

## A Clinical-pathological Study 2 Years Following Cardiomyoplasty: Intact Latissimus Dorsi Muscle and Metabolic Transformation of Myofibers

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### Abstract

A young patient died suddenly 2 years after cardiomyoplasty. The anatomic-pathological study showed cardiomegaly and confirmed a classic dilated cardiomyopathy. The Latissimus dorsi muscle (LDM) covered both ventricles and hard adhesions between epicardium and endocardium were seen. The electrodes remained in the original position. Some interstitial fibrosis and fiber atrophy and degeneration, were observed around the electrodes. Histological and enzyme-histochemical studies showed that the muscle morphology of the LDM flap stimulated up to 2 years was well preserved. Morphological changes seen in some fibers were isolated on occasional events. Also in the present case, muscle fiber transformation into fatigue resistant, oxidative type 1 fibers was almost complete after the long-term electric stimulation.

**Key words:** cardiomyoplasty, Latissimus dorsi muscle, fibers transformation.

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Dynamic cardiomyoplasty is a surgical method based upon the use of conditioned Latissimus Dorsi Muscle (LDM) for reinforcement of the cardiac ventricular wall. A program of chronic electrical stimulation of the muscle evokes an adaptive remodelling of the contractile apparatus of the muscle fibers and provides long-term cardiac assistance [7, 13, 19, 21]. In selected patients with chronic heart failure the method is considered a reliable alternative to heart transplantation [1, 16].

*Post mortem* studies on LDM utilised for cardiomyoplasty have recently been performed on 3 patients who deceased suddenly 15 months, 2 and 8 years after cardiomyoplasty [3, 5, 13, 23]. These studies generally indicated a sufficient preservation of histological characteristics of LDM and an enzyme-histochemical "plastic" reorganisation of fiber types after electric stimulation protocol. Additional LDM morphology findings of long-term dynamic Cardiomyoplasty patients at autopsy related to each patients clinical outcome has been recently reported [17].

The present case is a young patient who died suddenly 2 years after dynamic cardiomyoplasty. A pathological study of his heart and of the wrapped LDM give us the opportunity to study the morphological and enzyme-histochemical characteristics of a long-term conditioned LDM.

### The patient

A pathological study was performed on a patient, who died suddenly from ventricular fibrillation 2 years after dynamic cardiomyoplasty. The patient, a young male aged 18 year and native of Algeria, underwent aortic valve replacement with bioprosthesis in 1985, associated with mitral valve repair using a Carpentier's ring. The operation was done in emergency for refractory congestive heart failure following aortic subacute valvulopathy, with septic embolism. There was also an associated mitral rheumatic insufficiency without stenosis. In 1987 he was rehospitalized with congestive heart failure, class IV of the NYHA. The patient was in sinus rhythm. The whole heart was hypokinetic despite a normally functioning aortic valve prosthesis. A significant decrease of isotopic LV ejection fraction (9%) was observed. Ultrasonic Doppler echocardiography showed a heart failure with significant dilatation of the left ventricle, the end diastolic diameter being 72 mm. The cardiothoracic ratio was 0.68. Hemodynamic studies showed the following pressures: right atrium: 13 mm HG; right ventricle: 42/0.15 mm HG; pulmonary artery: 42/20 mm HG, mean; 30; PCW 30 mm Hg; CO: 3.23 l/min; CI: 2.02 l/min/M<sup>2</sup>.

Dynamic cardiomyoplasty was proposed and the operation took place at the Broussais Hospital, in March 1987.

At surgery, a posterior to anterior wrapping using the left Latissimus Dorsi was performed, the left ventricle being completely covered, as well as 80% of the right, by the Latissimus Dorsi muscle. Two Medtronic SP 5528 electrodes were used for Latissimus Dorsi pacing, and a Medtronic SP 5548 electrode for right ventricle sensing. A Medtronic Cardiomyostimulator model SP 1005 was implanted. For the first two months, a staged program of progressive pacing was used. Two months postoperatively, muscle stimulation parameters were the following. Synchronization delay: 4 ms; pulse amplitude: 5V; pulse width: 210  $\mu$ s; burst rate; 30 Hz; and burst duration: 185 ms. Four months after cardiomyoplasty temporary arrest of the stimulator was followed by pulmonary oedema. Postoperative heart scans, ultrasonic Doppler echocardiography, and hemodynamic studies showed improvement of ventricular function with 80% relative increase in fractional shortening, twofold increase in cardiac index from 1.8 to 3.6 l/min/M<sup>2</sup> and left ventricular isotopic ejection fraction increasing from 8% to 16%. The clinical outcome demonstrates that cardiomyoplasty was effective, with functional and hemodynamic improvement. However, two years later the patient died suddenly.

#### Post-mortem findings and methods

Macroscopic examination confirms cardiomegaly, with significantly enlarged cavities. The right atrium had a moderate dilatation, and endocardial thickness was evident but moderate. No thrombi nor atrial septal defects were found. The foramen ovale was not patent. There was no right ventricular dilatation. There was a small dilatation of the left atrium, with thinner endocardial wall. Mitral orifice, on which a Carpentier's ring had been sutured, was normal but the posterior valve was prolapsed. The left ventricular cavity was greatly dilated, with important and diffuse endocardial thickness, but without parietal hypertrophy. The aortic valvular prosthesis was strongly fixed, but the size seemed small in relation with the very important ventricular dilatation.

The Latissimus Dorsi muscle covered both ventricles and the electrodes remained in the original position. Peripheral bundles of muscle were thinner than found 2 years previously, at the time of surgery. Hard adhesion developed between the surface of the Latissimus Dorsi muscle flap and the epicardium and cleavage was hard nearly everywhere.

The great vessels, mediastinal organs, and the lymph nodes all had a normal appearance. The heart was dissected from the diaphragm and it was necessary to divide the strong adhesions between the Latissimus Dorsi and the heart. The coronary arteries were dissected and were found to be normal.

Many fragments were taken from the Latissimus Dorsi on both sides, the right being used as histological control. Paraffin-embedded specimens were stained with Hematein-Phloxin-Safron, Orcein, Masson's trichrome, and elastic Van Gieson. Specimens cooled in liquid nitrogen

were cut at the cryostat and then treated for ATP-ase pH 9.6 reaction.

#### Morphological Results

Heart. Histological feature suggested a dilated cardiomyopathy. An obvious anisocytosis of cardiomyocytes was present, with some nuclear anomalies. Cardiomyocytes were surrounded by a diffuse interstitial fibrosis with important areas of sclerosis usually hyaline. New vessels were associated, often with alteration of pre-existent arterioles whose wall were thickened. The endocardium was thickened in a diffuse but irregular mode and only small foci of lymphocytes were observed. The valvular leaflets of tricuspid and mitral valve with macroscopic prolapse, are histologically normal. The sinus node was normal as well as the atrio-ventricular node and the bundle of His that was found in an unusual position. In conclusion, histologically there was a typical dilated cardiomyopathy.

Latissimus dorsi muscle. The margin between the myocardium and the Latissimus Dorsi muscle was clearly defined, formed from a layer of collagen of various thickness (Fig. 1). Sometimes, this tissue was very dense and strong, elsewhere loose, with many blood vessels and some nerves. The grafted LDM overlapping the heart was in good conditions. However, myocytes with a pathological aspect were present, with anisocytosis and eosinophilic degeneration. These pathological features were infrequent, and usually in the periphery. There was mixing between rhabdomyocytes and moderate fibrosis was present near the electrodes surrounded by a thin layer of collagen. Enzyme-histochemical reaction for ATP-ase demonstrated a clear predominance of type 1 fatigue-resistant oxidative fibers (Fig. 2). The right Latissimus Dorsi, used as control, was normal. Transformation of muscle fibers is well documented in long-term dynamic cardiomyoplasty. Figure 3 shows that even eight years after cardiomyoplasty the muscle is well preserved and almost completely converted to type 1 fibers.

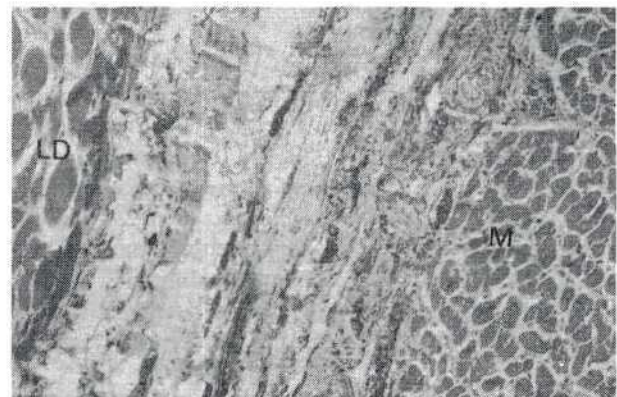


Figure 1. Latissimus Dorsi muscle and myocardium 2 years after cardiomyoplasty. A layer of loose collagen tissue forms the boundary between the myocardium (M) and the Latissimus Dorsi muscle (LD). Haematoxylin-Eosin-Safron, 120X.



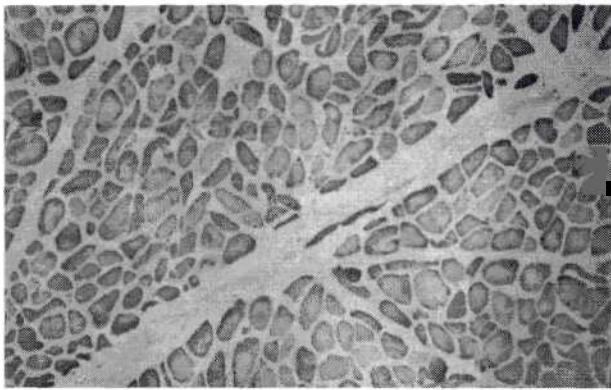


Figure 2. Latissimus Dorsi muscle 2 years after cardiomyoplasty. In this area, near the electrodes, some atrophic fibers are present. Most of the fibers are type 1 oxidative. Cross-section stained for ATP-ase (pH9.4), 320X.

### Discussion

While some reports have been published on clinicopathological and functional studies of LDM after long-term cardiomyoplasty [2, 6, 10, 14, 18, 20], post mortem investigations to evaluate the morphological conditions of the wrapped LDM graft following long-term stimulation, are scarce.

The previously described cases regarded patients with 15 months, 2 and 8 years cardiomyoplasty and subjected to the same protocol of electrostimulation [3, 5, 13, 23]. In these cases the grafted LDM showed focal unspecific fiber changes, as fiber atrophy and nuclear centralization, sarcoplasmic vacuolisation and degeneration of isolated fibers which did not seem to compromise the functional and metabolic aspect of the muscle. These alterations may be explained as changes secondary to the chronic heart failure, as recently described in patients with different chronic heart diseases and interpreted as subclinical ischemic damage to skeletal muscle [9, 22]. Major histological alterations have been confined in the region between the electrodes; in this area fiber atrophy and degeneration, internal subsarcolemmal nuclei (generally accepted as histological marker of muscle damage and/or regeneration) and interstitial fibrosis have been interpreted as direct damage by electric stimulation or by trauma at the time of electrode insertion (when small nerve branches, capillaries, and fiber could be injured) or during chronic displacements of electrodes due to muscle contractions. Indeed electric fields surrounding the large surface of the intramuscular electrodes is well below that required to cause tissue damage [5, 11, 23].

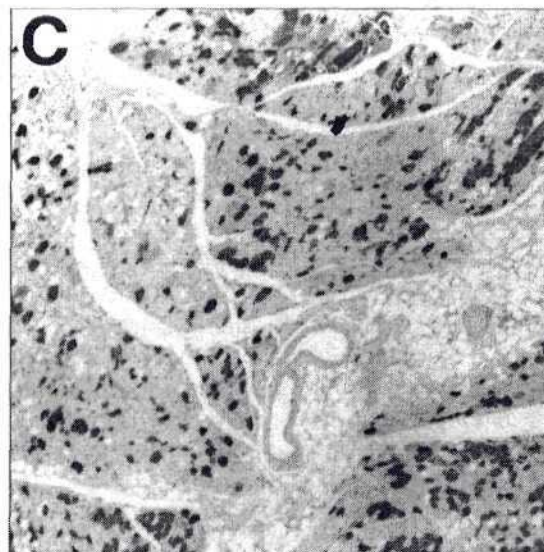
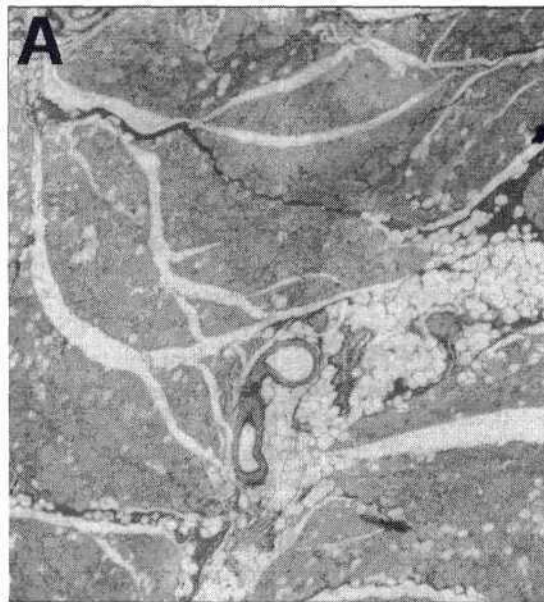


Figure 3. Latissimus Dorsi muscle 8 years after cardiomyoplasty: A, Eosin van Gieson stain; B, immunohistochemical analysis with R11D10 antibody (anti type 1 fibers); C, immunohistochemical analysis with MY-32 antibody (anti type 2 fibers).

In the present case, the LDM showed a strong adhesion developed between the epicardium and the epimysium. Histological studies revealed some interspersed fibers with anisocytosis and eosinophilic degeneration.

As well as in the previously described cases, the grafted LDM showed a clear predominance of type 1 fatigue-resistant oxidative fibers, as the result of the long-term electric stimulation. In the present case also the fiber conversion to type 1 was incomplete, indicating that in humans as well as in animals, some fast fiber types are maintained after long-term conditioning [12]. It is worth stressing that even 8 years after cardiomyoplasty the LD flap is well preserved and almost completely converted to type 1 fibers [3].

In conclusions, dynamic cardiomyoplasty may be considered a reliable clinical reality providing improvement in hemodynamic state and functional class of patients with pharmacologically-intractable heart failure.

At present, studies are in progress to optimise the electric stimulation of LDM for cardiomyoplasty using new stimulation protocols [4, 15] and to perform an optimal outcome for patients undergoing cardiomyoplasty [8].

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