Use What You Have
Biological Assistance for the Treatment of Heart Failure in the Caribbean

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ABSTRACT

Cardiovascular disease represents the main cause of death among adults in the Caribbean. Primary and secondary care facilities are efficiently managed. Cardiac surgical and interventional facilities, however, exist only in a small number of territories and are mainly privately funded and are only accessible to few patients. Patients with end-stage heart failure (ESHF) are given few options apart from palliative care or to seek treatmentoutside of the region. Transplantation remains the 'gold standard' therapy for ESHF. Establishing a Caribbeancardiac transplantation programme would require legislative and infrastructure changes. Tissue rejection poses aproblem and expensive immunosuppressants are needed. Mechanical assist devices are costly and associated withcomplications such as haemorrhage, thrombosis and infections. Both forms of therapy require significant technicaland financial investment and do not appear to be economically viable for the Caribbean. The use of the patient's own skeletal muscle to perform biological cardiac assistance is potentially the ideal alternative. The skeletalmuscle is conditioned by electrical stimulation to become fatigue resistant. It is then transposed and harnessed asan auxilliary circulatory pump. The required muscle stimulators are relatively inexpensive and the surgical techniques and postoperative care are not overly demanding. We discuss the financial and research implications of treating patients from the Caribbean who have end-stage heart failure.

INTRODUCTION

Mortality from cardiovascular disease continues to rise among Caribbean people. A review of Jamaican morbidity and mortality figures (1) has shown that cardiovascular disease has long replaced infectious disease as the leading cause of death among adults. Throughout the Caribbean, the average life expectancy at birth has been rising steadily. This Cardiac Bio-Assist has led to an ever-increasing population of people over the age of sixty years. The incidence of hypertension and diabetes mellitus among the largely African and East Indian Caribbean populations is high. Both of these chronic non-communicablediseases predispose patients to the development of cardiac disease. McSwain *et al* (2) showed that in Antigua and Barbuda in 1995 – 96, the prevalence of congestive cardiac failure in the general population was 1% in the 40 to 65 year age-group and 4% in those over 65 years-of-age. Considerable resources have been devoted to establishing and maintaining primary and secondary care facilities for the management of these conditions.

Cardiovascular disease can result in myocardial dysfunction and congestive cardiac failure (CCF). End-stage heart failure (ESHF) results when CCF is refractory to pharmacotherapy, surgery or ercutaneous intervention (PCI). For a long time, cardiac transplantation has been the only reasonable option for patients with ESHF. Mechanical devices have been used to provide circulatory assistance during recovery from myocardial injury during the wait for a suitable donor heart. Recently, the Food and Drug

Administration (FDA) of the United States of America has approved their use as destination therapy.

Unfortunately, both transplantation and mechanical devices are very expensive and are available only in centres that can provide the necessary clinical, technical and financial support. Transplantation also requires access to an adequate organ donor support network. This rules out most of the Caribbean. While developments in mechanical devices and transplantation biology continue to attract commercial research funding internationally, comparatively little is spent on low-cost solutions. Biological cardiac assist offers the potential for an inexpensive, effective and accessible treatment for ESHF that seems ideal for the Caribbean population.

End-stage heart failure

The loss of functional myocardium results in an inability of the heart to meet circulatory demands. If the condition is allowed to progress, the clinical result is CCF. Early diagnosis and assessment presents the opportunity for appropriate intervention which can lead to limitation and regression of myocardial damage. If CCF is refractory to conventional pharmacotherapy, PCI or surgery, the extent of myocardial dysfunction makes it impossible for the heart to satisfy circulatory demands. The result is ESHF with patients typically showing an ejection fraction of less than 20%.

Management options

For a long time, the emphasis in the Caribbean has been onpreventative care. However, once the diagnosis of ESHF is made, there are a variety of treatment options available (3). Optimal medical management must be continued, whether or not a PCI or surgery is performed. The survival benefits of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta-adrenergic receptor blockers and aspirin have all been adequately demonstrated in various clinical trials (3). These drugs also improve patient quality of life. Cardiac transplantation still remains the goldstandard surgical option. Other options include ventricular reduction or remodelling surgery; mitral valve repair; implantation of a mechanical ventricular assist device; implantation of a cardioverter-defibrillator; and cardiac resynchronization therapy. Combinations of transmyocardial revascularization, cellular myoplasty and gene therapy may hold promise for the future. Availability governs the choice of management option and there are only a few centres in which multiple treatment options are available. Centres with a high caseload of high-risk or experimental procedures often achieve better results than those in which the throughput of cases is sporadic. Specialty referral centres are therefore becoming more common. The trend in the United Kingdom, for example, has been to seek improved outcomes by reducing the number of cardio-pulmonary transplant and paediatric cardiac surgical centres, although this makes the facilities less accessible.

Unfortunately, very few of these surgical options are available in the Caribbean. Most patients in ESHF are managed only with pharmacotherapy and supportive care or are forced to seek other treatments outside the region at considerable expense.

Cardiac transplantation

Although cardiac transplantation is still the treatment of choice for ESHF, the total number of cardiac ransplant operations performed annually has declined over the last ten years due to the reduced availability of suitable donor hearts. There is a mortality of 20 to 30% among patients on transplantation waiting lists. For those who receive a transplant heart, the one-year survival approaches 85% in the best centres. Major long-term complications of cardiac transplantation include graft vasculopathy, rejection, infection and malignancy (due to immunosuppression). Young female transplant recipients are advised against pregnancy because of the risks of teratogenesis and miscarriage. There remains a large population of patients with ESHF in whom cardiac transplantation is contraindicated. Old age and insulin-requiring diabetes are relative contraindications to transplantation. These problems highlight the need for suitable alternatives to transplantation.

Facilities and personnel exist for successful human transplantation in the Caribbean but drugs and equipment for immune regulation and the management of complications are neither cheap nor readily available. The establishment of a cardiac transplantation programme would also require several medical, legal, social and ethical issues to be addressed (4).

Mechanical cardiac assist

The intra-aortic balloon pump (Fig.1) is the device most commonly used to provide short-term circulatory support. It inflates in diastole (augmenting the aortic pressure) and deflates in systole (off-loading the heart). Ventricular assist devices (VADs, Fig. 2) are used as a bridge-totransplantation, providing temporary support for the failing right or left ventricles. The use of VADs has been extended to long-term support and this may be accompanied by some recovery of cardiac function.

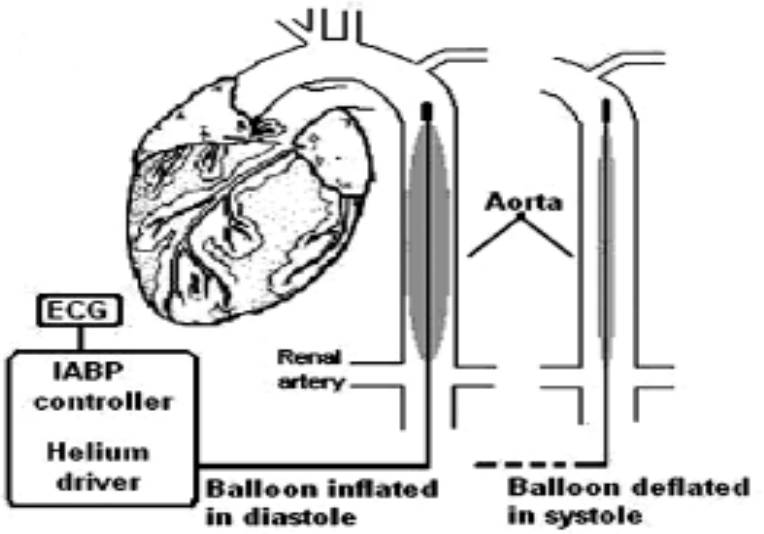

Fig. 1: The intra-aortic balloon pump (LABP) is placed via the femoral artery into the descending thoracic aorta. The LABP is inflated in diastole (increasing the diastolic blood pressure and the diastolic coronary artery blood flow) then deflated in systole (decreasing the workload of the heart). This is called counterpulsation.

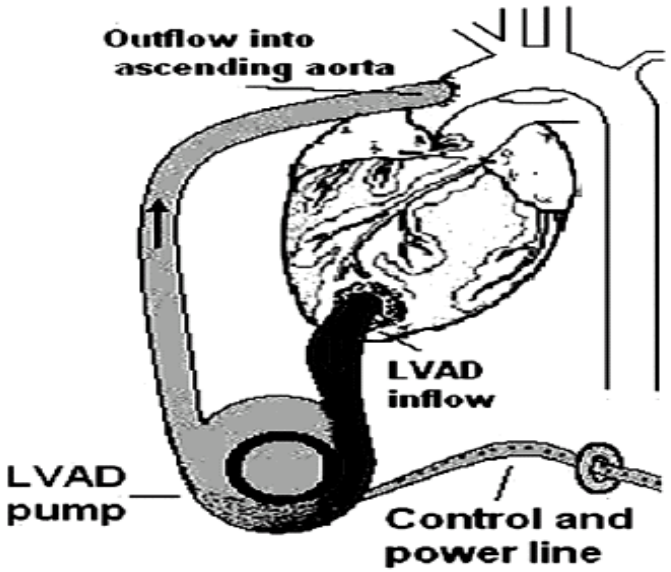

Fig. 2: A left ventricular assist device (LVAD). Blood is diverted from the left ventricle into the LVAD where it is pumped into the ascending aorta. The heart is allowed to 'rest' while the LVAD provides cardiovascular support.

Many VADs have been successfully explanted without the patient needing cardiac transplant.

A variety of VAD pump designs have been used. These include displacement pumps, centrifugal, rotary and axial flow pumps. All provide circulatory assistance with the dysfunctional heart *in situ*. They are implanted within the chest cavity but require the patient to wear an external power supply, linked to the implanted device by inductive transfer of power or by cables that pass through the skin. Removal of the native heart followed by replacement with a total artificial heart has been performed.

Despite the promise offered by mechanical assist devices, common complications include haemorrhage, thrombosis and drive-line related infection (5). There may also be adverse psychological reactions to the wearing of life-supporting external apparatus (6). Centres providing mechanical cardiac support and cardiac transplantation require a lot of personnel as well as financial and technical resources to maintain good results (3).

Biological cardiac assist

Skeletal muscle (usually the latissimus dorsi muscle) can be conditioned by electrical stimulation to become fatigue resistant (7). The conditioned muscle has the capacity to provide a continuous power output similar to that of the resting heart. If the muscle is transposed and reconfigured it can serve as an auxilliary circulatory pump (8, 9). In dynamic cardiomyoplasty (Fig. 3) transposed skeletal muscle is wrapped around the heart and stimulated to contract synchronously with the heart. In aortomyoplasty, the transposed muscle is wrapped around the aorta and stimulated to contract during diastole.

Such configurations are constrained by the geometry of existing structures and do not harness the full power available from skeletal muscle. A solution to this problem is to wrap transposed skeletal muscle around an independent structure to form a skeletal muscle ventricle (SMV) (Fig. 4). The SMV is then connected to the circulation and blood is pumped when the muscle is stimulated to contract.

With biological assist, there is neither danger of tissue rejection nor any need to modulate the immune system, as in transplantation. The need for the percutaneous power and control lines required by mechanical assist devices is avoided, greatly reducing the risk of infection. The muscle stimulator required for biological assist is a self-contained device the size of a normal pacemaker and can be placed in a subcutaneous pocket.

Cardiomyoplasty and aortomyoplasty have been used clinically (10,11). More than 2000 patients worldwide have undergone cardiomyoplasty. Unfortunately, it has fallen out of favour as a clinical treatment for end-stage heart failure, partly because haemodynamic benefits were promised that proved elusive (12) and the clear symptomatic benefits to the patients did not translate into improvements in long-term survival. The protocols that were widely used for the procedure were far from optimal. Over-stimulation of the transposed muscle resulted in a loss of available power and, in some cases, muscle damage. Inadequate precautions were taken to maintain an adequate blood supply to the functional graft (13). Demand dynamic cardiomyoplasty offers better muscle stimulation protocols and has already resulted in haemodynamic improvement (11). Clinical trials are needed to confirm the long-term benefits.

Support facilities

The surgical procedures required for biological assist are described elsewhere (10, 14) and are not technically demanding. Neither cardiopulmonary bypass nor uncommon drugs are required. Muscle stimulators, programmers, special electrodes and intensive care facilities are essential. Both the cardiac surgical teams and operating facilities within the Caribbean are more than adequate for biological assist surgery. Demand dynamic cardiomyoplasty has already been successfully performed in the Bahamas (15).

Financial implications

The cost of performing major cardiothoracic surgical procedures involves a number of factors. Suitable facilities (often privately funded) are available at a number of Caribbean centres. The support staff (including medical, nursing and technical), operating theatres, equipment and wards are already in place. Drugs necessary for the prevention and treatment of complications are available. The cost of having a cardiothoracic surgical procedure in the Caribbean varies between the different centres. In Barbados and Jamaica public funds are used to provide most of the cardiothoracic surgical services and the cost of an operation can be less than one performed in Europe or North America. The withdrawal of Medtronic Inc from the cardiomyoplasty field means that there is currently no FDA approved cardiomyostimulator available for biological cardiac assist in North America. However, other companies have developed alternative and improved stimulators for this purpose (16).

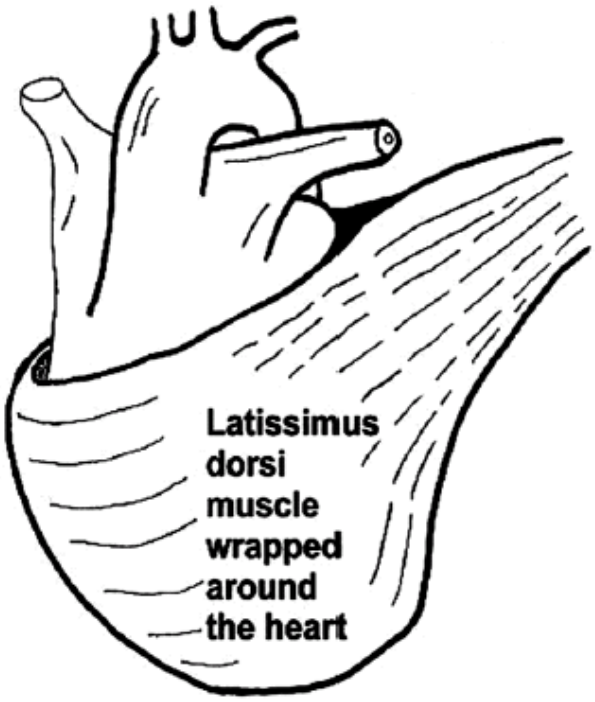

Fig. 3: The latissimus dorsi muscle is wrapped around the heart in cardiomyoplasty. Muscle stimulation during systole was designed to augment the cardiac contraction.

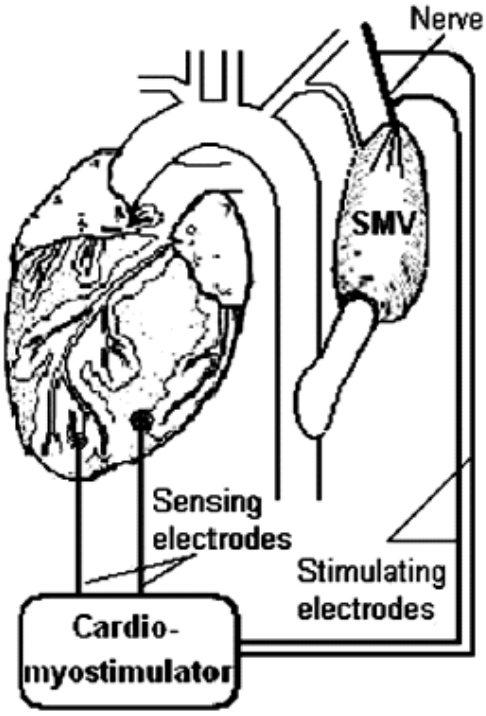

Fig. 4: The skeletal muscle ventricle (SMV) fills in systole and is stimulated to eject during diastole providing counterpulsation. This results in increased diastolic pressure and coronary artery flow (similar to the effects of the IABP).

Research and future implications

Aarons (17) and others have highlighted the resources that are available for clinical research in the Caribbean and have emphasized the need for regulatory bodies. The clinical application of biological cardiac assist lends itself to such a trial. Clinical research in the treatment of ESHF demands extra vigilance and rigid patient selection criteria, and trial end-points must be defined. For example, when a procedure is performed in a patient with ESHF and is successful, but the patient dies, it does not necessarily mean that the procedure was responsible for the death.

Biological cardiac support does not require sophisticated equipment and technical support. In comparison with other long-term surgical approaches it is cheaper, 'low tech,' and requires little more than the patient's muscle and a suitable muscle stimulator. The lack of a major technological (and therefore commercial) component has meant that research into biological assist has traditionally been less well funded than for mechanical assist. Despite this handicap, small research groups have continued to the IABP). Cardiac Bio-Assist 68 demonstrate the advantages of biological cardiac assist (9,18, 19). The needs and economy of the Caribbean would make it ideal as a niche for the development of clinical biological cardiac support. In addition to the benefits to the local population, this may lead to referrals and resulting income from outside the region.

CONCLUSION

Spencer *et al* (20) reported a case of a child with a rare congenital cardiac deformity (ectopia cordis) who died after corrective surgery. They questioned whether the use of precious resources such as operating time and intensive care beds could be justified in such an attempted salvage surgical procedure. The alternative is to label a patient's condition as incurable and to use supportive measures only. Patients with ESHF pose a similar problem. They can be labelled as having an incurable condition and be treated only with palliative care. Biological cardiac assist offers the potential for a better quality of life and prolonged survival for these patients. There is a need for such a service to be developed.

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