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Quadriceps weakness contributes to exercise capacity in nonspecific interstitial pneumonia

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Summary
Background and objective: It has been shown that peripheral muscle dysfunction is a critical factor in determining exercise intolerance in patients with several chronic lung diseases, including idiopathic pulmonary fibrosis. We hypothesized that exercise capacity would be, at least in part, determined by peripheral muscle dysfunction in patients with fibrotic nonspecific interstitial pneumonia (f-NSIP), another major subtype of fibrotic interstitial lung disease. The aim of the current study was to elucidate the relevance of peripheral muscle dysfunction and its contribution to exercise intolerance in f-NSIP.
Methods: The six-minute walk test was evaluated in 30 consecutive patients with f-NSIP along with potential determinants of exercise capacity, including respiratory muscle force and peripheral muscle force.
Results: Among 30 patients, the median age was 61 years, and 21 were female. Sixteen patients showed significantly decreased quadriceps force (QF), and 17 had significant decreases in maximum expiratory pressure. Exercise capacity and muscle power were clearly related to sex. Adjusted for sex, QF showed a significant relation to exercise capacity measured by six-minute walk distance (6MWD), whereas pulmonary function parameters such as vital capacity showed marginal correlations. In stepwise multiple regression analysis, only QF was an independent predictor of 6MWD.

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Conclusions: Quadriceps weakness is often observed in patients with f-NSIP. It seems that QF significantly contributes to exercise capacity in this population.

Introduction

The importance of evaluating exercise capacity is widely recognized in chronic lung diseases. Its clinical relevance has been intensely investigated especially in patients with chronic obstructive lung disease, and its impacts on their prognosis as well as their quality of life have been elucidated.[1] More recently, attention is also being directed to evaluation of exercise capacity in patients with interstitial lung diseases. Several recent studies have reported that six-minute walk distance (6MWD) is an independent and discriminating predictor of mortality among patients classified as having idiopathic pulmonary fibrosis (IPF).[2]

Fibrotic nonspecific interstitial pneumonia (f-NSIP) has been recognized, along with IPF, as one of the major types of chronic idiopathic interstitial pneumonias.[3–5] F-NSIP has come to be recognized as a distinct disease entity with characteristic clinical, radiologic, and pathologic features that differ from other idiopathic interstitial pneumonias.[5] However, the number of previous studies that have conducted exercise testing in f-NSIP patients is very limited.[2,6]

Previously, we reported factors related to exercise capacity in IPF and demonstrated that quadriceps weakness was related to exercise capacity.[7] However, the determinants of exercise tolerance in interstitial pneumonias other than IPF remain uncertain.

In considering the mechanisms of exercise limitation in patients with f-NSIP, we hypothesized that peripheral muscle weakness may exist in patients with f-NSIP and may contribute to exercise intolerance. We therefore assessed exercise tests and respiratory and peripheral muscle function of patients with f-NSIP along with tests of pulmonary function to explore the determinants of exercise capacity.

Materials and methods

Study subjects

Consecutive patients with f-NSIP diagnosed at Tosei General Hospital from April 2003 to March 2011, who consented to the study and underwent subsequent measurements in pulmonary function, exercise capacity and muscle strength, were retrospectively reviewed. During the study period a total of 257 cases of interstitial lung diseases were diagnosed by surgical lung biopsy at this hospital. One hundred and thirty patients were diagnosed as having fibrotic idiopathic interstitial pneumonia, and 38 of them were diagnosed with f-NSIP. The diagnosis of f-NSIP was confirmed by two lung pathologists. F-NSIP was newly diagnosed by a physician using the diagnostic criteria in the ATS/ERS consensus statement.[8] Patients who had received corticosteroids or similar medical treatment prior to the evaluation were excluded. Patients were also excluded if they had (1) clinically evident connective tissue disease (CTD), (2) cardiac disease, (3) obstructive lung disease such as COPD or asthma, and (4) other pathologic conditions (arthritis, malignancy, cerebrovascular disease).

This analysis was approved by our local institutional review board.

Exercise capacity

To evaluate exercise capacity, the current study adopted the six-minute walk test (6-MWT), a reliable, valid, and responsive measure of exercise tolerance in patients with interstitial lung diseases.[9] It also has major advantages over maximal exercise testing in terms of reproducibility in the routine evaluation of fibrotic interstitial pneumonias.[10]

The 6-MWT was conducted in all patients who participated in the study, according to the ATS statement.[11] Briefly, all patients were tested under standardized conditions by trained technicians. Baseline heart rate and oxygen saturation were measured. Patients were instructed to walk as far as possible in 6 min. The distance the patients could walk was recorded. Oxygen saturation was monitored and recorded continuously throughout the test by pulse oximetry. No supplemental oxygen was given during the test.

Pulmonary function tests and arterial blood gas tensions

All patients underwent pulmonary function testing including lung volumes and spirometry (CHESTAC-55V; Chest; Tokyo, Japan), according to the method described in the ATS 1994 update.[12] Single-breath diffusing capacity of carbon monoxide (DLco) was also measured (CHESTACV; Chest). The values for vital capacity (VC) and DLco were also related to predicted values. Arterial blood gas tensions were measured at rest.

Respiratory muscle force

Maximal inspiratory pressure (PI max) and maximal expiratory pressure (PE max) were determined in all patients. PI max was measured at residual volume, and PE max was measured near total lung capacity, according to the well-validated method proposed by Black and Hyatt (Vitalopower KH-101; Chest).[13] The highest value from at least three maneuvers was recorded. Reproducibility of the measurements was fairly good.

To determine patients with significant weakness in respiratory muscle power, the values were related to the predicted values[13] and those less than 80% of the prediction were considered to be significantly weak.[14]

Peripheral muscle force

The measurements of peripheral muscle forces were done with the methodologies well validated in the previous studies.[7,15]

Hand grip force (HF) was measured with a hydraulic hand dynamometer (Smedley's Dynamometer; TTM; Tokyo,