Heart Metab. (2014) 64:28–30

Skeletal muscle myopathy in advanced heart failure: a case report

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Abstract

Chronic heart failure (CHF) is a progressive myocardial disease characterized by the inability of the heart to pump enough blood to meet the body's demand and by a reduced exercise tolerance. Recently, the presence of a skeletal myopathy has received much attention as the main player responsible for the reduced aerobic capacity in patients with CHF. Herein, we describe a case of a patient with advanced CHF with skeletal myopathy who underwent a cardiopulmonary test as well as dobutamine and exercise echocardiography stress tests for the determination of peak cardiac output. A blunted increase in cardiac output, attained with either dobutamine or during exercise, suggests that forward failure is still a major determinant of reduced aerobic capacity. ■ *Heart Metab*. 2014;64:28–30

Keywords: cardiac output; cardiopulmonary exercise test; echocardiography; heart failure; skeletal muscle myopathy

Chronic heart failure (CHF) is characterized by an intolerance to exercise that causes early fatigue and shortness of breath. Intuitively, cardiac output (CO) is expected to be a stronger determinant of aerobic capacity in patients with CHF. However, it is now well recognized that patients with CHF may reach a peak oxygen consumption (peak $\dot{V}O_2$) during symptom-limited exercise on a treadmill or bicycle before exhausting the capacity of the left ventricle to increase CO.[1] A number of authors suggested that peripheral skeletal muscle abnormalities prominently contribute to the exercise intolerance associated with CHF, whereas, central hemodynamic parameters, such as CO, are far less predictive of clinical symptoms and outcomes.[2-7] Herein, we describe a case of a patient with advanced CHF with skeletal myopathy who underwent cardiopulmonary exercise tests (CPXs) as well as dobutamine and exercise echocardiography stress tests for the determination of peak CO.

Case report

The patient was a 65-year-old man with a history of hypertension, type 2 diabetes, cigarette smoking, mild chronic renal failure, and sleep-related Cheyne-Stokes respiration. In January 2013, he was hospitalized for anterior ST-segment elevation myocardial infarction complicated by cardiac failure followed by cardiogenic shock, ventricular fibrillation, and cardiac arrest. After resuscitation, an intra-aortic balloon pump was inserted until the patient was clinically stabilized. At that time, the patient underwent coronary angiography, which showed a 75% stenosis of the proximal left anterior descending artery with total occlusion of the middle

Abbreviations

ACE inhibitors: angiotensin-converting enzyme inhibitors; **BNP:** brain natriuretic peptide; **CHF:** chronic heart failure; **CO:** cardiac output; **CPX:** cardiopulmonary exercise test; **EMG:** electromyography; **LV:** left ventricular

segment of the same vessel. He was then revascularized with percutaneous angioplasty and stenting of the coronary lesions. The following month, he was implanted with an automatic cardioverter-defibrillator.

In October 2013, the patient was hospitalized due to worsening decompensation symptoms, including shortness of breath at rest, orthopnea, and paroxysmal nocturnal dyspnea. Physical findings included tachycardia, S3 gallop, and diffuse pulmonary rales. An echocardiogram showed an enlarged left ventricle with global hypokinesia and apical, anterior, inferior, lateral, and septal akinesia. The patient's left ventricular (LV) ejection fraction was 0.26, the ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity (E/E') was 17.6, and resting cardiac index was 1.75 L/min/m^2. He received optimal medical therapy with aspirin, angiotensin-converting enzyme (ACE) inhibitors, β-blockers, antialdosterone antagonists, and loop diuretics. On admission, brain natriuretic peptide was 802 pg/mL and N-terminal pro-brain natriuretic peptide was 2704 pg/mL. At the time of hospital discharge, they were 418 pg/mL and 1980 pg/mL, respectively.

After stabilization of the clinical status, the patient underwent CPX, dobutamine, and exercise echocardiography stress tests. Peak $\dot{V}O_2$ was 13.0 mL/kg/min. During the stress tests, CO showed similar responses to direct inotropic stimulation as well as to exercise. A blunted increase in CO was apparent either with dobutamine (from 3.5 to 4.8 L/min) or with exercise (from 3.0 to 4.7 L/min). The total workload (40 W) and time to exhaustion were similar with CPX and exercise echocardiography. The patient underwent electromyography (EMG) to detect the electrical activity generated by skeletal muscle cells of the lower limbs. A decrease in action potential duration and a reduction in the area to amplitude ratio of the action potential were reported on the right quadriceps femoris. The responses were totally absent on the left quadriceps femoris. These findings were interpreted to be a result of a reduction in the number of motor units secondary to increased interstitial cellularity and decreased capillary density.

Discussion

This case report shows that the presence of the skeletal myopathy, as diagnosed by EMG, cannot solely explain a patient's inability to perform exercise. The blunted LV response either to inotropic stimulation or during exercise is indicative of the importance of central hemodynamics and that CO should be regarded as a key limiting factor of exercise capacity.

Skeletal myopathy refers to a clinical disorder of the skeletal muscles. Abnormalities of muscle cell structure and metabolism lead to various patterns of weakness and dysfunction. Many reports claim that alterations in skeletal muscle morphology, metabolism, blood flow, and function play a major role in exercise intolerance in patients with CHF, the so-called "skeletal muscle hypothesis." However, our findings show that, even in the presence of documented skeletal muscle myopathy, cardiac dysfunction is still a major determinant of reduced exercise tolerance in CHF.[8-12] As a matter of fact, it is remarkable that, in this patient, the CO responded similarly using either the dobutamine stress test or exercise. Since CO greatly contributes to peak $\dot{V}O_2$, this observation suggests that LV pump failure rather than muscle skeletal myopathy is the primary determinant of the reduced exercise capacity, even in the presence of documented muscle abnormalities. The role of LV systolic and diastolic parameters in predicting cardiopulmonary exercise performance has been addressed by several authors.[13-15] In the study by Scrutinio et al, the cardiac response to low-dose dobutamine, as assessed by echocardiography, correlated well with peak $\dot{V}O_2$.[13] In another study, the E/E' ratio was found to be the most powerful predictor of peak oxygen consumption.[15]

Recently, some authors have proposed an alternative view to "the skeletal muscle hypothesis" that can account for the influences played by the periphery on central hemodynamics.[16-18] It is highly probable that the inability to enhance ventricular contractility during stimulation plays a pivotal role in the inability of CHF patients to increase stroke volume. The overactivation of signals originating from skeletal muscle receptors (mechano-metaboreceptors) is an intriguing hypothesis proposed to explain the origin of symptoms and the beneficial effect of exercise training in the CHF

syndrome. The so-called metaboreflex has been reported to be hyperactive in CHF and to be responsible for a paradoxical increase in systemic vascular resistance and decrease in cardiac output whenever it is activated in these patients.

Conclusion

Although skeletal muscle abnormalities may contribute to the ability of the left ventricle to increase CO with exercise and to the early occurrence of fatigue and dyspnea, in this particular case report, the blunted cardiac response to dobutamine cannot be explained by the presence of skeletal myopathy. Impaired myocardial responses during dobutamine and exercise stress echocardiography indicate that central hemodynamics are always a primary determinant of exercise capacity in patients with CHF. It is likely that most symptoms resulted mainly from a forward cardiac failure secondary to the large myocardial infarction, in spite of the presence of documented skeletal muscle myopathy. ■

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