VENTILATORY ANAEROBIC THRESHOLD BEFORE AND AFTER CARDIAC VALVE SURGERY

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The purpose of this study was to objectively assess exercise tolerance before and after cardiac valve surgery by using an objectively determined ventilatory anaerobic threshold (AT). Nine patients (mean age: 38.2±8.1 years) with predominantly mitral regurgitant lesions were studied by a symptomatic maximal treadmill exercise test which included a determination of AT. The mean lengths of time from preoperative exercise testing to cardiac surgery, and from surgery to postoperative exercise testing were 5.9±4.0 and 12.1±8.3 months, respectively. The determination of AT on data plots was performed after blinding to patient identification and pre- vs postoperative status.

After surgery, the clinical symptoms and NYHA class improved significantly with a decrease in the cardio-thoracic ratio and echocardiographic diastolic dimensions. The mean peak VO$_2$ (ml/kg/min) increased significantly from 20.2±7.1 to 29.7±7.9 (p<0.01). Together with these changes, AT (ml/kg/min in VO$_2$) increased from a mean of 14.8±4.8 to 22.8±5.5 (p<0.01).

In conclusion, symptomatic improvement and an increase in peak oxygen uptake after cardiac valve surgery were accompanied by a significant increase in the objectively determined AT. AT determined in a blind manner provides an objective means of evaluating exercise tolerance when a double-blind intervention cannot be performed.

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THE ventilatory anaerobic threshold (AT) has been proposed as an objective index of exercise tolerance$^1,2$ because the end point in symptomatic maximal exercise is subjective. This signifies that the peak oxygen uptake at the end point is also subjective unless a definite plateau is observed. Recently, the application of exercise tolerance tests has been extended to the evaluation of drug efficacy for heart failure.$^3–6$ However, in many cases, the improvement in peak oxygen uptake or AT has been rather small and questions have been raised regarding the sensitivity of incremental maximal exercise tests and their related parameters, including AT, in detecting changes in exercise tolerance?

Against this background, it seems pertinent to test the sensitivity of an incremental exercise test which includes an evaluation of AT in a population in which one of the greatest symptomatic improvements in cardiac therapy has been observed, i.e., in patients who have undergone cardiac valve surgery without irreversible cardiac muscle damage.$^8–10$ In this case, however, the

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physician who is administering the exercise test cannot be blind regarding the patient’s pre- or postoperative status. Accordingly, the peak oxygen uptake and exercise duration determined by such a test may be to some degree subjectively biased. Therefore, in this study, the actual procedure of determining AT from respiratory plots was carried out in a blind manner. To date, studies of exercise tolerance comparing pre- and post-cardiac valve surgery have not been conducted in this way.11–13

SUBJECTS AND METHODS

Study patients

Nine patients (6 males and 3 females) who underwent successful valve surgery were studied. Selection for inclusion in this report was based on the availability of a symptomatic maximal exercise test before and after cardiac surgery which included VO₂ measurement. The mean age was 38.2 ± 8.1 years (range; 30–54). The underlying valvular lesions of each patient are summarized in Table 1. The lesions were mainly mitral and regurgitant in nature with varying degrees of stenosis. The mean value of the pre-operative NYHA functional class was 2.6 ± 0.5. Preoperatively, atrial fibrillation was present in six patients and sinus rhythm was present in the remaining three. The basic rhythm did not change postoperatively. Preoperatively, eight patients were on digoxin and furosemide, and one was on digoxin only. Postoperatively, digoxin was administered to all patients at the same dosage Furosemide was also administered but at a reduced dosage.

Exercise testing

Symptomatic maximal treadmill exercise testing was performed using a 3-minute incremental protocol (either Bruce or modified Bruce). Before maximal exercise testing, one or two submaximal tests were performed. The exercise testing was requested by the attending physician for pre- and postoperative evaluation of exercise tolerance. The mean duration from the preoperative exercise testing to the cardiac surgery was 5.9 ± 4.0 months (range; 1–12 months). The mean duration from the cardiac surgery to the postoperative exercise testing was 12.1 ± 8.3 months (range; 4–24 months). All of the patients had either returned to work or were performing housework at the time of postoperative exercise testing. No particular postoperative rehabilitation or training program was employed.

Oxygen uptake was measured with an Oxylóg (Morgan) every minute in the first 4 patients and with an Autoaerobics R 1500S (Anima, Japan) every 30 sec in the remaining 5 patients (neither of these instruments was a breath-by-breath apparatus). Each

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**TABLE I CLINICAL DETAILS OF 9 PATIENTS**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Op.</th>
<th>Rhythm</th>
<th>CTR</th>
<th>NYHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>30</td>
<td>MR</td>
<td>MVR</td>
<td>AF</td>
<td>71</td>
<td>III</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>36</td>
<td>ASR, MSR, TR</td>
<td>AVR, MVR, TVR</td>
<td>AF</td>
<td>72</td>
<td>III</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>32</td>
<td>MR</td>
<td>MVR, AVR</td>
<td>AF</td>
<td>62</td>
<td>II–III</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>54</td>
<td>MS, AR</td>
<td>OMC, ARC</td>
<td>AF</td>
<td>52</td>
<td>III</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>40</td>
<td>AR</td>
<td>AVR</td>
<td>S</td>
<td>55</td>
<td>II</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>34</td>
<td>MR (MVP)</td>
<td>MRC</td>
<td>S</td>
<td>61</td>
<td>II</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>36</td>
<td>MR</td>
<td>MVR</td>
<td>AF</td>
<td>77</td>
<td>II</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>33</td>
<td>AR, MS</td>
<td>AVR, OMC</td>
<td>S</td>
<td>64</td>
<td>II–III</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>49</td>
<td>MR</td>
<td>MVR</td>
<td>AF</td>
<td>62</td>
<td>III</td>
</tr>
</tbody>
</table>

Op.=operation; CTR=cardio-thoracic ratio; NYHA=NYHA functional class; AF=atrial fibrillation; S=sinus rhythm; MR=mitral regurgitation; MS=mitral stenosis; MSR=mitral stenosis and regurgitation; AR=aortic regurgitation; ASR=aortic stenosis and regurgitation MVP=mitral valve prolapse; TR=tricuspid regurgitation MVR=mitral valve replacement; AVR=aortic valve replacement; TVR=tricuspid valve replacement; OMC=open mitral commissurotomy; MRC=mitral valve reconstruction. ARC=aortic valve reconstruction
Fig. 1. An example of VE vs VO₂ (top) and VCO₂ vs VO₂ (bottom) plots before and after cardiac valve surgery (patient no. 7). The initial portions of the plots (marked by ←→) were omitted from the analysis (see Methods). Marked increases in AT and VO₂ were observed after surgery.

patient used the same instrument before and after surgery. There were no significant differences between the VO₂ or VE of these 2 instruments in experiments in which normal subjects exercised with them connected in tandem. Correlation coefficients (r) for VO₂ and VE measurements between these two instruments were 0.993 and 0.999, respectively. The exertion perceived by the patient was scaled into 5 grades (1: very light, 2: light, 3: moderate, 4: strong, 5: very strong). The percentage of the predicted peak VO₂ for a given patient’s age and sex was calculated from the mean values of peak VO₂ in normal Japanese men and women. The main symptom at the endpoint of exercise was either shortness of breath or leg fatigue. None of the patients stopped exercise because of chest pain or arrhythmia. AT was determined from plots of VE vs VO₂ and/or VCO₂ vs VO₂. The increase in VE and VCO₂ was delayed when compared to the increase in VO₂ in the initial portions of the plots, which represented the resting and very early exercise changes. This initial “hump” was usually readily observed.
| TABLE II  CHANGES IN CLINICAL AND EXERCISE VARIABLES |
|---|---|---|---|
| n | Preop | Postop | p |
| Weight (Kg) | 9 | 52.9±8.9 | 55.1±9.6 | NS |
| NYHA | 9 | 2.6±0.5 | 1.5±0.5 | <0.001 |
| CTR (%) | 9 | 66.0±7.6 | 57.9±5.3 | <0.05 |
| LVDD (mm) | 8 | 70.9±15.9 | 51.6±6.1 | <0.01 |
| LVDs (mm) | 8 | 49.9±10.8 | 38.5±7.5 | <0.01 |
| FS (%) | 8 | 28.0±7.4 | 25.9±6.7 | NS |
| LAD | 8 | 58.1±14.9 | 46.3±12.6 | <0.01 |
| peak VO₂ (ml/Kg/min) | 9 | 20.2±7.1 | 29.7±7.9 | <0.01 |
| (ml/min) | 9 | 1071±428 | 1670±620 | <0.01 |
| % of predicted VO₂ (%) | 9 | 47.6±23.3 | 78.3±17.3 | <0.01 |
| AT (ml/Kg/min VO₂) | 8 | 14.8±4.8 | 22.6±6.0 | <0.01 |
| (ml/min VO₂) | 8 | 785±286 | 1282±492 | <0.01 |
| relative AT (%) | 8 | 76.6±7.4 | 80.4±6.7 | NS |
| peak HR (beats/min) | 8 | 171±25 | 162±19 | NS |
| peak syst. BP (mmHg) | 8 | 152±31 | 163±26 | NS |

NYHA = NYHA functional class; CTR = cardio-thoracic ratio; LVDD = left ventricular diastolic dimension; LVDs = left ventricular systolic dimension; FS = fractional shortening; LAD = left atrial dimension; HR = heart rate; syst. BP = systolic blood pressure

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Fig. 2. Changes in peak VO₂ (left) and AT (right) from preoperative to postoperative periods.

*marked by ← in Fig. 1*. This portion of the plot was not analyzed in the determination of AT. A similar procedure to eliminate the initial data has been used by Beaver et al. After omitting this early data, a linear increase in VE and VCO₂ was assumed, and the departure point from linearity was taken as AT. The co-plots of VE vs VO₂ and VCO₂ vs VO₂ for each patient before and after surgery were randomly numbered for the blind reading of AT. Pre- and postoperative data for the same patient were not

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paired. AT was then determined by one of the investigators, who was therefore unaware of the patient's identity or operative status. In two of the plot, which belonged to the same patient, AT could not be determined.

M-mode echocardiography was performed with an SSD810 (Aloka, Japan) in 8 patients. Left ventricular diastolic (LVDd) and end-systolic diameters (LVDs) in the short axis were measured and fractional shortening (FS) was calculated from these values.

Statistical analysis
All data are expressed as the mean ± SD. A paired t-test was used to compare the values before and after cardiac surgery. A probability value of < 0.05 was considered to be statistically significant.

RESULTS
Clinical and echocardiographic data (Table II)
All of the patients exhibited a marked subjective improvement in symptoms after surgery. The NYHA functional class improved from a mean of 2.6 ± 0.5 before surgery to a mean of 1.5 ± 0.5 after surgery (p < 0.001). The cardio-thoracic ratio (CTR) decreased from 66.0 ± 7.6% to 57.9 ± 5.3% (p < 0.05). LVDD, LVDs and left atrial diameter measured by echocardiography significantly decreased after surgery. Fractional shortening did not change significantly. Overall, the mean change in body weight was not statistically significant (from 52.9 ± 8.9 Kg to 55.1 ± 9.6 Kg).

Exercise testing
The mean peak VO2 (ml/Kg/min) increased from 20.2 ± 7.1 pre-operatively to 29.7 ± 7.9 post-operatively (p < 0.01, Fig.2(a)). The mean AT (ml/Kg/min) increased from 14.8 ± 4.8 to 22.8 ± 5.5 (n = 8; p < 0.001, Fig.2(b)). AT as a percentage of peak VO2 (relative AT, %) did not change significantly (from 76.6 ± 7.4 to 80.4 ± 6.7, NS). As a result, there was a significant correlation between the percentage increase in AT and peak VO2 (r = 0.78, p < 0.05). The mean level of perceived exertion at the point of peak exercise did not significantly differ between the pre- and postoperative periods (4.6 ± 0.5 vs 4.8 ± 0.3, NS). The peak heart rate and systolic blood pressure did not change significantly from the preoperative to the postoperative period.

Correlations between the improvement in peak VO2 after surgery and various preoperative clinical, echocardiographic and exercise variables were assessed. By simple correlation, only the peak VO2 and the percentage of predicted VO2 before surgery were significantly correlated with the percentage increase in peak VO2 (r = -0.672 and r = -0.79, respectively; p < 0.05); the greater increase was observed in patients who had a greater base-line functional disability. Neither the increase in peak VO2 nor that in AT was related to the length of time from surgery to postoperative exercise testing. Changes in body weight were not significantly related to the increases in peak VO2 or AT.

DISCUSSION
A marked improvement in exercise capacity as determined by NYHA functional class, has been reported in symptomatic patients with valvular heart disease who underwent successful valve replacement or reconstruction before the onset of irreversible cardiac muscle damage8–10 However, the NYHA functional class has been criticized for not being objective. A more objective means of evaluating exercise capacity would be multistage exercise testing, but there has been a paucity of studies of maximal exercise testing which include a determination of maximal oxygen uptake before and after valve surgery11–13 Therefore, the magnitude of the improvement in exercise capacity in quantitative terms, such as peak VO2 or MET, has not been well delineated. Furthermore, to confound the issue, the end point in symptomatic maximal exercise is subjectively determined by the patient, as well as by the physician who supervises the test. This may invalidate a treatment-induced change in peak VO2 or exercise duration unless the treatment be administered in a double blind manner. Blinded studies, however, are not possible in valve surgery. One way of circumventing this problem is to use the ventilatory anaerobic threshold, which usually appears at about

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60% of peak VO₂, and is determined objectively independent of the peak effort. This method has worked well for us and others in classifying patients according to exercise capacity and in validating the peak effort (which must be preceded by AT). However, there may be a problem when evaluating a change induced by treatment, particularly when the magnitude of the change in AT is small, i.e., usually less than 3 ml/kg/min VO₂ in drug trials for chronic congestive heart failure, or when AT can only be determined with difficulty (i.e., with a certain margin of error rather than as a discrete point). Under these circumstances, valid evaluation of the treatment is difficult to obtain, unless the process of AT determination from the plots can be performed blindly. This has been accomplished in an exercise training study involving cardiac patients, where the treatment (exercise training) could not be administered in a double blind manner. Therefore, in this study, we have objectively determined the magnitude of quantitative changes in exercise capacity after cardiac surgery. AT increased by an average of 8 ml/kg/min during the postoperative period. The increase in AT and peak VO₂ observed in our study is one of the largest induced by any intervention reported in the literature. This was reflected by an equally marked symptomatic improvement experienced by the patients. As a result, the predicted functional capacity of the patients, adjusted for age and sex, increased from an average of 48% preoperatively to 78% postoperatively. However, AT as a percentage of peak VO₂ (relative AT) did not change significantly after surgery. Although an increase in AT can theoretically be disproportionately greater than that of peak VO₂, in most of the drug trials, and even in an exercise training study, relative AT did not change because the absolute values of both AT and peak VO₂ increased proportionally. The calculated relative AT in this study was rather high, (77% preoperatively and 80% postoperatively), although it varied among patients. This was probably due to the fact this study was rather small-scale and in addition included patients who terminated the exercise test just beyond AT.

A limitation of this study is the wide variability in the length of time from cardiac surgery to postoperative exercise testing. Cardiac, as well as peripheral (vascular and metabolic), training effects are known to be important determinants of exercise tolerance in both normal and cardiac subjects. In this study, however, there was no correlation between the change in peak VO₂ or AT and the length of time from surgery to postoperative exercise testing. Both peak VO₂ and AT may be increased by cardiac as well as peripheral effects. The relative contribution of each factor, however, cannot be determined from this study. Relatively long durations between the valve operation and the post-operative exercise testing in some cases may make the interpretation of changes in exercise capacity difficult. However, without valvular surgery, exercise capacity is expected to decrease over time in patients with significant valvular lesions. Therefore, we concluded that the marked improvement in exercise capacity observed in this study was primarily due to the effect of valve surgery on cardiac function and the training effect which took place based on this improved cardiac function.

Another criticism may be that this was not a prospective study and that the decision to perform exercise testing was left to the attending physicians. Certainly there may have been bias concerning the selection of patients for exercise testing. Nevertheless, the significant decrease in exercise capacity with general preservation of left ventricular function preoperatively in our group of patients, we believe, provided ideal conditions for the large increase in exercise capacity observed after valve surgery.

Although there was no significant change in the average body weight between the pre- and postoperative periods, the range of the changes was relatively large (from -7 to +8 Kg). Changes in the muscle mass are expected after major cardiac surgery, and muscle mass has been proposed as one of the major factors which determine exercise capacity. In this study, however, no significant correlation was observed between changes in body weight and changes in peak VO₂ or AT. Ideally, this issue must be assessed in reference to lean body mass, which was not measured in this study.

Several earlier studies have examined exercise tolerance before and after cardiac
valve surgery, and a few have determined AT. In none of these studies, however, has AT been determined in a blind manner.

In conclusion, a significant increase in exercise capacity was observed after cardiac valve surgery in association with an improvement in the patients' symptoms. This was validated by AT, which was determined in a blind manner.

REFERENCES


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