Dynamic Cardiomyoplasty: Insights into the Mechanisms of its Success


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Abstract
Dynamic cardiomyoplasty is a recently developed operation for the treatment of end-stage heart failure. Recent studies have focused on the potential mechanism by which it may work. We have shown in a canine model of heart failure, using transformed muscle, that CMP has at least two mechanisms. First, it stabilizes ventricular function and volumes chronically by a girdling mechanism. Secondly, dynamic assistance acts acutely to augment systolic contraction. These two mechanisms act to stabilize cardiac function and may potentially allow for reversal of the chronic remodeling process seen with progressive heart failure.

Key words: cardiomyoplasty, heart failure, left ventricular assistance, skeletal muscle, remodeling.

BAM 7(1): 5-7, 1997

Dynamic cardiomyoplasty (CMP) is a promising new surgical therapy for end-stage heart failure. In this procedure, the latissimus dorsi muscle is mobilized and wrapped around the heart, and then stimulated electrically to contract in synchrony with the heart-beat. CMP has been performed in over 400 patients worldwide [7], and currently Phase III trials comparing its efficacy to medical therapy are underway. Despite numerous clinical and experimental studies, the effects of the procedure are poorly understood and data has been inconclusive in demonstrating any hemodynamic benefit [1, 4, 7, 8, 11, 12]. However, CMP does appear to improve both quality of life and symptoms of heart failure [8].

The discordant results over the past decade can be attributed to a number of reasons [7, 11]. First, a large number of these studies were done using normal hearts. Hearts that are dilated and failing superimpose different conditions on the wrap than normal hearts. Other studies have been done using untrained muscle. It is well known that chronic electrical stimulation results in changes in skeletal muscle among which include a conversion of muscle fiber type from one that is easily fatiguable to one that is fatigue resistant. The physiologic consequences of fiber switch include a decrease both in fiber size and in maximum power output. The time required for training would also allow for other physiologic processes to occur such as epicardial-epimysial adherence and development of collateral blood supply. Thus studies using untrained muscle may not be relevant. Finally, the modalities used to study the heart may be flawed. Imaging studies do not account for translational motion of the heart out of the plane of view that occurs after CMP. Also, commonly measured load-sensitive indicators of cardiac function are dependent not only on the state of the heart at the time of study, but also on the loading conditions such as preload and afterload. These conditions may alter the perceived functional state.

Our studies have started with the effects of a conditioned muscle wrap on normal hearts and have progressed to studies mimicking the clinical situation using dogs in heart failure and using conditioned wraps. These studies attempting to elucidate the mechanism by which CMP works will be discussed here.

Surgical Technique
The operation is performed with the patient initially in the right lateral decubitus position and a standard incision is made over the lateral border of the left latissimus dorsi muscle. A latissimus dorsi pedicle flap is raised and nerve stimulator leads are placed around the thoracodorsal nerve. Through a partial second rib resection, the flap is then passed into the thoracic cavity. The right thoracic wound is then closed over three bulb suction drains.

The patient is then turned into a supine position and the heart is exposed via a median sternotomy. After bringing the flap down from the left chest, the muscle is wrapped around the heart circumferentially. Often the flap is inade-
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quate in covering both ventricular epicardial surfaces and a portion of the pericardium is needed for complete closure. After the sensing leads is placed on the right ventricular surface, the chest is closed. The nerve stimulator output and QRS sensing leads are then connected to a subcutaneous cardiomyostimulator. The muscle is then programmed to turn on after a two week vascular delay period, and then conditioned over a progressive burst stimulation (i.e. delivering multiple pulses per stimulus train) protocol lasting typically about ten weeks.

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Recent reports on results in patients have demonstrated that primary dynamic effects of cardiomyoplasty may not be important determinants in its mechanism. Kass and colleagues [9], by using serial pressure-volume analysis before and after CMP in three patients, have suggested that CMP decreases left ventricular volumes over time. In addition, pressure-volume loops did not change in that study after turning the cardiomyostimulator on suggesting minimal effects secondary to wrap stimulation.

Our initial studies focused on the effects of a conditioned muscle wrap on normal hearts [5]. Five mongrels underwent left CMP followed by a subsequent graded muscle conditioning protocol of burst stimulation. Pressure-volume analysis (PVA) after the protocol was complete revealed that dynamic effects existed with an improvement in cardiac function with the stimulator on at the 1:1 muscle: heart-beat setting and for the assisted 1:2 beats. In addition, the end-diastolic volumes (EDV) also shifted downward with the stimulator on those settings.

We have since attempted to model the clinical situation by creating a model of heart failure by rapid ventricular pacing (RVP) dogs for three to four weeks at 215 beats/min. This produces a situation analogous to human pacing (RVP) dogs for three to four weeks at 215 beats/min. This produces a situation analogous to human

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erated at 2 Hz. This conditioning protocol has been shown to result in transformation of the muscle but does not result in sustained tetanic contractions as is seen with a burst (multiple pulses per train) stimulation. PVA at the end of the rapid pacing period showed a significant improvement in load independent indices of function in the asynchronous group when compared to controls. In addition, echocardiography suggested a stabilization of the chamber volumes after CMP while control hearts continued to dilate.

Finally, we have investigated the dynamic effects of CMP [13]. Twelve dogs underwent RVP for four weeks to create heart failure. Four dogs were then selected to undergo left cardiomyoplasty. RVP was then continued in all dogs for an additional six weeks. The four CMP dogs also received a six week graded muscle conditioning protocol of burst stimulation. Pressure-volume analysis at the end of the rapid pacing period showed that dogs with the myostimulator “off” had improved ventricular function when compared to controls. This suggested a chronic effect of CMP similar to that seen with the asynchronous experiments. In addition, turning the myostimulator on at 1:1 muscle: heart-beat improved function significantly when compared to the stimulator “off settings suggesting a dynamic effect of CMP. The augmented beats at 1:2 stimulation improved function when compared to myostimulator “off settings but did not reach significance.

Conclusions

Our preliminary work on the effects of CMP on left ventricular performance has suggested that the benefit seen after CMP may be attributable to several reasons. First, the presence of the conditioned muscle wrap alone may allow for stabilization of chamber volumes. This would then translate into more optimal loading conditions and stress/strain relations within the heart. It is unclear whether an unconditioned nonstimulated wrap could accomplish this in the long term, but this is unlikely since the muscle would then be subject to significant disuse atrophy. However, a recent study using an unconditioned wrap has demonstrated an attenuation of left ventricular enlargement during RVP when compared to unwrapped controls [3]. Secondly, dynamic CMP may actively augment cardiac function during systole. These effects are evident when one looks at load-independent measures of contractility and not the frequently clinically used load-sensitive measures such as cardiac output, ejection fraction, and maximum rates of pressure change.

Further research into long term hemodynamic effects of CMP, and effects of CMP on basic muscle mechanics and muscle cell biology would be helpful in determining its mechanism and are underway in our laboratory as well as others. In addition, research in optimization of the surgical procedure and in long term muscle preservation will help improve the outcomes seen with patients undergoing this procedure.
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References


