Skeletal muscle mass and exercise performance in stable ambulatory patients with heart failure

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Lang, Chim C., Don B. Chomsky, Glenn Rayos, T. K. Yeoh, and John R. Wilson. Skeletal muscle mass and exercise performance in stable ambulatory patients with heart failure. J. Appl. Physiol. 82(1): 257–261, 1997.—The purpose of the present study was to investigate the contribution of skeletal muscle atrophy to exercise intolerance in stable ambulatory patients with heart failure. Body composition and maximal exercise capacity were measured in 100 stable ambulatory patients with heart failure. Body composition was assessed by using dual-energy X-ray absorption. Peak exercise oxygen consumption (V̇O₂peak) and the anaerobic threshold were measured by using a Naughton treadmill protocol and a Medical Graphics CardioO2 System. V̇O₂peak averaged 13.4 ± 3.3 ml·min⁻¹·kg⁻¹ or 43 ± 12% of normal. Lean body mass averaged 52.9 ± 10.5 kg and leg lean mass 16.5 ± 3.6 kg. Leg lean mass correlated linearly with V̇O₂peak (r = 0.68, P < 0.01), suggesting that exercise performance is influenced by skeletal muscle mass. However, lean body mass was comparable to levels noted in 1,584 normal control subjects, suggesting no decrease in muscle mass. Leg muscle mass was comparable to levels noted in 34 normal control subjects, further supporting this conclusion. These findings suggest that exercise intolerance in stable ambulatory patients with heart failure is not due to skeletal muscle atrophy. Results in this population were compared with results in 1,584 normal control subjects. Leg lean mass was also correlated with maximal exercise capacity to investigate the relationship between muscle mass and exercise performance.

METHODS

Patient population. Studies were performed on 100 stable ambulatory patients followed by the Heart Failure and Heart Transplantation Program at Vanderbilt University Medical Center. All patients had a history of chronic heart failure for >6 mo, and all patients were ambulatory and receiving digoxin, an angiotensin-converting enzyme inhibitor, and diuretics. All patients were on optimal diuretic doses and did not have leg edema. Seventy-four patients were men and 26 were women. The average age was 51 ± 10 yr (range 26–67 yr). The left ventricular ejection fraction averaged 23 ± 7%. Heart failure was attributed to coronary arterial disease in 54 patients, to idiopathic cardiomyopathy in 42 patients, and to valvular heart disease in 4 patients.

Body composition studies and maximal exercise testing were performed on all patients as part of standard clinical evaluation of their heart failure. Body composition studies were used to assess obesity and bone density. Body composition was measured with dual-energy X-ray absorptiometry by using a total body scanner (model DPX, Lunar, Madison, WI) (10, 15, 19, 24). This scanner uses a constant potential X-ray source and a cerium filter to produce two stable radiation beams at 6.4 and 11.2 f. A series of transverse scans is made from head to toe at 1-cm intervals, for a total scan time of 20 min. When the two beams pass through the body, the attenuation depends on the mass and type of tissue. On the basis of regional attenuation, the fat mass, lean mass, and mineral content of the region are calculated.

Body composition was determined by using the DPX-L X-Ray Bone Densitometer (version 1.32) software program. The program identifies body regions by using bone edge markers and intervertebral space markers. The leg regions was defined as the area of the leg below the femoral neck. This area was initially identified by the software program but could be redefined if necessary by the technician on the basis of the total body scan.

Normal values for ideal body weight were calculated on the basis of gender, height, and weight (3). Normal lean body weight was calculated from ideal body weight and the percentage of weight normally due to lean body weight. This value was calculated on the basis of gender, age, and race (16).

Cardiopulmonary exercise testing. On the day of the test, the patient fasted for at least 3 h before arriving at the exercise laboratory. All medications were continued except for diuretics; these were held the morning of the study. The patient was connected to a MedGraphics CardioO2 System via a disposable pneumotach. After 3 min of resting data acquisition, maximum symptom limited treadmill exercise testing was performed by using a 3-min Naughton treadmill protocol and a Marquette treadmill. Arterial blood pressure was measured at each workload by using a cuff sphygmoma-
nometer. Arterial oxygen saturation was measured continuously by using a pulse oximeter; no patients exhibited arterial desaturation during exercise.

Respiratory gas analysis was used to identify the peak exercise oxygen consumption ($\dot{V}O_2$peak) and the anaerobic threshold. The anaerobic threshold was defined by using three criteria: the point after which the respiratory gas-exchange ratio [CO$_2$ production to O$_2$ consumption ($\dot{V}O_2$)] consistently exceeded the resting ratio; the point at which the ventilatory equivalent for oxygen [minute ventilation (VE)/$\dot{V}O_2$] was minimal followed by a progressive increase in VE/$\dot{V}O_2$; and the $\dot{V}O_2$ after which a nonlinear rise in VE occurred relative to $\dot{V}O_2$ (25, 26, 28). All patients achieved the anaerobic threshold, suggesting adequate motivation during exercise.

Data analysis. All data are expressed as means ± SD. Differences among groups were evaluated by using analysis of variance. Correlations among variables were assessed by using least square regression analysis. A P value < 0.05 was considered statistically significant.

RESULTS

Patients achieved a $\dot{V}O_2$peak level of 13.4 ± 3.3 ml·min$^{-1}$·kg$^{-1}$ (1,121 ± 382 ml/min). $\dot{V}O_2$peak was 43 ± 12% of $\dot{V}O_2$peak observed in normal sedentary aged-matched control subjects (4), 52 ± 14% of normal in the female patients, and 39 ± 9% of normal in the male patients.

Lean body mass and leg lean mass. Body composition for the entire population and for male and female patients are provided in Table 1. Lean body mass averaged 52.9 ± 10.5 kg and leg lean mass 16.5 ± 3.6 kg. There was a significant linear correlation between leg lean mass and both $\dot{V}O_2$peak and the anaerobic threshold (Fig. 1). There was also a relatively close correlation between $\dot{V}O_2$peak, when expressed as percentage of predicted normal, and $\dot{V}O_2$peak per kilogram of leg lean mass (Fig. 2).

However, there was little evidence of total muscle and leg muscle atrophy in the patients. Total body weight averaged 123 ± 21% of ideal body weight, whereas lean body weight averaged 112 ± 14% of ideal lean body. Only three women and two men exhibited ideal body weights <90% of predicted, and only two women and four men exhibited lean body weights <90% of predicted.

Table 1. Body composition in the patient population

<table>
<thead>
<tr>
<th></th>
<th>All Subjects</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>100</td>
<td>26</td>
<td>74</td>
</tr>
<tr>
<td>Age, yr</td>
<td>51 ± 10</td>
<td>51 ± 10</td>
<td>51 ± 10</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>83 ± 17</td>
<td>74 ± 17</td>
<td>86 ± 15</td>
</tr>
<tr>
<td>Height, cm</td>
<td>151 ± 8</td>
<td>142 ± 4</td>
<td>154 ± 7</td>
</tr>
<tr>
<td>%Fat</td>
<td>32 ± 9</td>
<td>39 ± 11</td>
<td>30 ± 6</td>
</tr>
<tr>
<td>Total tissue, kg</td>
<td>78.8 ± 16.0</td>
<td>70.2 ± 16.3</td>
<td>81.8 ± 14.8</td>
</tr>
<tr>
<td>Total fat, kg</td>
<td>25.9 ± 9.6</td>
<td>28.8 ± 12.1</td>
<td>24.9 ± 8.5</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>52.9 ± 10.5</td>
<td>41.3 ± 7.4</td>
<td>57.0 ± 8.2</td>
</tr>
<tr>
<td>Leg lean mass, kg</td>
<td>16.5 ± 3.6</td>
<td>12.8 ± 2.1</td>
<td>17.8 ± 3.0</td>
</tr>
<tr>
<td>Anaerobic threshold,</td>
<td>930 ± 305</td>
<td>809 ± 234</td>
<td>964 ± 316</td>
</tr>
<tr>
<td>$\dot{V}O_2$peak, ml/min</td>
<td>1,121 ± 382</td>
<td>926 ± 342</td>
<td>1,189 ± 373</td>
</tr>
<tr>
<td>% ideal body weight</td>
<td>123 ± 21</td>
<td>128 ± 26</td>
<td>121 ± 19</td>
</tr>
<tr>
<td>% ideal lean body weight</td>
<td>112 ± 14</td>
<td>110 ± 16</td>
<td>112 ± 13</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. $\dot{V}O_2$peak, peak exercise $O_2$ consumption.

Fig. 1. Relationship among leg lean mass, peak exercise $O_2$ consumption ($\dot{V}O_2$peak), and anaerobic threshold.

Lean body mass averaged 57.0 ± 8.2 kg in the male patients and 41.3 ± 7.4 kg in the female patients. The patients had no reduction in lean body mass when compared with normal values obtained in 1,584 normal control subjects, 529 female and 240 male subjects studied by the Lunar Corporation (J. R. Wilson, personal communication), and 815 normal subjects studied by Rico et al. (19) (Fig. 3). Lean body mass tended to decrease with age in the male patients, a trend also present in the normal subjects.

Fig. 2. Relationship between $\dot{V}O_2$peak and $\dot{V}O_2$peak per kilogram leg lean mass.
Leg lean mass averaged 12.8 ± 2.1 kg in the female patients and 17.8 ± 3.0 kg in the male patients. Heymsfield et al. (10) measured leg lean mass in 18 male and 16 female normal subjects with an average age of 52.3 ± 19.7 yr. Leg lean mass averaged 11.0 ± 2.2 kg in the female normal subjects and 14.1 ± 1.7 in the male normal subjects so that leg mass was slightly higher in the patients with heart failure.

Fat mass. Total fat mass averaged 25.9 ± 9.6 kg. Percent fat averaged 30 ± 6% in the male patients and 39 ± 11% in the female patients. Obesity was common in the population. Sixty-seven out of 74 male patients (91%) exhibited percent body fat >20%. Twenty-nine of the male patients (39%) had percent body fat >30%. Of the 26 female patients, 21 (81%) had percent body fat >30%, and 12 (46%) had percent body fat >40%. On average, both male and female patients tended to have greater percent fat than that observed in the large normal control population database obtained from the Lunar Corporation (Fig. 4).

DISCUSSION

There is a growing perception that skeletal muscle atrophy due to deconditioning is a major and universal contributor to exercise intolerance in patients with heart failure. This presumption has stemmed from two types of observations. First, a number of groups have reported findings consistent with skeletal muscle atrophy in patients with heart failure, including decreased leg muscle volume as assessed by magnetic resonance imaging (14, 17), decreased 24-h urinary creatinine excretion and decreased upper arm muscle circumference (6), and type II muscle fiber atrophy on biopsies of leg muscle (12, 23). Second, several groups have reported that exercise training can improve the maximal exercise capacity of patients with heart failure (1, 2, 5, 8, 22).

However, a careful review of prior studies raises serious questions about the presumed widespread prevalence of muscle abnormalities in heart failure. Studies of muscle characteristics have demonstrated statistical differences between heart failure patients and normal subjects, but they are often due to dramatic abnormalities in a relatively small number of patients rather than to major overall population differences. For example, Drexler et al. (6) found a significant reduction in mitochondrial size only in patients with severe exercise limitation, not in patients with less severe impairment. Studies of muscle mass appear to show a decrease in overall muscle size but are seriously limited by inclusions of very small study populations (14, 17). Population sizes have been so small that it was impossible to correct for differences in gender, age, and body size, all important determinants of skeletal muscle mass (7).

These observations raise the possibility that skeletal muscle abnormalities occur in a relatively small sub-

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**Fig. 3.** Comparison of lean body mass in patients with heart failure (hatched bars) with normal control values obtained by Lunar (filled bars) and by Rico et al. (Ref. 19; open bars; n = 1,584 normal subjects). A: men. B: women.

**Fig. 4.** Comparison of % body fat in patients with heart failure (filled bars) with normal control values obtained by Lunar (open bars; n = 769 subjects). A: men. B: women.
group of patients with severe heart failure and that most stable ambulatory patients, in fact, do not develop muscle abnormalities. By combining these two groups, investigators may have unintentionally skewed statistical observations to make it appear that muscle abnormalities are a pervasive problem in heart failure.

The present study was undertaken to reevaluate the contribution of skeletal muscle atrophy to exercise intolerance in ambulatory stable patients with heart failure. This study differed in two major ways from previous studies. First, only patients who were ambulatory and stable were enrolled in the study. This inclusion criterion tended to exclude patients with total body wasting or cardiac cachexia. Second, we enrolled more patients than in any previous study of skeletal muscle in heart failure and compared this group with an extremely large control population. This approach permitted us to compare body composition in patients and normal subjects with an adjustment for both age and gender. No previous study of skeletal muscle in heart failure has adjusted for these factors.

Body composition was measured by using dual-energy X-ray absorptiometry. This relatively new technology relies on differences in energy absorption between tissue types to distinguish fat, lean tissue, and bone mass (10, 15, 19, 24). A number of studies have shown that skeletal muscle mass assessed with this technology correlates closely with mass determined by more traditional techniques, including chemical analysis of beef phantoms (10, 15, 19, 24).

Using this technology, we found little evidence of generalized skeletal muscle atrophy in our patients. Lean body mass provides a general estimate of total skeletal muscle mass. When we compared our patients with two extremely large normal control groups, we found no evidence that lean body mass was reduced in the vast majority of patients; our patients and the two control groups had remarkably similar mass measurements. Only 6 of the 100 patients exhibited lean body mass <90% of predicted. We also found no evidence of muscle atrophy when we compared leg lean mass in our patients with normal levels noted by Heymsfield et al. (10). The only major abnormality of body composition detected in the patients was an extremely high incidence of obesity.

Although we found no evidence of reduced skeletal muscle mass in our patients, we did find a linear correlation between leg lean mass and both $V_{O_2}\text{peak}$ and the anaerobic threshold, suggesting that skeletal muscle mass influences exercise performance in patients with heart failure. Prior studies in normal subjects have also shown a linear correlation between muscle mass and maximal exercise capacity (7, 21) so that our results are not particularly surprising.

Such correlations provide indirect evidence that, should muscle atrophy develop, such atrophy could impair exercise performance. However, this conclusion may not apply to patients with heart failure. We observed a relatively close relationship between $V_{O_2}\text{peak}$, expressed as a percentage of the normal predicted level, and $V_{O_2}\text{peak}$ achieved per kilogram of leg lean mass (Fig. 2). This finding suggests that the impaired exercise performance of patients with heart failure is caused by qualitative changes in muscle oxidative capacity, due to factors such as reduced muscle oxygen delivery and/or mitochondrial density, rather than by changes in the quantity of muscle.

The presence of increased body fat in our population is not particularly surprising, given the prevalence of obesity in normal Americans. Patients with heart failure are more likely to develop obesity than the normal population due to their reduced activity level. However, it is worth noting that the presence of variable levels of body fat in patients with heart failure could influence the interpretation of $V_{O_2}\text{peak}$ levels. At present, $V_{O_2}\text{peak}$ is typically normalized for body size by dividing absolute $V_{O_2}$ by total body weight, including fat weight. This normalized measure of exercise performance is being increasingly used to evaluate patients with heart failure, particularly patients being considered for heart transplantation (13, 18, 20). By including fat weight in the normalization formula, one potentially will make obese patients appear more limited than nonobese patients, even in the presence of comparable levels of circulatory failure.

Clinical implications. Our findings suggest that ambulatory stable patients with heart failure usually do not develop significant skeletal muscle atrophy. This finding suggests that most ambulatory patients are sufficiently active to maintain normal levels of muscle mass. Given the general inactivity of patients with heart failure, this conclusion at first may seem surprising. Nevertheless, animal studies suggest that even brief periods of weight support during a day can markedly reduce the effect of immobilization-induced atrophy (9). Patients presumably are undertaking sufficient activity to avoid atrophy. The widespread obesity in this population may also serve to minimize atrophy because the added fat weight will increase the energy demands of activities and thereby help to maintain muscle mass.

The lack of significant atrophy in ambulatory patients with heart failure suggests that their maximal exercise capacity may not improve substantially with modest increases in activity levels. In fact, recent trials of exercise training have demonstrated only modest improvements in exercise capacity, with many patients exhibiting no improvement at all. In a randomized trial by Coats et al. (5), nearly two-thirds of the patients
exhibited no improvement in maximal exercise time. Belardinelli et al. (2) and Barlow et al. (1) noted that most patients in their training studies did not exhibit increases in VO2peak.

However, it should be emphasized that this study focused exclusively on muscle mass. Patients with heart failure may develop clinically important qualitative changes in skeletal muscle, such as alterations in mitochondrial density or vascular characteristics, with no overall change in muscle mass. Such qualitative changes potentially could improve with exercise training. In addition, training studies to date have utilized exercise protocols adapted from other populations. Patients with heart failure may require different training protocols to achieve optimal effects.

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