Dynamic Cardiomyoplasty: Effect of Discontinuing Latissimus Dorsi Muscle Stimulation on Left Ventricular Systolic and Diastolic Performance and Exercise Capacity

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Objectives. This study sought to assess the short-term effect of discontinuing latissimus dorsi muscle stimulation on left ventricular systolic and diastolic performance and exercise tolerance in patients with improved functional status by cardiomyoplasty, in whom latissimus dorsi muscle was fully conditioned.

Background. Cardiomyoplasty has consistently improved the functional status of patients, but the short-term effect of latissimus dorsi muscle contraction has not been assessed in these patients.

Methods. Right-heart catheterization, Doppler-echocardiography and maximal exercise testing with expired gas analysis were performed in 10 patients with congestive heart failure who had undergone cardiomyoplasty at least 6 months earlier. Data were obtained when the latissimus dorsi muscle was stimulated every other systole and after stimulation was discontinued for 1 h. The power of this study to detect a 10% difference was >80%.

Results. After cardiomyoplasty, left ventricular ejection fraction increased from 0.22 ± 0.08 (mean ± SD) to 0.27 ± 0.07 after 6 months (p < 0.02 vs. before cardiomyoplasty) and to 0.24 ± 0.09 after 1 year; functional class went from 3.0 ± 0.0 to 2.0 ± 0.5 after 6 months and to 2.0 ± 0.7 after 1 year (both p < 0.001 vs. before cardiomyoplasty). After discontinuation of latissimus dorsi muscle stimulation, cardiac index did not change (2.28 ± 0.45 vs. 2.30 ± 0.46 liters/min per m²). Mean systemic arterial and pulmonary capillary wedge pressures were also similar (85.2 ± 6.0 vs. 88.4 ± 5.6 mm Hg and 14.9 ± 7.1 vs. 13.6 ± 6.8 mm Hg, respectively). Doppler E/A ratio decreased from 1.04 ± 0.33 to 0.83 ± 0.25 (p < 0.02), suggesting that left ventricular diastolic function may have been improved by latissimus dorsi muscle stimulation. Peak oxygen consumption was unaltered (1,633 ± 530 vs. 1,596 ± 396 ml/min).

Conclusions. Alterations in left ventricular diastolic rather than systolic function may be responsible for the long-term clinical benefits of cardiomyoplasty.

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multicenter Medtronic study (Maastricht, The Netherlands) and fulfilled entry criteria, including isotopic left ventricular ejection fraction $<0.40$, mean capillary wedge pressure or left ventricular end-diastolic pressure $>15$ mm Hg and New York Heart Association functional class III despite optimal medical therapy. None of them had had concomitant surgical intervention. Mean age was $51.2 \pm 7.3$ years (range 43 to 63). Congestive heart failure was secondary to coronary artery disease in two patients and to idiopathic dilated cardiomyopathy in eight. Before cardiomyoplasty, all patients were treated with angiotensin-converting enzyme inhibitors and loop diuretic drugs. Six patients were given nitrates, six amiodarone and three cardiac glycosides. At the time of the study, angiotensin-converting enzyme inhibitors were discontinued in one patient because of severe symptomatic hypotension; loop diuretic drugs were discontinued in one patient; six patients were receiving amiodarone, three digoxin, and only one was still receiving nitrates. All patients provided written informed consent, and the protocol was approved by the Comité d’Éthique de l’Université Claude Bernard et des Hôpitaux Civils de Lyon.

**Stimulation protocol.** Two weeks after latissimus dorsi muscle implantation, stimulation was started every two systoles, with one impulse of 3.5 V/burst. The number of impulses was then increased every 2 weeks (by increasing the frequency of the burst from 5 to 30 Hz) until each burst included six impulses (burst duration 185 ms). The delay between the R wave detected by the sensing electrode placed on the right ventricle and the first impulse was set up so that the burst began at the onset of mitral valve closure on M-mode echocardiography. This timing was checked at each visit during follow-up. The impulse amplitude was increased systematically until it reached 4.5 V or if the patient requested it (one time) or if hemodynamic deterioration occurred (two times). However, no patient could withstand impulses $>5$ V. At the time of the study, the mean amplitude of stimulation was 4.23 V (range 3.5 to 5 V), and trains of six pulses were delivered in all patients.

**Hemodynamic study at rest.** A Swan-Ganz catheter was inserted through a peripheral vein of the arm and advanced into the right pulmonary artery under fluoroscopic guidance. Pressures were measured with a Siemens Mingograph III or a Hewlett-Packard monitoring device and recorded during end expiration or held expiration. Systemic arterial pressures were obtained by cuff with an automated device (Dynamap). Cardiac output was measured by the thermodilution technique (Baxter-Edwards). Radial and pulmonary artery blood samples were withdrawn for gas analysis and for derivation of arteriovenous oxygen content difference.

**Echocardiographic–Doppler study at rest.** Echocardiographic–Doppler studies were performed with an Interspec or a Hewlett-Packard machine with a 3.5-MHz duplex probe. Left ventricular echocardiographic diameter was measured in the parasternal long-axis view using the M-mode guided by two-dimensional echocardiography. Transaortic and transmirtal flow velocities were recorded from the apical view. For mitral flow recording, the sampling volume was placed at the level of the mitral leaflet tips and just below the aortic valves for aortic flow recording. All studies were recorded on a 0.5-in. videotape for subsequent analysis.

Mitral flow was digitized and analyzed using a personal program, allowing calculation of A and E wave peak velocities; A and E acceleration and deceleration times; A, E and total velocity–time integrals; RR interval; and total filling time (mitral inflow duration). Similarly, aortic flow was digitized and analyzed according to a previously described technique (8), allowing calculation of acceleration, deceleration and ejection times; peak and mean aortic velocities; maximal and mean acceleration times; and RR interval. Six consecutive beats were averaged. Premature ventricular beats and the two following beats were avoided.

**Protocol.** With the patient in the fasting state, the Swan-Ganz catheter was positioned in the pulmonary artery. A complete echocardiographic–Doppler study was performed (baseline), and hemodynamic data were obtained. Blood samples were withdrawn from the radial and pulmonary arteries for gas analysis. The stimulator was then switched off, and the hemodynamic and Doppler variables were recorded after 1, 3 and 5 min. Because of the technical impossibility of simultaneously recording aortic and mitral Doppler flows, and pulmonary artery and pulmonary capillary wedge pressures, the stimulation was set on again for 30 min, and new transitions allowed the measurement of missing variables. After completion of intermediary studies, the latissimus dorsi was left unstimulated for 1 h, and a complete set of hemodynamic and Doppler variables was obtained. The pulse generator was then switched back on.

**Exercise test.** Exercise was conducted in a temperature-controlled room at 20 to 22°C. Exercise testing was performed in the upright position on a magnetically braked bicycle ergometer (Ergoline) with both feet secured to the pedals. All the patients were familiar with bicycle exercise testing and had undergone several previous tests with continuous expired gas analysis. Work rate was increased by 12.5 W/min.

Expired gas was collected continuously during exercise through a low resistance three-way valve (Hans Rudolph). Oxygen uptake and carbon dioxide production were determined in ml/min at 15-s intervals (CPX Medical Graphics). Respiratory exchange ratio was calculated as carbon dioxide production/oxygen uptake. Every minute, the patient was asked to quantify the perceived intensity of exercise from 0 (nothing) to 10 (maximal) (9).

Blood pressure (standard cuff technique) and the electrocardiogram were continuously monitored during the exercise and recovery periods. Exercise tests with the cardiomyostimulator on and off were performed on separate days, at the same time of the day, in random order.

**Statistics.** Data are reported as mean value $\pm 1$ SD. The measurements obtained when the stimulator was on and off for 1 min, 3 min, 5 min, and 1 h were compared with repeated-measures analysis of variance as well as measurements obtained before cardiomyoplasty and after 6 months and 1 year. A paired Student $t$ test was used to compare 1) the measurements obtained when the stimulator had been discontinued for...
Figure 1. Evolution of New York Heart Association functional class (left), left ventricular ejection fraction (middle) and peak oxygen consumption (right). 0 = values obtained before cardiomyoplasty; +6 and +12 = values obtained 6 and 12 months after cardiomyoplasty, respectively. After 6 months, functional class improved significantly (p < 0.01), as did mean left ventricular ejection fraction (p < 0.02). However, mean peak oxygen consumption remained unchanged. After 1 year, no significant change in peak oxygen consumption or ejection fraction could be demonstrated. Symbols refer to individual patients.

1 h with those obtained when the stimulation was on, and 2) values obtained during the two exercise tests.

This study was able to detect a 10% change in peak oxygen uptake or rest cardiac index with a power of 80%, according to the published reproducibility data for these measurements (10,11).

Results

After latissimus dorsi muscle implantation, radionuclide left ventricular ejection fraction increased from 0.22 ± 0.08 up to 0.27 ± 0.07 at 6 months (p < 0.02 vs. before cardiomyoplasty). However, after 1 year, it was no longer significantly different from the baseline value (0.24 ± 0.09, p = NS). Mean functional class status improved from 3.0 to 2.0 ± 0.5 after 6 months and was 2.0 ± 0.7 after 1 year (both p < 0.001 vs. before cardiomyoplasty) (Fig. 1). In contrast, after latissimus dorsi muscle implantation, rest cardiac output remained unchanged (2.4 ± 0.4 liters/min per m² before cardiomyoplasty vs. 2.6 ± 0.4 liters/min per m² after 6 months and 2.4 ± 0.5 after 1 year, all p = NS) as well as peak oxygen consumption (18.9 ± 3.7 ml/kg per min before cardiomyoplasty vs. 17.9 ± 2.2 ml/kg per min after 6 months and 18.3 ± 3.1 after 1 year, all p = NS). Echocardiographic left ventricular end-diastolic diameters were not modified after cardiomyoplasty (72.8 ± 10.8 mm before cardiomyoplasty vs. 71.5 ± 12.2 mm after 6 months and 71.7 ± 12.5 mm after 1 year). Similarly, rest heart rate remained stable.

Hemodynamic study. Table 1 includes hemodynamic measurements with latissimus dorsi muscle stimulation off for 1 h. During latissimus dorsi muscle stimulation, arteriovenous oxygen content difference was 51 ml/liter. Systolic and diastolic pulmonary artery pressures averaged 31.0 ± 9.8 and 16.2 ± 7.3 mm Hg, respectively. Systolic and diastolic systemic blood pressures averaged 113 ± 9 and 71 ± 6 mm Hg, respectively. Systemic and pulmonary vascular resistance indexes averaged 1,457 ± 277 and 113 ± 36 dynes·cm⁻⁵, respectively. None of these variables were significantly altered 1, 3, 5 min and 1 h after discontinuing the stimulation. Even when the three patients with the lowest cardiac index were considered (all <2.2 liters/min per m² and capillary wedge pressure >18 mm Hg), no effect was observed.

Doppler study. Mitral flow. Three patients whose mitral regurgitation was graded 2+ or greater were excluded from mitral flow analysis, so that only data obtained from seven patients were analyzed. Heart rate and total filling time were not altered by stopping stimulation of latissimus dorsi muscle (Table 2). After discontinuation of latissimus dorsi muscle stimulation, left ventricular filling tended to occur later in diastole: although total velocity-time integral did not vary, E wave peak velocity decreased (p = 0.056), whereas A wave peak velocity was unchanged, so that the E/A velocity ratio decreased significantly (p < 0.02). Similarly, E wave velocity-time integral decreased (p < 0.001), whereas that for the A wave was not significantly modified. Despite the decrease in E wave peak velocity and velocity-time integral, E wave decel-

<table>
<thead>
<tr>
<th>Table 1. Hemodynamic Data</th>
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<tr>
<td><strong>Stimulation</strong></td>
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<tr>
<td><strong>On</strong></td>
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BP = blood pressure; CI = cardiac index; HR = heart rate; LVSWI = left ventricular stroke work index; PAS = pulmonary artery blood oxygen saturation; PCWP = pulmonary capillary wedge pressure; Stimulation = stimulation of latissimus dorsi muscle every other systole (On), and off for 1 h (Off); SVR = systemic vascular resistance.
Table 2. Mitral Doppler Data (mean ± SD)

<table>
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<tr>
<th>Stimulation</th>
<th>Stimulation Off 1 h</th>
<th>p Value</th>
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<tbody>
<tr>
<td>RR (s)</td>
<td>0.89 ± 0.13</td>
<td>0.88 ± 0.14</td>
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<tr>
<td>Filling time (s)</td>
<td>0.48 ± 0.13</td>
<td>0.45 ± 0.11</td>
</tr>
<tr>
<td>VTI (cm)</td>
<td>13.3 ± 2.9</td>
<td>12.3 ± 2.0</td>
</tr>
<tr>
<td>VTI E (cm)</td>
<td>8.3 ± 1.0</td>
<td>7.4 ± 0.9</td>
</tr>
<tr>
<td>VTI A (cm)</td>
<td>5.1 ± 2.3</td>
<td>4.9 ± 1.2</td>
</tr>
<tr>
<td>E velocity (m/s)</td>
<td>0.54 ± 0.10</td>
<td>0.48 ± 0.10</td>
</tr>
<tr>
<td>A velocity (m/s)</td>
<td>0.56 ± 0.12</td>
<td>0.60 ± 0.11</td>
</tr>
<tr>
<td>VE/VA</td>
<td>1.04 ± 0.33</td>
<td>0.83 ± 0.25</td>
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RR = RR interval duration; VE/VA = ratio of maximal E wave velocity to maximal A wave velocity; VTI = velocity-time integral; other abbreviations as in Table 1.

 contraction time remained stable, suggesting that left ventricular relaxation was delayed after discontinuation of latissimus dorsi muscle stimulation.

Aortic flow. Aortic flow variables were unchanged by discontinuing latissimus dorsi muscle stimulation for 1, 3, 5 min or 1 h. Aortic velocity–time integral and RR intervals specifically remained unchanged, and this was consistent with the stability of the thermodilution cardiac output.

Exercise studies. Exercise was limited by general fatigue or leg discomfort, or both, in all patients. None had symptoms compatible with angina or peripheral vascular disease. Discontinuation latissimus dorsi muscle stimulation for 1 h did not produce any symptom in any patient (Table 3).

At maximal exercise, the muscle flap was contracting every two systoles in one test, every three systoles in seven tests and every four systoles in two tests. Discontinuation of latissimus dorsi muscle stimulation did not affect maximal exercise variables. Derived variables, such as rate–pressure product or oxygen pulse, the latter being an indirect estimate of left ventricular stroke volume, also remained unchanged (18.667 ± 4,833 vs. 19.242 ± 5,515 [beats/min]·mm Hg and 11.4 ± 3.0 vs. 11.2 ± 2.2 ml/beat, respectively).

The anaerobic threshold was identified in all patients but one. At anaerobic threshold, the heart–muscle flap contraction ratio was 1:3. Exercise variables at anaerobic threshold, including oxygen pulse (9.0 ± 2.1 vs. 9.2 ± 2.4 ml/beat), were unchanged by discontinuation of latissimus dorsi muscle stimulation. However, at anaerobic threshold the perceived intensity of exercise tended to be lower during the stress test performed when latissimus dorsi muscle stimulation was on (3.7 ± 3.0 on vs. 4.9 ± 3.4 off, p = NS).

Discussion

Our study clearly indicates that discontinuation of latissimus dorsi muscle stimulation for 1 h did not alter rest left ventricular systolic function in patients with congestive heart failure who had undergone cardiomyoplasty at least 6 months earlier. In contrast, echocardiographic–Doppler-derived variables of left ventricular diastolic function were altered by discontinuation of latissimus dorsi muscle stimulation in the absence of change in loading conditions of the heart.

Stimulation on versus off. The short-term hemodynamic effects of latissimus dorsi muscle stimulation, using a heart muscle flap contraction ratio of 1:1, have been studied in several animal models with variable results. Many investigators have reported an increase in cardiac output in both failing and nonfailing hearts (12–15), but others have not (16,17). Of note, animal models using unconditioned skeletal muscle may not be relevant to the human clinical situation because the rate of contraction and relaxation is slowed in conditioned skeletal muscle (18). In 21 patients alive >2 years after cardiomyoplasty (4), stimulation of the latissimus dorsi muscle with 1:2 ratio was reported to increase cardiac output by 12 ± 3%
compared with values recorded after discontinuation of latissimus dorsi muscle stimulation. Bocchi et al. (19) reported a decrease in angiographic left ventricular ejection fraction after a discontinuation of 1:1 latissimus dorsi muscle stimulation for 24 h.

**Preoperative versus postoperative findings.** Cardiac output or left ventricular ejection fraction, or both, have been reported to increase after cardiomyoplasty in humans (4,19,20) and animal models of heart failure (21). In our patients, cardiac output remained unchanged, whereas mean left ventricular ejection fraction increased significantly from 0.22 ± 0.08 preoperatively to 0.27 ± 0.07 after 6 months (Fig. 1). This finding might suggest that the main effect of cardiomyoplasty was either an increase in mitral regurgitation or a decrease in left ventricular volume (not substantiated by a decrease in left ventricular end-diameter measured with M-mode echocardiography). However, these measurements are approximate because of geometric changes of the left ventricle. The reason for the absence of a sustained improvement of left ventricular ejection fraction after 1 year is unclear and could merely be related to the small number of patients studied.

**Diastolic function.** In seven patients, mitral regurgitation was absent or minimal, and because preload and afterload estimated by mean capillary wedge and blood pressures were unchanged, as was diastolic filling time, left ventricular end-diastolic function could be assessed using Doppler mitral inflow velocity. Left ventricular filling tended to occur later after discontinuation of latissimus dorsi muscle stimulation, suggesting that contraction of the skeletal muscle improved left ventricular filling: The peak velocity and velocity-time integral of the E wave significantly decreased after latissimus dorsi muscle contraction stopped, and E/A ratio decreased, suggesting that at least left ventricular diastolic function was not impaired by muscle contraction. This is in keeping with the increase in peak filling rate reported by Cheng et al. (21) in an animal model of congestive heart failure.

**Exercise.** Discontinuing latissimus dorsi muscle stimulation did not alter maximal graded stress test variables. The stability of peak oxygen consumption suggests that muscle stimulation did not impair left ventricular filling during exercise so as to reduce cardiac output and exercise capacity, and this is in keeping with our echocardiographic-Doppler study at rest. Furthermore, the finding that peak oxygen consumption was not higher with stimulation on is consistent with the hypothesis that muscle stimulation did not improve left ventricular systolic performance during exercise. This may result from the absence of effect of muscle contraction on hemodynamic variables, as suggested by our study at rest, or from the low stimulation rate of the skeletal muscle flap, limited to 55/min and therefore occurring every three systoles at the anaerobic threshold or even less at maximal exercise. Alternatively, peak oxygen consumption might be unchanged because, similar to patients with severe heart failure, our patients were limited by peripheral factors, so that a short-term change in cardiac output would not be associated with a corresponding change in peak oxygen consumption (22-24). However, our patients were less severely limited than patients with congestive heart failure in whom such a peripheral limitation has been demonstrated (25).

The absence of any effect of muscle flap contraction on left ventricular systolic performance is not readily explainable by technical factors. The surgical technique and conditioning protocol used were those developed by Chachques et al. (26). The mean amplitude of stimulation was 4.23 V, a value similar to that used by Carpentier et al. (4) (4.0 ± 0.6 V), which has been reported to produce hemodynamic benefit in humans (27). The delay between operation and hemodynamic studies was >3 months, and according to Jatene et al. (28), most of the beneficial effect occurred at 3 months and was maintained thereafter. Because hemodynamic variables at rest were subnormal, one can speculate that no distinct change could be expected. However, in three of our patients with a cardiac index <2.2 liters/min per m² and a mean pulmonary capillary wedge pressure >18 mm Hg, discontinuing latissimus dorsi muscle stimulation did not alter hemodynamic variables. One possible reason for this lack of efficacy could be, as suggested by Magovern et al., that the distal half of the muscle graft does not contract to the same degree as its proximal half or even lengthen, with most of the shortening occurring in the proximal part (18).

**Conclusions.** Our study suggests that the improvement in left ventricular function reported in patients after cardiomyoplasty is not directly related to dynamic compression of the left ventricle by latissimus dorsi muscle, as initially proposed. No short-term effect of skeletal muscle stimulation (with the variables used during clinical follow-up) could be evidenced on rest hemodynamic or exercise stress test variables. The functional improvement reported by our patients may thus not reflect the mechanical action of the muscle flap contraction on left ventricular systolic function. A myocardial oxygen consumption-saving effect has been reported (29), and some experiments suggest that preventing further left ventricular dilation may be the main effect of cardiomyoplasty. Our Doppler studies suggest that cardiomyoplasty might improve left ventricular diastolic function.

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**References**

6. Silverman NA. Invited letter concerning: left ventricular function changes


