Relationship between exercise tolerance and muscle strength following cardiac rehabilitation: Comparison of patients after cardiac surgery and patients with myocardial infarction

Takahiro Sumide (MS)\textsuperscript{a,∗}, Kazunori Shimada (MD, FJCC)\textsuperscript{a, b}, Hirotoshi Ohmura (MD)\textsuperscript{b}, Tomo Onishi (MS)\textsuperscript{a}, Kazunobu Kawakami (MS)\textsuperscript{a}, Yoshiyuki Masaki (MD)\textsuperscript{b}, Kosuke Fukao (MD)\textsuperscript{b}, Miho Nishitani (MD)\textsuperscript{b}, Atsumi Kume (MD)\textsuperscript{b}, Hiroyuki Sato (MD)\textsuperscript{a, c}, Satoshi Sunayama (MD)\textsuperscript{b}, Sachio Kawai (MD, FJCC)\textsuperscript{a, b}, Akie Shimada (MD)\textsuperscript{d}, Taira Yamamoto (MD)\textsuperscript{d}, Keita Kikuchi (MD)\textsuperscript{d}, Atsushi Amano (MD, FJCC)\textsuperscript{d}, Hiroyuki Daida (MD, FJCC)\textsuperscript{b}

\textsuperscript{a} Juntendo Sports Clinic, Juntendo University Hospital, 3-1-3 Hongo, Bunkyo-ku, Tokyo 113-8431, Japan
\textsuperscript{b} Department of Cardiovascular Medicine, Juntendo University School of Medicine, Tokyo, Japan
\textsuperscript{c} Department of General Medicine, Juntendo University School of Medicine, Tokyo, Japan
\textsuperscript{d} Department of Cardiovascular Surgery, Juntendo University School of Medicine, Tokyo, Japan

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Summary

Background and purpose: Previous studies have demonstrated that cardiac rehabilitation (CR) improves exercise tolerance and muscle strength in patients with myocardial infarction (MI) and in patients after cardiac surgery. However, the association between exercise tolerance and muscular strength following CR and the comparison of relationships among various disease categories has not been fully examined. The purpose of the present study was to assess the relationship between exercise tolerance and muscle strength following CR in patients after cardiac surgery and patients with MI.

Methods and results: One hundred and four patients who participated in CR for 6 months were enrolled [post-cardiac valve surgery (VALVE), \textit{n} = 28; post-coronary artery bypass grafting (CABG), \textit{n} = 42; post-acute MI, \textit{n} = 34]. The exercise tolerance, thigh/calf circumferences, and muscle strength were measured before and after CR. At the baseline, the thigh circumference was significantly smaller in the VALVE...
group than in the MI group. There were significant positive correlations between peak VO₂ and muscle torques of the lower muscles in all groups. After 6 months, peak VO₂ and muscle torque were significantly increased in all groups (p < 0.001). A positive significant correlation between percent increases in peak VO₂ and muscular strength was observed in the VALVE group (r = 0.51, p < 0.01), but not in the other groups. In addition, the changes in peak VO₂ and calf circumference after CR were significantly higher in the VALVE group than in the MI group.

Conclusions: These data suggest that exercise intolerance in patients after heart valve surgery may in part depend on decreased muscular strength. Further studies are needed to assess whether the strategy of increasing muscular strength of lower limb by programmed resistance training could be effective for improving exercise intolerance in patients after heart valve surgery and symptomatic patients with heart failure.

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Introduction

Cardiac rehabilitation (CR) has been applied to patients receiving open-heart surgeries such as cardiac valvular surgery and coronary artery bypass grafting (CABG), and patients with ischemic heart disease following myocardial infarction (MI). It has been clearly established that CR reduces mortality and morbidity in patients with chronic heart failure [1,2].

Physical deconditioning is frequently observed in patients after cardiac surgery and in patients with MI [3,4]. These patients often have skeletal muscle abnormalities including demand-perfusion mismatch, muscle atrophy, shifts in the muscle fiber type, and metabolic dysfunction [5]. Indeed, skeletal muscle strength is closely correlated with exercise tolerance, in patients with chronic heart failure [6]. Previous studies have clearly demonstrated that CR improves exercise tolerance and muscle strength in patients with MI and in patients after cardiac surgery. However, the association between exercise tolerance and muscular strength following CR and the comparison of relationships among various disease categories has not been fully examined. The purpose of the present study was to assess the relationship between exercise tolerance and muscle strength before and after CR in patients who had cardiac valve surgery, CABG, or acute MI.

Methods

Patients

One hundred and four patients who participated in CR for 6 months at Juntendo University Hospital between February 2002 and April 2005 were enrolled. They were divided into three groups: patients after valve surgery (VALVE) (n = 28), after CABG (n = 42), and with acute MI (n = 34). Preoperative diagnoses in the VALVE group were as follows: six patients with aortic stenosis, nine with aortic regurgitation, 11 with mitral regurgitation, and two with aortic and mitral regurgitation. Ten patients were in New York Heart Association functional classification I, 15 patients were in class II, and three patients were in class III. Written informed consent was obtained from each patient before participation. This study was approved by the Ethical Committee of Juntendo University Hospital.

Study protocol

All patients performed a symptom-limited cardiopulmonary exercise test using an electronically braked upright ergometer (Corival 400, Lode B.V., Groningen, Netherlands). After a period of resting, warm-up was performed for a few minutes at 20 W, followed by ramp loading (15 W/min) until patients felt fatigued. Heart rate and rhythm were monitored continuously by a 12-lead electrocardiographic system (Marquette CASE 8000, GE Healthcare Bio-Sciences Corp., Piscataway, NJ, USA), and blood pressure was assessed every minute throughout the test. The respiratory gas exchange was measured by the breath-by-breath method using a gas analyzer system (Vmax-29S, SensorMedics Co., Yorba Linda, CA, USA). Oxygen uptake (VO₂), carbon dioxide production (VCO₂), minute ventilation, and the respiratory exchange ratio were measured. Peak VO₂ was determined as highest VO₂ achieved during exercise. The anaerobic threshold was measured by the V-slope method. To measure the isokinetic muscle strength of the quadriceps and hamstrings, we used the Cybex-770
isokinetic dynamometer (Lumex Co., Ronkonkoma, NY, USA), as we described previously [7—9]. Patients were tested in a seated position with hip flexion. Stabilization straps were applied to the trunk, waist, and thigh. The range of motion during testing was set between 0° and 90° of knee flexion. All patients performed three consecutive repetitions of knee extension and flexion movements at an angular velocity of 60° per second. The highest value was regarded as the peak torque. The peak torques of the knee extensor and flexor muscles were adjusted by body weight according to the following formula: strength (Nm) × 100/body weight (kg), since it is well known that the peak muscle power is closely associated with body weight [10]. The circumferences of thigh and calf were also measured. These measurements were performed after surgery or acute MI onset (from 4 to 11 days) and 6 months after rehabilitation in the same manner.

Exercise session

Supervised exercise training, which was composed of warm-up, aerobic exercise, resistance training, and cool-down sessions, was performed once or twice a week for 6 months, as we described previously [7—9]. In brief, warm-up and cool-down sessions consisted of 12 types of stretching. Aerobic exercise, including a treadmill, cycle ergometer, and walking on in-room tracks, was prescribed on the basis of heart rate at the anaerobic threshold (maximum of 20 min/each). The total aerobic exercise time was approximately 60 min. Resistance training consisted of four types of training (sit-ups, diagonal arm and leg lifts, squats, and push-ups) using the patients’ own weight. Resistance training was gradually added to the exercise program at least a month after the beginning of participation. In addition to the supervised exercise, patients were encouraged to perform home-based aerobic exercise, more than 20 min at 11—13 of rating perceived exertion on the Borg scale twice a week.

Statistical analysis

The mean ± SD was calculated for all continuum values. The paired t-test was used to compare the data within each group before and after exercise training. For two and three group comparisons, the significance levels were calculated by an unpaired t-test and a one-way analysis of variance followed by Scheffe’s test, respectively. Linear regression analysis was used to determine the correlations between changes in peak˙VO2 and muscle torque. p < 0.05 was defined as significant.

Results

Baseline characteristics

At the baseline, the body mass index was significantly lower in the VALVE group than the CABG and MI groups (CABG: 23.3 ± 2.8 kg/m², MI: 24.0 ± 2.6 kg/m², VALVE: 21.6 ± 2.6 kg/m²; CABG vs. VALVE, p < 0.05; MI vs. VALVE, p < 0.05) (Table 1). The prevalence of dyslipidemia (CABG: 67%; MI: 53%; VALVE: 14%; CABG vs. VALVE, p < 0.01; MI vs. VALVE, p < 0.01) and that of diabetes (CABG: 50%, MI: 38%, VALVE: 7%; CABG vs. VALVE, p < 0.01; MI vs. VALVE, p < 0.01) were significantly higher in the CABG and MI groups than in the VALVE group. There were no significant differences in the number of supervised training sessions in each group (VALVE: 28.0 ± 12.3; CABG: 30.4 ± 12.6; and MI: 26.4 ± 13.7 sessions).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics.</th>
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<tbody>
<tr>
<td></td>
<td>VALVE</td>
</tr>
<tr>
<td>N</td>
<td>28</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>22/6</td>
</tr>
<tr>
<td>Age (year)</td>
<td>56 ±13</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>21.6 ±2.6</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>13 (46)</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>4 (14)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>57.3 ±17.5</td>
</tr>
</tbody>
</table>

Values are expressed mean ± SD. Examination of statistical significance was followed by Scheffe test or chi-square test. VALVE, cardiac valve surgery group; CABG, coronary artery bypass grafting group; MI, acute myocardial infarction group.

* p < 0.05 denotes statistically significant difference from the value of VALVE.

** p < 0.01 denotes statistically significant difference from the value of VALVE.
Table 2  Effects of cardiac rehabilitation for 6 months among three groups.

<table>
<thead>
<tr>
<th></th>
<th>VALVE Before</th>
<th>VALVE After</th>
<th>CABG Before</th>
<th>CABG After</th>
<th>MI Before</th>
<th>MI After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak VO₂ (ml kg⁻¹ min⁻¹)</td>
<td>15.7 ± 5.5</td>
<td>24.0 ± 7.2²</td>
<td>15.1 ± 3.7¹</td>
<td>21.7 ± 5.7³</td>
<td>18.5 ± 5.1</td>
<td>23.8 ± 6.1³</td>
</tr>
<tr>
<td>ΔPeak VO₂ (%)</td>
<td>58.2 ± 45.3¹</td>
<td>46.9 ± 33.3</td>
<td>12.5 ± 3.2³</td>
<td>11.0 ± 3.0</td>
<td>14.7 ± 3.3³</td>
<td></td>
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<tr>
<td>ΔAT (ml kg⁻¹ min⁻¹)</td>
<td>10.0 ± 2.2</td>
<td>14.1 ± 3.7²</td>
<td>9.2 ± 2.0¹</td>
<td>11.0 ± 3.0</td>
<td>14.7 ± 3.3³</td>
<td></td>
</tr>
<tr>
<td>ΔAT (%)</td>
<td>41.1 ± 34.3</td>
<td>42.8 ± 55.6</td>
<td>12.5 ± 3.2³</td>
<td>11.0 ± 3.0</td>
<td>14.7 ± 3.3³</td>
<td></td>
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<tr>
<td>Peak RER</td>
<td>1.13 ± 0.13</td>
<td>1.16 ± 0.07</td>
<td>1.09 ± 0.11</td>
<td>1.17 ± 0.07³</td>
<td>1.14 ± 0.08</td>
<td>1.16 ± 0.07²</td>
</tr>
<tr>
<td>Knee Ex (Nm × 100/BW)</td>
<td>170.1 ± 61.4</td>
<td>195.1 ± 58.5³</td>
<td>161.0 ± 48.4</td>
<td>189.1 ± 53.5³</td>
<td>174.3 ± 54.6</td>
<td>189.5 ± 56.1³</td>
</tr>
<tr>
<td>ΔKnee Ex (%)</td>
<td>19.5 ± 22.4</td>
<td>20.9 ± 27.5</td>
<td>11.0 ± 17.3</td>
<td>10.9 ± 17.3</td>
<td></td>
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<tr>
<td>Knee Flex (Nm × 100/BW)</td>
<td>97.3 ± 31.2</td>
<td>116.7 ± 34.6³</td>
<td>92.3 ± 28.7</td>
<td>114.6 ± 30.9³</td>
<td>101.1 ± 30.7</td>
<td>113.0 ± 32.6³</td>
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<tr>
<td>ΔKnee Flex (%)</td>
<td>26.4 ± 35.5</td>
<td>29.9 ± 34.0</td>
<td>14.1 ± 19.3</td>
<td>14.1 ± 19.3</td>
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<tr>
<td>Thigh circumference (cm)</td>
<td>47.5 ± 4.2¹</td>
<td>49.2 ± 4.3³</td>
<td>48.4 ± 3.9³</td>
<td>49.8 ± 4.3³</td>
<td>50.7 ± 3.9³</td>
<td>51.2 ± 4.9³</td>
</tr>
<tr>
<td>ΔThigh circumference (%)</td>
<td>3.5 ± 4.3</td>
<td>2.9 ± 5.3</td>
<td>1.2 ± 9.0</td>
<td>1.2 ± 9.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calf circumference (cm)</td>
<td>33.5 ± 3.2</td>
<td>35.7 ± 3.0³</td>
<td>34.5 ± 2.9³</td>
<td>35.5 ± 2.7³</td>
<td>35.3 ± 2.9³</td>
<td>35.2 ± 4.4³</td>
</tr>
<tr>
<td>ΔCalf circumference (%)</td>
<td>6.8 ± 8.0²</td>
<td>2.9 ± 2.7</td>
<td>-0.1 ± 11.1</td>
<td>-0.1 ± 11.1</td>
<td></td>
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</tbody>
</table>

Values are expressed mean ± SD. Examination of statistical significance was followed by paired t-test. VALVE, cardiac valve surgery group; CABG, coronary artery bypass grafting group; MI, acute myocardial infarction group; peak VO₂, peak oxygen consumption; AT, anaerobic threshold; RER, respiratory exchange ratio; Ex, extensor torque; Flex, flexor torque; BW, body weight.

² Denotes statistically significant difference from initial value within group (p < 0.001).

¹ Denotes statistically significant difference from the value of MI (p < 0.01).
Exercise tolerance and muscle strength

At the baseline, the peak $\dot{V}O_2$ (15.1 ± 3.7 ml kg$^{-1}$ min$^{-1}$) vs. 18.5 ± 5.1 ml kg$^{-1}$ min$^{-1}$, $p < 0.01$) and AT (9.2 ± 2.0 ml kg$^{-1}$ min$^{-1}$ vs. 11.0 ± 3.0 ml kg$^{-1}$ min$^{-1}$, $p < 0.01$) in the CABG group were significantly lower than those in the MI group (Table 2). After 6 months, the peak $\dot{V}O_2$, AT, and peak lower limb torques significantly increased in all groups (all $p < 0.01$). There were no differences in the peak $\dot{V}O_2$, AT, or peak torques of the knee extensor/flexor muscles among the three groups after CR. The value of the peak respiratory exchange ratio was similar in the three groups before and after CR. Most patients stopped exercise testing due to leg fatigue and few patients were terminated due to myocardial ischemia (CABG, $n = 1$; MI, $n = 1$) before CR. The reason for stopping exercise was similar after 6 months (leg fatigue, $n = 102$; ischemia, $n = 2$).

Correlations among peak $\dot{V}O_2$, peak torque, and thigh/calf circumferences

At the baseline, significant positive correlations between the peak $\dot{V}O_2$ and knee extensor torque were observed in all groups (VALVE: $r = 0.70$, $p < 0.001$; CABG: $r = 0.45$, $p < 0.01$; and MI: $r = 0.35$, $p < 0.05$) (Fig. 1). There were positive correlations between the peak $\dot{V}O_2$ and knee flexor torque in the CABG and VALVE groups, but not in the MI group (VALVE: $r = 0.41$, $p < 0.05$; CABG: $r = 0.32$, $p < 0.05$; and MI: $r = 0.21$, $p = NS$). There were positive correlations between the knee extensor torques and thigh circumferences in the CABG and VALVE groups, but not in the MI group (VALVE: $r = 0.46$, $p < 0.05$; CABG: $r = 0.37$, $p < 0.05$; and MI: $r = 0.25$, $p = NS$). There were positive cor-
Correlations between changes of peak $\dot{V}O_2$ and peak knee torques before and after cardiac rehabilitation in each group. VALVE, cardiac valve surgery group; CABG, coronary artery bypass grafting group; MI, acute myocardial infarction group; Ex, knee extensor torque; Flex, knee flexor torque.

The percent changes of peak $\dot{V}O_2$ were significantly correlated with those of knee extensor and knee flexor torques in the VALVE group (Ex: $r=0.43$, $p<0.05$; Flex: $r=0.51$, $p<0.01$) (Fig. 2). However, no correlation between the percent changes of peak $\dot{V}O_2$ and those of extensor or flexor torques was observed in the CABG or MI groups (CABG: Ex $r=0.004$, Flex $r=0.02$, and MI: Ex $r=0.004$, Flex $r=0.28$, all $p=NS$). No significant correlation between the percent changes of thigh/calf circumferences and those of exercise capacity was observed in all groups.

Discussion

The present study demonstrated the following major findings: (1) the combined aerobic and resistance training for 6 months significantly increased exercise tolerance and lower limb muscle strength in all groups; (2) the circumferences of the thigh and calf significantly increased in the VALVE and CABG groups; and (3) the improvement in exercise tolerance was significantly correlated with the changes in lower limb muscle strength in the VALVE group, but not in the CABG nor MI group. To the best of our knowledge, this is the first report demonstrating the effect of CR with respect to exercise tolerance, thigh/calf circumferences, and muscle strength in patients after cardiac valve surgery, patients after CABG, and patients with acute MI, simultaneously.

It has been clearly established that exercise tolerance measured by oxygen consumption, is a good predictor of prognosis in patients with cardiovascular diseases [2,11]. In addition, muscular strength is also associated with all-cause mortality [12,13]. Muscular strength is one of the determinants of exercise tolerance; however, there are few published data regarding these correlations before and after CR. In the present study, the supervised CR with home-based exercise significantly increased exercise tolerance and lower limb muscle strength without a serious incident during the entire training period. As is widely accepted, these results suggest that hospital-based CR in patients with cardiac disease is safe and can be beneficial [1–3,5–9].
In the present study, the improvement in exercise tolerance was significantly correlated with the changes in lower leg muscle strength only in the VALVE group. It has been demonstrated that patients who received heart valve surgery and patients with congestive heart failure have several disorders, including a disrupted central cardiac function, peripheral maladaptations such as an abnormal skeletal muscle morphology and metabolism, increased oxidative stress, and an inappropriate neurohumoral axis [5,12,14]. Volterrani et al. demonstrated that the muscle strength of the quadriceps and the cross-sectional area of the thigh were correlated with the peak VO₂ in patients with chronic heart failure [15]. In the present study, the circumference of the calf was larger than in the MI group (Table 2). Moreover, the change in circumference of the calf was larger than in the MI group. These data might support the reason why the improvement in exercise tolerance was significantly correlated with changes in muscle strength in the VALVE group. The lower limb circumference may be a good marker of physical deconditioning in patients after open-heart surgery and patients with acute MI. The circumference of lower leg includes not only the muscle diameter, but also the thickness of soft tissue, such as subcutaneous fat. In the present study, there were significant positive correlations between the circumference of thigh/calf and lean body mass (LBM) at baseline (data not shown). The LBMs in the VALVE and the CABG groups, but not the MI group, significantly increased after 6 months, as well as the circumferences of thigh and calf. In addition, the percent changes of the circumference of thigh and calf were significantly correlated with the percent change of LBM (data not shown). Therefore, we believe that the circumference in thigh and calf may reflect, at least in part, muscle volume. In general, the duration of deconditioning is much longer in patients with valvular disease than other patients, such as those with acute MI. The mean duration from the diagnosis or onset of clinical symptoms to operation in the VALVE group was 4.7 years. We speculate that the deconditioning of the skeletal muscle structure and metabolism was ameliorated by CR, resulting in improved exercise tolerance, especially in the VALVE group. Further prospective investigations are needed to clarify these points.

Resistance training has been recently recommended in CR for not only patients with atherosclerotic diseases, but also patients with chronic heart failure [12,16]. Indeed, dynamic moderate-load resistance training, such as that found in our exercise program, has been established as a safe and effective mode of exercise in CR [16—19]. Hare et al. reported that resistance training resulted in increased muscle strength and endurance, whereas the peak VO₂ did not increase [16]. Numerous studies have shown that aerobic training improves exercise tolerance and muscle strength in patients following open-heart surgery and patients with MI [20—24]. However, the peak VO₂ increased by less than 25% after exercise training, especially in patients who had undergone cardiac valvular surgery [25,26]. In contrast, improvement of the peak VO₂ was approximately 50% in the VALVE group after CR with combined aerobic and resistance training in the present study. The obvious amelioration might have been derived from the combination of aerobic and resistance training rather than from aerobic or resistance training alone. Marzolini et al. demonstrated that combined aerobic and resistance training elicited more marked changes in physiological adaptations such as muscular strength and endurance, and body composition compared to aerobic training alone in patients with coronary artery disease [27]. We believe that an increased lower limb muscle strength might be an effective strategy for improving exercise tolerance in patients after cardiac valve surgery and patients with chronic heart failure.

There are several limitations in this study. First, we cannot conclude that the improvement in exercise tolerance and muscle strength was only caused by CR because patients in both VALVE and CABG groups underwent open-heart surgery. However, as mentioned above, the improvement in exercise tolerance was clearly greater than in previous reports [25,26]. We therefore believe that CR improves exercise tolerance through the amelioration of peripheral deconditioning in patients after cardiac valvular surgery. Another limitation is that we obtained data regarding neither central function nor peripheral effects, such as muscular structure and metabolism, endothelial function, oxidative markers, nor neurohumoral factors. There are no data regarding pre-surgical state or home-based exercise volume in each group. We need to clarify the precise mechanism of improvement for CR and assess the effects of home-based exercise in the next step. Finally, the present investigation was a single center study with a small sample size. Further randomized investigations involving more subjects and institutions are required to confirm our findings.

In conclusion, exercise intolerance in patients after heart valve surgery may in part depend on decreased muscular strength. Further studies are
needed to assess whether the strategy of increasing muscular strength of lower limb by programmed resistance training could be effective for improving exercise intolerance in patients after heart valve surgery and symptomatic patients with heart failure.

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