Improved Exercise Capacity After Cardiac Rehabilitation Is Associated with Reduced Visceral Fat in Patients with Chronic Heart Failure

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Summary

Participation in a comprehensive cardiac rehabilitation (CR) program has been shown to reduce mortality and improve exercise capacity and symptoms in patients with chronic heart failure (CHF). Reduced exercise capacity leads to a concomitant reduction of skeletal muscle mass and accumulation of body fat. However, it is currently unknown whether CR reduces visceral adipose tissue (VAT) and/or subcutaneous abdominal adipose tissue (SAT) in patients with CHF. In addition, the body composition associated with improved exercise capacity after CR in patients with CHF has not been previously studied. Nineteen CHF patients who were categorized as NYHA functional class II or III and had received optimal medical treatment including a CR program for 5 months were enrolled in this study. The CR program significantly increased peak VO2 and reduced B-type natriuretic peptide. In addition, fat and body composition analysis showed reductions in the visceral fat tissue (VAT) area, subcutaneous abdominal adipose tissue (SAT) area, body weight, and total fat weight after CR. There were no changes in total water weight and total muscle weight. Single regression analysis revealed that the amelioration of reduced exercise capacity seen after CR is associated with reduced VAT area but not with SAT area or body weight. In conclusion, CR reduces VAT and improves exercise capacity in patients with CHF. This suggests that reducing VAT is important for CR to be most effective in the treatment of CHF.

Key words: Visceral adipose tissue, Subcutaneous abdominal adipose tissue, Peak VO2

Patients with chronic heart failure (CHF) have reduced exercise capacity due to dyspnea and fatigue. This reduced exercise capacity leads to a reduction in skeletal muscle mass and function. Muscle wasting has been shown to have prognostic importance in patients with CHF; therefore, maintaining muscle mass and function is an important part of CHF treatment.

Reduced exercise capacity and reduced skeletal muscle mass lead to accumulation of body fat, especially visceral adipose tissue (VAT). Increased VAT has been shown to be associated with cardiac remodeling and is a predictor of cardiovascular events. In addition, subcutaneous abdominal adipose tissue (SAT) volume may also be associated with cardiovascular events, although this association has not been definitively proven. Reduction of VAT/SAT volume without a concomitant reduction in muscle mass may lead to better outcomes for patients with CHF.

It has been established that a comprehensive cardiac rehabilitation (CR) program can reduce mortality and improve functional cardiac capacity and symptoms in patients with CHF. However, it is currently unknown whether CR reduces VAT and/or SAT in patients with CHF. The body composition after CR that is associated with optimal amelioration of the reduced exercise capacity seen in CHF patients is also unknown. The aim of this study was to investigate the effects of CR on VAT/SAT and skeletal muscle mass and to investigate whether the improved exercise capacity seen after CR is associated with changes in VAT and/or SAT.
Methods

Subjects: Nineteen CHF patients who were categorized as NYHA functional class II or III and had received optimal medical treatment including a CR program in the Department of Cardiovascular Medicine of Tokushima University Hospital were enrolled in this study between November 2014 and March 2016. Patients were enrolled when CHF was stabled with medication and/or coronary revascularization. Eighteen patients were enrolled as outpatients and one patient was enrolled during hospitalization for percutaneous coronary intervention. Patients were defined as having CHF if they had documented evidence of: 1) symptoms including dyspnea, fatigue, and/or peripheral edema; 2) physical signs of heart failure at the time of hospital admission, including increased jugular venous pressure, a displaced apex beat, the presence of a third heart sound, and/or crepitation on chest auscultation; or 3) significant radiographic and/or echocardiographic findings suggesting heart failure. Patients were excluded from this study for the following reasons: terminal illness, severe cognitive dysfunction, and psychological or physical disabilities. Patients who were waiting for coronary revascularization, insertion of an implantable cardioverter defibrillator, or cardiac resynchronization therapy, were also excluded.

Exercise training program: The exercise training program was supervised by a nurse and/or a physiotherapist with specialist training in CR. The duration of the CR program was approximately 5 months for all patients. The CR was performed 5 days per week during hospitalization. Each supervised session consisted of 5 minutes of warm-up, 30 minutes of pedaling on a bicycle ergometer, 10 minutes of calisthenics, and 5 minutes of cool down. After hospitalization, patients continued to perform the supervised exercise training program one to three times per week, as well as home exercise training at least twice a week for 5 months. Home exercise training consisted of 5 minutes of warm-up, 30-40 minutes of walking, 10 minutes of calisthenics, and 5 minutes of cool-down exercises. The exercise intensity of the ergometer portion of the supervised session was performed at a watt strength equivalent to the work level 1 minute before the anaerobic threshold during the patients’ maximal symptom-limited cardiopulmonary exercise tests. If exercise capacity was improved during the program, exercise intensity was modified by additional cardiopulmonary exercise test and/or the 6-20 scale perceived rating of exercise (original Borg’s score) reaching to the level.

Clinical data: Clinical measurements were performed before beginning the CR program and again 5 months after starting the CR program. The VAT area and SAT area at the level of the umbilicus were measured using the bioelectrical impedance method with a fat area analyzer (Dual Scan HDS-2000; OMRON, Japan). Previous studies have shown a strong correlation between VAT area measured by the fat area analyzer and VAT area measured by computed tomography. Whole body skeletal muscle weight and total body water were measured using multifrequency bioelectrical impedance methods with a body composition analyzer (Inbody720; Biospace, Korea). The intra-assay coefficients of variability for VAT area and whole body skeletal muscle weight and total body water in our laboratory were 0.99%, 2.7%, and 0.11%, respectively, which was evaluated by measuring 15 healthy subjects.

Peak VO2 was measured by a maximal symptom-limited cardiopulmonary exercise test. Plasma B-type natriuretic peptide (BNP) concentrations, lipid profiles including low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides, and hemoglobin A1c (HbA1c) were measured by enzymatic methods. Estimated glomerular filtration rate (eGFR), serum levels of C-reactive protein (CRP), and electrolytes were also evaluated.

Echocardiography was performed to assess left ventricular end-diastolic volume and left ventricular systolic function by left ventricular ejection fraction based on the modified Simpson’s method and to assess left ventricular diastolic function by the ratio of peak transmural flow velocities of E to A (E/A) and the ratio of peak E velocity to early diastolic mitral annuls velocity (E/E’).

Informed consent was obtained from all subjects before enrollment, and the study was performed in accordance with protocols approved by the Tokushima University Hospital Ethics Committee.

Statistical analysis: All data are expressed as means ± SD. One-way repeated analysis of variance was used to compare patient variables at baseline and after the 5-month CR program. Simple regression analysis was used to assess the relationship between the % change in peak VO2 and % change in VAT/SAT area or body weight. All statistical analyses were performed using JMP 10 software. Statistical significance was defined as P < 0.05.

Results

Patient characteristics: The patients’ characteristics are shown in Table I. Fourteen of the patients had developed CHF due to ischemic cardiomyopathy while the other five patients suffered from CHD due to non-ischemic cardiomyopathy. The mean left ventricular ejection fraction was 49 ± 17% (Table II). No patients dropped out of the study or experienced worsening of CHF or re-hospitalization during the study period.

The effects of CR on symptoms, systemic hemodynamics, cardiac function and laboratory parameters: The CR program did not change blood pressure, systemic and diastolic left ventricular function evaluated by echocardiography, and eGFR, but improved NYHA functional classification, and decreased heart rate and level of CRP (Table II).

The effects of CR on exercise capacity and BNP level: The CR program increased peak VO2 from 13.5 ± 3.6 mL/kg/minute to 15.3 ± 3.3 mL/kg/minute (P < 0.01) and reduced BNP from 116 ± 112 pg/mL to 72 ± 55 pg/mL (P < 0.05; Figure 1).

The effects of CR on total fat mass, total muscle mass, and VAT area/SAT area: Fat area analysis showed that the CR program significantly reduced the VAT area from 99 ± 36 cm2 to 92 ± 36 cm2 (P < 0.05) and SAT area from 203 ± 74 cm2 to 182 ± 61 cm2 (P < 0.05; Figure 2).
In addition, body composition analysis revealed reductions in body weight (from 71 ± 13 kg to 70 ± 13 kg; \( P < 0.05 \)) and total fat weight (from 20 ± 7 kg to 19 ± 6 kg; \( P < 0.05 \)), and no changes in total water weight (from 38 ± 7 kg to 37 ± 7 kg) and total muscle weight (from 28 ± 6 kg to 28 ± 6 kg; Figure 3).

**The effects of CR on metabolic parameters:** The CR program did not result in changes in metabolic parameters including LDL-C (from 98 ± 28 mg/dL to 88 ± 34 mg/dL), HDL-C (from 57 ± 15 mg/dL to CR 61 ± 12 mg/dL), triglycerides (from 119 ± 63 mg/dL to 111 ± 40 mg/dL), and HbA1c (from 6.4 ± 0.6% to 6.2 ± 0.5%; Figure 4).

The % change in peak VO\(_2\) was correlated with the % change in VAT area (\( P < 0.05 \)) and total body water, while simultaneously improving exercise capacity in patients with CHF. The improvement in exercise capacity was associated with a reduction in VAT area.

**Excessive accumulation of abdominal fat, as seen in**

**Discussion**

Our results demonstrate that CR reduces both the VAT and SAT areas without changing the weight of skeletal muscle and the total body water, while simultaneously improving exercise capacity in patients with CHF. The improvement in exercise capacity was associated with a reduction in VAT area.

**Table I. Clinical Characteristics of Patients**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of patients</th>
<th>Male, n (%)</th>
<th>Age, years</th>
<th>Body mass index, kg/m(^2)</th>
<th>Body mass index, kg/m(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>14 (74)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>59 ± 11</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m(^2)</td>
<td>26 ± 3.3</td>
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<td></td>
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</tbody>
</table>

**Table II. The Effects of Cardiac Rehabilitation on Symptoms, Systemic Hemodynamics, Cardiac Function and Laboratory Data**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before CR</th>
<th>After CR</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline demographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA functional classification</td>
<td>II 10</td>
<td>18</td>
<td>0.01</td>
</tr>
<tr>
<td>II</td>
<td>9</td>
<td>1</td>
<td>0.15</td>
</tr>
<tr>
<td>III</td>
<td>56 ± 22</td>
<td>116 ± 14</td>
<td>0.81</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>115 ± 22</td>
<td>116 ± 14</td>
<td>0.81</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>71 ± 17</td>
<td>70 ± 12</td>
<td>0.70</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>75 ± 12</td>
<td>68 ± 9</td>
<td>0.01</td>
</tr>
<tr>
<td>Echocardiographic data</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>LVDD, mm</td>
<td>55 ± 8</td>
<td>54 ± 8</td>
<td>0.33</td>
</tr>
<tr>
<td>LVEDV, mL/m(^2)</td>
<td>143 ± 55</td>
<td>134 ± 52</td>
<td>0.22</td>
</tr>
<tr>
<td>LAVI, mL</td>
<td>42 ± 19</td>
<td>39 ± 18</td>
<td>0.48</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>49 ± 17</td>
<td>52 ± 13</td>
<td>0.05</td>
</tr>
<tr>
<td>E/e'</td>
<td>1.1 ± 0.5</td>
<td>1.0 ± 0.8</td>
<td>0.54</td>
</tr>
<tr>
<td>E/e'</td>
<td>12 ± 9</td>
<td>11 ± 6</td>
<td>0.28</td>
</tr>
<tr>
<td>Laboratory data</td>
<td></td>
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<tr>
<td>Serum sodium, mEq/L</td>
<td>141 ± 26</td>
<td>142 ± 27</td>
<td>0.69</td>
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<tr>
<td>Serum potassium, mEq/L</td>
<td>4.3 ± 0.4</td>
<td>4.4 ± 0.4</td>
<td>0.08</td>
</tr>
<tr>
<td>CRP, mg/dL</td>
<td>0.3 ± 0.4</td>
<td>0.15 ± 0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>eGFR, mL/minute/(1.73m(^2))</td>
<td>73 ± 16</td>
<td>72 ± 13</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Unless indicated otherwise, data are presented as mean ± standard deviation. CR indicates cardiac rehabilitation; NYHA, New York Heart Association; LVDD, left ventricular diameter at end diastole; LVEDV, left ventricular end-diastolic volume; LAVI, left atrial dimension volume index; LVEF, left ventricular ejection fraction; CRP, C-reactive protein; and eGFR, estimated glomerular filtration rate.

**Figure 1.** CR increases peak VO\(_2\) and reduces BNP (*\( P < 0.05 \), **\( P < 0.01 \)).
metabolic syndrome, is associated with a variety of metabolic changes. These include insulin resistance, hyperlipidemia, and hypertension, all of which promote the development of atherosclerotic lesions. Thus, abdominal fat accumulation is considered a risk factor for the development of coronary artery disease. In patients at risk for coronary artery disease, treatment of obesity results in an improved coronary risk profile. In addition, abdominal fat accumulation is a highly prevalent condition in patients with CHF, and epidemiologic studies have shown that the accumulation of abdominal fat contributes to the incidence and severity of CHF.

It has not previously been shown whether CR changes VAT/SAT volume and skeletal muscle mass in patients with CHF, although several studies have shown that exercise and lifestyle modification reduce VAT in patients with diabetes, hyperlipidemia, and obesity without CHF. The accumulation of abdominal fat leads to the accumulation of cardiovascular risk factors, including insulin resistance, lipid abnormalities, and abnormalities of muscle metabolism. In this study, most of the patients are affected with metabolic syndrome as well as CHF. CR might reduce VAT in a comprehensive manner, dependent/independent of increased exercise capacity. Thus, reduction of VAT may be through improvement of CHF and through improvement of metabolic syndrome.

In addition, abdominal fat accumulation has been shown to be involved in cardiac dysfunction; this effect is partially mediated through chronic inflammation and increased oxidative stress. It has been reported that the
The effects of CR on metabolic parameters.

- LDL-C (mg/dL)
- Triglyceride (mg/dL)
- HDL-C (mg/dL)
- HbA1c (%)

Figure 4. The effects of CR on metabolic parameters.

\[ r^2 = 0.22 \]
\[ P < 0.05 \]

Figure 5. Correlation between % change of VAT/ SAT or body weight and % change of peak VO\(_2\).

anti-inflammatory effect of CR is due to increased expression of IL-10 and decreased expression of IL-6,\(^{25}\) and that the anti-oxidative effects of CR are due to down-regulation of NADPH oxidase, ERK1/2, and SAPK/JNK.\(^{26}\) Moreover, exercise-induced increased level of adiponectin, an insulin-sensitizing hormone, may improve cardiac energy metabolism via AMP-activated protein kinase.\(^{24,25}\) These mechanisms might be involved in the reduction in VAT area and increased exercise capacity seen in CHF patients who undergo CR.

We have shown an association between increased exercise capacity and decreased VAT area, but this increased exercise capacity is not associated with changes in SAT area or body weight. VAT represents a pathological adipose tissue accumulation. Relative to SAT, VAT is more sensitive to lipolysis and secretes more inflammatory cytokines,\(^{26}\) indicating that VAT may be more associated with exercise capacity than SAT and body weight in patients with CHF.

This study had several limitations. First, this was a pilot study with a small sample size. Second, there was considerable heterogeneity of the patient characteristics. Larger-scale investigations are required to assess and clarify the relationship between improved exercise capacity and decreased VAT after CR in patients with CHF.

Conclusion

Our results revealed that CR reduces VAT and improves exercise capacity in patients with CHF. This suggests that reducing the VAT area is important for CR to be most effective in the treatment of CHF.
Acknowledgments

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Disclosures

Conflict of interest: The authors declare that they have no conflicts of interest to disclose.

References