Physical training improves exercise capacity in patients with mitral stenosis after balloon valvuloplasty

H. Douard, L. Chevalier, L. Labbe, A. Choussat and J. P. Broustet

Hôpital Cardiologique du Haut Lévêque, Pessac, France

Background  Haemodynamic measurements taken at rest and during exercise showed that percutaneous transvenous mitral commissurotomy results in both acute and long-term improvement. However, the time lag before there is an increase in exercise and in peak oxygen uptake appears to be delayed and irregular.

Patients and methods  To assess the potential of physical training to restore better physical capacity after percutaneous transvenous mitral commissurotomy, 26 patients with mitral stenosis were studied after the procedure. The group was split into two. Thirteen underwent a 3-month rehabilitation programme, and the other 13, who did not, acted as controls.

Results  The mitral valve orifice area increased similarly, from 1.12 ± 0.17 to 1.88 ± 0.28 cm² in the training group and from 1.04 ± 0.16 to 1.88 ± 0.19 cm² in the control group. Cardiopulmonary parameters were similar before percutaneous transvenous mitral commissurotomy (peak VO₂: 19.9 ± 2.4 vs 18.9 ± 4.5 ml min⁻¹ kg⁻¹; peak workload: 94.6 ± 29.3 vs 96.1 ± 25 watts; VO₂ at anaerobic threshold: 17 ± 3.4 vs 16.1 ± 5.2 ml min⁻¹ kg⁻¹; all P=ns). Three months later the results were higher in the training group (peak VO₂: 26.6 ± 4.7 vs 21.6 ± 3.8 ml min⁻¹ kg⁻¹, P=0.001; peak workload: 125.4 ± 26.6 vs 108.5 ± 23 watts, P=0.03; VO₂ at anaerobic threshold: 19.6 ± 5.8 vs 15.8 ± 2.9 ml min⁻¹ kg⁻¹, P=0.02).

Conclusion  These results indicate that patients should take up exercise after successful percutaneous transvenous mitral commissurotomy for better functional improvement. (Eur Heart J 1997; 18: 464-469)

Key Words: Physical training, mitral valvuloplasty, exercise.

Introduction

In recent years, percutaneous mitral valvuloplasty has become an efficient curative treatment for many patients suffering from severe mitral stenosis[1,2]. However, the excellent haemodynamic results obtained during interventions or during subsequent follow-up are in contrast with an often disappointing short-and mid-term objective functional result[3,4]. In fact, although the functional classes of patients having received valvuloplasty are often improved, objective criteria (exercise performance or peak VO₂) measured after valvuloplasty are only slightly improved. This low increase in functional improvement seems associated with muscular and vascular peripheral anomalies which are similar to those observed in patients with cardiac failure[5,6].

Rehabilitation of patients with cardiac failure, even if severe, makes it possible to increase their exercise capacity[7,8]. We therefore undertook to rehabilitate patients who had received mitral valvuloplasty and to assess the benefits on a prospective basis.

Methods

Study population

Thirteen patients (eight women, five men) who had received mitral valvuloplasty were included in a rehabilitation programme. This began 15 ± 4 days after valvuloplasty and included three sessions of 1 h per week (exercise performed at a heart rate corresponding to 70% of the peak VO₂ measured before valvuloplasty). Each session consisted of approximately 15 min of warm-up exercises, followed by 30 min of continuous upright aerobic and dynamic exercise, and approximately 15 min of cool-down stretching and calisthenics. Moreover, the patients were encouraged to resume regular physical activity. Only those in sinus rhythm and whose valvuloplasty had succeeded (mitral surface after valvuloplasty > 1.5 cm²) without the appearance or
aggravation of preexisting mitral insufficiency were included.

The rehabilitated group (T) was compared with a control group (C) strictly matched for age, sex and body surface. The 13 controls were selected from a registry of 138 patients who had undergone valvuloplasty and reassessment 3 months later, but had not taken part in a programme of exercise. No specific recommendations concerning activity were given to this group. Matching was carried out with the patients' consent and 3 months of controlled rehabilitation was performed without knowing the functional results of the control group. Initial clinical, functional and haemodynamic parameters were similar for both groups (Table 1). Although patients in the C group had had percutaneous transvenous mitral commissurotomy 1 or 2 years before patients in the T group, the protocol of the procedure was similar. No patient was taking digoxin or beta-blockers. Eight and nine patients in groups T and C, respectively, were administered a diuretic, four patients (two in group T, two in group C) were receiving amiodarone, and one patient (group C) was receiving verapamil. Four and five patients in groups T and C, respectively, had moderate mitral insufficiency, and three and two patients in groups T and C, respectively, had minimal aortic insufficiency.

**Cardiac catheterization and valvuloplasty**

Patients underwent left and right heart catheterization with coronary arteriography before percutaneous transvenous mitral commissurotomy; the coronary arteries were found to be normal in all patients. Mitral valvuloplasty was performed by the transeptal approach using an Inoue balloon (Toray, Japan) in all cases, except for two patients in the C group. The mitral valve orifice area was calculated by the Gorlin formula before and immediately after valvuloplasty. Cardiac output was determined by the thermodilution technique. The mitral valve area was calculated by the Doppler pressure half-time method 3 months after percutaneous transvenous mitral commissurotomy in all patients.

**Exercise protocol**

Symptom-limited maximal upright bicycle exercise, during which respiratory gases were measured, was performed 24 h before and 3 months after valvuloplasty. All subjects underwent one or more familiarization maximal exercise tests with respiratory gas analysis before the study. On each occasion, the patients were asked to exercise until symptoms forced them to stop. Medications were unchanged throughout the study except for two patients in group C who stopped diuretics.

After a 3-min rest period on the ergometer, exercise was begun at an initial workload of 10 watts, followed by a continuous ramp protocol, corresponding to increments of 10 watts \( \text{min}^{-1} \) to a symptom-limited maximum. The ECG was monitored throughout exercise, and a 12-lead ECG was recorded at 1-min intervals. Blood pressure was measured with a cuff sphygmomanometer every 3 min. Respiratory gas analysis was performed with an automated on-line system (CPX, Medical Graphics System, Minneapolis, U.S.A.) to measure oxygen uptake \((\text{VO}_{2})\) and carbon dioxide production \((\text{VCO}_{2})\) every 15 s. For each exercise test, the following parameters were calculated: expired minute ventilation \((\text{VE})\), peak oxygen consumption (peak \(\text{VO}_{2}\)) corresponding to the highest attained oxygen consumption, \(\text{CO}_{2}\) output \((\text{VCO}_{2})\), and the respiratory exchange ratio \((\text{RER} = \text{VCO}_{2}/\text{VO}_{2})\). Oxygen consumption at anaerobic threshold \((\text{VO}_{2})\) was defined as the \(\text{VO}_{2}\) at which VE/\(\text{VO}_{2}\) was minimal followed by a progressive increase, the \(\text{VO}_{2}\) after which a non-linear increase in VE or \(\text{VCO}_{2}\) occurred relative to \(\text{VO}_{2}\), and the \(\text{VO}_{2}\) where the respiratory exchange ratio began to rise more steeply.

**Statistical analysis**

All data were expressed as mean±SD. Exercise responses between equivalent groups before and after valvuloplasty were calculated by a two-tailed t-test. Correlations were calculated by the least squares method, and examined using the Spearman’s rank test. A \(P\) value <0.05 was considered significant.

**Results**

Clinical, haemodynamic and cardiopulmonary parameters at exercise were similar before percutaneous transvenous mitral commissurotomy in both groups (Tables 1 and 2). The mean left ventricular ejection fraction and systolic pulmonary arterial pressures were 65 ±9% and 36 ±13 mmHg in group T, and 62 ±13% and 41 ±14 mmHg in group C. The maximal workload was 94.6 ±29.3 watts in group T and 96.1 ±25 watts \((P=\text{ns})\) in group C. Peak \(\text{VO}_{2}\) and \(\text{VO}_{2}\) at the aerobic threshold were 19.9 ±2.5 and 17 ±3.4 ml \(\text{min}^{-1}.\text{kg}^{-1}\) in group T, and 18.9 ±4.5 and 16.1 ±5.2 ml \(\text{min}^{-1}.\text{kg}^{-1}\) in group C. Percutaneous transvenous mitral commissurotomy increased the mitral surface area from 1.04 ±0.16 to 1.88 ±0.28 in group T, and from 1.12 ±0.17 to 1.88 ±0.28 in group C; the cardiac output index increased from 2.7 ±0.5 to 3 ±0.41 ml \(\text{min}^{-1}.\text{m}^{-2}\) (group T) and from 2.6 ±0.5 to 2.9 ±0.41 ml \(\text{min}^{-1}.\text{m}^{-2}\) (group C).

The mean valve gradient decreased from 14.2 ±3.8 to 4.5 ±2.5 mmHg (group T) and from 12.7 ±4.9 to 3.4 ±2.5 mmHg (group C). The mitral surface area measured by echo Doppler 3 months later remained at 2 ±0.3 cm\(^2\) (group T) and at 1.9 ±0.4 cm\(^2\) (group C) \(P=\text{ns}\).

All group T patients completed the training programme without side-effects, and were re-evaluated, as were group C, by cardiopulmonary tests 3 months after percutaneous transvenous mitral commissurotomy.
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>MVA (cm²)</th>
<th>LAP (mmHg)</th>
<th>MVG (mmHg)</th>
<th>CI (l. min⁻¹, m⁻²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>3 Months</td>
<td>Before</td>
</tr>
<tr>
<td>Group C</td>
<td>41.8 ± 10.9</td>
<td>1.12 ± 0.17</td>
<td>1.88 ± 0.28**</td>
<td>19 ± 0.4**</td>
</tr>
<tr>
<td>Group T</td>
<td>43.8 ± 11.1</td>
<td>1.04 ± 0.16</td>
<td>1.98 ± 0.19**</td>
<td>2 ± 0.3**</td>
</tr>
</tbody>
</table>

MVA = mitral value area; LAP = left atrial pressure; MVG = transmitral value gradient; CI = cardiac output index.  
*P < 0.01, **P < 0.001 vs before valvuloplasty.
Table 2  Cardiopulmonary parameters before and after balloon valvuloplasty in the control and training groups

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Training group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3 Months</td>
</tr>
<tr>
<td>Rest HR (beats . min⁻¹)</td>
<td>76.1 ± 13.8</td>
<td>80.5 ± 11.2</td>
</tr>
<tr>
<td>Peak HR (beats . min⁻¹)</td>
<td>155.3 ± 24.3</td>
<td>156.8 ± 22.2</td>
</tr>
<tr>
<td>Peak SAP (mmHg)</td>
<td>143.4 ± 14.8</td>
<td>145.8 ± 29.8</td>
</tr>
<tr>
<td>Rate-pressure product</td>
<td>22 211 ± 3949</td>
<td>22 933 ± 6385</td>
</tr>
<tr>
<td>VE max (l . min⁻¹)</td>
<td>43.9 ± 13.1</td>
<td>45.7 ± 15.8</td>
</tr>
<tr>
<td>Max RER</td>
<td>1.16 ± 0.09</td>
<td>1.15 ± 0.01</td>
</tr>
<tr>
<td>Max Ve/VCO₂</td>
<td>37 ± 3.8</td>
<td>34.4 ± 3.8</td>
</tr>
</tbody>
</table>

HR=heart rate; SAP=systolic artery pressure; AT=anaerobic threshold, RER=respiratory exchange ratio.

*P<0.05.

Figure 1  Peak VO₂ before and 3 months after percutaneous transvenous mitral commissurotomy in control (a) and trained (b) patients.

In group C, peak workload increased to 108.5 ± 23 watts (+16% vs pre-percutaneous transvenous mitral commissurotomy, P=0.01); peak VO₂ (Fig. 1(a)) was 21.6 ± 3.8 ml . min⁻¹ . kg⁻¹ (+18%, P=0.02), and VO₂ aerobic threshold was 15.9 ± 2.9 ml . min⁻¹ . kg⁻¹ (1%, P=ns). In group T, peak workload increased to 125.4 ± 26.6 watts (+40% vs pre-percutaneous transvenous mitral commissurotomy, P<0.001); peak VO₂ (Fig. 1(b)) was 26.6 ± 4.7 ml . min⁻¹ . kg⁻¹ (+33% P=0.001), and VO₂ aerobic threshold was 19.6 ± 5.8 ml . min⁻¹ . kg⁻¹ (+17%, P=0.008). The increases in peak workload and peak VO₂ were significantly greater 3 months after percutaneous transvenous mitral commissurotomy in group T than in group C.

Total ventilation at the end of exercise was unchanged in group C (from 43.9 ± 13.1 to 45.7 ± 15.8 l . min⁻¹) and increased from 45.5 ± 13.4 to 52.1 ± 11.7 l . min⁻¹, P=0.06, in group T. The ventilatory equivalent for CO₂ (Ve/VCO₂) at the end of exercise decreased from 37 ± 3.8 in group C and from 37.3 ± 3.3 in group T before percutaneous transvenous mitral commissurotomy to 34.4 ± 3.8 (P=0.002) and 32.6 ± 2.4 (P=0.0001), respectively, 3 months later.
Although there was a trend towards a reduced resting heart rate in group T at control, heart rates and systolic pressures were similar in both groups before and after percutaneous transvenous mitral commissurotomy at rest and at the end of exercise (Table 2). We found no correlation between haemodynamic (mitral area or transmitral gradient) and exercise performance (workload or peak VO₂ improvements) in either group (Fig. 2).

**Discussion**

The haemodynamic response to exercise in patients with severe mitral stenosis includes an attenuated cardiac output response and a rapid rise in pulmonary artery pressures and mean mitral valve gradients. This rapid haemodynamic improvement at rest and during exercise persists at 3 months and at longer follow-up periods. However, we and others have described a lack of improvement in exercise performance or peak VO₂ immediately after the procedure and only a modest increase some months later.

Nevertheless, subjective improvement in dyspnoea and exertional fatigue is experienced by most patients immediately after percutaneous transvenous mitral commissurotomy; this has recently been attributed to a decrease in excessive exercise ventilation due to a decrease in physiological dead space. This in turn can be put down to a decrease in left atrial pressure values and interstitial congestion post percutaneous transvenous mitral commissurotomy. In our study, the control patients increased their performance by only 96.1 ± 25 to 108.5 ± 23 watts and their peak VO₂ from 19.1 ± 4.9 to 21.6 ± 3.8 ml.min⁻¹.kg⁻¹ 3 months after successful percutaneous transvenous mitral commissurotomy.

However, haemodynamic results were satisfactory and similar to those reported in the literature. A possible restenosis or mitral insufficiency was also eliminated by Doppler reassessment, which confirmed the good result of the procedure 3 months later. The clinical and haemodynamic data of rehabilitated patients were the same as those of the controls. Training made it possible to clearly increase their exercise capacity from 94.6 ± 29.3 to 125.4 ± 26.6 watts and their peak VO₂ from 21.7 ± 3.6 to 25.8 ± 6 ml.min⁻¹.kg⁻¹. Rehabilitation, which was initially developed for managing coronary patients, has been proposed in recent years for patients suffering from cardiac failure. Interestingly, results have been reported, with an increase in peak VO₂ and VO₂ at anaerobic threshold. Although not completely understood, the main mechanism in this improvement is restoration of peripheral muscle extraction capacity.

Histological and biological muscle anomalies close to those observed in cardiac failure have been reported in patients with mitral stenosis. More recently, Barlow et al. reported that these anomalies persisted 2 weeks after mitral valvuloplasty, followed by their correction 4 months later (increase of quadriceps cross-sectional area measurement, percentage of type I fibres and dynamic maximal quadriceps torque and fatigue improvement). However, these patients were not included in a supervised rehabilitation programme and compared to controls as in our study.

We did not take muscle samples in our patients to check the histological and biochemical muscle modifications usually induced by rehabilitation. Yet the ventilatory changes observed (increased peak VO₂, VO₂ at anaerobic threshold, and decrease in Ve/VO₂) were similar to those observed after rehabilitation in patients with cardiac failure. We did not observe any correlation in our patients between improved peak VO₂ and haemodynamic changes induced by valvuloplasty. Nevertheless, haemodynamic measurements were only performed at rest and not during exercise. These results differ from those of Marzo et al. who reported a significant correlation between change in mitral valve area and change in peak VO₂ at 3 months.

The supplementary increase in functional capacity obtained by rehabilitation is therefore independent. It mainly corrects the peripheral vascular and muscle anomalies due to the limitation in activity that mitral stenosis causes. An enhanced cardiac output enables improved muscular fitness and reversal of ongoing peripheral muscular atrophy.

**Limitation of the study**

The patients rehabilitated in our study were not randomized but were compared with a control group taken from a registry of patients who had received percutaneous transvenous mitral commissurotomy. Owing to the low number of rehabilitated patients, they were strictly matched for age, sex and technique used before the beginning of rehabilitation. Moreover, we included only those patients who were in sinus rhythm, so the benefit of rehabilitation for patients with atrial fibrillation cannot be fully verified. The spontaneous improvement of cardiorespiratory parameters after percutaneous transvenous mitral commissurotomy in patients with atrial fibrillation is generally less pronounced, except when there is a reduction in the disturbance of the supraventricular rhythm. It may be that in the long term, the improvement in the cardiorespiratory data of non-rehabilitated patients is the same as that of rehabilitated patients. Indeed, some authors have reported very late improvement.

The mitral valve area was assessed before and immediately after percutaneous transvenous mitral commissurotomy by the Gorlin formula. For ethical reasons, reassessment of the mitral area was by echocardiogram only; however, comparability of both methods are good, although the haemodynamic method is prone to error in the presence of a significant atrial septal defect.

The indications for rehabilitation have been widened in recent years to patients with cardiac failure, and the functional results have been substantial. Similar
muscle anomalies in patients with mitral stenosis explains the modest functional benefit often observed after percutaneous transvenous mitral commissurotomy, but as we have shown, this benefit may be considerably increased by patients taking part in rehabilitation programmes.

References


