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Adiposity facilitates increased strength capacity in heart failure patients with reduced ejection fraction ☆

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ABSTRACT

Background: Obesity is associated with relatively improved prognosis among heart failure (HF) patients. Mechanisms explaining this so-called "obesity paradox" have been unclear. We hypothesized that increased adiposity may contribute to increased strength capacity, and may thereby facilitate clinical benefits.
Methods and results: In a controlled, cross-sectional study, adults aged ≥50 years with HF with reduced ejection fraction (HFREF) (LVEF ≤40%) were compared to age matched controls. Body composition was determined by dual-energy X-ray absorptiometry (DXA). Aerobic (cardiopulmonary exercise testing), maximum strength (one repetition maximum [1RM]), and power (submaximal resistance/time) were assessed.
70 adults (31 HFREF, 39 controls; mean age 66.2 ± 9.6 years) were studied. Peak oxygen consumption (VO_2) (15.4 ± 4.2 vs. 23.4 ± 6.6 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$, $p<0.0001$), 1RM (154.8 ± 52.0 vs. 195.3 ± 56.8 kg, $p<0.01$) and power (226.4 ± 99.2 vs. 313.3 ± 130.6, $p<0.01$) were lower in HFREF vs. controls. 1RM correlated with total fat ($r=0.56$, $p<0.01$), leg fat ($r=0.45$, $p<0.05$) and arm fat ($r=0.39$, $p<0.05$) in HFREF. Moreover, among HFREF patients with a high (≥30 kg/m^2) body mass index (BMI), 1RM and fat mass were significantly greater than those with lower (<30 kg/m^2) BMIs. Correlations between 1RM and total fat ($r=0.65$, $p<0.05$) and leg fat ($r=0.64$, $p<0.05$) were particularly notable in the high BMI subgroup.
Conclusion: Increased adiposity correlates with relatively greater strength in HFREF patients which may explain some of the clinical benefits that result from obesity.

1. Introduction

While obesity is generally considered detrimental to those who are healthy [1,2], increased adiposity is associated with a relatively better prognosis among older adults with heart failure with reduced ejection fraction (HFREF) [3]. This so-called *obesity paradox* is often attributed to the "cardio-protective benefits" [4–7], of adipose tissue wherein adipose tissue is thought to impart neuroendocrine and metabolic benefits [8–10]. While a multitude of studies corroborate the favorable implications of obesity in heart failure (HF) patients, mechanisms of cardiac benefit remain controversial [11]. We hypothesized that the benefits of adiposity may relate to functional implications of body composition. Adults with surplus body fat carry extra weight throughout the course of daily living. Differences in prognosis may result from what is a defacto resistance training stimulus and relates to differences in body composition and strength.

Although elevated body mass index (BMI) of ≥30 kg/m^2 is usually used to demarcate excess adiposity, simple quantification of body habitus does not discriminate between lean muscle and fat tissue [12]. Using dual energy X-ray absorptiometry (DXA) to more accurately quantify adiposity and fat distribution in HF patients and age-matched controls, we studied the impact of aerobic and strength performance relative to fat and lean body tissue.

Functional decline is typical among HFREF patients, with poor prognostic implications as well as diminished quality of life, increased

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frailty, and reduced independence [13,14]. Diminished muscular strength is also typical [15,16]. The relationship of lean body mass, fat mass, and the relative implications on aerobic and strength abilities have not been delineated. High fat mass may impart paradoxical health benefits by its favorable functional ramifications.

2. Materials and methods

Non-cachectic (BMI ≥ 18.5), clinically stable, male HFREF patients aged 50 years and older were compared to age-matched controls. All patients were on a standard regimen of evidence-based HF therapy with medications and doses determined by their primary cardiologists. All HFREF patients were euvolemic during a physical exam immediately prior to the functional assessments. Additionally, each HFREF patient completed an echocardiogram within 6 months of enrollment to confirm a left ventricular ejection fraction (LVEF) ≤40%. Both HF patients and control subjects were excluded if they had neurological dysfunction, musculoskeletal problems, or severe pulmonary disease, which might have confounded functional assessments. Control subjects had no history of cardiovascular disease. Control candidates or HFREF patients who exercised ≥150 min/week for the three months prior to enrollment were also excluded to avoid confounding effects of exercise training. The study was approved by the VA Institutional Review Board and informed consent was obtained from each subject.

Exercise testing was completed on a motorized treadmill using a modified Balke protocol [17] in conjunction with ventilatory expired gas analysis through a snorkel device [18]. The ventilatory expired gas analysis system (MedGraphics BreezeSuite St. Paul, MN) was calibrated prior to each test. ECG waveforms, blood pressure, oxygen saturation, and subjective symptoms were assessed before, during, and after exercise, in routine clinical fashion.

Peak oxygen consumption (VO_2) was defined as the 30-second averaged value during the last stage of exercise. Ventilatory anaerobic threshold (VAT) was determined by the V-slope method [19]. Ventilatory efficiency represented as the ventilation to carbon dioxide production (VE/VCO_2) slope was evaluated during exercise. VE and VCO_2 values, acquired from the initiation of exercise to maximal exertion, were input into a spreadsheet software (Microsoft Excel, Microsoft Corp., Bellevue, WA) to calculate the VE/VCO_2 slope via least squares linear regression ($y = mx + b$, m = slope). All of the subjects achieved a minimum peak respiratory exchange ratio (RER) of 1.0, ensuring a standard of high physical exertion [20] among patients who had predominantly sedentary lifestyles.

Muscle strength and power were measured using a pneumatic leg press (Keiser A420, Fresno, CA). To assess maximal strength capacity, participants performed a leg press (i.e. knee extension and flexion) initially using a minimal weight. Subjects rated the leg press according to the rating of perceived exertion (RPE) using the Borg scale [21] The physiologist then increased the weight and the participant completed another leg press with the heavier weight and rated the difficulty of the leg press. The weight was progressively increased until the participant was unable to complete a full repetition. The last weight that was used to complete a full repetition was recorded as the one repetition maximum (1RM). Thereafter, the resistance was reduced to 60% of the 1RM, and subjects completed up to 30 repetitions continuously to assess submaximal power. A desktop computer was connected to the leg press machine, which generated power curves (watts) for each leg press. Upon completion of the 30 repetitions, the peak for each curve was determined and averaged with one another.

Total and anthropometric lean and fat mass were measured with iDXA (GE Lunar, Madison, WI) and analyses were performed using Encore 13.60 software. The DXA scanner (Lunar iDXA, Madison, WI 53718,) was calibrated with a phantom provided by GE Healthcare, prior to each scan, according to manufacturer's specifications [22]. iDXA is a fan beam system which uses a staggered array of sixty-four detectors (CZT-HD digital detectors) to enhance precision and eliminate dead space between detectors, thus creating a high resolution image [23]. DXA measurements were normalized to height.

SAS statistical software version 9.0 (SAS, Cary, NC) was used to analyze the data and values are reported as mean ± SD (unless otherwise indicated). Comparison of HF and controls was determined using non-paired t-tests and Pearson correlations were used to evaluate the correlation coefficients. A p-value of <0.05 was used to define statistical significance for all tests.

3. Results

Seventy subjects (31 HF patients [mean age 67.4 ± 8.9 years] and 39 controls [mean age 65.3 ± 10.1 years]) were assessed. All subjects were male. Table 1 lists the demographics and medications among the study population.

Table 2 demonstrates impaired aerobic ability in HF patients evidenced by a significantly decreased peak VO_2 and VAT and an increased VE/VCO_2 slope. Strength and power were also decreased in HF patients, suggesting further abnormalities in peripheral skeletal muscle function. Leg lean muscle mass was diminished in HF patients but since "lean tissue" measures incorporate both bone and muscle tissues, isolated skeletal muscle implications are uncertain. Total adiposity was similar between HF patients and controls.

Table 1
Participant demographics.

	HF	Controls	Significance
Age (years)	67.4 ± 8.9	65.3 ± 10.1	0.37
Weight (kg)	86.0 ± 27.4	86.6 ± 14.9	0.91
Height (meters)	1.7 ± 0.07	1.7 ± 0.09	0.98
Medications			
Beta-blocker	23	2	<0.0001
ACE-inhibitor	25	6	<0.0001
ARB	2	2	0.80
Statin	24	16	<0.001
Diuretics	20	5	<0.0001

HF indicates heart failure; ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker.

Table 3 demonstrates the lack of correlation between lean mass and aerobic indices in HF patients. However, Table 4 shows that lean mass is significantly associated with strength capacity in HF patients, suggesting that lean mass has a greater influence on strength than aerobic ability. Table 4 also shows that fat mass correlates with strength; correlations were stronger in the HF group than in the controls.

To further compare the effects of fat and lean body mass on strength capacity, HF patients were stratified into groups according to a <30 kg/m^2 ($n = 21$) and ≥ 30 kg/m^2 ($n = 10$) BMI threshold; mean BMI 25.0 ± 3.1 vs. 37.0 ± 7.5 kg/m^2, $p<0.001$, respectively. Although aerobic indices were similar between the two groups [peak VO_2 (14.9 ± 4.3 vs. 15.6 ± 4.2 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$, $p = 0.66$), VAT (11.0 ± 2.7 vs. 10.9 ± 1.7 $mlO_2 \cdot kg^{-1} \cdot min^{-1}$, $p = 0.84$), and VE/VCO_2 slope (36.9 ± 13.2 vs. 35.1 ± 9.4, $p = 0.67$)], those in the high BMI group had a significantly higher 1RM (181.0 ± 55.6 vs. 141.6 ± 46.0 kg, $p<0.05$).

Fat mass, as assessed by DXA, was increased in the high BMI subgroup: total fat mass (26.5 ± 10.1 vs. 12.1 ± 3.9 kg, $p<0.01$) as well as leg fat mass (7.2 ± 3.4 vs. 3.3 ± 1.2 kg, $p<0.01$), and arm fat mass (2.4 ± 1.0 vs. 1.2 ± 0.5 kg, $p<0.01$). 1RM correlated positively with total fat ($r = 0.65$, $p<0.05$) and leg fat ($r = 0.64$, $p<0.05$) only in the HF group with high BMI.

Patients in the high BMI group also had increased total lean mass (36.4 ± 4.3 vs. 29.7 ± 2.6 kg, $p<0.0001$) as well as leg lean mass (12.3 ± 2.1 vs. 9.4 ± 1.2 kg, $p<0.01$) and arm lean mass (4.3 ± 0.7 vs. 3.5 ± 0.5 kg, $p<0.01$). However, there were no significant correlations between lean mass and function in this group.

Table 2
Differences in function and body composition between HF patients and control subjects.

	HF	Controls	Significance
Aerobic capacity			
Peak VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	15.4 ± 4.2	23.4 ± 6.6	<0.0001
VAT ($ml \cdot kg^{-1} \cdot min^{-1}$)	10.9 ± 2.1	14.4 ± 4.0	<0.0001
VE/VCO_2 slope	35.7 ± 10.6	29.1 ± 4.6	<0.01
Strength capacity			
1RM (kg)	154.8 ± 52.0	195.3 ± 56.8	<0.01
Power (watts)	226.4 ± 99.2	313.3 ± 130.6	<0.01
DXA fat and lean body mass distributions (normalized to height)			
Total lean (kg)	31.2 ± 4.8	32.5 ± 3.8	0.20
Legs lean (kg)	10.3 ± 2.0	11.1 ± 1.4	<0.05
Arms lean (kg)	3.8 ± 0.7	4.0 ± 0.9	0.24
Total fat (kg)	16.7 ± 9.4	16.3 ± 5.0	0.82
Leg fat (kg)	4.6 ± 2.8	4.3 ± 1.4	0.62
Arm fat (kg)	1.6 ± .9	1.6 ± 0.6	0.80

Peak VO_2 indicates maximal oxygen consumption; VAT oxygen consumption at anaerobic threshold; VE/VCO_2 slope ventilatory efficiency; 1RM the one repetition maximum.