Dynamic Cardiomyoplasty: Now and in the Future

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Abstract

Dynamic Cardiomyoplasty has reached a juncture at which the clinical evolution of the procedure has slowed. Basic research on skeletal muscle assist continues to make rapid strides, and at this point has advanced beyond the clinical application of dynamic cardiomyoplasty. Herein lies the static paradox of dynamic cardiomyoplasty. There must remain a synergy between basic scientific research and the clinical application of the procedure so that improvements in the clinical realm continue to draw upon, and at the same time stimulate, advances in the basic sciences. This paper reviews recent improvements in the basic sciences and looks at the future trends for research and the clinical application of dynamic cardiomyoplasty.

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The advent of clinical cardiomyoplasty in 1985 ushered in a new era of surgical possibilities for the cardio-thoracic surgeon. Alain Carpentier in Paris and George Magovern in Pittsburgh initiated a surgical procedure which was the culmination of over 20 years of experimental study. The clinical application of dynamic cardiomyoplasty was drawn from the work of a multitude of investigators in a variety of fields. Engle [10] first established the myofibrillar ATPase theory of skeletal muscle type, and Buller [3] later showed that muscle transformation and plasticity could take place with his cross-innervation studies. In the mid 1960’s Salmons and Sreter [29] discovered that low frequency chronic electrical stimulation of a skeletal muscle could result in total transformation of muscular fiber type. Dewar and Chiu [8] proved that sequential addition of electrical stimuli in short pulse trains, or "bursts", resulted in summation of skeletal muscle twitches. This resulted in greater maximal force generation than single stimulation with little or no increase in fatigue. Rapid advances in microchip technology allowed this burst myostimulator to be coupled to a cardiac pacemaker creating the first cardiomyostimulation device.

In addition to these monumental advancements in the understanding of skeletal muscle physiology, there were also major advances in the surgical evolution of cardiomyoplasty prior to 1985. Petrovski [27] first suggested the use of diaphragmatic muscle as a pedicle or free graft for multiple intrathoracic operations. This included revascularization of the heart (as in Beck’s operation) and the repair of defects left by ventricular aneurysmectomy. Termet [30] was the first to report the use of pedicled latissimus dorsi flaps around the heart. However, this work predated Salmons’ studies and this failed as a chronic support model secondary to muscle fatigue.

The clinical culmination of these surgical, physiological and electrical advancements was the clinical application of dynamic cardiomyoplasty by Carpentier in France in 1985 [4]. A paced left latissimus dorsi muscle was used to repair the defect created when a large fibroma was resected from the left ventricle of a 37 year old woman. The ventricular defect was covered with a pedicled latissimus dorsi flap which was wired for stimulation. Over the ensuing weeks the patient’s left latissimus cardiomyoplasty was gradually conditioned. This resulted in an increase in left ventricular ejection fraction. A similar pioneering operation was performed 3 months later in Pittsburgh by George Magovern [23]. He used a paced latissimus dorsi pedicle flap to cover the defect created by a large left ventricular aneurysmectomy.

Since 1985 the clinical application of dynamic cardiomyoplasty has experienced at first gradual followed by exponential growth in numbers (figure 1). Laboratory investigation into the physiology and mechanisms in dynamic cardiomyoplasty has increased exponentially as well. This is evidenced by the volume of publications on dynamic cardiomyoplasty in the English literature (figure 2). Despite this parallel growth, the relationship between clinical cardiomyoplasty and the experimental investiga-
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Theoretical and experimental advances

The advent of a new surgical technique spurred cardiothoracic laboratories around the world to begin investigations on dynamic cardiomyoplasty. There are several approaches to investigation. The first and most obvious one was to identify the mechanisms through which dynamic cardiomyoplasty improved functional class. This has been elegantly demonstrated at a number of centers [2, 6, 19]. These studies have collectively shown that although dynamic cardiomyoplasty acutely impairs diastolic function of the left ventricle this does not seem to hold true over the long term. A definite reduction in left ventricular wall stress has been demonstrated in a canine model of dilated cardiomyopathy [18] and implies that a decrease in myocardial oxygen consumption may be the basis for improvement in clinical symptoms. No experimental results have shown improvement in the left ventricular ejection fraction or outflow with the left latissimus cardiomyoplasty without the induction of severe pharmacologic hypotension and heart failure.

Because of the inability to show objective circulatory improvement in minimally failed experimental hearts, a second broad category of investigation has sprung up which attempts to identify ways to improve the dynamic cardiomyoplasty technique. These optimization protocols could be further divided into those that focus on optimization of muscular stimulation and those that look towards more radical changes in muscle wrap configuration for better compression of the ventricles.

A basic tenet of effective repetitive muscle contraction is that there must be enough time allowed for full relaxation and repolarization of myofibrils [21]. The actual optimal frequency for repetitive contraction of latissimus dorsi muscle has shown to be as low as 40 and as high as 88 stimulations per minute [7, 20]. In addition to modification of pacing parameters, the application of new types of muscle electrodes has been shown to improve the force of muscle contraction. A multi-channel stimulation device adapted from studies of distal spinal cord stimulation has been shown to provide proton contractions of latissimus muscle [31]. A somewhat less complex 180 degree perineural electrode was shown to significantly decrease the threshold voltage of muscle contraction and significantly decrease the amount of voltage required for maximal stimulation [15]. These studies conclusively reveal that perineural leads demonstrate better efficiency for muscle stimulation than do intramuscular leads. These perineural leads have been used in chronic experimental studies for up to one year without detrimental effects to motor nerves [16]. Currently only intramuscular leads are approved for clinical dynamic cardiomyoplasty, despite the fact that perineural leads have been shown to be superior and safe. A recent electrophysiological study [28] revealed that for intramuscular lead stimulation the location of the interelectrode field rather than the location of the cathode determines the mechanical performance of the skeletal muscle. Furthermore, tension development of...
skeletal muscle with an intramuscular lead was found to be primary nerve activation rather than direct muscle stimulation. The higher tension generation that resulted from perineural activation was produced by activating a higher number of muscle fibers through the neuromuscular junctions.

Anatomical [32] and physiologic [17] studies of the latissimus muscle show that the distal (origin) portion of the muscle is poorly vascularized following acute mobilization. Performance of the cardiomyoplasty wrap immediately following muscle takedown may lead to distal muscle ischemia and fibrosis. A more rational approach would be to mobilize the distal latissimus dorsi muscle 7 to 10 days prior to wrapping the heart. This would allow adequate collaterals to develop prior to muscle transfer.

The surgical technique and configuration of latissimus dorsi cardiomyoplasty has long been the subject of investigation. The left latissimus muscle has produced hemodynamic augmentation in an acute model of severe left ventricular depression [25]. However, similar proof in an animal model of normal ventricular function has not been obtained with the left latissimus muscle [1]. Because of these inadequacies using left latissimus alone, investigators in both Stephensons’s [26] and Magovern’s [22] laboratories conceived of bilateral cardiomyoplasty as a method of covering both ventricles with skeletal muscle to provide superior hemodynamic augmentation. These studies were the first ever to show hemodynamic augmentation of a non-failed ventricle. Investigations into the mechanism of this superior augmentation [13] reveal that the right anterior cardiocostal myoplasty was solely responsible for the hemodynamic effects seen with the bilateral cardiomyoplasty. The right cardiomyoplasty minimally depressed the native hemodynamics of the ventricles in their static state while providing superior augmentation of the ventricular function in the dynamic state. Further investigations led to a randomized paired comparison of the left posterior and right anterior cardiomyoplasty in an acute non-failed ventricle [12]. This study demonstrated that the right latissimus cardiomyoplasty configuration was significantly better than the left latissimus configuration for hemodynamic augmentation. The mechanism of action of the right latissimus myoplasty has been shown by MRI to be compression of the apex of the ventricle towards the base [5] as was originally hypothesized. The same study revealed that left latissimus cardiomyoplasty did not compress the ventricle in either the short or long axis.

These findings with the right latissimus cardiomyoplasty were put into clinical use through a variance in the FDA Phase II protocol. Fifteen patients at Allegheny General Hospital underwent a right anterior cardiocostal cardiomyoplasty sling. Significant improvements in left ventricular ejection fraction were seen at 3 and 6 months [24]. However, by 12 months ejection fraction had returned to baseline. Because there was no difference between the improvement and ejection fraction between the right and left cardiomyoplasty patients, the FDA denied further re-

quests for right cardiomyoplasty implantation. Nonetheless, the experience with the 15 patients who received the right anterior cardiomyoplasty sling remains the only one to date which shows significant clinical improvement in left ventricular ejection fraction in the early postoperative period.

Another field of investigation aimed at optimizing benefits of cardiomyoplasty is the field of risk analysis. To date, most centers’ experiences have been too small to produce a multivariate analysis of risk. Recently a multivariate analysis of risk was produced by combining the studied patients from both the Pittsburgh, Pennsylvania and Portland, Oregon groups [14]. This study included 45 patients and evaluated preoperative variables for their effect on overall survival. Significant predictors of death were low right ventricular ejection fraction and preoperative atrial fibrillation. Specifically atrial fibrillation increased the risk of death postoperatively 6.1 times, while a decreasing right ventricular ejection fraction had progressively larger effects on postoperative mortality. Covariates of low right ventricular ejection fraction were high pulmonary artery pressures and resistances and high left ventricular end diastolic pressure.

Future trends

Although there have been tremendous strides in the experimental optimization of the dynamic cardiomyoplasty procedure, few if any of these improvements have been applied clinically. The cardiomyoplasty procedure as it is performed today exists basically in the same form as it was first performed in 1985 by Carpentier.

There thus exists a large dichotomy between what is practiced clinically and what may be more beneficial experimentally.

The FDA has refused to accept any further modifications in the surgical technique of cardiomyoplasty at this time, even though the technique as originally described remains largely unproven clinically and experimentally in terms of significant magnitude of systolic improvement. The FDA has requested that the next phase cardiomyoplasty study be a randomized study with medical therapy. This is due to large multi-center trials with calcium channel antagonists showing a decrease in overall mortality. Implicit in the concept of randomization is the assumption that the cardiomyoplasty technique, as it exists today, is already optimized and cannot be improved despite experimental studies to the contrary. The pressure from the FDA to do a randomized study with medical therapy as the sole clinical trial represents an enormous change in the evolution of cardiac surgery. In this particular study, while the cardiomyostimulation device is regulated and is the same in every patient, the operation should still be in the phase of evolution. It is not a homogeneous structure which has been fully developed, and because of this, it is not comparable to a single pharmacological agent or device which can be easily randomized.

There is however a role for randomization of certain aspects of an operation which is in the early stages of
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development. If one were to accept randomization of muscle wrap configurations, stimulation leads, the use of pre-myoplasty conditioning, different stimulation protocols, and the application of multi-variate risk factors to the selection process, then the possibility exists that randomization of this procedure could help and indeed speed its evolution. In this setting, randomization could help us look at other ways of improving and optimizing the operation. It would also help to apply lessons learned in the laboratory and remove the dichotomy which currently exists between the experimental results and the clinical application of dynamic cardiomyoplasty.

We have reached a point at which the application and pace of development of clinical dynamic cardiomyoplasty has slowed. While basic science is far ahead of clinical work, there must remain a synergy between the two so that improvements in the clinical realm draw upon, and at the same time, stimulate advances in the basic sciences. There have been many improvements to date in the laboratory which have not been incorporated in the clinical application of dynamic cardiomyoplasty. Further advances may occur if we are free to take a clinical leap forward and critically challenge the procedure and our idea of how it works. Randomization should occur, but only alongside of continuing clinical advancements in the procedure. It should not be the only pathway through which dynamic cardiomyoplasty is evaluated, but it should be an accessory pathway in which its continuing improvements are judged against standard medical therapy. Continuing to challenge the conventional wisdom through incorporating experimental improvements in cardiomyoplasty into the clinical realm may break the static paradox of dynamic cardiomyoplasty.

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References


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