Clinical Perspective

Dynamic cardiomyoplasty: how well does it work?

Introduction

Despite great advances recently, congestive heart failure remains a therapeutic challenge. Heart transplantation offers a valuable treatment option for patients with end-stage disease and yields excellent functional improvement, but donor organs are scarce and chronic rejection limits survival to about 38% at 12 years [1]. Permanently implanted mechanical assist devices will probably play a major role in the future, but the problems of thromboembolism and infection are not yet entirely overcome and the devices may not be available for all patients. In dynamic cardiomyoplasty, an autologous skeletal muscle is wrapped around the patient's heart. It obviates the need for immunosuppression, is available to many patients, is independent of energy supply and less expensive than other methods. However, while the first clinical application of cardiomyoplasty dates back to 1985 [2], it has failed to become an established treatment method. In the past, the diversity of the underlying heart diseases, of the pre-operative functional status and of the differences in surgical technique have led to inconsistent results. In addition, when the technique was first used the operative mortality was high [3]. To date, more than 500 patients have been operated on worldwide. In recent years, the surgical technique and the indications have been more uniform, which makes results eligible for comparison. On the basis of these more recent data, we have attempted to determine the current value of cardiomyoplasty in the treatment of congestive heart failure.

Procedure

The surgical technique for dynamic cardiomyoplasty has been developed by the pioneering work of Carpentier and Chachques [4] (Fig. 1). Due to its plasticity, skeletal muscle can be trained and transformed into a 'fatigue resistant' tissue by chronic electrical stimulation [3]. This is achieved by gradually increasing the frequency and duration of electrical stimulation impulses. A specific postoperative stimulation protocol was developed by Carpentier and Chachques [4]: in the first 2 weeks after operation the muscle is left without stimulation, during which time adhesions between muscle and epicardium develop and residual seroma and muscle oedema is resorbed. From the 3rd to the 10th week after operation, muscle stimulation is gradually increased at weekly intervals until the muscle receives a complete burst with six single impulses (Fig. 2). Burst impulse stimulation increases the contractile force by tetanic contraction and prolongs the duration of muscle contraction. The onset of the burst impulse is programmed to the closure of the mitral valve determined by M-mode echocardiography.

Patient selection criteria

Patients with ischaemic or dilative cardiomyopathy and severely impaired left ventricular function are eligible for cardiomyoplasty. They should be deteriorating or unstable despite maximal medical therapy. Patients with biventricular failure are excluded, because of an increased peri-operative risk. At the time of the operation the patient should be in NYHA III. Patients in permanent NYHA IV, who may be receiving inotropic or mechanical support have a high risk of dying from the procedure [6,7]. Mitral and tricuspid insufficiency should not exceed grade I. Atrial fibrillation and severe pulmonary hypertension have been shown as incremental risk factors for survival and are considered relative contraindications. Vital lung capacity may be reduced by 10–20% after cardiomyoplasty, which has to be taken into account with significant pulmonary dysfunction (FEV1 <50% of predicted). Patients with serum creatinine >2.5 mg. dl⁻¹ should be selected with caution, because they may develop peri-operative renal insufficiency, requiring haemofiltration with the risk of developing sepsis and multi-organ failure. In patients with previous heart surgery and associated cardiac defects, cardiopulmonary bypass is usually required. Patients with a history of ventricular tachycardia or ventricular fibrillation receive a combined procedure: cardiomyoplasty coupled with the implantation of an implantable cardioverter defibrillator. Patients with degenerative muscular disease are not eligible (Table 1).
Figure 1. Left: M. latissimus dorsi in situ. Right: Posterior cardiocostal wrap with the left latissimus dorsi.

ECG:

Muscle contraction

3, + 4, week

5, + 6, week

7, + 8, week

"Burst"

After 2 months

Figure 2. Postoperative stimulation protocol: during the first 2 weeks after operation the muscle is left without stimulation. From the 3rd to the 10th week after operation muscle stimulation is gradually increased at weekly intervals until the muscle receives a complete burst with six single impulses. Burst impulse stimulation is chosen to increase the contractile force by a tetanic contraction pattern and to prolong the duration of muscle contraction.

Results from Heidelberg

The Heidelberg experience is based on eight patients who were all in NYHA III prior to the operation (Table 2). Follow-up is now 42.8 ± 19.3 months. One patient died 57 days after surgery from liver cirrhosis, which had excluded him from heart transplantation. Two patients died late, 34 and 55 months after the operation from 'sudden death'. Actuarial survival is 62.5% at 67 months. Recently, two more patients were operated on receiving cardiomyoplasty and simultaneous cardioverter defibrillator implantation. The simultaneous implantation of an implantable cardioverter defibrillator was uneventful and there

Eur Heart J. Vol. 18, February 1997
example, every second cardiac systole is supported by
cardiac index at rest. Resting systolic pulmonary
capillary pressure was 13.7 ± 3.1 mmHg. The increase in
peak systolic aortic pressure suggests a muscle contraction, as
evidenced by the burst signal in the ECG. The increase in
peak aortic flow suggests an active improvement of myocardial
wall motion in assisted beats.

Table 1 Contraindications for cardiomyoplasty

<table>
<thead>
<tr>
<th>NYHA IV</th>
<th>Inotropic support/l.ABP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrioventricular valve insufficiency &gt;11°</td>
<td></td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>(&gt;600 dyn x s x cm^-2)</td>
</tr>
<tr>
<td>Decreased pulmonary function (VC/FEV &lt;55% of predict.)</td>
<td></td>
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<tr>
<td>Renal insufficiency</td>
<td>(Creatinine &gt;2.5 mg . dl^-1)</td>
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<tr>
<td>Previous heart surgery</td>
<td></td>
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<tr>
<td>Muscular disease</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Pre-operative haemodynamics

<table>
<thead>
<tr>
<th>Patient</th>
<th>PAP (mmHg)</th>
<th>PCWP (mmHg)</th>
<th>EF (%)</th>
<th>CI (l . min^-1 . m^-2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.H.</td>
<td>46/18</td>
<td>19</td>
<td>20</td>
<td>2.9</td>
</tr>
<tr>
<td>N.L.</td>
<td>56/22</td>
<td>20</td>
<td>20</td>
<td>2.8</td>
</tr>
<tr>
<td>Mô.H.</td>
<td>85/37</td>
<td>35</td>
<td>14</td>
<td>1.9</td>
</tr>
<tr>
<td>G.H.</td>
<td>27/10</td>
<td>14</td>
<td>16</td>
<td>2.2</td>
</tr>
<tr>
<td>K.H.</td>
<td>25/15</td>
<td>11</td>
<td>21</td>
<td>1.9</td>
</tr>
<tr>
<td>W.N.</td>
<td>50/27</td>
<td>18</td>
<td>15</td>
<td>1.6</td>
</tr>
<tr>
<td>G.M.</td>
<td>50/30</td>
<td>27</td>
<td>32</td>
<td>1.3</td>
</tr>
<tr>
<td>B.L.</td>
<td>38/22</td>
<td>18</td>
<td>27</td>
<td>1.7</td>
</tr>
</tbody>
</table>

PAP=pulmonary artery pressure; PCWP=pulmonary capillary
wedge pressure; EF=ejection fraction; CI=cardiac index.

was no hindrance in the electrical communication
between the cardiomyostimulator and the implantable
cardioverter defibrillator. Haemodynamic results
on these patients are not yet available.

One patient did not improve after the operation
and remained in NYHA III. All other patients
exhibited considerable symptomatic improvement
and the mean NYHA decreased from 3.0 to 1.9 ± 0.7
(P<0.01). Three patients went temporarily back to
part-time work. Mean left ventricular ejection fraction
increased from 21.2 ± 5.2% prior to operation,
to 38.1 ± 15.9% (n=7, P<0.015) at 1 year and to
36.6 ± 17.7% (n=6, P<0.05) at 2 years. Further
changes were not significant (Fig. 3). Maximal O_2
consumption was 13.7 ± 3.1 ml . min^-1 . kg^-1 before
operation and did not change significantly. Right
heart catheterization revealed no consistent change of
cardiac index at rest. Resting systolic pulmonary
artery pressure tended to decrease after the operation,
but changes were not significant. An example of a
Doppler echocardiographic examination 12 months
after cardiomyoplasty is given in Fig. 4. In this
example, every second cardiac systole is supported by
a muscle contraction, as evidenced by the burst signal
in the ECG. The increase in peak aortic flow suggests
an active improvement of myocardial wall motion in
assisted beats.

Worldwide results

NYHA class and ventricular function

There is general agreement that cardiomyoplasty
leads to a notable decrease in NYHA class with only
moderate improvements in objective haemodynamic
parameters. Similar to our results, Chachques et al.
reported a significant increase in ejection fraction
from 24 ± 6.2% to 30.6 ± 5% (P<0.05) in a larger
population of 44 patients after a mean follow-up of
21 months[8]. The mean NYHA class decreased from
3.3 to 1.6 (P<0.01). The group in Sao Paulo, Brazil,
showed an increase in left ventricular ejection fraction
from 19.7 ± 3.3 to 23.3 ± 6.5% (P<0.05) and in left
ventricular stroke work index from 17.5 ± 5.2 to
25.6 ± 9.4 g x m x m^-2 (P<0.05) in 22 patients one
year after operation[9]. Again, the mean NYHA class
decreased from 3.2 ± 0.4 to 1.7 ± 0.7 (P<0.01). The
'Medtronic Dynamic Cardiomyoplasty Clinical Study' of
360 patients showed a significant increase in
left ventricular ejection fraction from 21.3 ± 6.8% to
24.2 ± 9.5% (P<0.02) and in stroke volume index
from 29.3 ± 8.2 to 32.3 ± 10.6 ml. beat^-1 . m^-2
(P<0.03). Seventy-nine percent of these patients
showed an improvement in their predominant post-
operative NYHA class. Magovern et al., using the
right latissimus dorsi, showed no change in left ven-
tricular ejection fraction in nine patients 6 months
after cardiomyoplasty, but a decrease in the mean
NYHA class from 3.0 ± 0.2 to 1.8 ± 0.2 and in left
ventricular end-diastolic volume from 316 ± 23 ml to
261 ± 22 ml (P<0.05)[10].

It is important to note that the functional
results of the cardiomyoplasty procedure are significa-
cantly affected by the pre-operative condition of the
patient. Experimental data from our laboratory have
shown that the residual function of the heart is of
considerable importance for the performance of the
heart/skeletal muscle complex[11]. A subanalysis of
the data from the Medtronic Dynamic Cardiomyo-
plasty Clinical Study divided 47 patients into two
groups, one group with less advanced disease, lower
incidence of symptomatic arrhythmia and better
aerobic capacity prior to the operation than the other[12].
The patients with less advanced cardiac
symptoms exhibited an increase in left ventricular
ejection fraction from 23% to 30%, in left ventricular
stroke work index from 28.7 gm . m^-2 . beat^-1 to
37.6 gm . m^-2 . beat^-1 and in peak oxygen
uptake from 17.6 ml . min^-1 . kg^-1 to
20.5 ml . min^-1 . kg^-1. The mean NYHA class
decreased in this group from 3.0 to 1.6. In the other
group, the only change in NYHA class was from
3.1 to 2.0, without a concomitant change in haemo-
dynamic parameters.

Eur Heart J, Vol. 18, February 1997
All patients but one exhibited a moderate increase in left ventricular ejection fraction. The mean increased from 21.2 ± 5.2% prior to the operation to 36.6 ± 17.6% (P<0.05) at 2 years.

Doppler echocardiography of left ventricular ejection flow 1 year after cardiomyoplasty. In this patient, every second cardiac systole is supported by a muscle contraction, as seen by the burst signal in the ECG. In this example the peak velocity of aortic ejection flow is higher in assisted than in non-assisted beats.

Quality of life

The predominant improvement in functional status (NYHA class) following cardiomyoplasty is not necessarily incompatible with the haemodynamic results, since no correlation exists between functional status, exercise capacity and left ventricular ejection fraction in patients with severe congestive heart failure[13]. Upon questioning, six of seven patients in our study exhibited a marked improvement in their physical, psychological and social behaviour. The group in São Paulo, Brazil, explicitly addressed the issue of quality of life in a prospective study of 14 patients, 13 ± 9 months following cardiomyoplasty. They found an important improvement in physical activity, sleep patterns, and social activity[14]. This is confirmed by the data from the Medtronic Dynamic Cardiomyoplasty Clinical Study[12]: prospective investigation by questionnaires prior to, and not less than 6 months following cardiomyoplasty revealed an improvement in activities of daily living in 86.5% and of social activities in 74% of the patients.

Mortality

The operative mortality for the cardiomyoplasty procedure lies to date between 0 and 18%[7-9,12,15,16].
Death has been attributed to myocardial failure, haemorrhage, sepsis, pulmonary infection, multi-organ failure or arrhythmia\(^8\)\(^{12}\). In our own experience actuarial survival is 62.5% at 67 months. Carpentier et al. reported 70.4% actuarial survival in 40 patients after a mean follow-up of 36 ± 7 months (range 2 months to 7 years)\(^6\)\(^{11}\). The strongest determinant for postoperative mortality is proper patient selection, as emphasized by the results of the Medtronic Dynamic Cardiomyoplasty Clinical Study: 298 patients in pre-operative NYHA III had a 1-, 2- and 3-year survival of 71.8%, 62.9% and 55.1%, respectively. In contrast, 46 patients in pre-operative NYHA IV had a 1-, 2- and 3-year survival of only 47.3%, 32.8%, and 24.7%, respectively\(^{12}\). Exclusion of patients who died from sudden death improved survival in the NYHA III patients at 2 years to 72%. In contrast, in NYHA IV patients this had no effect on survival, suggesting that these patients die from heart failure rather than from sudden death. Sixty-four more recently operated patients were selected, on the basis of pre-implant left ventricular ejection fraction, maximal O\(_2\) consumption and a statistical model, as having less than 10% predicted operative risk (Current practice). In these patients 1-, 2- and 3-year actuarial survival was 89.0%, 80.4% and 71.0% (Fig. 5).

**Mechanism of action**

Clinical data suggest that the stimulated muscle graft exerts some ‘active’ systolic improvement in left ventricular wall motion. Generating 40 W.kg\(^{-1}\), the power of transformed skeletal muscle equals the power developed by cardiac muscle during systole\(^{17}\). Due to the short neurovascular bundle, only the less efficient distal part of the muscle is available for ventricular assist. Furthermore, according to LaPlace’s law, myocardial wall tension in severely enlarged ventricles presents a high load for the muscle. This may explain why the improvement in left ventricular ejection fraction is only small and why larger improvements in left ventricular function have been observed in experimental animals with smaller hearts\(^{11}\)\(^{18}\).

The concept of ‘active reinforcement’\(^{6}\) is also supported by a recently published investigation of the left ventricular pressure–volume relationship in nine patients 6–24 months following cardiomyoplasty. Single beat comparison with and without skeletal muscle stimulation showed a significant increase in stroke volume by 20 ± 15%, in maximal systolic ejection velocity by 68 ± 24%, and in systolic aortic pressure by 7 mmHg\(^{19}\).

However, as opposed to ‘active reinforcement’, passive mechanisms have also been proposed: Moreira et al. found a significant fall in pulmonary capillary wedge pressure from 24.7 ± 6.3 to 18.2 ± 5.8 mmHg (\(P<0.05\)) in 22 patients 12 months following cardiomyoplasty\(^9\). Together with the decrease in left ventricular end-diastolic volume, which was demonstrated by the Magovern group\(^{10}\), this may suggest that the heart/skeletal muscle complex works at a reduced volume load following cardiomyoplasty, while maintaining cardiac output, suggesting improved ‘contractility’.

The concept of ‘passive reinforcement’ is supported by experimental data: It was shown that a simple muscle wrap around the heart, which is not electrically stimulated, slows progressive ventricular dilatation in dogs in a rapid pacing model\(^{20}\) and in goats in a model of chronic volume overload\(^{21}\). Carpentier reported that in patients the cardio-
thoracic ratio remained unchanged up to 3 years following cardiomyoplasty\[6\], suggesting that the intrinsic tension of the muscle prevents progressive dilation of the ventricles. Using the conductance catheter technique, Kass et al. found a chronic lowering of cardiac end-diastolic volume in three patients 6 and 12 months after cardiomyoplasty when the muscle stimulator was turned off. The end-systolic pressure–volume relationship shifted leftward, with only minimal changes in the diastolic pressure–volume relationship. Turning the muscle stimulator on yielded only minimal active enhancement of systolic function from skeletal muscle contraction. These results are consistent with a chronic ‘reverse remodelling’ of the heart, conceivably due to the external elastic constrain provided by the muscle wrap\[22\]. As another conceivable mechanism of action, Chiu suggested a ‘myocardial sparing effect’\[23\]. According to the law of Laplace, myocardial wall tension at any given pressure is directly related to the radius, and inversely related to the wall thickness. Assuming that the skeletal muscle wrap contributes to myocardial wall thickness, it achieves ‘functional ventricular hypertrophy’, thus lowering myocardial oxygen demand. Consistent with this theory, a decrease in the transmural tension time index and in the transmural pressure volume area was demonstrated in experimental animals after cardiomyoplasty\[24\]. Direct measurement of myocardial oxygen consumption in a goat model showed a significant reduction in MVO$_2$ and an increase of load independent measures of left ventricular function, such as Ees and Emax\[22\]. Such an improvement in myocardial energetics could lead to recovery of intrinsic myocardial function.

**Conclusion**

Cardiomyoplasty was conceived as a surgical alternative for the treatment of end-stage congestive heart failure. Clinical experience has shown that cardiomyoplasty leads to a considerable symptomatic improvement in NYHA III patients, while the improvement in haemodynamic parameters fell short of the initial expectations. Recently, survival was shown to be considerably improved by proper patient selection. Heart transplantation yields excellent functional results and permanently implanted mechanical assist devices gain increasing importance. However, both methods have obvious drawbacks. We currently define the indications for cardiomyoplasty at the University of Heidelberg as follows: (1) Patients with contraindications for heart transplantation, for whom cardiomyoplasty remains the only surgical alternative; (2) Patients with severely impaired left ventricular function and a history of ventricular tachycardia or fibrillation, in whom primarily the implantation of an implantable cardioverter defibrillator is indicated. These patients are threatened by the progression of heart failure. The combined treatment of the arrhythmia and the impaired left ventricular function may thus be a promising option, which could conceivably gain further importance as a bridge to transplantation; (3) Patients in NYHA III, who exhibit recurrent episodes of myocardial decompensation despite maximal medical therapy. In these patients cardiomyoplasty could conceivably slow progression of ventricular dilation and delay the time until organ replacement needs to be performed as the ‘ultima ratio’.

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**References**


