Inspiratory Muscle Weakness Is Associated With Exercise Intolerance in Patients With Heart Failure With Preserved Ejection Fraction: A Preliminary Study

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ABSTRACT

Background: The relationship between inspiratory muscle weakness (IMW) and exercise intolerance in patients with heart failure with preserved ejection fraction (HFpEF) remains unestablished.
Methods and Results: The present study enrolled 40 patients with HFpEF (EF ≥45%). IMW was defined as maximum inspiratory pressure <70% normal predicted values. The function of the diaphragm was assessed by means of ultrasound measurement of muscle thickening of the diaphragm. IMW was prevalent in 27.5% of patients. Patients with IMW had significantly lower vital capacity relative to normal predicted values (%VC), lower knee extensor muscle strength in relation to body weight (%KEMS), poorer nutritional status as assessed by means of the Geriatric Nutritional Risk Index, and shorter 6-minute walk distance (6MWD) compared with patients without IMW (all $P < .05$). Impaired diaphragm muscle thickening at end-inspiration (median value < 3.9 mm) was significantly associated with a high prevalence of IMW and reduced 6MWD (all $P < .05$). Subgroup analysis showed that IMW was accompanied by a further decrease in 6MWD in patients with restrictive pulmonary dysfunction (%VC <80%) or lower-limb muscle weakness (median %KEMS <30%; all $P < .05$).
Conclusions: IMW is associated with exercise intolerance in patients with HFpEF. (*J Cardiac Fail 2016;22:38–47*)
Key Words: Exercise intolerance, diaphragm, skeletal muscle.

The prevalence of heart failure with preserved ejection fraction (HFpEF) has increased with advancing age over the past decades. This has imposed a considerable burden on the health care system.[1] The primary symptom of patients with HFpEF is reduced exercise tolerance with fatigue and dyspnea, contributing to a poor prognosis and quality of life (QOL).[2] Despite the importance of HFpEF, the precise mechanisms of exercise intolerance in patients with HFpEF have not been well established. Therefore, there is an absence of effective therapeutic strategies.

Earlier studies have suggested that inspiratory muscle weakness and peripheral skeletal muscle dysfunction are a part of the underlying mechanisms for exercise intolerance in patients with heart failure with reduced ejection fraction (HFrEF).[3] Patients with HFrEF show reduced inspiratory muscle strength and endurance, which are currently recognized as additional factors implicated in a limited exercise response and QOL, as well as in their poor prognosis.[3–8] The precise cause of inspiratory muscle dysfunction remains speculative. However, diaphragm biopsies have shown a variety of histologic abnormalities, including fiber type I atrophy. These abnormalities are involved in a generalized skeletal muscle disorder in HFrEF.[6] Recent studies have shown beneficial effects of inspiratory muscle training in patients with HFrEF on inspiratory muscle strength, respiratory endurance, functional capacity, QOL, and subjective symptoms.[3,6–8] Many epidemiologic studies have concluded that HFpEF has a different pathophysiology from HFrEF. However, there is currently little information on inspiratory muscle weakness and its relation to exercise intolerance in patients with HFpEF.

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Therefore, we investigated the effect of inspiratory muscle weakness on limited exercise tolerance in patients with HFpEF.

Methods

Patients

A flow chart of study participants is shown in Fig. 1. The present study enrolled 69 consecutive patients. These patients were hospitalized and discharged from Tottori University Hospital with a primary diagnosis of HFpEF from January 2012 to September 2014. Patients with HFpEF were defined as follows: 1) patients with symptoms of heart failure (HF) defined by the Framingham criteria, 2) patients with preserved left ventricular ejection fraction ≥45% as previously described,[9] and 3) patients without the HF etiologies of severe valve disease, congenital disease, complete atrial ventricular block, sick sinus syndrome, pericardial disease, primary pulmonary hypertension, pulmonary artery embolism, or acute myocardial infarction.

The following patients were excluded: 1) patients who could not take physical functional tests because of poor exercise performance, dementia, or motor dysfunction because of cerebrovascular or orthopedic diseases (n = 18), 2) patients with missing data (n = 9), and 3) patients with pyothorax and a history of pneumonectomy (n = 2). Finally, data of 40 patients were used for analysis in this study. All of the patients were treated with diuretics, vasodilators, and/or inotropes for relief of symptoms after admission. Following stabilization for HF, they received cardiac rehabilitation during their hospital stay, including endurance exercise training consisting of cycle ergometer exercises or walking, as well as resistance training for the upper and lower limbs, as previously described.[10]

Data Collection

Medical records were retrospectively reviewed with regard to demography, medical history, comorbidities, laboratory data, echocardiograms, medications, and physical functional tests. All measurements were taken at hospital discharge.

Inspiratory Muscle Strength and Pulmonary Function. Measurements of maximum inspiratory pressure (MIP), vital capacity (VC), forced expiratory volume in 1 second (FEV1), and forced vital capacity (FVC) were obtained with the use of a multifunctional spirometer (HI-801; Chest, Tokyo, Japan) as recommended by the American Thoracic Society.[11,12] MIP and VC were expressed as the percentage of normal predicted value (%MIP, %VC).[6,13,14] Inspiratory muscle weakness was defined as %MIP <70%.[6] Restrictive and obstructive pulmonary dysfunction were defined as %VC <80% and an FEV1/FVC ratio <0.7, respectively.

Handgrip Strength. Handgrip strength was measured with the use of a grip dynamometer (Grip-D; Takei, Tokyo, Japan) set at the 2nd grip position. Three measurements were made on each hand. We calculated the average value of the right- and left-side handgrip strength.[15]

Knee Extensor Muscle Strength. Knee extensor muscle strength (KEMS) was measured with the use of a hand-held dynamometer (μTas F-1; Anima, Tokyo, Japan). All patients sat on a bench, and the dynamometer was fixed to a rigid bar. Testing was carried out for both legs at a maximum of 3 times the maximal isometric voluntary contraction of the knee extensor muscles and at a knee flexor angle of ~80°–90°. The hip joint angle was set at ~80°–90° of flexion. After measurements were performed, we calculated the average values of the right- and left-side knee extensor strength, which was corrected for body weight (%KEMS).[15] Lower-limb

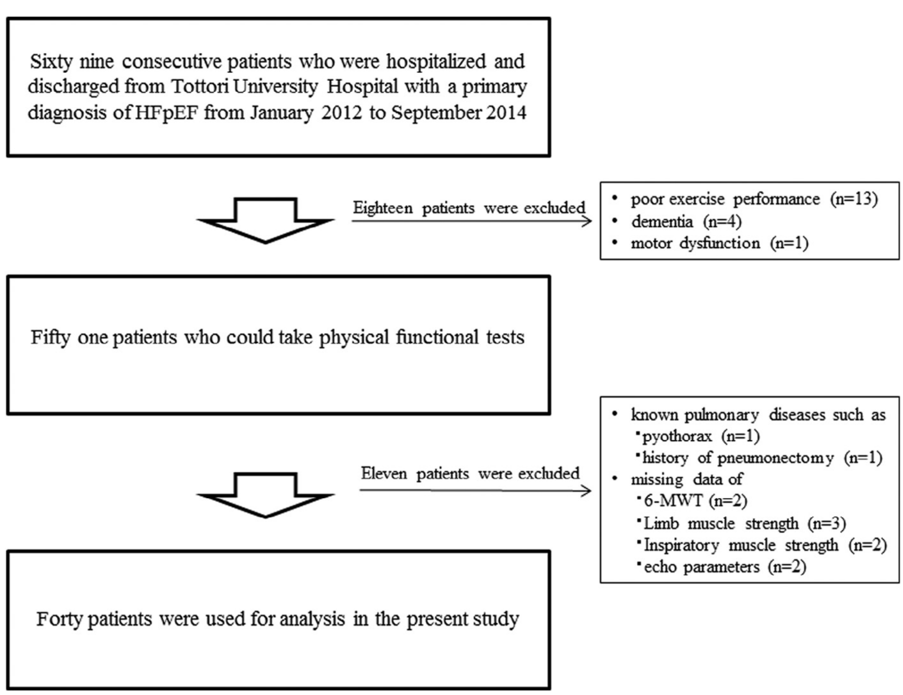

Fig. 1. Flow chart of study participants. 6-MWT, 6-minute walk test.