RESEARC
IN
SURGERY

e of Unstimulated *Latissimus Dorsi* nsposed Into the Chest and Applied Cardiomyoplasty

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RACT

e aim of characterizing qualitative and quantitative aspects of unstimulated striated ske
s involved in cardiomyoplasty, four goats had clockwise anterior-posterior cardiomyopl
latissimus dorsi was dissected and stimulating electrodes were implanted, but the muscle
jected to the usual activating-transforming stimulation protocol. Histological and mor
aspects of muscle were assessed during surgery, once during follow-up in two animals
and at sacrifice (2-12 months later). A biochemical study of the muscle was also done ir
. In each case, impressive atrophy with retraction of the muscle was noticed; after 12 mo
aining flap covered only half to two-thirds of the left ventricular free wall. Microsco
howed neither vascular nor neurological damage, though fiber degeneration and an increa
ous and adipose content were noted. Histoenzymology and biochemical analysis confi
eneration of both oxidative and glycolytic fibers. The interface between the heart an
sed muscle, and the muscle reaction to the implanted electrodes were characterized. This
and documents the less favourable evolution (excluding technical errors) of muscle inv
omyoplasty: it strongly suggests that, due to tenotomy, modified length-tension relatio
k of stimulation, extensive time-dependant disuse atrophy occurs. Neural influx throug
ed thoracodorsalis nerve seems to exert little influence in maintaining significant muscle
 months.

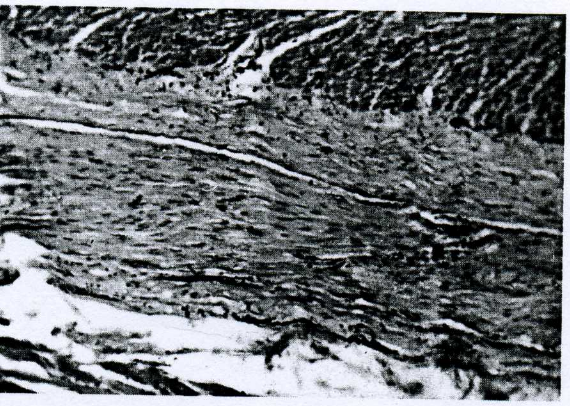
ords: Striated muscle. Cardiomyoplasty. Muscle transposition.

RODUCTION

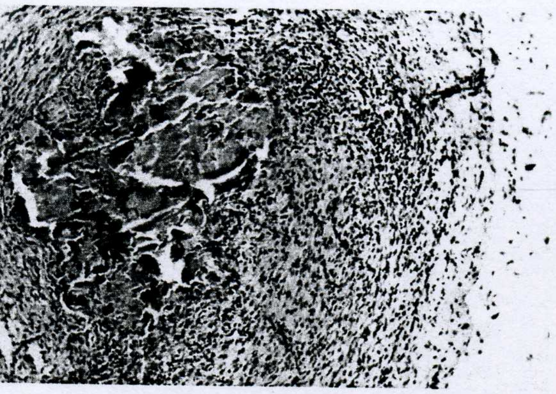
nalytical approach to study the evolution of *s dorsi* used for cardiomyoplasty requires that oints of major concern be taken into account. most such points may dramatically influence the come of the involved muscle.

e aspects are: (a) The consequences of complete al dissection leading to proximal and distal y with suppression of the peripheral vascular riginating from perforating branches of inter- d lumbar arteries; (b) The influence and possible s effects of intramuscular or epineural electrode ation; (c) Transposition into the chest via a window; (d) The concentric disposition of the muscle around the heart, where it is possibly subje remodeling and to the beat-to-beat variatio intracardiac volume and pressure; and (e) The effects stimulation protocol that contributes to the acquisi fatigue-resistance and maintains mechanical acti addition to that via self-innervation through the th dorsalis nerve.

The purpose of the present study was to investig short- and middle-term follow-up the effe transposition into the chest and concentric wr independently of any external pacing. This aspect evolution of *latissimus dorsi* involved in cardiomy has not been carefully documented in the literature (1). Furthermore, it constitutes a prerequisi



Interface between the latissimus dorsi (LD) and the hematoxylin-eosin, x40). A fibrous layer with a ry separates the transposed LD (top) from the dium (bottom).



. Inflammatory reaction surrounding implanted ting electrodes (hematoxylin-eosin, x40). A usual n against foreign body is seen (Medtronic SP5528 les removed prior to histological preparation), with cleated and epithelioid cells completely encircling trode.

rative studies to understand the modifications ng in muscles stimulated under currently used ls.

TERIAL AND METHODS

r goats had clockwise cardiomyoplasty following a sly described technique (2). Briefly, anesthesia was with xylasin and ketamine, and was maintained by on of fluothane 1-2.5% in O_2-air. Prophylactic ics (streptomycin and penicillin) were routinely stered. The left *latissimus dorsi* was carefully d via an oblique left lateral thoracic incision, with ar attention to the neurovascular pedicle. After e mobilization, stimulating electrodes (Medtronic) were implanted and tested for adequate threshold e proximal electrode (cathode) was inserted just 1-2 cm) to the division of the neurovascular The anode was sutured transversally into the mass 3-5 cm away. The neurovascular structures eserved and incomplete recruitment of the muscular ring stimulation was avoided. The flap was then sed into the chest through a second intercostal space was performed to allow access after pericar to the left side of the heart. Epicardial sensing le not implanted. Clockwise anterior-posterior car plasty was performed. The muscle was suture atrioventricular groove following the superior ar edge and finally fixed to the lateral margin. N stretch was applied to the muscle. The chest was standard fashion.

Two goats had a muscle biopsy to assess histology 6 weeks after the initial operation. Thi was carried out through a fourth intercostal space under general anesthesia (2).

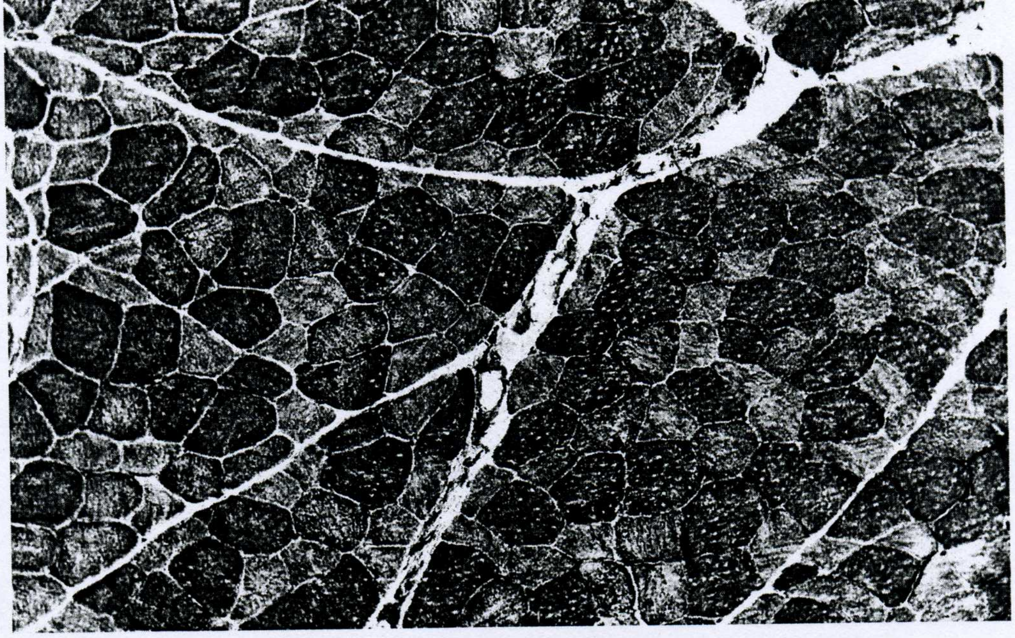
The biopsy samples (0.4/0.5 cm) were analyz routine histological techniques (hematoxylin-eos specimens for histochemistry were sectioned thickness in a cryostat; routine ATPase stainin 4.35 and 9.4) and NADH tetrazolium reductase sta performed. Determination of the percentage of Ty II fibers was made, along with a general micr examination.

Mitochondrial oxidase activities were meas spectrophotometry at 30°C (Aminco Chan 2UV/VIS spectrophotometer) according to Schneic (3) for NADH-cyt c OR and for succ-cyt c C according to Möller and Palmer (4) for cyt c lactate dehydrogenase (LDH) activity was dete according to Bergmeyer and Bernt (5) at a p concentration that does not inhibit H-isozyme (0.5

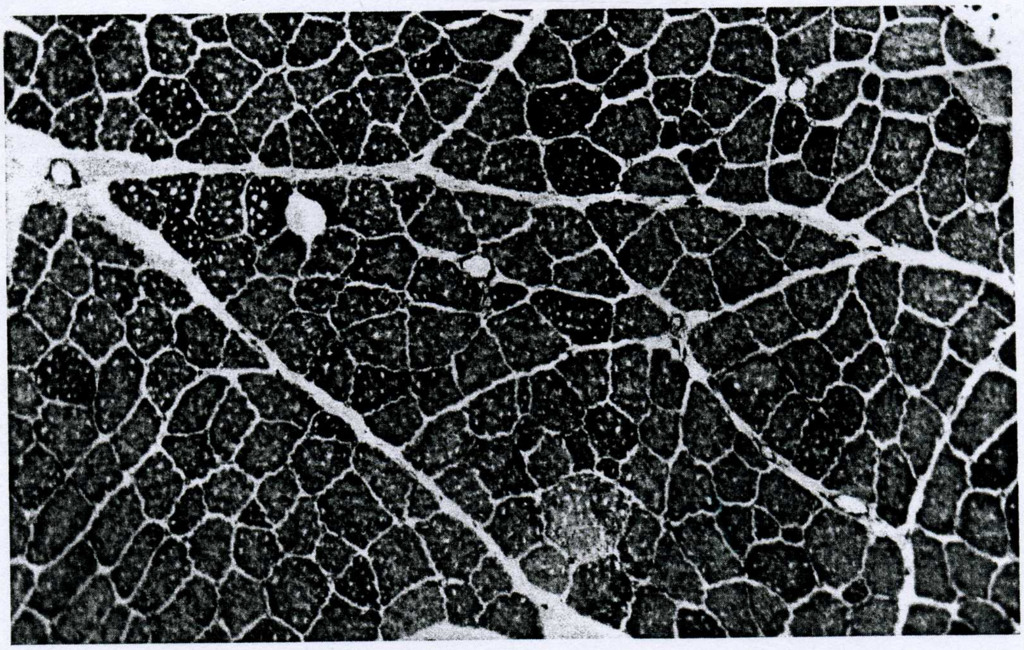
At autopsy, the aspect of the cardiomyopla appraised, as well as the dimension and the surface by the muscle (planimetry). Special attention wa to the contacts between the muscle and the surr structures. Systematic analysis of the pedic electrode implantation site, and the muscle-heart i was done.

RESULTS

The surface area of the *latissimus dorsi* at the surgery was sufficient to achieve complete coverag left and right ventricular free walls. Goats 1, 2 and autopsied after 12 months, and goat 4 after two Goats 2 and 3 were biopsied at 6 weeks postoper In each autopsy, at all intervals since surgery, th evidence of atelectasis of the left lower lobe a adhesions of the proximal part of the *latissimus* the left thoracic wall. The neurovascular pedicle e from the second intercostal space and transsectio artery and vein showed patency and persistent pe The stimulating electrodes were positioned at thei site. In the first 3 muscles, the *latissimus dorsi* pr evidence of extreme atrophy and had a pale grey asp to considerable fibrous and fatty content. Size re was approximately 80%, compared to preop measurements, and only half to two-thirds of ventricular free wall was found to be covered muscle. In muscle 4, 50% atrophy was seen, and red aspect was observed. In all cases, the musc firmly adherent to the myocardium, from which separated by a 0.5-4 mm layer of fibrous con tissue. Apart from few capillaries, no significant were found to cross this interface (Fig. 1). Micros



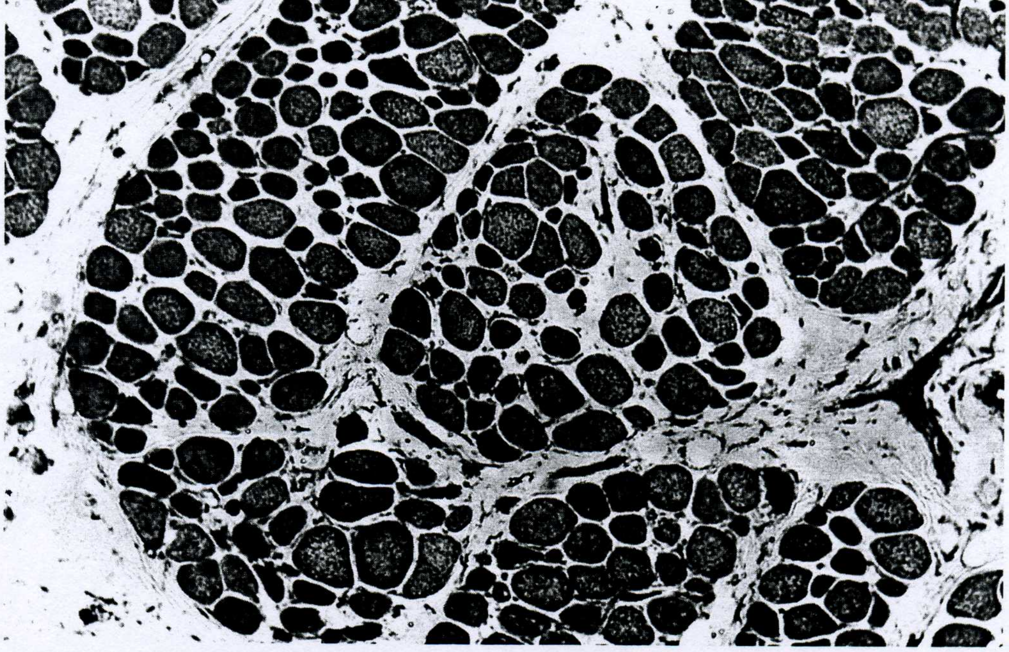
3. Normal goat latissimus dorsi (LD)(NADH stain, x100). The size heterogeneity and checkerboard ngement of Type I and Type II fibers is demonstrated. The connective tissue is narrow and regular.



. 4. Biopsy sampled at 6 weeks postcardiomyoplasty (NADH stain, x100; proximal third of latissimus si). The muscle which was not stimulated has retained its initial gross aspect. Fibers have a smaller diameter, lerscoring ongoing atrophy. Absence of inflammatory infiltration or sequellae of coagulative necrosis.

vessels, without thrombosis. In the vicinity of ode implantation site, a typical foreign body atous reaction (with multinucleated giant cells) rved (Fig. 2). Histologically, the normal goat *dorsi* (Fig. 3) showed irregularity in fiber size, yhedric aspect. The mean major axis diameter of s 9.76±2.92 mm. The percentage of fibers and l space was about 95% and 5%, respectively. fiber and interfascicular connective tissue were narrow and regular without apparent fibrosis. M fibers were closely arranged within a fascicle. H enzymology demonstrated that goat *latissimus* consists of a mixed population of Type I and Ty fibers. Within a fascicle, muscle fibers were organize checkerboard pattern. The different proportions of T and Type II fibers were respectively ±30% and ±70%

After 6 weeks this general aspect was prese However, a significant decrease in muscle fiber



ig. 5. Autopsy sample after 12 months postcardiomyoplasty (NADH stain, x100; proximal third of latissimus orsi). The increase in the collagen and adipose content is prominent. Fibers are small, with a round shape, but etain a checkerboard aspect. The overall aspect is compatible with extensive disuse atrophy.

79 mm) was found, with a slight homogenous in the connective tissue. The checkerboard pattern recognizable (Fig. 4).

r twelve months there was persistence of Type I nd Type II (65%) fibers, with obvious size eneity. Fibers had a rounder shape and were d in an abundant interstitial stroma (59±5%) g in a widening of septae and interfiber spaces. ere atrophic, with a mean diameter of 4.425±1.83 generated fibers were replaced by fatty infiltration almost complete in the most distal part of the . 5).

hemical analysis in goats 1 and 2 (*latissimus* mpled in its proximal part during surgery and at showed greatly reduced values for maximal of LDH (329 vs. 28 nmol/min./mg, and 365 vs. /min./mg for goats 1 and 2, respectively), and s in succ-cyt c oxidoreductase activity (1.37 vs. ol/min./mg, and 1.10 vs. 0.10 nmol/min./mg) chrome oxidase (5.7 vs. 0.45 nmol/min./mg, and 0.51 nmol/min./mg). NADH cyt c reductase decreased slightly (0.36 vs. 0.10 nmol/min./mg, 4 vs. 0.13 nmol/min./mg) in goats 1 and 2, ely.

CUSSION

s previously been suggested that, assuming an model (goat) is used, the distal vascular supply of *imus dorsi* can be suppressed without ischemia if is left at rest, because of the connections between itudinal arteries arising from the thoracodorsal and the distal supply (2,6). Furthermore, prior to ing the feasibility of the technique, it was shown hques et al. that transposition into the chest does to injury of the neurovascular pedicle (1). This

no signs of vascular pedicle thrombosis, muscle ne or evidence of neurologic impairment were seen. I the histoenzymological study showed, after 8 wee one year, a persistent checkerboard aspect w grouping phenomenon. These findings indica absence of major nerve injury and fiber reiner Available biochemical data confirm the persiste markers of oxidative metabolism: terminal oxidases mitochondrial respiratory chain and glycolytic ana metabolism (LDH activity). The sharp decrease in enzymatic activities is a result of the atrophy o Type I and II fibers and their dilution in an inc interstitial stroma. The progressive increase in co and adipose content was always diffuse and homog This is an argument for the absence of acute isc necrosis. Furthermore, evidence of coagulative ne was never encountered. The muscle was fr inflammation, with neither polymorphonuclea lymphomonocytic infiltrates, thus excluding major or aseptic phenomena. These data also support th that, providing there is an adequate knowledge intramuscular distribution of neurovascular stru implantation of an intramuscular stimulating ele does not lead to irreversible damage. Hence, the rem factors such as tenotomy, modified stretch and l stimulation, appear to play a crucial role i determination of muscle outcome.

McNin and Urbova (8) observed that tenotomy pale muscles produces only minimal changes, wh slow red muscles, this maneuver induced co degeneration of most fibers. The remaining fibers w very small diameter, and were distributed within a n fatty and fibrous tissue. In the *soleus*, these change already present after three weeks. The degeneration af both Type I and Type II fibers in our study.

size and proportions of Type II and Type I
is may be explained by the preponderance of
fibers in the native *latissimus dorsi* (an
ate between pale and red muscle) and the
e of some stretch when the muscle is wrapped
e myocardium. Indeed, muscles used in cardio-
retain a stretch intermediate between that at
c and equilibrium length.

eponderant role of tenotomy is emphasized by
periments (using the rabbit *femoris anterior*)
hat transposition done with preservation of the
- and thus presumably basal stretch - induces a
f about 25% of the initial mass and 17% of the
ut (9). It thus seems that tenotomy in itself, and
no overstretching is applied, necessarily leads to
ee of muscle atrophy. Stretch removal entails a
comeres in series leading to muscle shortening,
nd accumulation of connective tissue. This
also characterized by rapid proteolysis with a
itrogen balance (12). On the other hand, passive
has been shown to promote protein synthesis
on of sarcomeres in series, thus increasing both
gth and mass. Overstretching is also capable of
regardless of any stimulation protocol, some
fast-to-slow transformation, by substituting
bers (13).

The muscles involved in this study retain a pote
activation pathway via the intrinsic innervation.
effect was however negligible, since it did not preven
dramatic muscle atrophy well beyond anything seen
muscle stimulated following usual conditioning
activation protocols. This further suggests that altho
voluntary activation may interfere with the ca
myoplasty (14), it plays a negligible role in preve
muscle atrophy.

Conclusions

Wrapped around a normal heart, unstimul
latissimus dorsi muscle applied in cardiomyopl
showed no evidence of vascular or neural injury, b
time-dependant atrophy was noted (50% at 2 mo
progressing to 80% at 12 months) leading to comp
disappearance of the wrap performed during surgery.
histological analysis showed regression of both Ty
and Type II fibers that may be explained by
modifications of the length-tension relationship follo
proximal and distal tenotomy. Since self-neural infl
have little influence on maintaining muscle mass,
because external stimulation was not applied, conside
disuse atrophy ensued. Our study thus defines an ext
evolution of muscles involved in cardiomyoplasty
illustrates heart-muscle and muscle-electrode relations

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