Demand Cardiomyoplasty: Dynamic Girdling is Superior to Adynamic Girdling

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Abstract

In order to avoid full transformation and early degeneration of the latissimus dorsi (LD), giving better systolic assistance, a new stimulation protocol was developed: fewer impulses per day were delivered, providing the LD wrap with daily periods of rest, based on a heart rate cut-off (Demand activation). We aimed to determine whether Demand dynamic girdling (DemDyn) is superior to passive girdle effect (Adynamic) in term of cardiac assistance, survival and freedom from cardiovascular events. Fourteen patients with dilated myocardiopathy (13/1 = M/F, mean age 58.2 ± 5.8 years, sinus rhythm/atrial fibrillation = 12/2) were submitted in the years from 1993 to 1996 to CMP and at different intervals to Demand protocol. Patients were divided on the basis of mechanographic measurement of the tetanic fusion frequency (TFF) at start of Demand: DemDyn patients with faster LD (high TFF, 7 patients) and Adynamic girdling patients with slower LD (low TFF, 7 patients). Clinical, echocardiographic, mechanographic and cardiac invasive assessment records were reviewed as well as cardiovascular events (death and arrhythmias) occurrence.

The mean duration of follow-up was 41.4 ± 21.1 months (range 23 to 69). DemDyn group showed a major decrease in NYHA class (2.14 ± 0.7 vs 0.43 ± 0.5, $p = 0.007$), a higher percent increment of ejection fraction (13.7 ± 7.1 vs 5.3 ± 2.4%, $p = 0.002$), a better survival (85.7% vs 28.6%, $p = 0.037$) and a higher TFF value (38.3 ± 5.8 vs 24.3 ± 2.9, $p = 0.002$) than Adynamic girdling group.

Early started "Demand" girdling offers better results than Adynamic girdling in term of both symptomatic improvement and survival.

Key words: cardiomyopathy, heart-assist device, heart failure.

Basic Appl Myol 13 (2): 89-93, 2003

Poor systolic assistance and latissimus dorsi (LD) degeneration have been retained the main drawbacks of Dynamic Cardiomyoplasty, many authors agreeing only in recognizing a passive girdling as the beneficial effect of this procedure ("adynamic cardiomyoplasty") [3, 7, 8, 12, 14, 17].

In order to give a better systolic assistance, long-term partial transformation of the LD wrap and less muscular degeneration should obtained delivering fewer impulses per day than in standard clinical stimulation. This is attained by providing the LD wrap with daily periods of rest based on a heart rate cut-off (Demand stimulation) [1]. Our studies [15-16] proves that a real measurable systolic assistance is effective in patients early submitted to demand stimulation protocol. Furthermore, its value is higher when demand protocol is started early after surgery, while it is much lower to virtually not valuable when demand protocol was started several months after invariable stimulation.

Moreover, we proved that systolic assistance is strictly correlated to muscular properties of LD as speed of contraction expressed in Tetanic Fusion Frequency (TFF) value [5].

Basing on these premises, we report our attempt to demonstrate whether Demand dynamic girdling (DemDyn) is superior to passive girdle effect.

Methods

From 1993 to 1996, 14 patients suffered from idiopathic dilated cardiomyopathy and refractory congestive heart failure (13/1 = M/F, mean age 58.2 ± 5.8 years, sinus rhythm/atrial fibrillation = 12/2) underwent cardiomyoplasty (CMP) according to the original Broussais Hospital procedure by Carpentier et al [11].

Demand stimulation was programmed at the Department of Cardiology, Cardiomyoplasty Project Unit-Center for Advanced Heart Failure, Legnago Teaching Hospital, Verona, Italy, whereas follow-up was performed in this center and also in the Division of Cardiology and Rehabilitation, Montescano Medical Center, Maugeri Foundation, Montescano, Pavia, Italy.

The demand protocol was electively introduced in a pool of patients forming the Italian Trial of Demand Dynamic Cardiomyoplasty and in patients previously operated of CMP following the criterion of no amelioration, or worsening of clinical conditions with CMP continuous stimulation, without short-mid term perspective of heart transplantation. Informed consent to the intervention and then to demand stimulation protocol has been obtained from all patients.

Demand stimulation protocol

Demand stimulation protocol was introduced [5] in order to avoid complete LD wrap transformation caused by the continuous stimulation protocol of the FDA phase II trial in use by the American Cardiomyoplasty Group [9] and to homogenise patient response.

It is well established that a muscle fully transformed by continuous stimulation displays significant loss in power, generally attributed to fiber-type change or loss of type 2 myofibrils (fast contracting myofibrils). The insertion of rest periods during chronic electrical conditioning preserves myofibril cross-sectional area and produces fatigue-resistant fiber distributions; in this way, a more powerful fatigue-resistant muscle is created. The improved performance of such LD is though to be due to the maintenance of an intermediate level of transformation of the LD wrap, thanks to the demand regimen. The LD was stimulated with a single impulse at a 1:3 synchronization ratio after a healing period of 10-14 day. An impulse was then added every week at a 23 msec interval (43 Hz) for a final burst of four impulses, with a cardiac amplitude > 5 Volts and pulse width of 1.5 msec. After 6-12 months of this "light" daily stimulation, the patients were submitted to the "demand regime", allowing the LD wrap a daily period of rest.

In order to provide the LD wrap with daily periods of rest, a 24-hour Holter study was firstly performed to determine the average heart rate during the sleeping hours. The pacing parameters of the cardiomyostimulator (Transform, Model 4710, Medtronic, Inc., Minneapolis, MN, USA) were programmed at a rate of 70-80 bpm, with minimum pulse amplitude (< 1 Volts) and pulse width (< 0.05 msec). Muscle output was programmed to "Sense", occurring only with sensed cardiac events, not with paced events. In this way, the lower rate was set just above average nocturnal heart rate and the cardiomyostimulator worked during the resting hours at an energy level well below the one required for capturing the heart. During these pacing episodes, muscle output was inhibited. The result was that muscle stimulation was inhibited during the resting hours and occurred at the programmed synchronization ratio during the active hours, providing an activity-rest stimulation regimen.

Monitoring muscle functionality: the mechanogram

Contractile characteristics of LD wrap, such as speed of contraction and relaxation, can be monitored using a standard polygraph (MegaCart or Mingophon, Siemens Elema, Solna, Sweden): electrocardiogram and the pressure changes due to LD contraction can be simultaneously recorded as previously described [5]. The dynamic characteristics of the LD wrap are determined from the LD response to stimuli delivered at increasing frequency up to tetanic fusion frequency (TFF). In this way, a smooth contraction curve can be plotted: the faster the fibres, the higher the TFF. As described elsewhere [10-11], the normal value of TFF for human muscle is expected to be 43 Hz (the tetanic contraction with pulses delivered at 23 msec intervals).

Assuming that a TFF of 43 is expected for normal functioning muscle which can give the best systolic assistance, whereas TFF < 26 is expected for a muscle capable of a very low or not measurable systolic assistance, the patients have been divided in two groups on the basis of TFF cut-off value of 26: one with an expected systolic assistance, the other acting as adynamic girdling group. Results of DemDyn and adynamic girdling patients have been compared.

Follow-up

Non-invasive evaluation was performed by clinical and echocardiographic examination. Invasive evaluation of right cardiac pressure was obtained during the follow-up by means of right heart catheterisation.

Statistical analysis. Paired Student's t-test was used to compare data before and after demand dynamic girdling , whereas frequencies were compared using the chi-square test. A p value < 0.05 was considered significant. Clinical and laboratory data were expressed as mean ± SD or as percentage. Survival rate was expressed as mean ± SEM. Patients switched to heart transplantation program due to worsening clinical conditions, occurrence of malignant ventricular arrhythmias or need for ICD implantation were calculated as deaths, whereas a death due to non cardiovascular related causes was calculated as censored data. StatView (SAS Institute Inc., Cary, NC, USA) and GraphPad Prism 3 (GraphPad Software Inc., San Diego, CA, USA) systems were used for data analysis and graphic output.

Results

The mean duration of follow-up was 41.4 ± 17.5 months (range 23 to 69 months).

Cumulative results. There were no perioperative deaths. The mean NYHA class was significantly lower when compared with pre-operative values whereas the mean ejection fraction (EF) at follow-up was significantly higher than pre-operative value. The mean end-diastolic volume did not change significantly during the follow-up as well as the capillary wedge pressure. At last mechanographic interrogation, the value of TFF was significantly higher than before the start of demand protocol.

See table I for cumulative results.

During the follow-up, one patient died of hepatic cancer at 36 months and another died of massive pulmonary embolism at 18 months from operation. Both were in NYHA class I one month before death. One patient implanted with a bi-ventricular and defibrillator for the development of left bundle block and ventricular arrhythmias died after 60 months for cardiogenic shock. Three patients, in whom continuous stimulation had been performed for several months (107,41 and 57 months, respectively) were switched to the heart transplant program, two patients for worsening clinical conditions (NYHA class III, also treated with biventricular pacing) and the other due to the dysfunction of the myostimulator, previously in NYHA class II. The global actuarial 5-year survival rate was 46.36%. In all patients, an oral therapy with personalized doses of diuretics, ace-inhibitors and beta-blockers was maintained.

DemDyn versus adynamic girdling. Seven patients had TFF > 26 (DemDyn) and other 7 had TFF < 26 (Adynamic girdling). Patients' data and result comparisons are showed in table II.

DemDyn group showed a major mean class decrease in NYHA, a higher mean percent increment of LVEF, a better survival as showed in Figure 1, and a higher tetanic fusion frequency value than Adynamic girdling group. Event-free survival rate was higher (50 vs 45%, p = 0.217) in DemDyn patients. There was a good correlation between duration of continuous stimulation and TFF value (r = 0.64, p = 0.014) and EF increment (r = 0.61, p = 0.009).

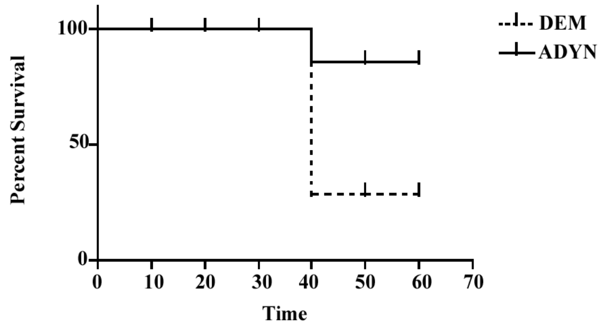

Figure 1. Actuarial survival in the two groups of patients. Data are expressed as mean ± SEM.

Discussion

Many authors failed to prove a real systolic assistance explaining the clinical amelioration observed in patients responding to CMP. An enhancement of systolic contraction has been suggested but not proven by studies revealing only low-to-moderate increase in left ventricular ejection fraction and stroke volume, despite a notable improvement in NYHA class. Therefore, there is a commune consensus in attributing to classic CMP only a passive girdle effect.

The muscular degeneration caused by continuous long-term stimulation had an important role in the development of this general opinion. The concept that an intermittent stimulation may result in less muscular damage and maintain muscle viability, contributing to a more effective cardiac support [15] constitutes the premise for the development of the demand protocol able to improve the results of classic CMP [2, 6].

Table I. Cumulative results.

	Pre-operative	Post-operative	p
NYHA class	3.17 ± 0.38	1.67 ± 0.77	< 0.0001
EF	22.6 ± 4.38%	32.0 ± 7.0%	< 0.001
EDLV (ml/m^2)	114 ± 41.1	104 ± 9.9	0.67
Wedge Pressure (mmHg)	12.2 ± 6.11	11.7 ± 7.19	0.83
TFF (Hz)	33 ± 7.86	15.8 ± 11.1	< 0.0001

Table II. Clinical data of DemDyn and Adynamic girdling groups and results comparison.

	DemDyn	Adynamic	p
Male/female	6/1	6/1	-
Age (years)	58.4 ± 5.3	58.1 ± 5.9	ns
TFF value	30 ± 2.3	21 ± 4.2	0.01
Chronicle stimulation (months)	18.9 ± 10.2	47 ± 22.4	0.012
Mean decrease in NYHA class	2.14 ± 0.7	0.43 ± 0.5	0.007
Mean percent increment of LVEF	13.7 ± 7.1	5.3 ± 2.4	0.002
Actuarial survival	85.7%	28.6%	0.037
TFF (MHz)	38.3 ± 5.8	24.3 ± 2.9	0.002
Significance set at p < 0.05			

As suggested by our studies, the LD properties are well correlated with amount of systolic assistance [15-16], and are maintained over time. This explains the higher values of TFF measured and the good survival rate, as well as the improvement in NYHA class and in LVEF value in the DemDyn group of patients. Moreover, in those patients in whom demand protocol started later after a continuous stimulation period, the TFF not only maintained its initial value but in many cases increased, this being a sign of enhanced muscle properties.

This data suggests that demand protocol provides an active systolic assistance by preserving LD from atrophy. This protocol has beneficial effects in term of quality of life also in patients previously submitted to long-term continuous stimulation.

Our study carries some limits such as the absence of randomization and the small number of patients, both ones due to the difficulty to enroll patients to a procedure that remains experimental and to the negative opinion of cardiologists aware of the results of the old dynamic cardiomyoplasty.

We believe that the Demand protocol is the most effective protocol for dynamic cardiomyoplasty, providing an amelioration of the response to CMP in terms of systolic assistance and survival by preventing excessive muscle degeneration. Moreover it offers noticeable advantages in comparison to passive adynamic containment techniques. In the era of heart transplantation and great technological advances in the field of circulatory assist devices and of the artificial heart, we think Demand stimulated muscular girdling may still play a role. In comparison with transplantation, ventricular assist devices, and containment heart dilation support devices, the Demand dynamic girdling have the advantages to be moderately expensive, to require neither extracorporeal circulation, nor immunosuppression, nor anticoagulation therapy, nor cumbersome follow-up modalities, while acting as a real systolic assist.

Acknowledgements

Supported in part by funds from the Italian National Research Council to the Unit for Muscle Biology and Physiopathology. Supported by the Italian Ministry of University and Scientific and Technologic Research (M.U.R.S.T. n. 9806192428): Trial Italiano sulla Cardiomioplastica Dinamica a Domanda (TiCDD).

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