

Early Latissimus Dorsi Stimulation after Cardiomyoplasty Procedure: a Preliminary Study

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Abstract

We studied early *Latissimus Dorsi* (LD) conditioning following cardiomyoplasty surgery. A counterclockwise wrapping procedure was performed in eight goats and LD post-operative electrical training was started one day later (Cardiomyostimulator model SP 1005, Medtronic, Minn., USA). Stimulation parameters included pacing frequency of 10 pulses/sec, pulse amplitude of 5 V and LD-heart contraction ratio of 1:3. In order to create temporarily proper intermuscular fixation, a fibrin glue (Tissucol, Immuno AG, Austria) was applied. LD contribution to cardiac function was assessed two weeks later. On macroscopic evaluation no sign of wrapped muscle damage or displacement was observed.

Histological studies furtherly confirmed the absence of intramuscular degenerative reaction. Partial transformation of type II into type I fibers was already present. Hemodynamic measurements, after two weeks, revealed efficient and significant LD contribution to cardiac performance ($p < 0.05$ for Right Ventricular Pressure). This study clearly shows early post-operative LD conditioning feasibility. For transposed muscle fatigue preventing, initial pacing parameters and proper LD-heart contraction ratio are determinant factors. Fibrin sealant appeared to be a valuable surgical tool to enhance adhesion formation in order to avoid muscle displacement.

Key words: cardiomyoplasty, *Latissimus dorsi* conditioning, early stimulation, fibrin glue.

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Because of limited heart transplantation application due to donor shortage transformed skeletal muscles have been proposed as alternative power source for cardiac support. The use of such biomechanical pumps proved to provide efficient contribution to global ventricular function either experimentally or clinically [1-8]. Since the first patient was submitted to *Latissimus Dorsi* (LD) transplant onto the heart in 1985 several investigators reported successful operative as well as long-term results [9-18]. Current Cardiomyoplasty (CM) technique implies LD recovery period after surgery. This span has been shown to be necessary in order to prevent muscle ischemia due to collateral vessel ligation and to obtain proper LD-heart fusion through optimal adhesion formation [3,19,20,21]. Skeletal muscle atrophy due to immobilization has been reported [24,25]. Furthermore, post-operative hemodynamic deterioration has been described during muscle flap recovery, because of failing heart overload (6,11,15). This study presents preliminary findings regarding modified surgical and post-operative procedures to avoid such adverse effects.

Material and methods

Eight adult female goats with a weight range of 40-60 kg were submitted to the study and cared in conformity to the principles for research use of experimental animals of the American Society of Physiology.

The left LD was exposed through a left lateral thoracic incision. After proper muscle dissection the proximal portion was carefully examined and the pedicle structures identified. Two intramuscular electrodes (Model SP 5528, Medtronic, Maastricht, The Netherlands) were then implanted, with the proximal lead woven at the branching level of the thoracodorsal nerve and the second lead placed 6-8 cm distally. Any neural or vascular damage was avoided. LD and electrode impedance as well as threshold were measured with a proper device (Model 3028, Medtronic). The skeletal muscle transposition into the left thoracic cavity was performed through a window obtained by a partial resection of the second rib. The humeral insertion of the muscle was divided and sutured to the periosteum of the first rib. The pericardial sac was visualized through a left anterolateral thoracotomy in the fifth intercostal space and resected to allow optimal cardiac exposure.

The LD wrapping procedure was performed according to the counterclockwise technique. Before completing ventricle reinforcement a fibrin sealant (Tissucol, Immuno AG, Austria) was applied at the intermuscular level (anteriorly and posteriorly) using a spray device (Duploject-Tissomat, Immuno AG, Austria).

A sensing electrode was implanted on the right ventricle and the related threshold assessed by the Medtronic analyser. The cardiomyostimulator (Model SP 1005, Medtronic) was then

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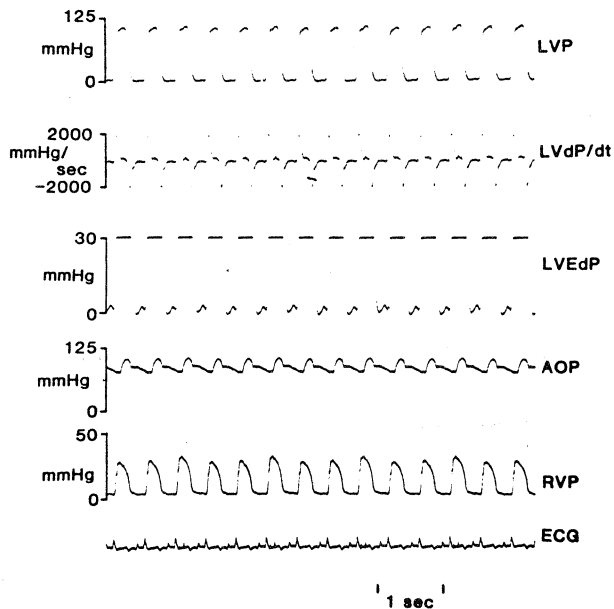


Figure 1: Hemodynamic recording obtained with 10 pulses/sec pacing frequency, 100 msec interpulse interval, 5 V pulse amplitude and 3:1 LD-heart contraction ratio. Left ventricular pressure, left ventricular dP/dt, left ventricular diastolic pressure, aortic blood pressure, right ventricular pressure and ECG are shown. Note marked LD support to right ventricular function during assisted beats.

connected to the leads and finally positioned in a properly fashioned pocket.

In all animals LD electrical conditioning was started one day after surgery. The stimulation parameters included pacing frequency of 10 pulses/sec, pulse amplitude of 5 V and LD-heart contraction ratio of 1:3. After stimulation programming, LD contraction was assessed by ECG recording (pulse observation) as well as by axilla palpation. During the following two weeks stimulated muscle flap function was periodically evaluated by palpation to verify muscle contraction.

After fourteen days accurate muscle dissection was performed to precisely evaluate LD condition after early training submission and to carefully examine the extent of adhesion degree at the intermuscular level. Fiber typing was also performed to elucidate whether efficient muscle transformation was proceeding. Attention was paid, moreover, to search for any sign of occurring intramuscular degenerative or inflammatory reactions. Hemodynamic LD contribution to cardiac performance was assessed at 10 pulses/sec pacing frequency. In order to further stress muscle flap contractile force or to elicit any previously induced muscle damage stimulation was also performed at 30 pulses/sec. Hemodynamic data were obtained using catheters placed inside the right and left ventricles (Millar

Instruments, Houston, Texas) measuring internal related pressures concomitantly with left ventricular dP/dt. Aortic blood pressure was recorded through a femoral arterial line.

All hemodynamic data were subjected to statistical analysis with the paired t test. A p value of 0.05 or less was considered significant. The data are given as mean \pm SD.

Results

Eight goats entered into the study. Ventricular fibrillation refractory to any resuscitation technique occurred in one animal during left ventricle catheter insertion (tip induced arrhythmia).

Macroscopic as well as histological evaluations were performed in all 8 animals whereas 7 goats were submitted to hemodynamic measurements.

LD contribution to heart performance was immediately evident soon after catheter positioning for hemodynamic function recording (figure 1). Right ventricular pressure was markedly influenced and increased during assisted beats.

Slight LD support was also noted on LV pressure curve, attesting skeletal muscle flap viability after early post-operative electrical stimulation.

Of note, on autopsy all the early trained LD muscles appeared in perfect condition and properly wrapped onto the heart; no purple area (ischemic segment) was observed. LD radio-labeled blood flow measurements were not performed, but all muscle flaps appeared healthy attesting optimal cellular substrate supply and absence of blood flow impairment.

Histology confirmed no muscular tissue damage or atrophy either at the proximal or distal portion. Adequate LD conditioning was moreover demonstrated by fiber typing: partial type II fatigue-prone fibers and partial type I fatigue-resistant fibers were observed demonstrating the fiber transformation process (figure 2).

Gross LD muscle examination at the time of death revealed that optimal intermuscular fusion, and strong as well as uniformly spread adhesions were present (figure 3); no evidence of cardiac constriction was present.

Finally, it is important to note that significant cardiac assist on right ventricular function was observed (table I), despite both normal heart performance and low pacing frequency. Hemodynamic studies with 30 bursts further confirmed trained LD viability and showed significant improvement of heart function during supported beats.

Discussion

Despite recent advances, cardiac transplantation cannot provide effective treatment to end-stage heart failure because of limited donor pool. Dynamic Cardiomyoplasty, which implies unilateral *Latissimus Dorsi* mobilization and wrapping around the ventricles followed by electrical stimulation to allow muscle fiber transformation, has been proposed as one alternative procedure. Several reports described successful experimental LD cardiac assist during past years leading to the first clinical case in 1985 [1-9]. To date, almost one hundred patients have been submitted to Dynamic Cardiomyoplasty [10-16]. Optimal operative results as well as long-term survival have already been reported by some investigators [10-18]. Nevertheless improvement of the surgical technique to augment LD contractile contribution or post-operative patient care refinement have been proposed [6,21,22].

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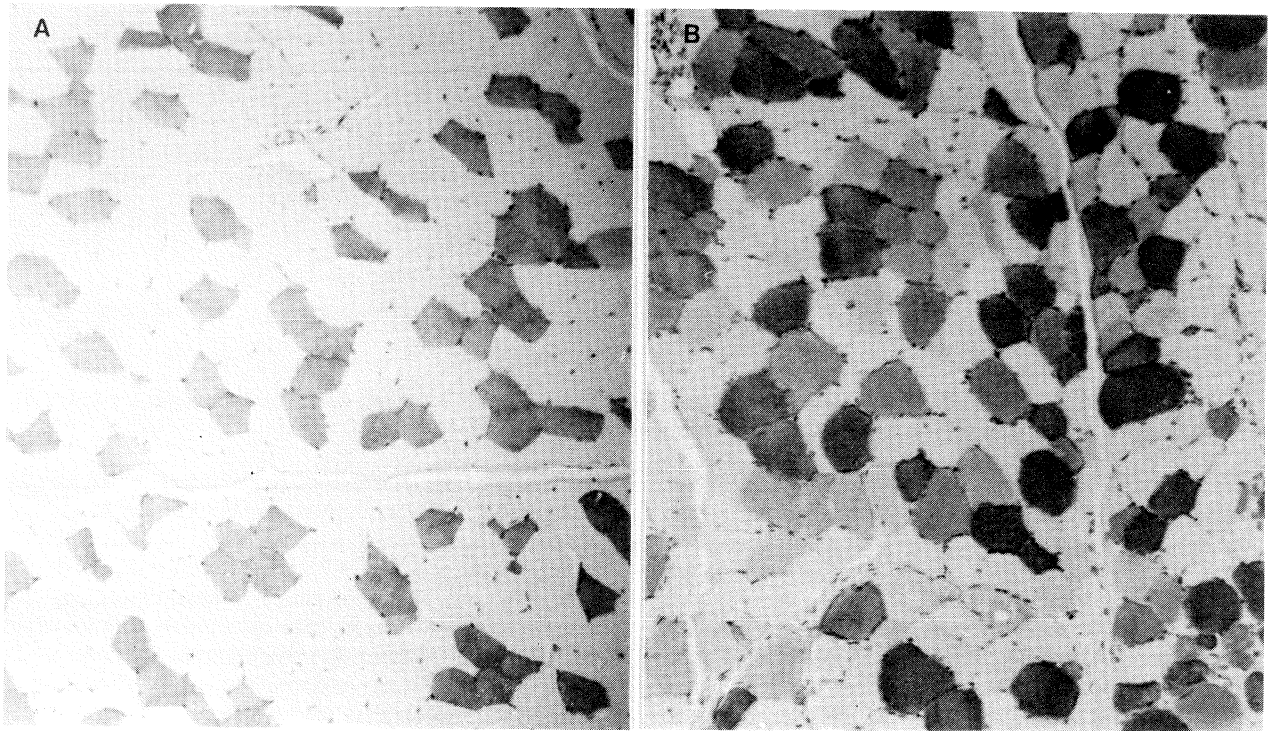


Figure 2: Latissimus Dorsi cross-section. A: non stimulated right skeletal muscle. B: Two-week conditioned left pedicled flap. The lightly stained fibers are classified as type II fast-twitch fatigue-prone fibers whereas darkly stained fibers as type I slow-twitch fatigue-resistant fibers. Note partial LD transformation after early electrical stimulation for 2 weeks.

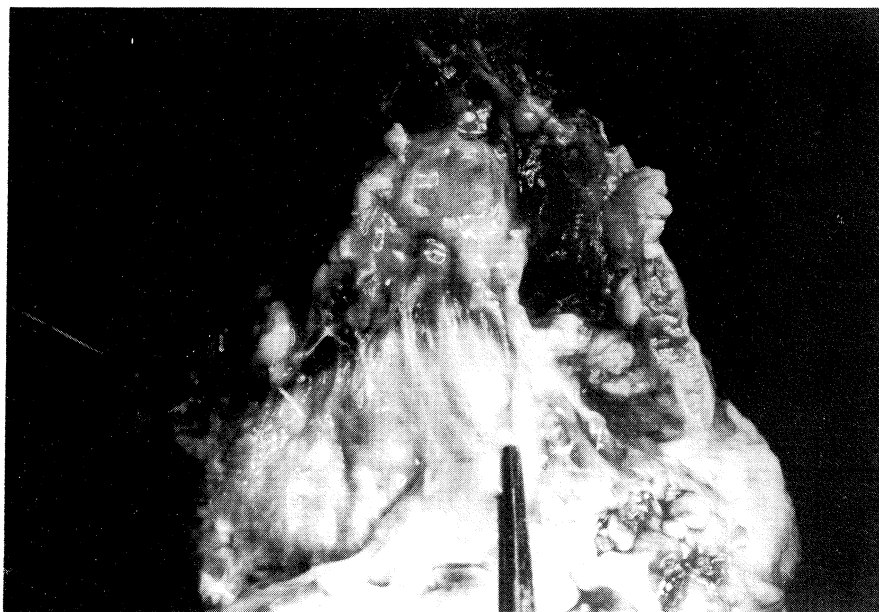


Figure 3: Latissimus Dorsi-Heart interface. Above: Latissimus Dorsi muscle flap. Below: ventricular chambers. Uniform and firm adhesion are evident after early-induced muscle conditioning. No cardiac constriction was observed.

The current Dynamic Cardiomyoplasty procedure requires a LD rest period of two weeks after surgery to allow muscle flap revascularization because of intra-operative collateral vessel severance [19,20,21,23]. Concomitantly this recovery span may give rise to proper adhesion development at the intermuscular site [21]. Actually, the preliminary clinical cases did not follow

such a protocol and the exact time to start electrical conditioning of the LD is not well established ranging from 5 to 14 days after surgery [9,11,15]. At present no muscle damage or pedicled graft dysfunction due to earlier stimulation had been reported.

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Table I: Hemodynamic parameters

	LVP	LVdp/dt	RVP	AoP
1) 10 pulses/sec:				
- non-assisted beats	110 ± 18	1740 ± 494	26 ± 6	118 ± 17
- assisted beats	112 ± 17	1897 ± 618	30 ± 8	120 ± 16
p value	0.143	0.08	0.014*	0.111
2) 30 pulses/sec:				
- non-assisted beats	112 ± 14	1646 ± 232	26 ± 8	118 ± 15
- assisted beats	113 ± 13	1859 ± 325	31 ± 11	120 ± 14
p value	0.656	0.018*	0.011*	0.018*

* = p value of 0.05 or less is accepted significant. Values are given as mean ± SD. LVP: left ventricular pressure; LVdp/dt: left ventricular dp/dt; RVP: right ventricular pressure; AoP: aortic pressure.

Mannion et al. [19], however, demonstrated negative early LD pacing effects, showing muscle ischemia and fatigue occurrence soon after muscle dissection. These results convincingly led to the current stimulation protocol.

Several investigators described deleterious effects of skeletal muscle immobilization, already after two-weeks, leading to muscle atrophy due to serial sarcomere loss and to intramuscular connective tissue remodelling with subsequent increased muscle stiffness [24,25]. Moreover, low cardiac output episodes have been reported following Cardiomyoplasty Surgery likely induced by an inactive wrapped LD muscle which might negatively affect functioning of the already failing heart [11,15].

These considerations led us to investigate a different protocol regarding an earlier muscle conditioning feasibility.

In our laboratory a low pacing frequency (10 pulses/sec) was chosen and applied 24 hours after the surgical procedure.

This short post-operative delay was selected because we observed that LD mobilization stress does not require a more prolonged recovery. A fibrin glue was applied during surgery in order to timely create proper LD-heart contact and to avoid LD displacement.

After two-weeks of synchronous electrical stimulation no transported flap showed any sign of damage or displacement.

Strong and effective LD-heart fusion was still maintained despite sustained contractions. No cardiac constriction was observed. All early trained LD muscles were viable in the proximal and distal area.

Histological studies confirmed no intramuscular degenerative reaction nor the occurrence of an inflammatory process.

Proper muscle transformation was furthermore demonstrated: partial transformation type II fast-twitch fatigue-prone fibers to type I slow-twitch fatigue-resistant fibers was obtained.

Despite observed hemodynamic improvement the adopted LD pacing protocol will not provide effective cardiac support.

However a minor LD contribution can be anticipated to improve rather than deteriorate ventricular performance.

The present study reports early LD conditioning feasibility.

Proper pacing frequency, that is low frequency stimulation, and synchronous LD-heart contraction ratio are the crucial factors for preventing muscle flap ischemia and subsequent dysfunction. Stimulation-induced increase in muscle blood flow will occur and the intramuscular hyperemia might compensate distal flow impairment due to collateral vessel ligation. Also restricted muscle contraction might trigger internal

collateral network recruitment. Finally, the use of fibrin glue during cardiomyoplasty surgery should be advocated even when a recovery period of 2 weeks follows, since LD displacement may occur during this period because of wrapping suture line weakness (atrio-ventricular fatty tissue). We do believe, moreover, that the technique to apply fibrin glue is crucial since the spray device gives a uniform adhesion layer whereas syringe technique provides only a few less effective anchoring spots.

Accomplishment of the complete conditioning protocol and the long-term effect of early LD stimulation still remain to be investigated.

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