

Clinical and Experimental Effects of the Unstimulated (Static) Right *Latissimus Dorsi* Cardiomyoplasty on Left Ventricular Function

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Abstract

Stimulation of the *latissimus dorsi* muscle (LD) is not started until several weeks after cardiomyoplasty (CMP). This study was designed to determine whether the presence of an unstimulated (static) CMP would adversely affect left ventricular function (LV) in an experimental animal model or after clinical CMP. Five normal mongrel dogs underwent staged right LD CMP. Left ventricular pressure was measured with a micromanometer. Left ventricular volume was measured with sonomicrometry. Indices of LV function were measured before and immediately after CMP, and then again two weeks later. Heart rate (HR, beat/min), end-systolic pressure volume relation (E-max, mmHg/mL), left ventricular end diastolic volume (LVEDV, mL), preload recruitable stroke work (PRSW, g · cm/cm³), left ventricular end diastolic pressure (LVEDP, mmHg), ejection fraction (EF), and the diastolic relaxation constant (Tau, msec) were measured and expressed as mean ± standard error of the mean (SEM). Indices of systolic and diastolic function showed no significant differences from baseline acutely and at two weeks. Seven patients who underwent right LD CMP were prospectively studied. Left and right ventricular ejection fractions were measured preoperatively, two weeks postoperatively (before initiation of muscle stimulation), and six weeks postoperatively (with muscle stimulation). Left ventricular ejection fraction (%) remained unchanged from baseline values at two weeks (25 ± 1.9 to 28 ± 3), with a significant increase at six weeks (33 ± 4 , $p < .05$). Right ventricular ejection fraction showed no significant change (58.4 ± 5 to 63 ± 3 to 63 ± 3). We conclude that the static right LD CMP does not impair indices of LV function in an animal model. Furthermore, the static right LD CMP does not impair LVEF or RVEF in patients with heart failure and is capable of producing a significant improvement in LVEF by systolic augmentation.

Keywords: cardiomyoplasty, *latissimus dorsi*, ventricular function.

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Dynamic cardiomyoplasty (CMP) is currently an experimental treatment for various forms of heart failure [8, 9]. The procedure entails wrapping the *latissimus dorsi* (LD) muscle around an impaired ventricle to augment cardiac function. Based on current protocols, the LD is not stimulated for two weeks and is not fully utilized for ventricular augmentation until six weeks postoperatively [1]. This delay period is necessary to allow recovery of the LD, adherence of the LD to the heart, and transition of the LD to fatigue-resistant status. Recent reports have examined the experimental effect of the static left LD CMP in animals [2, 3, 6], but to our knowledge no information about the effect of the static right LD CMP in experimental

animals or in patients has been published. This study was designed to determine whether the right static (unstimulated) LD CMP significantly depresses left ventricular (LV) function in an experimental animal model or in patients with congestive heart failure.

Materials and Methods

Animal Protocol

Five mongrel dogs were studied (25-35 kg). The animals received humane care in compliance with the "Principles of Laboratory Animal Care" (National Society for Medical Research) and the "Guide for the Care and Use of Laboratory Animals" published by the National Institutes of

Health (NIH Publication No. 86-23, revised 1985). They were sedated with acepromazine (0.25 mg/kg), and general anesthesia was induced with pentothal (20 mg/kg) and maintained with 1-2% isoflurane.

The LD muscle was mobilized three to five days prior to CMP to provide a vascular delay period. A longitudinal incision was made anterior to the LD muscle. Mobilization of the LD was performed by creating subcutaneous flaps, ligating intercostal perforators, and transecting lateral and distal tendinous insertions. The origin of the LD and thoracodorsal neurovascular pedicle were left intact. A paraneural bipolar stimulation lead (Model #4545, Medtronic, Inc., Minneapolis, MN) was placed in proximity to the neurovascular pedicle and secured with 4-0 silk. Following a 3-4 day vascular delay period, the third rib was removed, and the LD was translocated into the right chest. A left thoracotomy was performed with subperiosteal resection of the fifth rib. The pericardium was opened and tacked to the chest wall.

Piezoelectric crystals were placed for measurement of LV volume using a sonomicrometer (Model #120, Triton Technology, Inc., San Diego, CA). The long axis was measured using 5-mm hemispheric crystals (Model #HE3-2, Triton Technology, Inc.) secured at the base and apex of the heart. Short axis dimensions were measured from two 5-mm hemispheric crystals (Model #ED3-2, Triton Technology, Inc.) placed in opposition on the LV free wall. Wall thickness was measured midway between the apex and the base with a 5-mm hemispheric epicardial crystal and a 2-mm endocardial crystal (Model #W25-2, Triton Technology, Inc.). Two unipolar sensing leads (Model #6917A-53T, Medtronic, Inc.) were placed 1 cm apart on the right ventricle. The LD CMP was constructed by suturing the distal LD muscle to the atrioventricular groove along the LV epicardium using pledgeted 2-0 Tricron sutures, which resulted in a cardiocostal orientation [4]. A Millar micro-tipped pressure transducer was placed into the left ventricle via a left common carotid artery cutdown. A Swan-Ganz pulmonary artery flow-directed catheter was placed via the right external jugular vein. A 40-cc aortic occlusion Fogarty catheter was placed into the inferior vena cava via a femoral vein cutdown for intermittent occlusion of venous return.

Muscle stimulating and sensing leads were connected to a Prometheus myostimulator (Model #6100, Medtronic, Inc.), and baseline and acute data were collected. After a two week period, all animals were re-anesthetized and re-instrumented with an LV Millar micromanometer, Swan-Ganz pulmonary artery catheter, and aortic occlusion catheter. Sonomicrometry crystal leads were re-exposed from a subcutaneous pocket and connected to the sonomicrometer. All parameters were measured again with the CMP static. Measured and calculated variables of LV function included: end systolic pressure volume relation (E-max), preload recruitable stroke work (PRSW), left ventricular end diastolic volume (LVEDV), left ventricular end diastolic pressure (LVEDP), the diastolic relaxa-

tion time constant (Tau) and ejection fraction (EF). Heart rate (HR) was continuously recorded via electrocardiographic leads. Ejection fraction was stroke volume divided by LVEDV multiplied by 100. Occlusion of the inferior vena cava was used to obtain PRSW (the slope of SW vs. LVEDV) and E-max (slope of LV pressure vs. end systolic volume). Left ventricular volume (v) was calculated from the formula $v = \pi + 6(a - 1.1h)(b - 2h)^2$, where a is the major axis diameter, b is the minor axis dimension, and h is the wall thickness. Tau was defined as the negative reciprocal of the slope of the plot of the natural logarithm of LV pressure vs. time from maximal $-dP/dt$ to 5 mmHg above LVEDP. Data were entered into an IBM-AT personal computer using CODAS software (Dataq Inc., Akron, OH), and analyzed using Xanalyze software [10]. Statistical analysis was done by repeated measures of ANOVA for comparison of means.

Patient Protocol

Seven patients undergoing right LD CMP were studied prospectively. Mean age was 52.4 years (range 33 - 64). There were five men and two women. Causes of heart failure were ischemia in four and idiopathic cardiomyopathy in three.

All patients had a preoperative radionuclide multigated acquisition scan (MUGA) to determine right and left ventricular ejection fraction (RVEF), (LVEF). Patients were selected for right LD CMP based on inoperable coronary disease or contraindication to orthotopic heart transplant. Patients underwent a MUGA at two weeks after surgery (just prior to initiation of muscle training), and at six weeks after surgery (after four weeks of muscle stimulation at 1:2). The stimulation protocol is shown in Table 1. Repeated measures of ANOVA and paired t-test were used for comparison of means. $p < 0.05$ was significant.

Table 1. Muscle training protocol for inducement of latissimus dorsi fatigue resistance in humans.

Postoperative Week	Frequency (Hz)
0	0
1	0
2	2
3	10
4	15
5	20
6	30
7	30
8	30

pulse amplitude = 3 volts; pulse train duration = 185 msec; pulse width = 210 μ sec; synchronization ratio = 2:1.

Static cardiomyoplasty

Operative Technique

The technique of right LD CMP was performed by means of two separate incisions: a lateral approach for mobilization and testing of the LD muscle, followed by a median sternotomy. All right LD CMP's were performed in the right anterior cardiocostal orientation as previously described by Furnary (Figure 1) [4]. Normothermic cardiopulmonary bypass was used in 4 patients. No concomitant procedures were performed.

Results

Animal Protocol

Figure 2 compares baseline measurements in dogs with measurements showing the effect of static CMP on LVEF acutely and at 2 weeks. There were small decreases in ejection fraction, E-max, PRSW, SW, and CO immediately after construction of the CMP, but the changes were not statistically significant and returned nearly to baseline at two weeks (Tables 2 and 3).

There were no significant changes in indices of diastolic filling or relaxation acutely (Table 4). There was a trend for LV end diastolic volume and pressure to decrease by 2 weeks after operation, but the change was not statistically significant. The isovolumic relaxation time constant (Tau) also appeared to decrease with time, but the difference was not significant. Figures 3, 4, and 5 show representative pressure-volume loops at baseline, acutely, and at two weeks, with and without caval occlusions.

Table 2. Effect of static cardiomyoplasty in dogs on load-independent indices of systolic function at baseline, immediately postcardiomyoplasty (acute), and at two weeks (initiation of muscle training) (mean $\pm$ SEM).

	E-max mmHg/mL	PRSW g $\cdot$ cm/cm ³
Baseline	6.0 $\pm$ 1.0	78 $\pm$ 14.4
Acute	5.0 $\pm$.7	53 $\pm$ 8.0
Two weeks	8.0 $\pm$ 2.0	70 $\pm$ 10
p value	NS	NS
E-max = end systolic pressure volume relation; PRSW = preload recruitable stroke work.		

Patient Protocol

There were no operative or in-hospital deaths. There were no differences in RVEF between baseline, two-week, and six-week studies (58.4 $\pm$ 5 to 63 $\pm$ 3 to 63 $\pm$ 3%). Figure 6 compares baseline RVEF with studies at six weeks with the CMP stimulated.

No significant differences in LVEF occurred between baseline and MUGA scans at two weeks with CMP unstimulated (25 $\pm$ 1.9 to 28 $\pm$ 3). A significant increase in LVEF from baseline was observed six weeks after surgery, with the right LD CMP stimulated at a ratio of 1:2 for

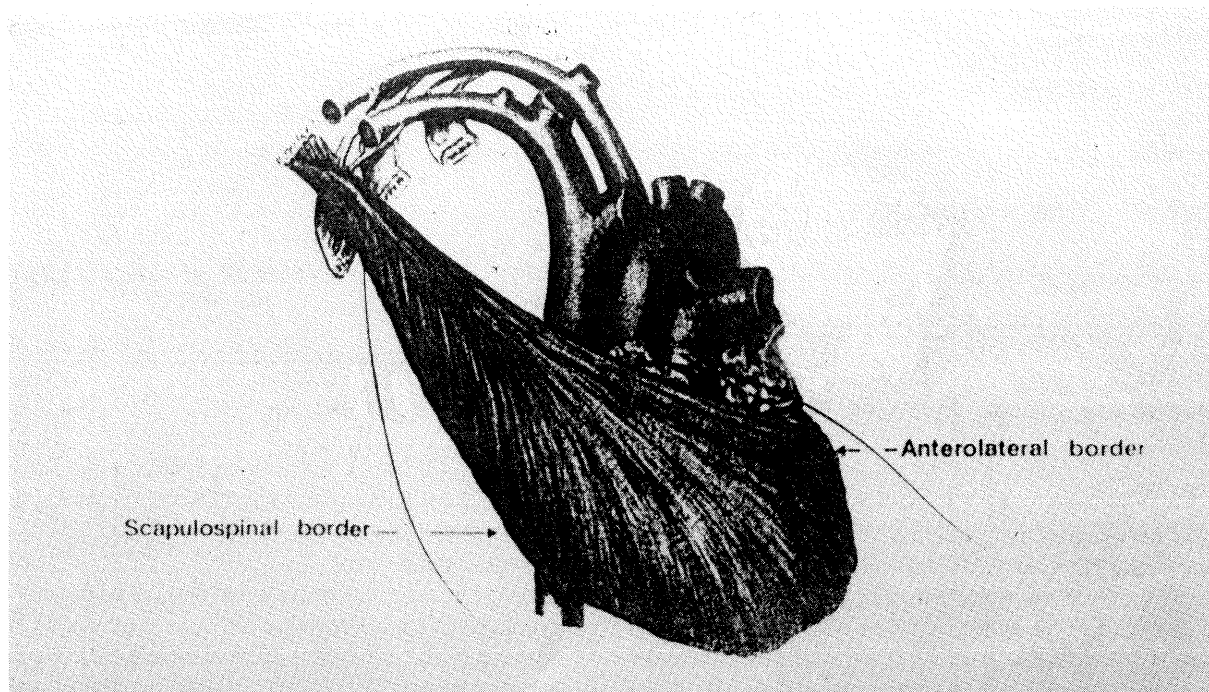


Figure 1. Schematic representation of human right latissimus dorsi cardiomyoplasty.

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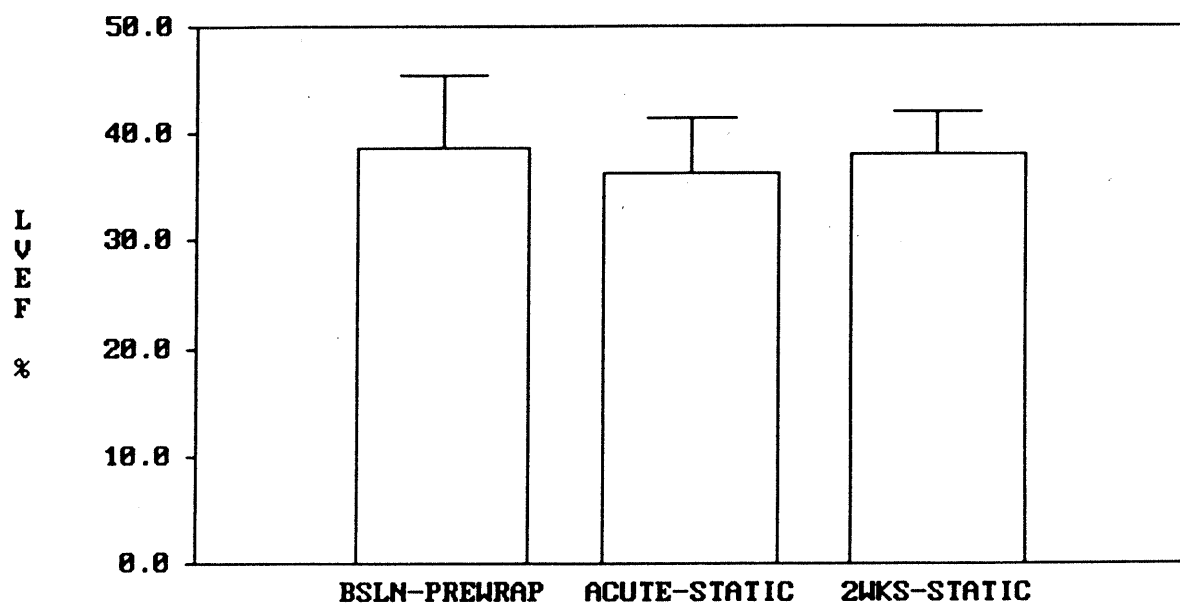


Figure 2. Effect of static right latissimus dorsi cardiomyoplasty on left ventricular ejection fraction in dogs comparing prewrap baseline with acute (immediate postwrap) and two week studies.

Table 3. Effect of static cardiomyoplasty in dogs on load-dependent indices of systolic function at baseline, immediately postcardiomyoplasty (acute), and at two weeks (initiation of muscle training) (mean ± SEM).

	HR (beats/min)	CO L/min	SW gm · cm ³
Baseline (n = 5)	113 ± 11	5.87 ± 0.92	1758 ± 383
Acute (n = 5)	115 ± 6	4.22 ± .60	1232 ± 254
Two weeks (n = 5)	125 ± 10	5.49 ± 1.1	1166 ± 174
p value (n = 5)	NS	NS	NS

CO = cardiac output; HR = heart rate; SW = stroke work.

Table 4. Effect of static cardiomyoplasty in dogs on indices of diastolic function at baseline, immediately postcardiomyoplasty (acute), and at two weeks (initiation of muscle training)

	LVEDV (mL)	LVEDP (mmHg)	Tau (msec)
Baseline (n = 5)	40 ± 3.6	14 ± 6.0	45 ± 8.1
Acute (n = 5)	38 ± 4.0	14 ± 6.0	48 ± 8.4
Two weeks (n = 5)	34 ± 4.9	12 ± 3.0	36 ± 4.3
p value (n = 5)	NS	NS	NS

LVEDP = left ventricular diastolic pressure; and LVEDV = left ventricular end diastolic volume.

ventricular augmentation (25 ± 1.9 to 33 ± 4 , $p < 0.05$) (Figure 7).

Discussion

A few previous animal studies [2, 3, 6] have documented deleterious effects of CMP on indices of systolic and diastolic function using the left LD CMP. To our knowledge, no studies have been carried out to evaluate the effects of the right LD CMP in the static (unstimulated) state on LV systolic and diastolic function either in an animal model or clinically. We have previously documented improved systolic function using the right LD

CMP in a right anterior cardiocostal orientation [5]. Therefore, we felt it important to document whether the right-sided wrap orientation had any deleterious effects on LV systolic and diastolic functional mechanics in the non-stimulated static form.

Chang and associates concluded that left LD CMP acutely reduces CO, and the reduction caused by static CMP is responsible for equivocal clinical results [2]. However, Chang performed left LD CMP with predetermined tensions (preload) on the LD, and generated wide variations in left ventricular peak pressure, mean systolic pressure,

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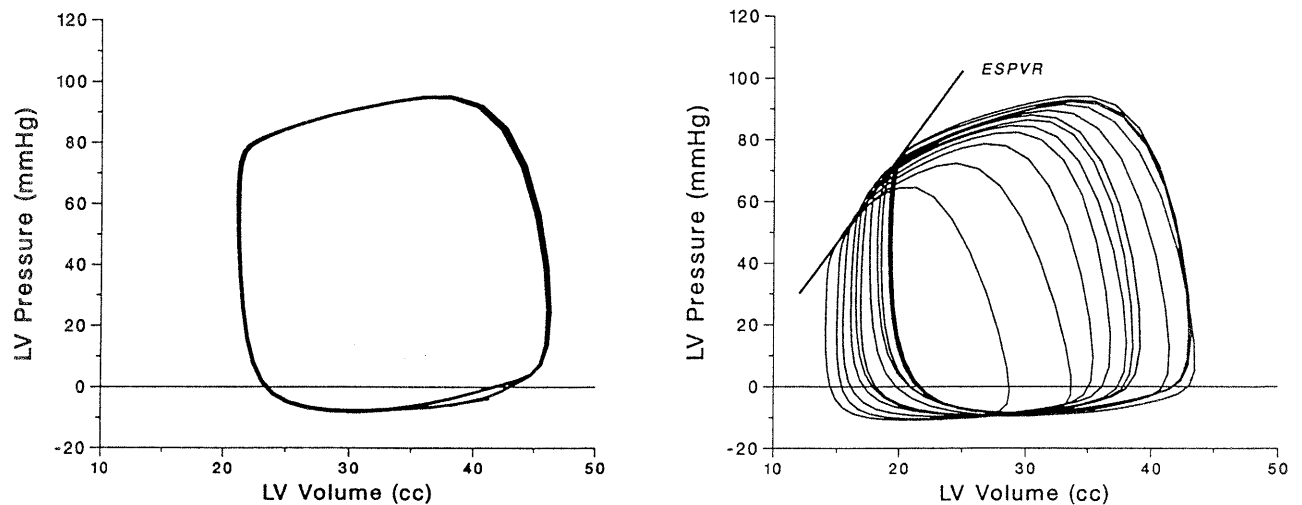


Figure 3. Representative pressure volume loops in dogs showing: a) prewrap baseline, b) prewrap baseline with caval occlusion. Slope of the line represents end-systolic pressure volume relation.

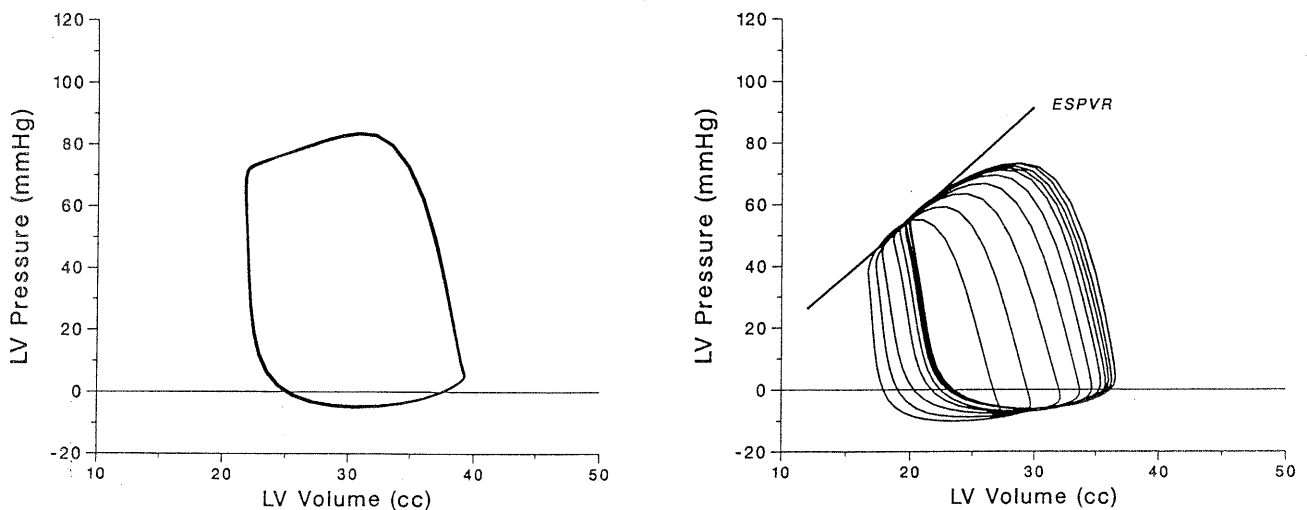


Figure 4. Representative pressure volume loop with CMP static in dogs: a) acute postwrap with cardiomyoplasty static; b) acute postwrap with cardiomyoplasty and caval occlusion. Slope of the line represents end-systolic pressure volume relation.

and left ventricular area compared with prewrap baseline. George and associates documented significant changes in maximal dP/dt and SW when comparing baseline to static CMP in a canine model [3]. However, they also administered beta-blockers to simulate heart failure, and thus confounded the static effect of CMP with the effect of beta-blockade. Corin and associates demonstrated negative changes in indices of left ventricular diastolic function comparing static to prewrap left CMP in normal canine hearts [6]. However, differences that occurred in active

diastolic relaxation, passive pressure decay, and passive stiffness may be related to the significant increase in end diastolic pressure caused by the performance of their CMP. In contrast to these studies, our studies showed no changes in left ventricular systolic or diastolic function following left LD CMP in a normal canine heart. Thus, it is possible to perform left LD CMP without comprising cardiac function, but the wrap must not be made tightly [7].

In this study there were no significant changes in indices of left ventricular systolic or diastolic functional mechan-

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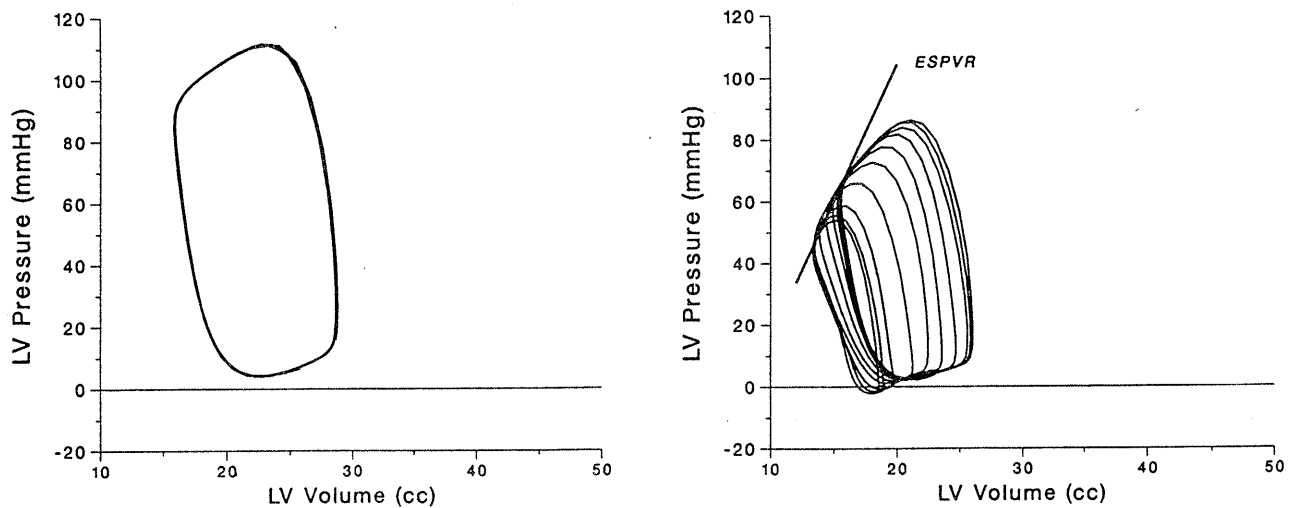


Figure 5. Representative pressure volume loops in dogs: a) two weeks with cardiomyoplasty static and caval occlusion. Slope of the line represents end-systolic pressure volume relation.

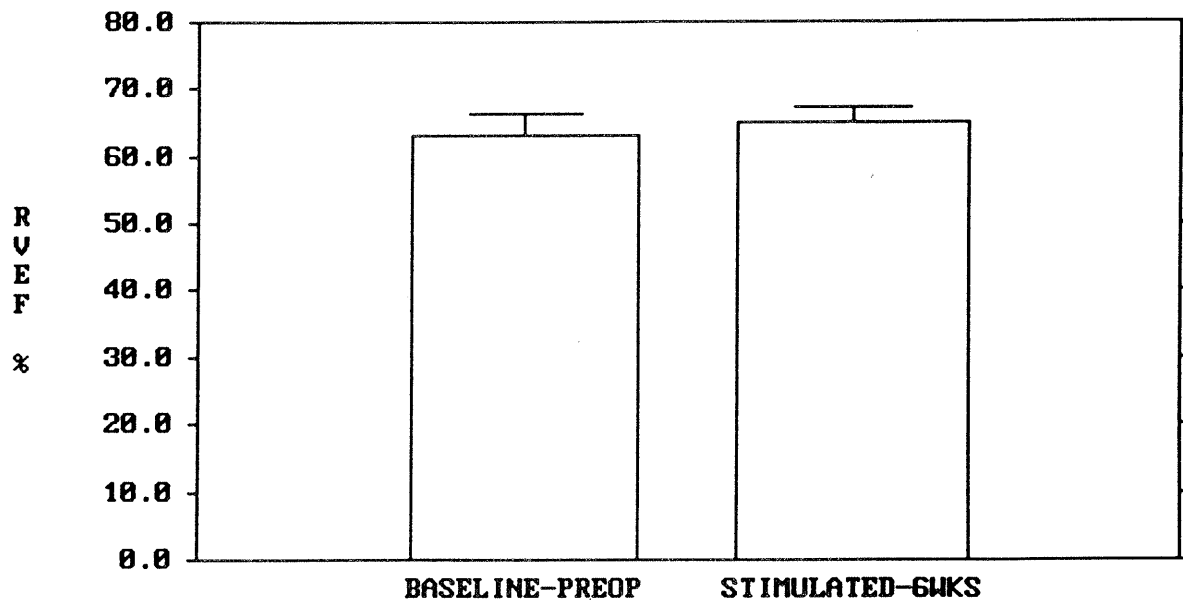


Figure 6. Right ventricular ejection fraction comparing preoperative data to data obtained at six weeks with the cardiomyoplasty stimulated to augment ventricular function.

ics by the static right LD CMP acutely or following the two week "resting" period during which time the muscle is allowed to revascularize. Findings in the experimental animals were confirmed by the clinical results. The lack of hemodynamic depression by the static right CMP may be related to the surgical technique of CMP. The right LD CMP can be consistently performed in the right anterior-cardiosternal orientation and is easily standardized. Performance of the left LD CMP, in both our clinical and

experimental experience, is prone to greater operative variation, depending upon operative approach (sternotomy vs thoracotomy), the intercostal space at which the LD is placed into the left chest, size and length of the muscle, and size of the heart. Hemodynamic deterioration occurs if the wrap is constructed too tightly in any situation. This increases preload on the LD muscle but impairs left ventricular function.

The important technical points in performing CMP are

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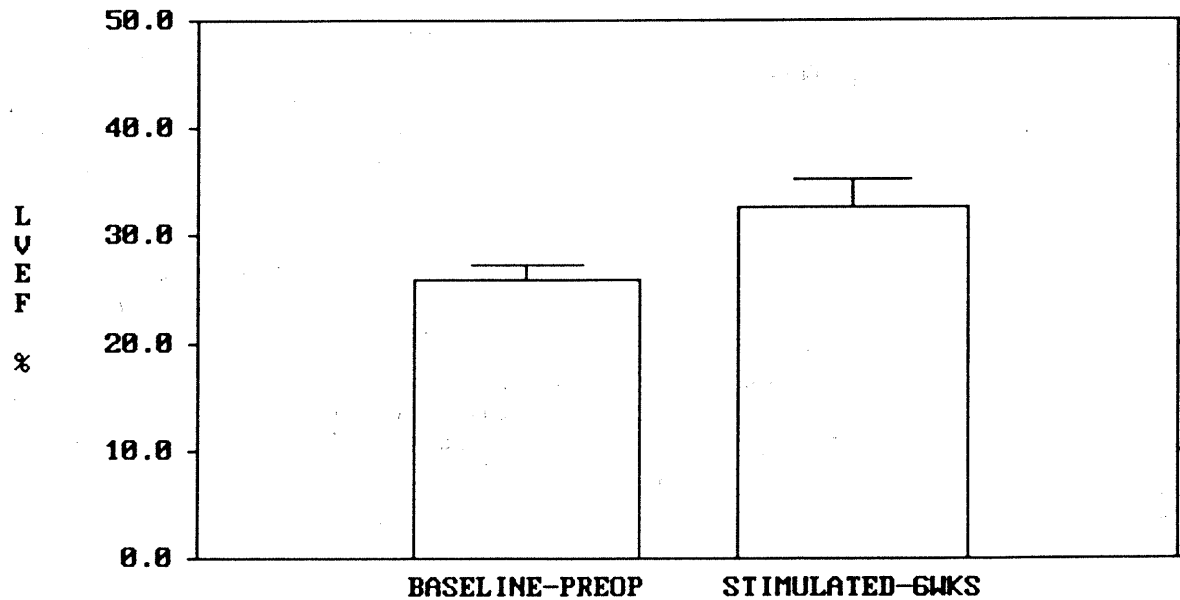


Figure 7. Left ventricular ejection fraction comparing preoperative data to data obtained at six weeks with the cardiomyoplasty stimulated to augment ventricular function. The difference between baseline and six week data is significant at the $p < 0.05$ level.

coverage of the left ventricle with viable LD and a loose CMP which does not disturb the normal anatomic orientation of the heart or impede venous return to the heart. These technical points will enable the procedure to be done without causing impairment of ventricular function. Molding of the myoplasty to the heart and the elevated end diastolic pressures seen in patients undergoing CMP will insure that sufficient preload is placed on the LD. This point is illustrated by the lack of effect of the static CMP on LVEF at two weeks followed by the significant increase in LVEF at six weeks with the CMP stimulated in the clinical group.

Our animal protocol also demonstrated no deleterious effect on LV function by the static right LD CMP. Ejection fraction, a load-dependent parameter of cardiac function, decreased in most animals following CMP, but returned to baseline. Cardiac output decreased acutely but remained within normal physiologic range, with an increase at two weeks. More importantly, load-independent parameters of cardiac contractility, i.e., preload recruitable stroke work and the end-systolic pressure volume relation, showed no significant differences over time. Calculated diastolic parameters also showed no significant changes. Left ventricular end diastolic volume and pressure as well as Tau, the diastolic relaxation time constant, stayed essentially the same following CMP, with nonsignificant decreases at two weeks. The drawback of our animal protocol is that non-failed hearts were used. The difficulty in reproducing chronic heart failure in animals that is pathophysiologically similar to that seen clinically is well known.

We conclude that the static (unstimulated) right LD CMP does not significantly impair ventricular function in either

non-failed animal models or clinically in patients with heart failure. Furthermore, despite minimizing preload on the LD as a measure to prevent hemodynamic compromise, the right LD CMP is clinically able to generate significant improvement in LVEF at six weeks. Subsequent refinement of operative techniques, muscle training protocols, improved patient selection, and continued physiologic studies will define CMP as a treatment for congestive heart failure.

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