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Skeletal Muscle Mass Independently Predicts Peak Oxygen Consumption and Ventilatory Response During Exercise in Noncachectic Patients With Chronic Heart Failure

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OBJECTIVES We sought to assess whether skeletal muscle mass might be a predictor of peak oxygen consumption (Vo_2) and relation of the ventilation to carbon dioxide production (VE/Vco_2) slope in patients with chronic heart failure (CHF) independent of clinical conditions, neurohormonal activation and resting hemodynamics.

BACKGROUND A variety of abnormalities characterize skeletal muscle and contribute to exercise intolerance in patients with CHF. Skeletal muscle mass is a determinant of peak Vo_2 both in healthy patients and in patients with CHF, but there are no reports on the independent predictive value of this parameter, which can be measured with great accuracy by whole-body dual energy X-ray absorptiometry (DEXA). The influence of skeletal muscle mass on VE/Vco_2 slope is not known either.

METHODS We prospectively evaluated 120 consecutive noncachectic patients with CHF. Every patient underwent a cardiopulmonary exercise test, an echo-Doppler examination and an evaluation of neurohormonal activation and body composition as assessed by DEXA.

RESULTS At the univariate analysis, New York Heart Association (NYHA) class ($p < 0.0001$), age ($p < 0.0001$), male gender ($p < 0.0001$) and plasma renin ($p < 0.0001$) significantly related with peak Vo_2. There was a significant correlation between lean mass and absolute peak Vo_2 ($r = 0.70$, $p < 0.0001$) and VE/Vco_2 slope ($r = -0.27$; $p < 0.01$). At the multivariate analysis, lean mass predicted peak Vo_2 and VE/Vco_2 slope independently of NYHA functional class, age, gender, neurohormonal activation and resting hemodynamics.

CONCLUSIONS Skeletal muscle mass is an independent predictor of peak Vo_2 and VE/Vco_2 slope in stable noncachectic patients with CHF. Future studies will determine whether an increase in skeletal muscle mass in the individual patient might result in an improvement in parameters of exercise capacity. (J Am Coll Cardiol 2001;37:2080–5) © 2001 by the American College of Cardiology

Chronic heart failure (CHF) is a syndrome characterized by impaired exercise capacity, fatigue and exertional dyspnea. Cardiopulmonary exercise testing with measurement of peak oxygen uptake (peak Vo_2) is a useful index of exercise capacity and a strong prognostic marker in patients with CHF (1). Classically, hemodynamic disturbances were thought to be responsible for the reduction of exercise capacity; however, there is only a poor correlation between hemodynamic abnormalities at rest and peak Vo_2 (2,3). Therefore, it is possible that noncardiac factors may contribute to exercise intolerance in patients with CHF. A separate abnormality has been found during cardiopulmonary exercise testing in patients with CHF. For a given rate of carbon dioxide production (Vco_2), patients with CHF ventilate at a higher level compared with normal subjects; therefore, the rate of increase in ventilation (VE) per unit increase in Vco_2 (VE/Vco_2 slope) is steeper in patients with CHF compared with controls (4). This parameter carries independent prognostic implications (5), but the mechanisms leading to increased ventilation during exercise in CHF are not fully understood yet.

A variety of skeletal muscle abnormalities develops in patients with CHF (6–10), many of which relate to impaired functional status. Skeletal muscle mass is another important determinant of exercise capacity in patients with CHF (11), but its role in the pathophysiology of CHF has not yet been adequately investigated. This parameter can be very accurately measured by dual energy X-ray absorptiometry (DEXA), which is a noninvasive, highly reproducible and accurate technique (12). Nevertheless, there are no reports on the independent predictive value of this parameter in determining exercise intolerance in stable, noncachectic patients with CHF. Therefore, we aimed at assessing: 1) whether skeletal muscle mass might predict exercise capacity independently of clinical, hemodynamic and neurohormonal parameters in patients with CHF without

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Abbreviations and Acronyms

ACE	= angiotensin-converting enzyme
CHF	= chronic heart failure
DEXA	= dual energy X-ray absorptiometry
LVEF	= left ventricular ejection fraction
NYHA	= New York Heart Association
VCO_2	= carbon dioxide production
VE	= ventilation
VE/VCO_2	= relation of the rate of ventilation to carbon dioxide production
VO_2	= oxygen consumption

cardiac cachexia, and 2) the relationship between skeletal muscle mass and VE/VCO_2 slope in this group of patients.

METHODS

Study population. We studied 120 consecutive patients in a stable clinical and nutritional status followed at our Outpatient Heart Failure Clinic. Every patient had a left ventricular ejection fraction (LVEF) <45% and a duration of heart failure of at least six months, was on standard therapy for heart failure and on optimal diuretic dose. We excluded patients with intermittent claudication, significant pulmonary disease, inducible ischemia or other disorders limiting exercise performance other than cardiac disease. Patients with signs of pulmonary or peripheral edema or ascites were not included in the study because fluid retention would interfere with the measurement of body composition (12). A clear relationship exists between cardiac cachexia and skeletal muscle abnormalities (13). Therefore, we excluded patients with cardiac cachexia, defined as a nonintentional weight loss >7.5% of previous normal weight over a period of six months (14). The protocol was approved by the local ethics committee, and every patient provided written informed consent before the beginning of the study.

Cardiopulmonary exercise testing. All patients underwent a symptom-limited bicycle ergometer exercise test at a constant cadence of 60 rpm. A continuous ramp protocol was used in which work rate was increased by 10 W/min. Gas exchange was monitored during the exercise test with a computerized metabolic cart (Vmax 229, SensorMedics, Yorba Linda, California). Oxygen uptake, carbon dioxide production, VE and respiratory exchange ratio were measured online every 10 sec using a standard inert gas dilution technique. Peak VO_2 was defined as the highest VO_2 achieved during exercise and was expressed both in ml/min/kg and in ml/min (absolute peak VO_2). The slope of the relation between ventilation and CO_2 (VE/VCO_2) was calculated from the exercise data and taken as an index of the ventilatory response to exercise (5).

Neurohormonal activation. Venous blood samples were drawn on the day of the study after a 30 min supine rest in a fasting state between 8 and 9 AM. The concentrations of aldosterone and renin were measured by a sandwich radioimmunoassay (Biochem Immuno System, Rome, Italy). Plasma norepinephrine and epinephrine levels were measured by high performance liquid chromatography with electrochemical detection. The reference values in our laboratory are 3.9 to 49.3 mU/L for renin, 0.04 to 0.42 nmol/l for aldosterone, 215 to 475 pg/ml for norepinephrine and <520 pg/ml for epinephrine.

Echo-Doppler examination. A complete echo-Doppler examination was performed immediately before the exercise test. Left ventricular end-diastolic volume and end-systolic volume (area-length method) and LVEF were measured from an apical four-chamber view. Mitral E and A wave velocities, E/A ratio and E wave deceleration time were measured at the mitral flow Doppler examination. Cardiac stroke volume was measured as the product of the left ventricular outflow tract annulus area, and time velocity integral was measured at the same level by pulsed wave Doppler. Mean pulmonary artery pressure was calculated as previously described (15). All measurements were obtained from the average of three beats for sinus rhythm patients and five beats for those with atrial fibrillation.

Body composition. Body composition was measured with DEXA by using a total body scanner (QDR 2000, Hologic, Bedford, Massachusetts). 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 fJ. A series of transverse scans is made from head to toe at 1-cm intervals for a total scan time of 7 min. When the two beams pass through the body, attenuation of the radiation depends on mass and type of tissue. On the basis of the regional attenuation, the total fat mass, total lean mass and lean mass of the legs and arms are calculated (12). Appendicular lean mass was calculated from the sum of the lean mass of arms and legs (16). Lean and fat mass were expressed as absolute values and as a percent of body weight.

Statistical analysis. Results are given as mean ± standard deviation for continuous variables and as median (interquartile range) for nonparametric variables. Comparison in body composition between men and women was made by using Student *t* test. Univariate regression analyses were performed in order to identify the relationship between variables. Significant predictors of peak VO_2 and VE/VCO_2 at the univariate analysis were used in different multivariate models to assess their independent predictive value. A commercially available statistical software package was used (STATA 4.0, Stata Corporation, College Station, Texas). A p value <0.05 was considered statistically significant.

RESULTS

The etiology of CHF was ischemic cardiomyopathy in 73 patients (61%), idiopathic dilated cardiomyopathy in 44 patients (37%) and valvular heart disease in three patients (2%). The detailed results relative to clinical status, echocardiography, neurohormonal activation and parameters of exercise tolerance are summarized in Table 1. Twenty patients (16%) were in New York Heart Association

Table 1. Clinical Characteristics of a Population of 120 Ambulatory Patients With CHF

Variable	Mean ± SD
Age (yr)	62.1 ± 8.8
n (men/women)	105/15
NYHA functional class I–II (%)	82/120
Plasma creatinine (μmol/l)	100.2 ± 26.4
Plasma sodium (mEq/l)	139.2 ± 3.1
LVEF (%)	34 ± 9
LVEDV (ml)	266 ± 96
LVESV (ml)	182 ± 87
DtE (ms)	222 ± 82
E max (m/s)	0.6 ± 0.2
A max (m/s)	0.7 ± 0.2
E/A ratio	1.0 ± 1.0
MPAP (mm Hg)	28.8 ± 8.6
Stroke volume (ml)	85 ± 9
Peak Vo_2 (ml/min/kg)	17.3 ± 5.0
Absolute Vo_2 (l/min)	1327.7 ± 470.4
VE/VCo_2 slope	36.9 ± 7.0
Rest SBP (mm Hg)	137 ± 20
Plasma norepinephrine (ng/l)	336 (182–480)
Plasma renin (ng/l)	46 (12.3–100.8)
Plasma aldosterone (nmol/l)	0.25 (0.2–0.34)

Data are given as mean ± SD or median (interquartile range).

A max = A wave velocity; ACE = angiotensin-converting enzyme; DtE = E wave deceleration time; E max = E wave velocity; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; MPAP = mean pulmonary artery pressure; NYHA = New York Heart Association; SBP = systolic blood pressure; VE/VCo_2 = relation of the ventilation to carbon dioxide production, Vo_2 = oxygen consumption.

(NYHA) class I, 62 (52%) in class II, 36 (30%) in class III and 2 (2%) were in class IV. A total of 93% of patients were on an angiotensin-converting enzyme (ACE)-inhibitor; the remaining patients were taking an angiotensin II receptor blocker due to intolerance of ACE inhibitors. A total of 73% of the patients were on beta-blockers and 88% were on diuretics.

Results of body composition for the entire population and for men and women are summarized in Table 2. Mean body mass index was 27.3 ± 3.9. Obesity was common in the population. A total of 38% of patients had >30% body fat, and 9% had >40% body fat.

Predictors of peak Vo_2 and VE/VCo_2. Univariate predictors of peak Vo_2 are reported in Table 3. Age ($p < 0.0001$; $r = 0.37$), gender ($p < 0.0001$; $r = 0.37$), renin ($p < 0.05$; $r = 0.2$), NYHA class ($p < 0.0001$; $r = 0.42$), cardiac stroke volume ($p < 0.0001$; $r = 0.3$) and E/A ratio ($p < 0.05$; $r = 0.13$) predicted absolute peak Vo_2. The relationship between appendicular lean mass and absolute peak Vo_2 is shown in Figure 1. At the multivariate analyses (Table 4), appendicular lean mass predicted peak Vo_2 independently of age, gender, NYHA class and renin. In the same model, gender lost its predictive power. We were able to predict 53% of the variability of peak Vo_2 in ml/min/kg and 66% of the variability of absolute peak Vo_2 with this model.

The detailed results of univariate predictors of VE/VCo_2 slope are reported in Table 3. At the multivariate analysis, appendicular lean mass ($p = 0.02$) predicted VE/VCo_2 independently of age ($p = 0.03$), aldosterone (NS) and percentage of LVEF ($p = 0.02$).

DISCUSSION

In this study we describe the role of skeletal muscle mass as assessed by DEXA in determining impaired Vo_2 and increased ventilatory response during exercise in noncachectic patients with CHF. In our population, skeletal muscle mass predicted peak Vo_2 and VE/VCo_2 independently of age, NYHA class, gender, resting hemodynamic and neurohormonal activation. Only few echocardiographic parameters predicted peak Vo_2 at the univariate analysis, and none of them predicted exercise capacity independently. This confirms previous reports that found that resting hemodynamics only poorly related with peak Vo_2 (17,18).

Role of skeletal muscle in the pathophysiology of CHF. Biochemical, histological and functional changes characterize skeletal muscle of patients with CHF (6,8,19,20). Many of these abnormalities closely relate to exercise intolerance (6,19,21–23). These findings have fuelled the muscle hypothesis (24), according to which many of the symptoms present in CHF are due to changes in the periphery rather than to central hemodynamics. Nevertheless, these parameters can only be obtained at the cost of high invasiveness and, therefore, are not widely used.

Skeletal muscle mass is an important determinant of exercise capacity in patients with CHF (11). The contribution of this parameter to exercise intolerance in patients with CHF has not yet been adequately investigated due to a lack of reliable measurement methods. Dual energy X-ray absorptiometry scanning is a relatively new technology that allows a very accurate, noninvasive and rapid estimate of body composition (12). Our main finding is in accordance with the work of Lang et al. (11) who described a significant relationship between skeletal muscle mass of the legs and peak Vo_2 in a population of ambulatory patients with CHF. Unfortunately, this study focused on skeletal muscle mass as the only predictor of peak Vo_2 and no data is available

Table 2. Body Composition of 120 Consecutive Patients With CHF as Assessed by Dual Energy X-ray Absorptiometry

Variable	Total CHF Patients (n = 120)	Men (n = 105)	Women (n = 15)	p Value*
Weight (kg)	74 ± 12	79 ± 12	67 ± 12	< 0.001
Height (cm)	168 ± 7	170 ± 7	158 ± 6	< 0.0001
Body mass index	27.3 ± 3.9	27.4 ± 3.9	26.7 ± 4.4	NS
Total fat mass (kg)	22.6 ± 7.6	22.1 ± 7.4	24.8 ± 7.4	NS
Total lean mass (kg)	51.5 ± 8.2	53.4 ± 6.7	38.5 ± 6.4	< 0.0001
Appendicular lean mass (kg)	20.2 ± 3.7	21.1 ± 3.1	14.6 ± 2.9	< 0.0001
Legs lean mass (kg)	14.7 ± 2.6	15.2 ± 2.2	10.8 ± 2.2	< 0.0001
Arms lean mass (kg)	5.6 ± 1.2	5.9 ± 1.1	3.8 ± 0.9	< 0.0001
Lean % body weight	67.0 ± 7.3	69.1 ± 6.4	59.7 ± 6.3	< 0.0001
Fat % body weight	28.7 ± 7.3	27.9 ± 6.4	37.5 ± 6.4	< 0.0001

* Men versus women.

All data are given as mean ± SD.

CHF = chronic heart failure.

Table 3. Clinical Predictors of Peak Vo_2 in ml/min/kg, peak Vo_2 in ml/min and VE/VCo_2 Slope in a Population of 120 Patients With CHF (Univariate Analysis)

	Peak Vo_2 (ml/min/kg)			Peak Vo_2 (ml/min)			VE/VCo_2 Slope		
Variable	p Value	b (95% CI)	r	p Value	b (95% CI)	r	p Value	b (95% CI)	r
Age (yr)	< 0.0001	−0.2 (−0.3 ÷ −0.1)	0.38	< 0.0001	−21.0 (−30.5 ÷ −11.5)	0.37	< 0.01	0.2 (0.1–0.3)	0.24
NYHA class	< 0.0001	−3.2 (−4.3 ÷ −2.0)	0.45	< 0.0001	−287.8 (−402.2 ÷ −173.4)	0.42	0.001	2.8 (1.1–4.6)	0.29
Gender	< 0.0001	−4.6 (−7.3 ÷ −2.0)	0.30	< 0.0001	−558.5 (−809.9 ÷ −307.1)	0.37	NS	—	—
Norepinephrine (ng/l)	NS	—	—	NS	—	—	NS	—	—
Renin (ng/l)	< 0.0001	−0.01 (−0.02 ÷ −0.006)	0.30	< 0.05	−0.9 (−1.7 ÷ −0.1)	0.19	NS	—	—
Aldosterone (nmol/l)	0.014	−7.1 (−12.7 ÷ −1.4)	0.23	NS	—	—	< 0.05	9.1 (1.3–16.9)	0.22
LVEF (%)	NS	—	—	NS	—	—	< 0.05	−0.2 (−0.3 ÷ −0.22)	−0.22
Stroke volume (ml)	0.016	0.06 (0.01–0.11)	0.22	< 0.001	8.2 (3.5–12.8)	0.30	< 0.01	−0.1 (−0.2 ÷ −0.3)	−0.27
Cardiac output (ml/min)	0.06	0.09 (−0.05–0.2)	0.21	< 0.01	0.1 (0.03–0.2)	0.30	NS	—	—
LVEDV (ml)	NS	—	—	NS	—	—	NS	—	—
LVESV (ml)	NS	—	—	NS	—	—	NS	—	—
E/A ratio	NS	—	—	NS	—	—	< 0.05	1.4 (0.2–2.7)	0.22
DtE (ms)	NS	—	—	NS	—	—	NS	—	—
MPAP (mm Hg)	0.06	−0.12 (−0.26–0.04)	0.21	NS	—	—	NS	—	—
Total lean mass (kg)	< 0.0001	0.2 (0.1–0.3)	0.40	< 0.0001	0.03 (0.02–0.04)	0.67	< 0.01	−0.2 (−0.3 ÷ −0.1)	−0.24
Appendicular lean mass (kg)	< 0.0001	0.6 (0.4–0.8)	0.46	< 0.0001	0.09 (0.07–0.1)	0.70	< 0.01	−0.5 (−0.8 ÷ −0.1)	−0.27
Leg lean mass (kg)	< 0.0001	0.5 (0.3–0.7)	0.45	< 0.0001	0.08 (0.06–0.1)	0.71	< 0.01	−0.3 (−0.5 ÷ −0.2)	−0.23
Total fat mass (kg)	0.017	−0.1 (−0.2 ÷ −0.02)	0.22	< 0.05	0.01 (0.001–0.02)	0.19	NS	—	—

CI = confidence interval. Other abbreviations as in Table 1.

concerning clinical and hemodynamic parameters in this population. Other authors (25) found a significant relationship between peak Vo_2 and thigh muscle cross-sectional area, but this finding is limited to a small number of patients, and, as in other studies (6), it is not clear whether cachectic patients were included. We believe this is important to establish. In fact, the relationship between skeletal muscle atrophy and functional impairment is well known (13,26). Therefore, we excluded patients with cardiac cachexia from the study.

Predictors of peak Vo_2. In our study at the univariate analysis, gender was a strong predictor of peak Vo_2. On the contrary, in a multivariate model including NYHA class, age, appendicular muscle mass, total fat mass and gender, the last parameter lost its predictive power. This suggests that differences in exercise capacity between men and women are probably due to differences in body composition. In the same model, both muscle mass and total fat mass were independent predictors of peak Vo_2, underlying the importance of body composition in determining exercise tolerance.

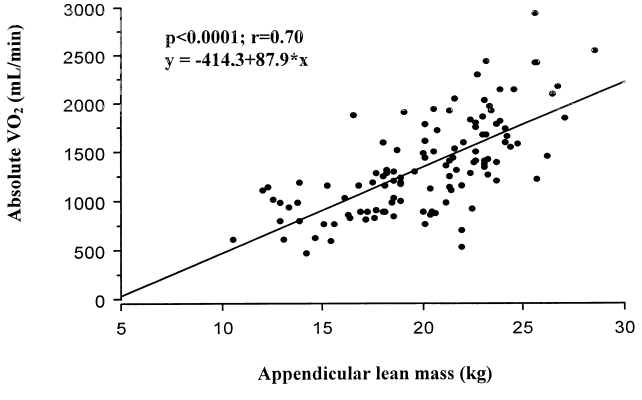

Figure 1. Linear regression analysis between appendicular lean mass and absolute peak oxygen consumption (Vo_2) in a population of 120 noncachectic patients with chronic heart failure.

The relationship between skeletal muscle mass and peak Vo_2 is quite clear. In fact, Vo_2 during maximal exercise occurs almost exclusively in the exercising muscles as blood is shunted away from the splanchic bed (27). On the contrary, total fat mass has a negative relationship with peak Vo_2, that is, the higher the fat content, the lower the exercise capacity. These findings have potential clinical implications, as the value of peak Vo_2 in defining functional status and predicting outcome might be enhanced by correcting absolute Vo_2 for skeletal muscle mass instead of for total body weight. In a recent paper, Osman et al. (28) reported the prognostic value of body fat adjusted peak Vo_2 compared with weight adjusted peak Vo_2 in a population of 225 patients with CHF. In their study, despite a nonoptimal evaluation method of body composition, encouraging results were found. In the future, an even more striking difference between the two variables might be expected by evaluating body composition with DEXA instead of the skinfold technique. This correction might be particularly useful in women and may increase the prognostic value of peak Vo_2 in this group of patients. Similar implications might concern

Table 4. Predictors of Peak Vo_2 (ml/min/kg) and Absolute Vo_2 (ml/min) in a Population of 120 Patients With CHF (Multivariate Analyses)

	Peak Vo_2 (ml/min/kg)		Absolute Peak Vo_2 (ml/min)	
Variable	**p Value**	**b (95% CI)**	**p Value**	**b (95% CI)**
NYHA class	< 0.0001	−2.3 (−3.3 − −1.3)	< 0.0001	−198.7 (−295.1 ÷ −102.3)
Gender	< 0.0001	−3.5 (−5.8 − −1.2)	< 0.0001	−389.2 (−598.7 ÷ −179.6)
Age (yr)	< 0.0001	−0.22 (−0.3 − −0.14)	< 0.0001	−199.3 (−272.7 ÷ −125.8)
Renin (ng/l)	< 0.0001	−0.01 (−0.02 − −0.001)	0.01	−0.9 (−1.6 ÷ −0.2)
Stroke volume (ml)	NS	—	< 0.05	4.7 (1.1–8.0)
	R^2 = 0.47		R^2 = 0.49	
Variable	**p Value**	**b (95% CI)**	**p Value**	**b (95% CI)**
NYHA class	< 0.0001	−2.1 (−3.1 ÷ −1.2)	< 0.0001	−13.4 (−19.5 ÷ −7.3)
App. lean mass (kg)	0.009	0.3 (0.1 ÷ 1)	0.002	−0.8 (−1.32 ÷ −0.3)
Age (yr)	< 0.0001	−0.18 (−0.26 ÷ −0.1)	< 0.0001	−149.8 (−224.3 ÷ −75.3)
Renin (ng/l)	< 0.0001	−0.015 (−0.02 ÷ −0.008)	< 0.0001	74.9 (56.7 ÷ 93.2)
Gender	NS	—	NS	—
	R^2 = 0.50		R^2 = 0.65	
Variable	**p Value**	**b (95% CI)**	**p Value**	**b (95% CI)**
Age (yr)	< 0.0001	−0.19 (−0.3 ÷ −0.1)	<0.0001	−13.3 (−19.3 ÷ −7.2)
Renin (ng/l)	< 0.0001	−0.01 (−0.02 ÷ −0.01)	< 0.0001	−0.95 (−1.47 ÷ −0.42)
NYHA class	< 0.0001	−2.0 (−2.9 ÷ −1.1)	< 0.0001	−157.4 (−231.4 ÷ −83.3)
App. lean mass (kg)	< 0.01	0.4 (0.1 ÷ 0.6)	< 0.0001	70.4 (51.7 ÷ 89.0)
Total fat mass (kg)	< 0.01	−0.1 (−0.2 ÷ −0.04)	NS	—
Gender	NS	—	NS	—
	R^2 = 0.53		R^2 = 0.66	

APP = appendicular; CHF = chronic heart failure; CI = confidence interval; NYHA = New York Heart Association; Vo_2 = oxygen consumption.

the effect of age on peak Vo_2; in fact, it is well known that the age-associated reduction in Vo_2 is related to the loss of skeletal muscle (29).

Potential therapeutic implications. After considering the relationship between skeletal muscle mass and exercise capacity, one might hypothesize that peak Vo_2 would increase after interventions directed towards the increase of skeletal muscle bulk. Cardiac rehabilitation (30,31), human growth hormone (32) and anabolic steroids (33) might provide some benefits to the periphery. In a recent study, Harrington et al. (34) showed beneficial effects of salbutamol on skeletal muscle in patients with CHF. Randomized studies are needed in order to define the possible effects of these means on skeletal muscle mass and, consequently, on functional capacity.

Ventilatory response to exercise and skeletal muscle mass. Another important finding of this study was the relationship between skeletal muscle mass and VE/VCo_2 slope. Appendicular lean mass predicted VE/VCo_2 slope independently of LVEF, age and neurohormonal activation. The increase of VE/VCo_2 in patients with CHF carries relevant clinical consequences as it predicts outcome independently of peak Vo_2 (35). A variety of abnormalities contribute to the increase in the ventilatory response to exercise in patients with CHF including increased anatomical dead space (36), ventilation-perfusion mismatch (37), pulmonary vasoconstriction (38) and altered chemosensitivity (39). It is not easy to explain why a reduced skeletal muscle mass is associated with a higher VE/VCo_2. In a small population Harrington et al. (40) observed that the amount and type of the exercising muscle can influence the VE/VCo_2 in patients with CHF, possibly because of a greater metabolic stress on a smaller group of active muscles. A muscle metaboreflex has been recognized as a stimulation to ventilation (41), and this reflex is increased in patients with CHF (42). Therefore, this might represent the link between skeletal muscle bulk and the abnormal ventilation we observed in our study. An increase of skeletal muscle mass might, theoretically, result in a decrease in ventilatory drive during exercise in these patients.

CONCLUSIONS

Our study further supports the role of skeletal muscle in the pathophysiology of CHF. Skeletal muscle mass is an important determinant of exercise capacity independent of central hemodynamics, neurohormonal activation, gender and age; furthermore, it relates to ventilatory response during exercise. Therefore, it seems important for patients with CHF to maintain a normal skeletal muscle mass in order to avoid functional impairment. Whether an increase of skeletal muscle mass would result in an improvement of exercise capacity and a reduced ventilatory drive during exercise needs to be confirmed by future studies.

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