text{end diastolic volume}}$$

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Table 1 American College of Cardiology/American Heart Association time line classification of heart failure

- ▶ Stage A: asymptomatic patients at risk of developing heart failure (with hypertension, coronary artery disease, for example)
- ▶ Stage B: those who are asymptomatic but have ventricular changes of heart failure (hypertrophy or ventricular impairment)
- ▶ Stage C: those with a current or past history of heart failure in association with structural changes, and
- ▶ Stage D: those with refractory heart failure

This third relationship is often used to describe ventricular function but it must be used with caution. It is a derived value and risks misinforming the clinician—for example, a fall in stroke volume can coincide with a rise in ejection fraction, such as in hypovolaemia.

The fourth:

$$\text{Intra-ventricular pressure (P)} = \frac{2 \times \text{ventricular wall tension (T)}}{\text{Ventricular radius (R)}}$$

or

$$T = \frac{P \times R}{2}$$

where ventricular wall tension (T) is directly related to oxygen consumption and ventricular work. This is La Place's law and its evolution was in the surface tension of a bubble. It is not clear how it relates to the working ventricle but probably has its influence during diastole. Starling's law relating stretch of the ventricle to power generated by subsequent contraction (to a finite limit of stretch) predicts systolic function.

Armed with these four relationships this article attempts to bring some clarity to the assortment of surgical solutions for the failing heart. An attempt will be made to offer levels of evidence for each operative approach (see appendix for definitions of evidence levels).

A SURGICAL APPROACH TO HEART FAILURE

Clearly improvement of cardiac output is the aim of any approach that seeks to improve the heart failure patient's well being. Can a surgical approach affect cardiac output? It would appear so:

- ▶ either by removing the primary ventricular insult, or permitting recovery, or
- ▶ by amelioration of the damaged ventricle with improvement of cardiac output (so called "reverse remodelling" or "ventricular restoration surgery").

Where possible it is preferable to identify the cause and remove it rather than accept attempts to surgically reverse remodel the failing ventricle. With this in mind an attempt to identify the possible causes of heart failure is shown in table 3.

There are components of structural change that appear to drive the ventricle to remodel. This process leads to problems with ventricular filling or ejection or both—that is, heart failure. Simply, an obstructed or pressure loaded chamber seems to primarily remodel through hypertrophy of its wall. On the other hand volume overload (for example, valvular regurgitation) leads to ventricular dilatation. An enlarging

Table 2 New York Heart Association (NYHA) classification of heart failure

- ▶ NYHA I: symptoms that appear only at levels of exertion that would limit normal individuals
- ▶ NYHA II: symptoms on ordinary exertion
- ▶ NYHA III: symptoms on less than ordinary exercise
- ▶ NYHA IV: symptoms of heart failure at rest

ventricle moves towards a spherical shape with consequent (secondary) mitral regurgitation. The increasing ventricular radius also leads to increased wall tension (fourth relationship above) and increased oxygen demand. As the remodelling process continues it appears that the hypertrophied, pressure loaded ventricle dilates and the enlarged, volume loaded ventricle develops hypertrophy.

Ventricular remodelling is malign and must be reversed, or at least halted if the patient's lot is to be improved. In the recent past, authors have described the need to remodel the failing ventricle surgically. This unfortunate misuse of nomenclature is confusing and emphasises the need for a universally acceptable and appropriate language.

Surgical approaches should have the aim of reverse remodelling or restoring the ventricle to normality. If this is unachievable then the compromise is to force a trend towards a more normal heart. Such normality must be recognised in three dimensions:

1. **Morphological** (both gross anatomic and microscopic level)
2. **Physiological** in terms of:
 - ▶ contractility: overall and as coordinated inter- and intraventricular contraction with normalisation of contractile reserve
 - ▶ electrical (normalisation of ECG and myocardial excitability)
 - ▶ biochemical: normalisation of:
 - high energy phosphate production, storage and oxygen use
 - enhanced natriuretic peptide secretion
 - raised renin-angiotensin values
 - catecholamine values
 - endothelin values
 - markers of inflammation
3. **Prognostic**, returning the patient's expectation of survival towards that of peers without heart failure, ideally.

THE OPERATIONS

The operations or interventions will be described in a standardised fashion according to whether:

- ▶ the primary insult can be identified and removed or
- ▶ the aim is to attempt to surgically reverse remodel the ventricle.

The outline of the procedure, efficacy, safety and level of evidence will be offered.

Removing the primary insult

In ideal circumstances the primary ventricular insult or remodelling force is identified and removed—for example, removing the pressure loading of the left ventricle by aortic valve replacement (AVR) in aortic valve stenosis. Following this operation hypertrophy may regress and morphology normalise. Physiology improves too, as does prognosis. Similarly, mitral valve repair for regurgitation corrects the volume overloaded

Table 3 Possible causes of heart failure

- ▶ Impaired filling before the ventricle:
 - extracardiac obstruction, eg, pericardial constriction or venous obstruction
 - intracardiac obstruction of inflow, eg, mitral valve stenosis or obstructing atrial tumour
- ▶ Impaired filling of the ventricle:
 - hypertrophy, eg, congenital (genetic, eg, HOCM), acquired (pressure loading in hypertension)
 - infiltration, eg, fibrosis, acute and chronic inflammatory (myocarditis), giant cell, sarcoidosis, amyloidosis
- ▶ Impaired ejection by the ventricle:
 - of the wall: iron overload or chronic alcohol or glycogen excess), ventricular aneurysm formation, dilating cardiomyopathy, ischaemia with hibernation, ischaemia with scarring, loss of ventricular interdependence (bundle branch block, pacing), outflow tract obstruction (dynamic: septal hypertrophy, systolic anterior mitral valve leaflet movement; fixed: subvalvar aortic stenosis)
 - miscellaneous: sustained excessive work load without obstruction: arteriovenous fistulae, super athlete, high output shock
- ▶ Impaired ejection after the ventricle:
 - valvular aortic stenosis, regurgitation
 - aortic coarctation (congenital or acquired)
 - hypertension

HOCM, hypertrophic obstructive cardiomyopathy.

left ventricle and dilatation may recede. Removing toxins such as iron in haemochromatosis and alcohol (supplemented with thiamine) in alcoholic cardiomyopathy has led to reverse remodelling of failing, dilated ventricles. Surgical strategies to control rate or rhythm in persistent atrial fibrillation may lead to reverse remodelling of the dilated heart of tachycardiomyopathy. These surgical approaches will not be discussed further as they are well described elsewhere. The sequential classification of heart failure by the ACC/AHA indicates that all cardiac surgical procedures can be regarded as “heart failure surgery” in their attempts to prevent, ameliorate or correct the condition. This paper would not be complete without some further attention to the hibernating ventricle, a consequence of ischaemia.

Revascularisation

Myocardial ischaemia is probably the most important cause of heart failure and is associated with a 30–50% annual mortality. However, reduced ventricular function may be reversible with ischaemia. This temporary reduction in function has been termed “stunning” and “hibernation”, depending upon the time course. Myocardial stunning follows an acute ischaemic episode and is characterised by reduced systolic and diastolic function with improvement with use of inotropes or restoration of blood flow. Hibernation has a longer history. It was described by Ramtoola in the late 1980s and is characterised by a reduction in myocardial function that parallels the fall in myocardial blood supply. Restoration of function with correction of ischaemia may take some time, occasionally months. Identifying the presence of hibernation is probably best achieved with labelled (F^{18} deoxyglucose uptake) positron emission tomographic (PET) metabolic studies. It can be demonstrated by dobutamine stress echocardiography and its

characteristic biphasic response to increasing concentrations of inotrope. There is an initial improvement in contractility followed by a fall off in function as dobutamine concentrations reach values of 25–40 $\mu\text{g/kg/min}$. Magnetic resonance imaging (MRI) is showing promise too by revealing scar or viable muscle (fig 1).

Procedure outline

This procedure requires the demonstration of hibernation as set out above. The patient then undergoes coronary artery bypass grafting, with the expectation of improvement in objective signs of heart function, heart failure symptoms and survival.

Safety and efficacy

Survival appears to be better after coronary artery bypass grafting in patients with evidence of hibernation compared to those without³ (fig 2).

A number of studies (STITCH and UK-HEART) are underway to improve confidence in this area.

Level of evidence

- ▶ Level B, ACC/AHA recommendation IIa

Ventricular restoration surgery (reverse remodelling surgery)

All too often the primary remodelling process is not identifiable (for example, idiopathic dilated cardiomyopathy) or if it is, it is not amenable to correction (identified genetic lesion—for example, hypertrophic obstructive cardiomyopathy). An attempt is made to summarise these operations in table 4.

INTERVENTION TO IMPROVE CARDIAC OUTPUT BY REDUCING VENTRICULAR AFTERLOAD

Intra-aortic balloon pumping

Kantrowitz introduced the intra-aortic balloon pump (IABP) four decades ago. The principle involves inflation of an intra-arterial balloon in early diastole augmenting coronary perfusion (D in fig 3) followed by pre-systolic (late diastolic) collapse which results in a lower afterload or effective lower systemic resistance for the left ventricle (E in fig 3).

Procedure outline

A 35 or 40 ml Helium intra-aortic balloon is inserted into the femoral artery and passed retrogradely into the thoracic aorta. Sensing of heart rate through ECG or arterial pressure monitoring allows the IABP to inflated on the dicrotic notch of the systemic arterial wave form (onset of diastole) and be collapsed at the latest point possible in diastole.

Efficacy and safety

IABPs are in common use and are regarded as important in the initial management of patients with acute coronary syndromes and those with heart failure. It is a percutaneous device and restricts the patient to an intensive care bed.

Evidence

- ▶ Level B, ACC/AHA recommendation level I

Resection of left ventricular outflow tract

Patients with hypertrophic cardiomyopathy (HCM) may be troubled by left ventricular outflow tract obstruction (LVOTO). Relief of this obstruction leads to improvement of cardiac

Figure 1 Magnetic resonance images of a poorly functioning left ventricle in association with coronary artery disease and (A) hibernating myocardium and (B) scar (arrows).

output and prognosis. This is, of course, not an example of reverse remodelling surgery but ameliorative surgery as the driving force for ventricular remodelling is genetic.

Procedure outline

Direct de-bulking of an LVOTO can be undertaken by open heart surgery or alcohol injection of the first septal artery.

Efficacy and safety

Echocardiographic evidence suggests that both direct surgical resection and alcohol injection are effective at relieving LVOTO in HCM. Open surgery appears to be more effective. Ommen and colleagues⁴ demonstrated, through retrospective review, that surgical resection of LVOTO restored survival to that of individuals unaffected by HCM.

Level of evidence

► Level B, ACC/AHA recommendation IIA

Figure 2 Survival of patients with no mismatched segmental flow and function compared to those with mismatches.³

SURGICAL STRATEGIES TO REDUCE LEFT VENTRICULAR SIZE (LA PLACE SURGERY)

The Myo-splint

Ventricular diameter is reduced by a series of transventricular buttons placed across the short axis of the ventricle. This tends to produce a figure of eight cross section to the ventricle, producing a reduction of internal radius (figs 4 and 5).

Procedure outline

The aim of this operation is to reduce wall stress using the La Place principle and so improve ventricular function. Targeted patients are those with heart failure resistance or who are intolerant of medical treatment.

Efficacy and safety

McCarthy and colleagues reported benefit in a canine model with improvement in ejection fraction, ventricular volumes and

Table 4 Operations to reverse remodel the failing heart

- Intervention to improve cardiac output by reducing ventricular afterload:
 - intra-aortic balloon pumping (IABP)
 - resection of obstructed left ventricular outflow in hypertrophic cardiomyopathy (HOCM)
- Surgical procedures to improve cardiac output by reducing left ventricular size ("La Place surgery"):
 - myo-splint
 - CorCap or Acorn device
 - Batista operation
 - left ventricular aneurysmectomy
 - mitral valve repair for secondary regurgitation
- Surgical strategies to re-power the failing heart:
 - *mechanical*:
 - cardiac resynchronisation therapy (CRT)
 - ventricular assist devices (left (LVAS), right (RVAS), bi- (BiVAS) and total artificial heart)
 - *biological*:
 - dynamic cardiac myoplasty
 - heart transplantation
 - cell transplantation
 - gene therapy
 - up-regulation of natural pathways

Figure 3 The arterial waveform with intra-aortic balloon pump (IABP) counter-pulsation. A: cardiac cycle; B: unaugmented diastole; C: peak systolic pressure; D: peak augmented diastolic pressure (full inflation of intra-aortic balloon (IAB)); E: maximum late diastolic pre-load reduction (collapse of IAB); F: reduced peak systolic pressure seen with IAB pump on.

wall stress. There are recent reports of clinical work in 2001⁵ concluding that careful patient selection with maintained medical treatment is crucial for successful treatment.

Evidence

► Level C, ACC/AHA recommendation IIb

The Acorn CorCap device

Pfeffer and Braunwald described progressive ventricular dysfunction leading to congestive cardiac failure after myocardial infarction. Five years later Kass's group⁶ concluded that dynamic myoplasty (see below) was probably nothing more than a sympathetic cardiac constraint limiting further dilatation of a damaged heart. Probably from these observations came the CorCap, a polypropylene mesh designed to be placed about the ventricles at open operation.

Procedure outline

There is evidence from animal models that such passive constraint improves left ventricular geometry and myocardial stresses after myocardial infarction. The aim is to constrain the failing and dilating left ventricle in patients with NYHA class III or less. Clearly no immediate benefit is offered by this cardiac device and requires an operation with all the hazards of surgery in those with compromised heart function.

Efficacy and safety

A randomised study including 300 heart failure patients was reported to the AHA in 2004.⁷ Those receiving a CorCap device appeared to fare better than those without. There was a significant reduction in left ventricular end-diastolic and end-systolic volumes with an improvement in quality of life, although there was no difference in mortality or hospital readmissions for heart failure.

Evidence

► Level B, AHA/ACC recommendation level IIb

Partial left ventricular resection

In contrast to scar resections of damaged left ventricles, this procedure requires the prescribed removal of muscle between anterior and posterior papillary muscles in dilating, failing left ventricles. This procedure was developed in Brazil 15 years ago

Where $R > r$

Figure 4 Impact of Myo-splint buttons on ventricular radius.

by Batista. Its intention was to offer a surgical solution for patients with heart failure symptoms in the context of dilating cardiomyopathy and specifically Chagas' disease.

Procedure outline

The aim is to normalise cardiac volume/mass ratio, so reducing left ventricular (LV) volume, LV wall stress and improving systolic function. This surgery is usually carried out on cardiopulmonary bypass but has been reported as having been completed off bypass. The surgeon is guided by the arithmetic relationship between circumference and diameter (where circumference = $\pi \times \text{diameter}$, and $\pi = 3.142$). Each 3 cm of circumference resected by the surgeon is equivalent to a 1 cm reduction of ventricular diameter. This is often combined with mitral surgery.

Efficacy and safety

Reports have demonstrated a reduction in LV end diastolic and systolic volumes, and improvements in ejection fraction, cardiac index and stroke volume. Unfortunately death is a frequent complication. Dowling and colleagues⁸ reported a 12 month freedom from death or transplant listing of 56%. This compares poorly with the results of heart transplantation. There are few if any centres undertaking this surgery now.

Level of evidence

► Level B, AHA/ACC recommendation III

Left ventricular aneurysmectomy

The aim of this surgery is to reduce an enlarged ventricular volume and to reverse the forces driving further ventricular remodelling. As with the Batista procedure, a dyskinetic segment of ventricle is removed, reducing ventricular diameter

Figure 5 The Myo-splint.

Figure 6 The CorCap.

and so reducing ventricular wall tension. However, the segment removed is scar and not ventricular muscle. Initially simple excision of post-myocardial infarction scar followed by ventricular placcation was undertaken. This produced distortion of ventricular geometry leading Jatene to recommend an encircling stitch about the aneurysm neck, and Cooley and Dor independently to recommend a patch to the remaining defect. The aim was to restore a more “normal” ventricular geometry.

Procedure outline

Patients with symptoms of heart failure, angina or ventricular arrhythmias are selected for this surgery. On cardiopulmonary bypass the scar is opened. If scarred or aneurysmal the septum is plicated from within the left cavity. The “neck” or edge of the scar is then identified and an encircling stitch placed about it. This is tied, reducing the enlarged ventricular cavity. The remaining defect is then patched with synthetic material. The exteriorised scar edges are finally closed over the repair. Cryotherapy may be applied to the myocardial edge of this repair in an attempt to abolish ventricular arrhythmias.

Efficacy and safety

Dor and colleagues reported⁹ their experience of resections of “akinetic” (without movement) and dyskinetic (paradoxical movement) ventricular scar resections with followed up over nine years (fig 7). Survival of those with akinetic scar was worse than heart transplantation at five years. Worryingly, further work by Marchenko and colleagues (table 5) describes a trend of redilatation of the left ventricle with time. This appeared to complicate all three surgical approaches to aneurysmal scar resection.

More data are required to describe the long-term outcomes of surgical resection of ventricular aneurysms before this common

Figure 7 Cumulative survival after resection of ventricular scar. Adapted from Dor *et al.*⁹

operation can be performed with confidence in a satisfactory long term outcome.

Level of evidence

► Level B, AHA/ACC recommendation IIb

Mitral repair for secondary mitral regurgitation

It seems counterintuitive to repair the valve in secondary mitral regurgitation (MR) in the face of poor left ventricular function. It would seem that this action would effectively raise the afterload to the failing heart, so worsening failure.

Procedure outline

However, MR with poor left ventricular function is associated with a dilated annulus and a tendency for the leaflets to be splinted open though chordal attachments, as the ventricle dilates and becomes more spherical. These mechanisms are added to in the case of ischaemia by papillary rupture, ischaemia or fibrosis.

Efficacy and safety

Bolling and colleagues¹⁰ reported a series of patients with severe MR, ejection fractions of 8–15% and NYHA status of III–IV in whom mitral valve repair was performed. Heart failure symptoms reduced significantly, ejection fraction increased and both LV diastolic and systolic volumes fell with a reduction in “sphericity” of the heart. Survival of these patients is shown in fig 8. The authors suggested that survival was much the same as that following heart transplantation. This is perhaps a little optimistic as recent reports suggest no difference in outcomes for MR patients who have had or not had mitral surgery.

Level of evidence

► Level C, AHA/ACC recommendation IIb

Table 5 End diastolic ventricular (EDV) volumes before, early after and late (12 months) after left ventricular aneurysmectomy with linear closure, septal remodelling or endoventricular patch plasty (endoVP)

Technique	EDV (ml) pre-	Early post-	Late post-
Linear	189 (25)	143 (291)	165 (24)
Septal	199 (36)	150 (27)	170 (26)
EndoVP	251 (64)	174 (32)	187 (27)

Values are presented as mean (SD).

Figure 8 Survival after mitral repair in heart failure. Adapted from Bolling *et al.*¹⁰

SURGICAL STRATEGIES TO RE-POWER THE FAILING HEART: (1) MECHANICAL SUPPORT Cardiac resynchronisation therapy (CRT)

Biventricular pacing is considered when there is evidence of lack of interventricular synchronous contraction—for example, bundle branch block.

Procedure outline

Pacing leads are positioned directly within the right ventricular cavity and onto the left ventricle through the coronary venous system. Simultaneous stimulation re-introduces coordination of right ventricular (RV) and LV contraction. This therapy is directed towards patients who have had heart failure for at least six weeks and who are in NYHA class III or IV despite standard pharmacological treatment and who have a reduced LV ejection fraction ($\leq 35\%$) and a QRS duration on ECG of >120 ms.

Figure 10 Destination therapy (chronic ventricular assist device, Velvas) compared to maximum medical treatment (Omm): REMATCH study.¹³

Efficacy and safety

CRT has been shown to result in reduced interventricular mechanical delay, an increased LV ejection fraction, reduce mortality and improved NYHA class. In addition improvement of symptoms and quality of life have been reported.^{11 12}

Level of evidence

► Level A, ACC/AHA recommendation I

Ventricular assist devices (VAD)

The intention here is to offload the failing heart. This is achieved by the unloading of blood from the ventricle and its delivery into the arterial tree (pulmonary for right ventricular assist device (RVAD) and systemic for left (LVAD)). Both ventricles may be supported simultaneously with biventricular devices (BiVADs). Total excision of a failing heart is occasionally undertaken followed by replacement with an artificial heart (Cardiowest, Abiocr). VADs may be continuous flow or pulsatile and there is currently little to discriminate between

Figure 9 A display of various ventricular assist devices. (1, 2) Percutaneous continuous flow transaortic valve VAD, Implella. (3) Diagram illustrating pulsatile BiVAD Thoratec devices. (4) Total artificial heart (Abiomed). (5) Chest x-ray illustrating Heartmate I as LVAD (with implantable cardioverter-defibrillator in position too).

Figure 11 Dynamic cardiac myoplasty.

them, except that pulsatile pumps are larger (fig 9). Pumps may be placed within the body or lie outside, being connected to the heart by pipes that cross the skin (para-corporeal). There is a risk of deposition of blood elements onto the inner lining of the pumps or connecting tubes. This pseudo-intima may be responsible for the generation of “cross-match antibodies” that are sometimes found with VADs.

Procedure outline

Generally a potential VAD candidate presents with severe, refractory heart failure with deterioration despite intensive medical treatment. A VAD is selected and may be temporary or long-term. Some are designed for percutaneous insertion into the systemic arterial tree lying across the aortic valve (Impella). More usually VADs are inserted via a sternotomy under general anaesthesia. Some devices permit insertion off cardiopulmonary bypass (Levitronix). Patients are often mortally ill with multisystem dysfunction. Bleeding, control of vascular resistance and multi-organ failure are early problems which are soon replaced by risks of infection and thromboembolism. This describes patients in whom heart failure accelerates too rapidly to realise heart transplantation. These individuals are bridged to transplantation safely by the VAD. Interestingly, some patients (often those with a short but aggressive history of failure or myocarditis) recover so that the VAD can be removed and heart transplantation avoided (bridge to recovery).

There is interest in the role of permanent mechanical support for heart failure, usually in patients ineligible for transplantation. Such chronic support is termed “destination therapy”.

Figure 12 Survival of patient with cardiac myoplasty (DCMP) and chronic heart failure (Reference patients).⁶

REMATCH¹³ was a landmark CRT trial exploring the efficacy of destination therapy. Survival with a VAD was significantly better than maximum medical treatment at both one and two years (fig 10).

Efficacy and safety

Mechanical support is carried out in very sick patients and has a substantial attendant mortality of 25% or so for LVAD and 40% for BiVAD. Infection is common but appears to be less so for small, electrical implantable devices with remotely placed transcutaneous cables. There is currently no totally implantable VAD because of problems with energy delivery and so power cables must cross the skin. Thromboembolic events are common, despite anticoagulation, and usually occur early. Haemolysis is often seen and is more likely with a BiVAD with renal support. Right-sided failure is often seen with LVADs and is usually an early postoperative event. Equally daunting to these profound complications is the cost of devices. Recent work suggests that this may be as high as £50 000 for each quality adjusted life-year gained. It may be fair to say that there is still no perfect device available to deliver a satisfactory long-term outcome.

Level of evidence

► Level B, AHA/ACC recommendation I

SURGICAL STRATEGIES TO RE-POWER THE FAILING HEART: (2) BIOLOGICAL

Dynamic cardiac myoplasty

The intention here is to re-power the failing heart using autologous skeletal muscle.

Procedure outline

Skeletal muscle (latissimus dorsi muscle) is mobilised on its neurovascular pedicle and brought into the chest through a small thoracotomy (fig 11) and wrapped about the heart to deliver increased muscle bulk in order to add power to ventricular contraction, thus improving systolic function. It is continuously paced in order to transform fast twitch muscle to slow twitch (Salmons and Streeter¹⁴) and secondly to synchronise the skeletal wrap contraction with cardiac contraction. Patients targeted are those in heart failure but who do not have NYHA class IV, mitral regurgitation, atrial fibrillation, pulmonary wedge pressure >25 mm Hg, ejection fraction <12%, multivessel coronary artery disease and peak oxygen consumption <10 ml/kg/min, as poor surgical outcomes have been reported in these groups.

Efficacy and safety

Despite promising animal work, improvement in systolic function in patients has been inconsistent. However, some improvement in load independent measures (Kass⁶) of diastole has been described. This procedure is rarely undertaken now. Figure 12 contrasts the survival of 68 skeletal myoplasty patients to a matched group of 58 patients with chronic heart failure.

Evidence

► Level B, AHA/ACC recommendation IIb.

Figure 13 Number of heart transplant procedures and their geographical distribution.

Heart transplantation

First undertaken by Barnard in South Africa in 1967, heart transplantation is now regarded as the best procedure that can be done for patients with severe, refractory heart failure (AHA/ACC stage D). Heart transplant activity is dictated by donor heart availability and can be seen to be in decline worldwide since a peak of just under 4500 procedures in 1994 (fig 13).

The insertion of several hundred grams of foreign protein by transplanting a human heart excites a rejection response. As a result the patient is dependent upon life-long immune suppression. This is based on ciclosporin, mycophenolate and steroids.

Procedure outline

The recipient is selected to avoid significant secondary complications that may arise through immunosuppression. Therefore, patients with a recent history of malignancy or persistent acute or chronic infection are excluded. There is evidence that the donor hearts manage poorly in the face of moderate pulmonary vascular hypertension. A right heart study defines the size of the transpulmonary pressure gradient (TPPG = mean pulmonary artery pressure – mean pulmonary wedge pressure). Patients are required to have a TPPG of 14 mm Hg or less. Rarely are patients selected with significant co-morbidity and consequently heart plus other solid organ transplantation is unusual.

The donor organ is reviewed by the donor team and its function assessed by pulmonary artery catheter or echocardiography. If satisfactory it is subjected to cold diastolic arrest and excised before being transported to the recipient hospital in cold saline. Donor to recipient matching is made by blood group (according to the rules of transfusion) and body size (either height or weight). The recipient heart is removed and replaced by suturing at mid left and right atrial and mid pulmonary and aortic arterial levels on cardiopulmonary bypass (CPB). The new heart is usually capable of supporting the recipient after 30 minutes of reperfusion.

Efficacy and safety

Survival with the diagnosis of severe refractory heart failure is appalling. The REMATCH study¹³ demonstrated 28% one-year

Figure 14 Actuarial survival after heart transplantation (ISHLT registry 2005).

survival, falling to 8% at two years in medically managed patients with severe refractory heart failure. The International Society of Heart and Lung Transplantation (ISHLT) registry (fig 14) of survival after heart transplantation compares well to this natural history with an overall half-life after heart transplantation of 11 years.¹⁵

Additionally, many studies have demonstrated quality of life of heart transplant recipients to be good. However, there are persisting concerns with personal appearance and sexual dysfunction. Surprisingly there have been no prospective randomised trials exploring the position of heart transplantation in the management of patients with class D heart failure.

Level of evidence

- ▶ Level B, AHA/ACC recommendation I

Cellular transplantation

The concept of re-powering the failing ventricle by cellular transplantation has attracted a great deal of attention. It requires that the new cells will:

- ▶ be retained within the tissue into which they have been injected
- ▶ engage as part of the cardiac syncytium
- ▶ differentiate into myoblasts
- ▶ lead to an improvement of contraction
- ▶ improve the outcome for the recipient.

Procedure outline

Stem cells, be they the pluripotent cells of bone marrow, adipose tissue, skeletal muscle or embryo, are injected into the myocardium where they are expected to grow. This injection is either via the coronary arterial system or directly into the myocardium.

Efficacy and safety

Results in the laboratory have been encouraging, with a suggestion of improvement in heart function. Skeletal myoblasts have been harvested from the quadriceps muscle in a series of patients with a region of poor ventricular function and who were expecting coronary artery bypass surgery. Autologous skeletal myoblasts were isolated and expanded in numbers by cell culture. Using this approach in a recent prospective, blinded randomised clinical trial (MAGIC study), patients received transport medium and either low or high concentration suspensions of autologous skeletal myoblasts as a series of injections into the area of poor ventricular function. This trial failed at interim analysis and has been suspended. A further study of 60 patients, five days after transmural myocardial

Figure 15 Myocardium of a patient with aortic stenosis showing evidence of myoblasts (vital staining: blue) and mitotic activity (white arrow).¹⁶

infarction, received autologous bone marrow cells at the time of angioplasty. There was a suggestion of improved ventricular function.

Level of evidence

► Level B–C, ACC/AHA recommendation IIB

Gene therapy

It is very early days in this arena. The aim appears to be upregulation of biochemical pathways by gene delivery.

Procedure outline

There is some animal work to suggest that upregulation of SERCA by adenovirus vecta may increase the likelihood of recovery of ventricular function with mechanical ventricular support.

Level of evidence

► Unknown

Upregulation of natural pathways

Promotion of intrinsic pathways that would result in improved power production by the heart is of current interest. For example, clenbutarol, an anabolic steroid with β -agonist properties (perhaps better known for its abuse by athletes), has been reported to increase the likelihood of recovery in patients being bridged to transplantation by VAD.

More excitingly, however, is the recent identification of the human cardiac myoblast. Recent clinical reports have demonstrated both cellular hypertrophy and new myocyte production within the myocardium stressed by aortic stenosis¹⁶ (fig 15).

Level of evidence

► Unknown

CONCLUSION

Interventions for heart failure are proliferating as interest in this patient group heightens. It is true to say that all heart surgery can be regarded as heart failure surgery in the light of the new, sequential classification of heart failure by the ACC and AHA. Direct surgical approaches to reverse remodel the dilated and failing left ventricle appear to be less successful at restoring normality than if the primary ventricular remodelling insult can be identified and removed. Where such approaches are not possible due to an advanced state of heart failure, the results of heart transplantation remain impressive 40 years after its introduction. Despite concerns over donor heart supply for transplantation, the future in this area is encouraging following the recent identification of a possible internal recovery system, the human cardiac myoblast. Perhaps it is not too romantic to imagine a future period of mechanical support buying time for a failing heart to be re-powered by upregulated autologous myocyte production; cells bourn into the syncytium and able to contract?

In compliance with EBAC/EACCME guidelines, all authors participating in Education in Heart have disclosed potential conflicts of interest that might cause a bias in the article

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APPENDIX

LEVEL OF EVIDENCE

- A.** Data are derived from multiple randomised clinical trials or meta-analysis.
- B.** Data are derived from a single randomised trial or non-randomised studies.
- C.** Only consensus opinion of experts, case studies, or standard of care.

LEVELS OF RECOMMENDATIONS (ACC/AHA)²

- Class I:** Conditions for which there is evidence and/or general agreement that a given procedure/therapy is beneficial, useful, and/or effective
- Class II:** Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure/therapy
 - IIa:** Weight of evidence/opinion is in favour of usefulness/efficacy
 - IIb:** Usefulness/efficacy is less well established by evidence/opinion
- Class III:** Condition for which there is evidence and/or general agreement that a procedure/therapy is not useful/effective and in some cases may be harmful.