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Early Exercise Training After Mitral Valve Repair*

A Multicentric Prospective French Study

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Background: **Surgical mitral valve (MV) repair is now the best technique to correct mitral regurgitation (MR). However, clinical studies have shown that without exercise training (ET), there is no significant postoperative exercise tolerance improvement. Moreover, healing duration of the MV wound is not well known; thus, the feasibility of an early ET program (ETP) may be discussed.**

Objectives: **To evaluate safety and feasibility of an early ETP after MV repair.**

Methods and results: **All patients hospitalized in 13 postoperative centers after MV repair from September 2002 to June 2003 were included in this prospective study. They underwent an ETP during 3 weeks on average. Transthoracic echocardiography and a cardiopulmonary exercise test were performed before and after the ETP.**

Patients: **Two hundred fifty-one consecutive patients (male gender, 70%; mean age, 59 ± 14 years [± SD]) were included 16 ± 10 days after MV repair. There was no MR occurrence or worsening after the ETP. Left ventricular ejection fraction slightly increased (53 ± 10% vs 55 ± 9%, p = 0.004). Peak oxygen consumption and anaerobic threshold increased from 16.3 ± 4.5 to 20.0 ± 6.0 mL/kg/min (22% increase) and from 12.2 ± 3.8 to 14.2 ± 4.3 mL/kg/min (16% increase) respectively, (p < 0.0001).**

Conclusion: **ET after MV repair does not deteriorate the outcome of recent surgery and seems efficient.**
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Key words: cardiac rehabilitation; exercise training; mitral valve; valvuloplasty

Abbreviations: AF = atrial fibrillation; AT = anaerobic threshold; CABG = coronary artery bypass grafting; CPT = cardiopulmonary exercise test; CRC = cardiac rehabilitation center; ET = exercise training; ETP = exercise training program; LAA = left atrial area; LAD = left atrial diameter; LVEDD = left ventricular end-diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; MV = mitral valve; NYHA = New York Heart Association; TTE = transthoracic echocardiography; $\dot{V}O_2$ = oxygen consumption

The emergence of mitral valve (MV) repair[1] clearly modified cardiac surgery habits. Indeed, valve replacement by either mechanical prostheses or bioprostheses is still associated with a number of problems (*eg*, thrombosis, hemorrhage, degeneration). MV repair has many advantages, including the absence of long-term antithrombotic therapy in patients with sinus rhythm and excellent long-term results.[2,3] This is why, if feasible, this type of reconstructive surgery is increasingly proposed to young patients who sometimes have few symptoms or even are asymptomatic.[4] Modern management of these patients aims at rapid recovery of a near-normal functional capacity. However, as demonstrated by Le Tourneau et al,[5] exercise tolerance measured 6 months after surgery does not significantly improve, despite mitral regurgitation (MR) correction, in the absence of exercise reconditioning. These disappointing results have recently been confirmed in a study[6] in which patients performed their second

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exercise test 1 year after MV repair. One possible explanation of this "paradox" could be peripheral deconditioning induced by both valvular heart disease and postoperative course. Physical training allows, among other effects, improved exercise performance in patients with coronary heart disease[7] and heart failure,[8–10] as well as in those who have undergone aortocoronary bypass grafting[11–13] or prosthetic valve replacement.[14] However, MV healing duration after MV repair is not well known, and only animal data are available. Takamura et al[15] showed (in sheep) that healing of a MV wound requires from 8 to 12 weeks after surgery. This could explain the daily life reluctance of some surgical teams to allow early exercise training (ET) after MV repair, especially in high-risk groups of patients: left ventricular ejection fraction (LVEF) $< 45\%$,[16] age > 70 years,[16] ischemic MR,[17] preoperative New York Heart Association (NYHA) functional class III or IV,[16] anterior or both mitral leaflets repair,[18] and concomitant coronary artery bypass grafting (CABG).[19]

To our knowledge, no assessment of the safety of exercise reconditioning after MV repair has ever been attempted. The main aim of our study was to evaluate the safety and feasibility of early ET in patients after MV repair.

Materials and Methods

Patients

This multicentric prospective study (13 centers) was conducted on behalf of the Working Group of Cardiac Rehabilitation of the French Society of Cardiology. All consecutive patients in whom MV repair had been recently performed (< 60 days before study entry) and who were hospitalized in cardiac rehabilitation centers (CRCs) from September 1, 2002, to June 30, 2003, were included. The only exclusion criteria was the inability to perform exercise testing. Drug treatment was left to the discretion of the investigator.

Assessment Criteria

Clinical, echocardiographic, and ergometric assessments were made before and after completion of the cardiac rehabilitation program. Clinical parameters were assessed at least twice a week, looking for the presence of arrhythmia, thromboembolic or hemorrhagic events, infection, signs of heart failure, and emergence or worsening of MR murmur. Doppler echocardiography was performed in all patients at least on two occasions: before and after the ET program (ETP). Each echocardiographic study was done jointly by two operators. Systolic and diastolic BP and heart rate were measured at the beginning of each session. Left ventricular end-diastolic diameter (LVEDD) was measured on the great axis parasternal plane. Left ventricular end-diastolic volume (LVEDV) and LVEF were measured using the Simpson method.[20] Left atrial diameter (LAD) and left atrial area (LAA) were measured during systole.[21] Mean transmitral gradient was measured by continuous Doppler echocardiography coupled with two-dimensional imaging in the apical position. The importance of residual MR was quoted from I to IV based on the following parameters: left atrial regurgitation flow area determined by color Doppler echocardiography,[22] regurgitating orifice area and regurgitated volume calculated using the proximal isovelocity surface area method,[23,24] and research of pulmonary venous flux inversion.[25] Pulmonary systolic BP was estimated from the tricuspid insufficiency flow.

All patients underwent two cardiopulmonary exercise tests (CPTs) before and after the ETP. CPTs were based on the classical methods and done in the upright position.[26] All patients performed an upright graded symptom-limited cycloergometer exercise with a workload increment of 10 W/min after an initial workload of 30 W. Most of the patients were familiar with the procedure and were regularly encouraged to exercise until maximal exhaustion. In order to stabilize resting gas measurements, subjects were asked to remain still on the bicycle for 3 min before exercising. A standard 12-lead ECG was continuously recorded. Heart rate was followed at each minute, and BP was measured by a mercury sphygmomanometer every 2 min during the exercise test and at the peak of exercise. Oxygen consumption ($\dot{V}O_2$), carbon dioxide production, and the other common ventilatory parameters (minute ventilation, breathing rate) were measured on a breath-by-breath basis. The results were averaged using a moving-average filter every seven breaths, excluding at each breath the highest and lowest values in order to reduce breath-by-breath noises. They were then averaged every 15 s and printed. The respiratory exchange ratio was always > 1 at peak exercise. Peak $\dot{V}O_2$ was defined as the highest $\dot{V}O_2$ obtained at the end of the test, and was expressed in milliliters per minute per kilogram. The anaerobic threshold (AT) was determined using classical methods.[27,28] The oxygen pulse was calculated as the $\dot{V}O_2$/heart rate ratio. At peak exercise, patients were asked to stop pedaling, and measurements were continued for 5 min.

ET

The ETP included calisthenics (started the day after arrival in the CRC) and endurance bicycle training (started after the first CPT) 5 days a week (during 3 weeks on average) for inpatients (84%) and 3 days a week (during 5 weeks on average) for outpatients (16%). Endurance training was performed using a bicycle set at an intensity determined by heart rate measured at the AT or, if not available, at 70% of the maximal heart rate of the first CPT. Each session lasted 40 min, beginning with a 5-min warm-up phase, followed by 30 min of rectangular cycling exercise, and ended by a 5-min cool-down period. The calisthenics consisted of 20 different dynamic and isometric arm and leg exercises during 30 to 40 min at each session. All sessions where held under the supervision of a cardiologist.

Statistical Analysis

Results were expressed as mean ± SD. A paired *t* test was used to compare continuous data collected in patients before and after completion of the rehabilitation program. Since multiple comparisons were performed, Bonferroni adjustment was used. Accordingly, statistical significance was achieved for the outcome variables when the p value was < 0.00625. This strategy was used to maintain the type I error rate at the 5% level.

A χ^2 test was used to analyze nominal data. Factors associated with changes observed after the training period were determined by means of logistic regression analysis. All statistical analyses were performed using statistical software (StatView 5.0; SAS Institute; Cary, NC).

Results

Patients

Among the 261 consecutive patients selected, 10 were excluded because of a contraindication to exercise testing (deteriorated general status, n = 5; postoperative grade IV mitral disease, n = 1; postoperative aortic dissection, n = 1; abundant pericardial effusion, n = 3). The 251 included patients 175 men and 76 women (mean age, 59 ± 14 years). Mean preoperative NYHA functional class was 2.3 ± 1.0.

Intraoperative MV disease analysis showed a leaflet prolapse in 214 patients (85%) [type II Carpentier functional classification]; the leaflet prolapse involved the posterior in leaflet in 154 patients, the anterior leaflet in 27 patients, and both leaflets in 33 patients. Sixteen patients (6%) had a normal leaflet motion (type I Carpentier functional classification), and 21 patients (8%) a restrictive leaflet motion (type III Carpentier functional classification).

In type I, a prosthetic ring remodeling annuloplasty was used alone or associated with closure of leaflet perforation. In type II, leaflet prolapse was treated with leaflet resection (85%) and/or chordal shortening or transposition (35%). In type III, commissurotomy, leaflet enlargement with autologous pericardium, and annuloplasty were usually performed. A prosthetic ring was used in all patients. Table 1 shows the distribution of patients by NYHA class and etiology of mitral disease.

Associated cardiac surgery was performed in 31.4% of cases (80 patients): aortic valve replacement (13.3%), CABG (12.8%), tricuspid valve repair (6.2%), Cox rhythmic surgery (2.3%), pacemaker implantation (2.3%), and others (2.7%). Patients were transferred to the CRC 16 ± 10 days after surgery.

Drug therapy comprised β-blockers in 111 patients (44.2%), angiotensin-converting enzyme inhibitors or angiotensin II antagonists in 106 patients (42.2%), amiodarone in 104 patients (41.4%), and diuretics in 51patients (20.3%). One hundred seventy patients received oral anticoagulant therapy (vitamin K antagonist) alone, 15 patients received aspirin (75 to 300 mg/d) combined with oral anticoagulant therapy, 40 patients received aspirin alone, and 26 patients received no antithrombotic treatment.

Table 1—*Preoperative Characteristics of Patients (n = 251)**

Characteristics	Data
Age, yr	59 ± 14
Range	18–87
Male gender, %	70
NYHA class, %	
I	18
II	34
III	36
IV	12
Mean	2.3 ± 1
LVEF, %	56 ± 11
Range	20–80
MR etiology, %	
Dystrophic	69
Ischemic	11
Rheumatism	10
Endocarditis	5
Others	5

*Data are presented as mean ± SD unless otherwise indicated.

ET Modalities

Duration of the ETP was > 21 ± 3 days for inpatients and 35 ± 7 days for outpatients, and comprised a mean of 13.7 ± 5.4 calisthenic sessions and a mean of 11.0 ± 4.0 ergometric bicycle training sessions. Mean training workload performed at the end of the program was 58 ± 27 W. Mean training heart rate observed during the sessions was 103 ± 17 beats/min.

Echocardiographic Results

The first transthoracic echocardiography (TTE) was performed 19 ± 10 days after surgery, and the second TTE was performed after completion of the training program, 39 ± 10 days after MV repair. At the first TTE, 52% of patients had residual MR (grade I, 43%; grade II, 9%; grade III, 0%; grade IV, 0%). Neither worsening of those MR cases (grade I, 39%; grade II, 9%; grade III, 0%; grade IV, 0%) nor emergence of new MR cases after completion of the exercise reconditioning program were observed (Fig 1). Moreover, postoperative MR grade did not change either after ET in the high-risk groups of patients: LVEF < 45% (n = 50), age > 70 years (n = 69), ischemic MR (n = 28), preoperative NYHA functional class III or IV (n = 120), anterior mitral leaflet repair (n = 27), repair of both mitral leaflets (n = 33), and concomitant CABG (n = 32).

No significant changes were observed in LVEDD (53 ± 8 at the first TTE vs 53 ± 7 mm at the second TTE), LVEDV (113 ± 39 mL vs 108 ± 35 mL), and LAA (23 ± 7 cm^2 vs 23 ± 7 cm^2), grade of residual MR (0.58 ± 0.7 vs 0.55 ± 0.7), and mean transmitral gradient (3.5 ± 1.7 mm Hg vs 3.8 ± 1.9 mm Hg) after the exercise reconditioning program (Table 2). LVEF slightly increased (53 ± 10% vs 55 ± 9%, p = 0.0043) after ET.

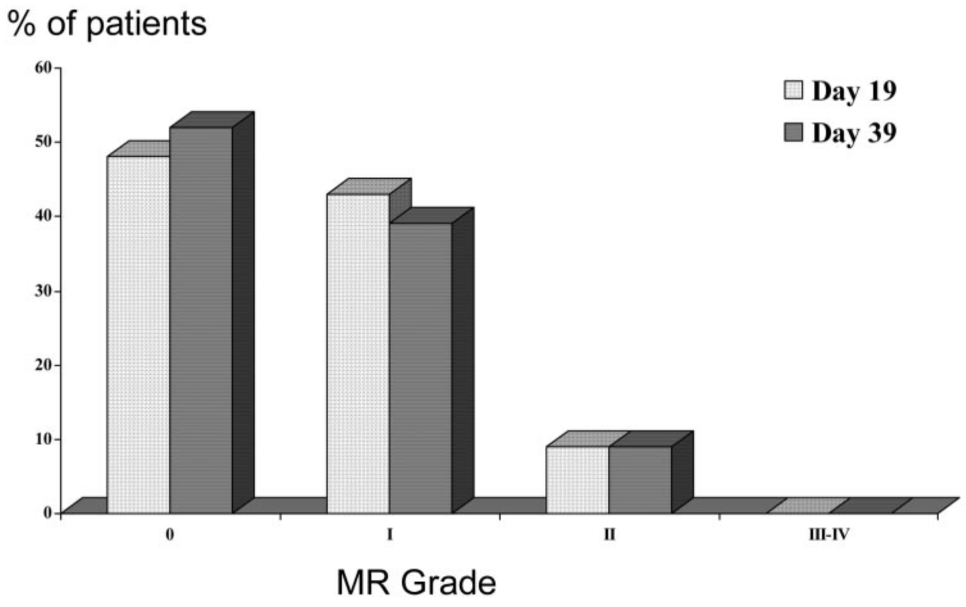

FIGURE 1. Postoperative MR grades evolution after training. Day 19: The first TTE, performed before ET. Day 39 = the second TTE, performed at the end of the ETP.

CPTs

The inclusion exercise test (the first CPT) was performed 21 ± 10 days after surgery and repeated at the end of the ETP 41 ± 14 days (the second CPT) after surgery. After completion of the ETP, there were significant increases in both peak $\dot{V}O_2$ (22% increase, $p < 0.0001$) and AT (16% increase, $p < 0.0001$). Detailed results are presented in Table 3. Univariate analysis showed that peak $\dot{V}O_2$ improvement was independent from age, sex, LVEF, presence of a β-blocker or an angiotensin-converting enzyme inhibitor treatment, presence or absence of atrial fibrillation (AF) and increase of hemoglobin concentration; therefore, the only parameter correlated with peak $\dot{V}O_2$ improvement was mean training workload ($r = 0.42$; $p = 0.001$).

Emerging Events During the Cardiac Rehabilitation Period

Before surgery, 52 patients (21%) had permanent AF. During their stay at the CRCs, a total of 66 patients (26%) had at least one AF episode lasting > 24 h; among those, 32 patients (12.7%) had still AF when discharged.

No severe heart failure exacerbation nor serious ventricular arrhythmia were observed. There were no ischemic or hemorrhagic strokes and no peripheral thromboembolic events. The adverse events observed were small or moderate pericardial effusion (12% of patients), pleural effusion requiring no pleural drainage (7%), urinary tract infection (5%), and transient ischemic attack (3.9%). Those transient ischemic attacks were not related to exercise since 70% occurred before the first training session.

Table 2—*Changes in Echocardiographic Parameters After Training**

Variables	First TTE (Postoperative Day 19 ± 10)	Second TTE (Postoperative Day 39 ± 10)	p Value†
LAD, mm	44 ± 8	43.8 ± 8	NS
LAA, cm^2	23 ± 7	23 ± 7	NS
LVEDD, mm	53 ± 8	53 ± 7	NS
LVEDV, mL	113 ± 39	108 ± 35	NS
LVEF, %	53 ± 10	55 ± 9	0.004
SPAP, mm Hg	32 ± 8	31 ± 8	NS
MR mean grade	0.58 ± 0.7	0.55 ± 0.7	NS
Transmitral gradient, mm Hg	3.5 ± 1.7	3.8 ± 1.9	NS

*Data are presented as mean ± SD. SPAP = systolic pulmonary arterial pressure; NS = not significant.
†Because multiple comparisons were performed, statistical significance was achieved at $p < 0.00625$.

Table 3—*CPT Test Evolution After Training*

Variables	First CPT (Postoperative Day 21 ± 10)	Second CPT (Postoperative Day 41 ± 14)	% Change	p Value*
Peak $\dot{V}O_2$, mL/kg/min	16.3 ± 4.6	20.0 ± 6.0	+ 22	0.0001
AT, mL/kg/min	12.2 ± 3.8	14.2 ± 4.3	+ 16	0.0001
Exercise duration, s	378 ± 150	509 ± 209	+ 34	0.0001
Maximal workload, W	81 ± 27	106 ± 37	+ 31	0.0001
Oxygen pulse, mL/kg/min/beats per min	10.3 ± 3	12.2 ± 3.7	+ 18	0.0001
Resting heart rate, beats/min	82 ± 13	78 ± 12	− 4	0.0001
Maximal heart rate, beats/min	115 ± 23	120 ± 26	+ 4	0.0001
Chronotropic reserve,† beats/min	38 ± 24	45 ± 37	+ 18	0.0001

*Because multiple comparisons were performed, statistical significance was achieved at $p < 0.00625$.
†Maximal − resting heart rate.

Discussion

Our multicentric study is the first one to prospectively evaluate the feasibility of early ET after MV repair. Our results demonstrate that ET is safe, without a deleterious effect on MV function or left ventricular remodeling, and does improve exercise tolerance in these postoperative patients.

MV repair provides beneficial effects on prognosis: after surgery, the life expectancy of operated patients becomes close to that of the general population.[2] Patients are therefore surgically treated increasingly earlier to avoid left ventricle dilation and complete arrhythmia onset. The registry published by Braunberger et al[2] in 2001, assessing outcomes of MV repair interventions performed > 20 years earlier, showed that only 3% of patients were asymptomatic before surgery. Interestingly, these were 15% in the Euro Heart Survey registry[4] and 18% in our study. However, we are now facing the following paradox: patients operated increasingly earlier often have very few symptoms, but their exercise capacity is worse after than before MV repair.[5,6]

The benefits of exercise reconditioning are very well documented in coronary heart disease[7,29] and heart failure patients.[8–10] However, few assessments of this therapeutic modality have been made after valvular surgery.[14,30–32]

Although postoperative exercise reconditioning might provide an opportunity to improve exercise tolerance in these patients, its efficacy and safety have been debated. Indeed, it might be feared that prolonged exercise could deteriorate the outcome of recent surgery performed on delicate valvular tissues, either because of the valve texture itself, or because of the time required for valve healing.

Our results clearly demonstrate that such concerns are groundless. Irrespective of the MV disease etiology of the surgical technique used and of the leaflet repaired, neither new onset nor worsening of MR were observed in patients who completed the ETP. In addition, the transmitral gradient at rest remained stable. Lastly, exercise had no deleterious effect on left ventricle remodeling since LVEDV remained stable. The improvement in ergometric parameters was similar to that usually observed in patients with coronary heart disease[7,29] and heart failure[8]: peak $\dot{V}O_2$ increased by approximately 20%.

The most powerful predicting factor for this improvement that we identified was the workload developed during training. The presence of AF had no impact on the ET outcome. Moreover, postoperative LVEF was slightly lower than before surgery, as commonly reported[33]; this parameter slightly improved after the ETP and returned to preoperative values, thus demonstrating that ET does not impair postoperative left ventricular recovery.

Study Limitations

The absence of control group is the main limitation of our study. However, it should be emphasized that the main purpose of this study was to assess the safety of an ETP after MV repair. No worsening of postsurgery residual MR was observed among the 251 trained patients, therefore, a control group was useless to demonstrate the safety of exercise reconditioning. In order to assess the improvement of ergometric parameters, a randomized control study could be warranted, but one can asks if it is an actual question to prove that ET does improve exercise capacities. Furthermore, the improvement of exercise capacities in our patients, similar to that obtained in both coronary heart disease[7] and heart failure patients[8–10] in randomized studies, is a strong argument to assume that ET is efficient in this particular population. Since our study only included patients transferred to a CRC, one cannot exclude that indications of ET might be more limited in more compromised patients.

Conclusions

Following MV repair, early ET is safe and is associated with an improvement in exercise capacity similar to that obtained in both coronary heart disease and heart failure patients.

Appendix

The members of the Working Group of Cardiac Rehabilitation of the French Society of Cardiology are as follows: Dr. Borgat, Centre Hospitalier de Maubreuil, Carquefou; Dr. Corone, Centre Médical de Bligny, Briis sous Forges; Dr. Feige, Clinique Rhone Durance, Avignon; Dr. Fischbach, Centre de Réadaptation, Chāteau-Lemoine, Cenon; Dr. Ghannem, Centre Medical Leopold Bellan-Ollencourt, Tracy le Mont; Dr. Henry, Clinique de l'Orangerie, Strasbourg; Dr. Iliou, Hôpital Broussais-HEGP, Paris; Dr. Kugler-Chambron, Beauvallon, Dieulefit; Dr. L'Heritier, Centre de Cardiologie, La Chenevière, Callian; Dr. Meurin, Centre de Réadaptation Cardiaque, Les Grands Prés, Villeneuve Saint Denis; Dr. Paemelaere, Centre de Réadaptation Fonctionnelle Cardio-respiratoire, Cambo les bains; Dr. Pierre, Centre de Médecine et de Réadaptation, IRIS, Marcy l'étoile; and Dr. Ross, Centre de Réadaptation Cardiaque, Abreshviller, France.

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