The Role of Cardiopulmonary Exercise Test in Mitral and Aortic Regurgitation : It Can Predict Post-Operative Results

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Background: We evaluated the efficacy of the cardiopulmonary exercise test as an objective indicator of functional status and as a pre-operative prognostic indicator in patients with mitral regurgitation (MR) and aortic regurgitation (AR).

Methods: Cardiopulmonary exercise tests and echocardiography were performed in 47 patients (MR: 30, AR: 15, MR + AR: 2) before surgery and repeated one year after surgery. We compared the New York Heart Association (NYHA) functional class, peak oxygen consumption rate (VO_2peak), exercise duration, left ventricular dimension and ejection fraction, before and after surgery.

Results: Initial VO_2peak and exercise duration were significantly different according to NYHA class. A year later, NYHA functional class improved from 2.1±0.1 to 1.4±0.1 ($p<0.001$). The VO_2peak was significantly increased (21.7±1.0 to 23.7±1.0 mL/kg per min, $p=0.008$) and exercise duration also increased (521.7±35.9 to 623.3±35.7 seconds, $p<0.001$). When patients were analysed according to their post-operative NYHA functional class, those with class I showed significantly different pre-operative VO_2peak (class I: 23.7±1.1, II: 18.3±1.5 mL/kg per min, $p=0.005$) and exercise durations (class I: 587.5±43.2, II: 415.6±55.7 seconds, $p=0.02$). Patients with higher pre-operative VO_2peak (19.0 mL/kg per min) more frequently became NYHA functional class I than those with a lower pre-operative VO_2peak (76.7% vs. 35.3%, $p=0.02$). But baseline left ventricular dimension and ejection fraction by echocardiography were not different between post-operative class I and II group.

Conclusion: VO_2peak and exercise duration are excellent parameters to evaluate the subjective functional class and to predict the post-operative functional class of patients with MR and/or AR. Patients with a pre-operative VO_2peak of 19.0 mL/kg per min or more will have a better functional status one year after surgery.

Key Words : Mitral valve insufficiency, Aortic valve insufficiency, Oxygen consumption, Exercise test

INTRODUCTION

It is often difficult to make decisions on surgery for patients with mitral regurgitation (MR) and aortic regurgitation (AR) because there are no accurate parameters to determine functional status[1, 2]. The functional status is an important prognostic factor because patients with poor pre-operative functional status often show poor post-operative prognosis. In patients with MR and/or AR, pre-operative echocardiographic findings, such as left ventricular dimension (LVD) and ejection fraction (EF), cannot exactly reflect their functional status or symptoms[3-6]. Even though the cardio

pulmonary exercise test is a standard tool to evaluate the patient's functional status, there are limited reports on the effects of surgical correction of MR and AR on later exercise capacity[7-10]. We, therefore, evaluated the efficacy of a cardiopulmonary exercise test as an objective parameter of functional status and as a pre-operative prognostic indicator for patients with MR and AR.

METHODS

Subjects

Forty-seven patients with severe valvular regurgitation (MR: 30, AR: 15, MR + AR: 2) who received surgery for valvular replacement or valvuloplasty were studied. We excluded any patients who had a component of valvular stenosis, significant respiratory or ischemic heart disease or severe claudication of a lower extremity.

The cardiopulmonary exercise test and echocardiography were performed before and one year after surgery. We compared the patients' New York Heart Association (NYHA) functional class, peak oxygen consumption rate (VO2peak), exercise duration, LVD and EF, before and after the operations.

Cardiopulmonary exercise test

An ergometer bicycle (SensorMedics 433DX-D, USA) was used for the exercise test. The use of cardiac drugs (diuretics, digoxin, angiotensin converting enzyme inhibitor, beta-blocker) was permitted. Patients were asked to cycle at a constant rate of 60 r.p.m. We recorded blood pressure and 12-lead electrocardiography every two minutes. The exercise test was stopped if the patients could not continue because of dyspnea or fatigue. Expired gases were analysed on a breath-by-breath basis, using a permanent zirconium oxide electrochemical cell. The gas analyser system was calibrated using a standard gas mixture before each test. After the tests, we recorded exercise durations and calculated VO2peak and ventilatory anaerobic thresholds (AT).

Statistics

Results are expressed as means standard error of mean. To compare NYHA classes, we used the nonparametric Mann-Whitney U-test. Comparisons between pre-operative and post-operative status on exercise tests were performed using Chi-squared or paired or unpaired Student's t-tests, according to the case. To determine the cut-off value of pre-operative VO2peak for post-operative functional class, we used Chi-squared method corrected with Lausen and Schumacher's method[11].

RESULTS

Clinical characteristics

The study included 47 patients: 30 with MR; 15 with AR and two with MR+AR. In echocardiographic evaluation, 30 patients showed degenerative valvular changes, and 14 patients were rheumatic valvular disease. There were 2 patients with ischemic valvular disease and 1 patient with bacterial endocarditis. Ten patients were in NYHA functional class I, 21 in class II and 16 in class III before surgery. Table 1 shows the baseline clinical characteristics of groups according to their NYHA functional class.

Table 1. Baseline clinical characteristics

	NYHA functional class		
	I	II	III
Number	10	21	16
Gender (M/F)	9 / 1	13 / 8	4 / 12
Age (years)	47.3±4.0	52.3±2.7	58.9±2.8
Pre-operative diagnosis			
MR	5	13	12
AR	5	6	4
MR+AR	0	2	0
Type of operation			
MVR	3	2	7
MV repair	2	11	5
AVR	5	6	4
DVR	0	2	0
Treatment			
Diuretics	4	13	14
Digoxin	1	5	6
ACE inhibitor	10	14	10
Beta-blocker	5	4	1

ACE inhibitor, angiotensin converting enzyme inhibitor; AVR, aortic valve replacement; DVR, dual valve replacement; MVR, mitral valve replacement.

Pre-operative functional status of patients

Table 2 shows the results of cardiopulmonary exercise tests and echocardiography before surgery. The VO2peak and exercise durations showed significant differences according to NYHA functional class ($p<0.001$). However, echocardiographic parameters were not different according to the patients' pre-operative functional status, as LVD and EF were not different among NYHA functional groups. The NYHA functional class of 12 patients were mismatched with groups categorized by pre-operative 95% confidence interval of VO2peak (VO2peak of Class I: 24.5, II: 20.5 and <24.5, III: <20.5 mL/kg per min).

Table 2. Findings of cardiopulmonary exercise test and echocardiography according to patients' NYHA functional class

| | NYHA functional class | | | p-value |
	I	II	III	
VO$_2$peak				
(mL/kg/min)	28.7±1.8	21.6±1.0	17.3±1.5	<0.001
Exercise				
duration (s)	766.0±66.4	510.6±46.9	383.5±48.6	<0.001
AT (%)	50.6±2.5	56.1±2.1	51.9±3.8	NS
LVD (diastole) (mm)	63.9±1.9	64.3±1.9	63.5±2.9	NS
LVD (systole) (mm)	42.9±2.1	43.5±2.2	42.0±2.7	NS
EF (%)	55.6±2.5	54.5±2.6	56.5±2.5	NS

AT, anaerobic threshold; EF, ejection fraction; LVD, left ventricular dimension

Table 3. Effects of surgery functional capacity and echocardiographic parameters in patients undergoing mitral and/or aortic valve surgery

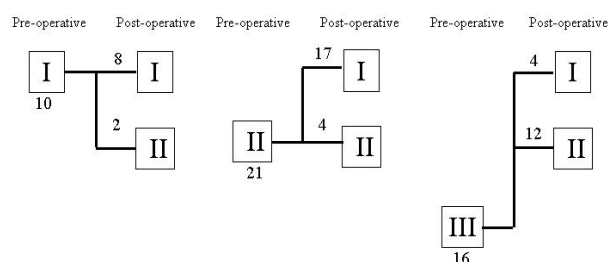| | Valve surgery | | p-value |
	Before	After	
NYHA functional class	2.1±0.1	1.4±0.1	<0.001
VO$_2$peak (mL/kg/min)	21.7±1.0	23.7±1.0	0.008
Exercise duration (s)	521.7±35.9	623.3±35.7	<0.001
AT (%)	53.4±1.7	57.1±1.5	NS
LVD (diastole) (mm)	64.0±1.4	50.9±1.0	<0.001
LVD (systole) (mm)	42.8±1.4	34.5±1.0	<0.001
EF (%)	55.5±1.5	55.6±1.4	NS

AT, anaerobic threshold; EF, ejection fraction; LVD, left ventricular dimension

Post-operative effects of surgery

In 47 patients who completed a one-year follow-up after surgery, there was no major adverse clinical events such as death, heart failure, major bleeding due to anticoagulation and embolism. Post-operatively, there was a significant improvement in their NYHA functional class (p<0.001), that is, 29 patients were placed in NYHA functional class I and 18 patients were in class II (Figure 1). The VO$_2$peak increased significantly (p=0.008) and exercise durations also increased (p<0.001). Although systolic and diastolic LVD decreased significantly after surgery (p<0.001), there was no significant change in EF (Table 3).

Cardiopulmonary exercise test in NYHA class III

Of 16 patients categorized as pre-operative NYHA functional class III, all improved to class I (n=4) or II (n=12), post-operatively. When the pre-operative factors determining post-operative NYHA functional class were compared, the pre-operative VO$_2$peak (class I: 23.5±2.8 vs. II: 15.3±1.4 mL/kg per min, p=0.01) and exercise duration (I: 621.5±72.9, vs. II: 304.2±39.0 seconds, p<0.01) were significantly different between post-operative class I and II.

Pre-operative parameters determining the post-operative NYHA functional class

Because pre-operative functional status is an important parameter that determines post-operative prognosis, we divided the patients into two groups according to their initial VO$_2$peak. The 30 patients with higher pre-operative VO$_2$peak (≥19.0 mL/kg per min) were more frequently categorized as post-operative NYHA functional class I than those with lower pre-operative VO$_2$ peak (76.7% vs. 35.3%, p=0.02) (Figure 2). In 16 patients with NYHA functional class III, there were 6 patients who had higher VO$_2$peak (≥19.0 mL/kg per min), and 4 of these patients were post-operative NYHA functional class I. Table 4 shows the difference in each parameter of cardiopulmonary test and echocardiography according to the value of pre-operative VO$_2$peak.

Figure 1. The NYHA functional status of patients before and one year after operation.

Figure 2. Comparison of the patients' NYHA functional classes after operation according to their pre-operative VO$_2$peak level. The patients with higher pre-operative VO$_2$peak (≥19.0 mL/kg/min) were more frequently categorized as post-operative NYHA functional class I than those with lower pre-operative VO$_2$peak (p=0.02).

Table 4. Comparison of parameters of cardiopulmonary test and echocardiography between 2 groups divided by pre-operative VO_2peak

	Pre-operative	VO_2peak	p-value
	≥19.0 mL/kg/min	<19.0 mL/kg/min	
Preoperative			
VO_2peak (mL/kg/min)	25.6±0.8	14.8±0.8	0.001
Exercise duration (sec)	648.5±38.8	297.9±23.5	<0.001
AT (%)	52.8±2.1	54.7±2.9	NS
LVD (diastole) (mm)	64.7±1.5	62.8±2.7	NS
LVD (systole) (mm)	43.4±1.6	41.9±2.7	NS
EF (%)	55.4±1.8	55.4±2.8	NS
Post-operative			
VO_2peak (mL/kg/min)	26.6±1.0	18.6±1.5	<0.001
Exercise duration (sec)	739.5±37.2	418.1±39.7	<0.001
AT (%)	55.2±1.7	60.3±2.3	NS
LVD (diastole) (mm)	50.7±1.1	50.7±1.8	NS
LVD (systole) (mm)	34.0±1.2	34.9±1.8	NS
EF (%)	55.4±1.6	56.1±2.8	NS

AT, anaerobic threshold; EF, ejection fraction; LVD, left ventricular dimension.

DISCUSSION

It is generally accepted that the cardiopulmonary exercise test can predict the patient's functional status[12]. However, there has been only limited study about the effects of cardiac surgery on exercise capacity[7-10]. Our study shows that cardiopulmonary exercise test parameters, especially VO_2peak and exercise durations, are highly correlated with the patient's NYHA class. VO_2peak and exercise durations improved in most patients in one year of valve surgery for significant MR and AR. Patients who had high VO_2peak values before their operation were categorized as a better post-operative NYHA class, even in those with NYHA class III. This means that the initial NYHA class is not enough to predict post-operative results in some patients. Because NYHA class is a subjective parameter, objective cardiopulmonary testing has an advantage for estimating the patient's status more accurately. Our results therefore suggest that the cardiopulmonary exercise test is an excellent modality to determine the point of operation, and that a pre-operative cut-off value of the VO_2peak of ≥19.0 mL/kg per min may be used to predict the better post-operative status in patients.

In one study carried out seven months after mitral valve surgery for severe chronic MR, although the patients' NYHA functional class improved, exercise performance parameters, such as VO_2peak and exercise duration, did not improve[13]. To explain this difference from our study, some points should be considered. The cardiopulmonary exercise test can be affected by many factors other than cardiac function, such as pulmonary and peripheral factors, skeletal muscle changes and alterations in blood flow distribution[14-17]. Improvement in these factors needs an adequate time of recovery to show significant changes in VO_2peak and exercise duration. Thus, seven months may be too short to reveal any change in a patient's exercise capacity. Because the patients in our study repeated their cardiopulmonary exercise tests one year after their operation, there may have been enough time to demonstrate improvements.

Although echocardiographic ejection fraction, end-systolic diameter and dP/dt are important parameters used to make a decision to perform cardiac surgery in patients with MR or AR[3-6, 18], such findings taken in the resting state do not always correlate with the patient's functional status. To reveal the exact functional status of patients, it is important to consider both the resting state of the patients and their exercise status[18-21]. The cardiopulmonary exercise test demonstrates integrated cardiopulmonary functional potential, so it has advantages to reflect the real functional status of patients[22-24].

In cases of left ventricular volume overload due to valvular regurgitation, patients with left ventricular systolic dysfunction have poorer prognosis after valvular operations[1, 2, 25], so it is reasonable to perform such operations before the dysfunction develops[26, 27]. However it is very difficult to predict the timing of left ventricular systolic dysfunction and the timing of the operation. In such a situation, it is thought that the cardiopulmonary exercise testing can be used to predict the timing of the operation. We found that patients who had lower pre-operative VO_2peak had poorer functional status than those with higher pre-operative VO_2peak when evaluated one year after surgery.

However, our study population was too small to calculate the exact cut-off value of VO_2peak, so a large prospective study would be needed to define the correct relationship between pre-operative VO_2peak and post-operative functional status. Another limitation is that we included both MR and AR in terms of left ventricular volume overload in spite of some differences in the hemodynamics of these two diseases[26]. In a further study, it is required to evaluate the effects of cardiopulmonary test in MR or AR alone. And the difference between operative methods of MR patients, such as mitral valve repair and mitral valve replacement, is an important parameter to affect the prognosis of post-operative prognosis, so it also should be considered in the next study.

CONCLUSION

Functional capacities, such as VO$_2$peak and exercise duration, are excellent parameters to evaluate the subjective functional class and estimate the post-operative functional class of the patients with MR and/or AR. We found that patients who had pre-operative VO$_2$peak of 19.0 mL/kg per min or greater showed better functional status one year after surgery. So, a large prospective trial will be necessary to determine an accurate cut-off value of the VO$_2$peak for adequate timing of surgery.

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