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Clinical significance of pectoralis muscle strength in elderly patients with idiopathic pulmonary fibrosis

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Abstract *Introduction:* Investigations of muscle dysfunction in patients with idiopathic pulmonary fibrosis (IPF) are limited to peripheral muscles. However, decreased thoracic muscle mass is known and deterioration of chest wall muscle strength is not clear. *Objective:* The aims of the present study were to evaluate pectoralis muscle strength located on the chest wall and to investigate the relationship of spirometric measurements and respiratory muscle strength with pectoralis muscle strength. *Methods:* Elderly patient with IPF (mean disease duration 7.47±7.04 years) and the age-and sex-matched healthy volunteers were recruited in this cross-sectional study. The pulmonary function test was performed by a portable spirometer for spirometric variables and a gas analyzer for diffusing capacity for carbon monoxide (DL_{CO}). Maximal inspiratory (MIP) and expiratory pressure (MEP) were measured with mouth pressure device. Modified Medical Research Council Dyspnea Scale (MMRC) was used to determined dyspnea severity. The pectoralis muscle strength was assessed isometrically during shoulder joint horizontal adduction movement with a handheld dynamometer. *Results:* A total of 17 patients with IPF (9 males, mean age 69.06±3.94 years) and 19 healthy controls (10 males, mean age 70.95 ±4.99 years) were included. Patients with IPF had lower pectoralis muscle strength than healthy controls ($p<0.001$). Significant relationships were found between pectoralis muscle strength and MIP ($r=0.79$, $p<0.001$), MEP ($r=0.81$, $p<0.001$), FEV_1% ($r=0.54$, $p=0.02$), FVC% ($r=0.68$, $p<0.003$) and DL_{CO} ($r=0.61$, $p=0.009$). With multiple linear regression analysis, pectoralis muscle strength was the only independent predictor of FVC% (adjusted $R^2=0.37$, $p<0.05$). *Conclusion:* In patients with IPF, pectoralis muscle strength decreases and is associated with pulmonary function. In particular pectoralis muscle strength is likely to have an important impact on FVC%. Therefore, we consider that this test should be included routinely in chest diseases and rehabilitation clinics. The trial was registered U.S. National Library of Medicine clinical trial registry (https://clinicaltrials.gov, Trial ID: NCT04803617)

Keywords: Idiopathic pulmonary fibrosis, Pectoralis muscle strength, Pulmonary function test, Chest wall muscle

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Introduction

Idiopathic pulmonary fibrosis (IPF) is a type of idiopathic interstitial pneumonia. It usually occurs in people older than 50 years and is associated with poor prognosis and survival (1). Exercise limitation and skeletal muscle dysfunction are observed due to exertion dyspnea, impaired lung function and oxidative capacity in patients with IPF (2).

Abnormal lung mechanics increase the respiratory workload and cause overload on respiratory muscles (3). In a study involving individuals with interstitial lung disease, it was reported to reduce transdiaphragmatic pressure and increase load on inspiratory muscles (4). When there is diaphragm fatigue, dysfunction or increased inspiratory effort, accessory respiratory muscles participate in ventilation (5). Although the diaphragm and internal intercostal muscles are the main inspiratory muscles involved in ventilation, accessory respiratory muscles have important roles in forced vital capacity (FVC) (6). It is considered that upper limb exercises which mainly involve horizontal adduction movements improve the ratio of dyspnea (7) and the pectoralis muscle may be associated with pulmonary function, especially in older people (8). Additionally, it was reported that low thoracic skeletal muscle mass is related to worse prognosis in patients with IPF (9) and the cross-sectional area of the pectoralis major muscle is associated with pulmonary function in chronic obstructive pulmonary disease (COPD) (10).

Research examining the skeletal and respiratory muscles in COPD are common but there are fewer studies about this issue in IPF and it is also unclear whether there is a relationship between peripheral muscle, chest wall muscle and respiratory muscles with lung mechanics (11,12). To the best our knowledge, there are no studies investigating changes in pectoralis muscle strength or the relationship between this muscle group and pulmonary function in IPF. This study aimed to examine changes in pectoralis muscle strength and the relationship between pectoralis muscle strength and pulmonary function in patients with IPF.

Method

Study population

This study was carried out with patients who attended to Sureyyapasa Chest Diseases and Thoracic Surgery Training Research Hospital from February 2017 to November 2018 and healthy controls who were recruited from the local community by invitation. Patients diagnosed with IPF by a multidisciplinary team according to the official ATS/ERS/ JRS/ ALAT statement (1) receiving stable antifibrotic drug therapy and aged 65-85 years were included. Patients with uncontrolled/active cardiovascular, metabolic, systemic or cancerous disease and/or significant orthopedic, neurologic or musculoskeletal comorbidity that limited functional independence and acute exacerbation history within last month due to IPF were excluded.

This cross- sectional study was approved by the Clinical Research Ethics Committee (Approval Number: 2016/5//17) and was performed in accordance with the Declaration of Helsinki. All participants signed written informed consent.

Clinical data

Baseline characteristics such as age, sex, body mass index (BMI), smoking history and disease duration were recorded. Pulmonary function was evaluated by measuring the spirometric values, diffusing capacity for carbon monoxide (DL_{CO}) and respiratory muscle strength. Pectoralis muscle strength was isometrically measured. The Modified Medical Council Research (MMRC) dyspnea score was used for evaluation of breathlessness. All assessments were performed in both groups at average one hour.

Pulmonary Function Test

The spirometric parameters were performed with portable spirometer (M.E.C. PFT Systems Pocket-Spiro) in accordance with American Thoracic Society and European Respiratory Society (ATS/ ERS) guidelines for pulmonary function tests. Forced expiratory volume in one second (FEV_1), FVC and FEV_1/FVC variables were measured and recorded as percentages of the predicted values (13). DL_{CO} values were measured in only patient groups according to ATS/ ERS guidelines for pulmonary function tests (14)

Respiratory Muscle Strength

Respiratory muscle functions were evaluated by measuring maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) using a mouth pressure device (M.E.C. PFT Systems Pocket- Spiro) in sitting position. Participants breathed through a

flanged mouthpiece inside the lips at near residual volume for the MIP value and near total lung capacity for MEP value (15). The maximum effort was sustained for at least one second. The test was repeated at least 3 times until no more than 10% difference was present between highest and previous measurement (16). The best value and percentage value of predicted best value were recorded.

Pectoralis Muscle Strength

The test was performed in supine position using with handheld dynamometer (Medical Commander Powertrack II; JTECH, Salt Lake City, UT, USA). The shoulder joint of participant was positioned at 90º abducted and at 0º internal/external rotation and the elbow joint was flexed at 90º. The other shoulder joint was fixed by the physiotherapist. While the participant performed isometrically horizontal adduction movement, the measurement was performed on the distal part of the upper arm by the physiotherapist and the contraction was sustained for at least 5 seconds by the participant (8). The test was performed three times and with 60 seconds rest between tests. The mean of the best value on both sides was recorded.

Dyspnea Assessment

Dyspnea severity during the various physical activities was assessed with MMRC dyspnea scale. The scale consists of 5 items scored from 0 to 4. 0 means that "I am not too breathless except during vigorous exercise" and 4 "I am too breathless during self-care activities like dressing, undressing, taking bath, etc. and I don't leave the house due to breathlessness" (17).

Statistical Analyses

Categorical variables were presented as frequency and percentages. Normally distributed continuous variables were presented as mean± standard deviation and non- normally distributed variables were presented median and interquartile range (IQR). Normality of continuous variables was tested with the Shapiro-Wilk test. Chi-square and Fisher's Exact Test were used to compare categorical variables between patient and healthy control groups. The Student's T-Test and Mann Whitney U test were used to compare continuous variables between the groups. Adjusted of pectoralis muscle strength according to age and sex were tested with analyses of covariance (ANCOVA). The correlations between pectoralis muscle strength and FVC%, DL_{CO}%, FEV_1%, MIP and MEP values were examined using Pearson's and Spearman's Rank Correlation Coefficients according to normality tests. Independent predictor variables for FVC% value were determined by using multiple linear regression analysis. Statistical analyses were performed with SPSS 22.0 (IBM Corp., Armonk, NY, USA). P value <0.05 was considered significant.

Results

A total of 28 patients with IPF were assessed initially. Eleven patients were excluded because 4 patients had just begun antifibrotic drug therapy, 4 patients had neck-shoulder pain comorbidity and 3 patients refused to participate in the study. In total, 17 patients with IPF and 19 healthy controls were recruited in this study. The percentage of male participants was higher in the both groups. Participants in both groups were overweight according to BMI. No significant difference was present for age, sex, BMI, and smoking history between patients and healthy controls. Baseline characteristics of the participants are shown in Table 1.

The results of pulmonary function test, respiratory muscle strength, pectoralis muscle strength and MMRC dyspnea score of all participants are presented in Table 2. According to percentage of predicted FVC and DL_{CO} values, 5.9% of patients had severe disease and 23.5% of patients had moderate disease severity. Percentages of the predicted FVC, FEV_1, and FEV_1/FVC value of patients were significantly less than healthy controls. The results for respiratory muscle strength value were similar between the groups. The pectoralis muscle strength was significantly different between patients and healthy controls. No patients were observed to have resting desaturation. While none of the healthy controls had breathlessness, 5.9 percent of patients were breathless to a serious degree, while 23.5% had moderate degree of dyspnea.

Table 1. Baseline characteristics for IPF patients and healthy controls

Variables	Patients (n=17)	Healthy Controls (n=19)	P value
Male sex, n (%)	9 (52.9)	10 (52.6)	0.98
Age, years	69.06±3.94	70.95 ±4.99	0.22
Weight, kg	72.99±13.19	76.05±12.61	0.48
Height, cm	161.26±10.69	164.73±8.74	0.33
BMI, kg/m^2	28.21±3.83	27.97±4.10	0.86
Smoking history, n(%)			
Current smoker	0	3 (15.8)	0.22
Ex smoker	8 (47.1)	8 (42.1)	
Pack- years	0(70)	16(70)	0.75
Disease duration	7.47±1.71	0	<0.001*
Comorbidity (n.%)			
None	3(17.6)	9(47.3)	0.01*
1	11(64.8)	9(47.3)	
>1	3(17.6)	1(5.3)	

* Statistically significant data
Data are presented in mean and SD, n(%) and median (IQR). Abbreviation: BMI, body mass index.

Table 2. Comparison of clinical variables between patients and healthy controls

Variables	Patients (n=17)	Healthy controls (n=19)	P value
FVC, L	2,21±0,89	2,70±0,58	0.05
FVC% predicted	66.94±13.68	82.14±14.34	0.003*
FEV_1, L	1,81±0.66	2,21±0.56	0.06
FEV_1% predicted	72.14±13.77	82.78±14.56	0.03*
FEV_1/FVC ratio %	84.17±9.16	83.78±12.79	0.55
DLCO, mmol.min^{-1}. kPa^{-1}	3.3±0.97	-	-
DLCO % predicted	42.76±8.84	-	-
MIP, cmH_2O	55 (37.23)	57.52 (50)	0.58
MIP %	81.17±34.17	87.57±31.76	0.56
MEP, cmH_2O	71.71±24.66	81.58±29.31	0.28
MEP%	70.76±21.83	79.00±17.72	0.22
MMRC score	1(2)	0(0)	<0.001*
MMRC grade≥2 (n,%)	7(41.2)	0(0)	<0.001*
PM, N	154.85±55.65	241.10±65.75	<0.001*
PM_{pred}, N	154.64±12.11	241.29±11.44	<0.001*

* Statistically significant data.
Data are presented as median (interquartile range) for MIP cm-H2O and MMRC scores, n (%) for MMRC grade≥2 and mean ± SD for other variables. Abbreviations: FVC, forced vital capacity; FEV1, forced expiratory volume in the first second; DLCO, diffusion capacity for carbon monoxide; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; MMRC, modified Medical Research Council dyspnea scale; PM: pectoralis muscle, PMpred; pectoralis muscle value adjusted for age and sex

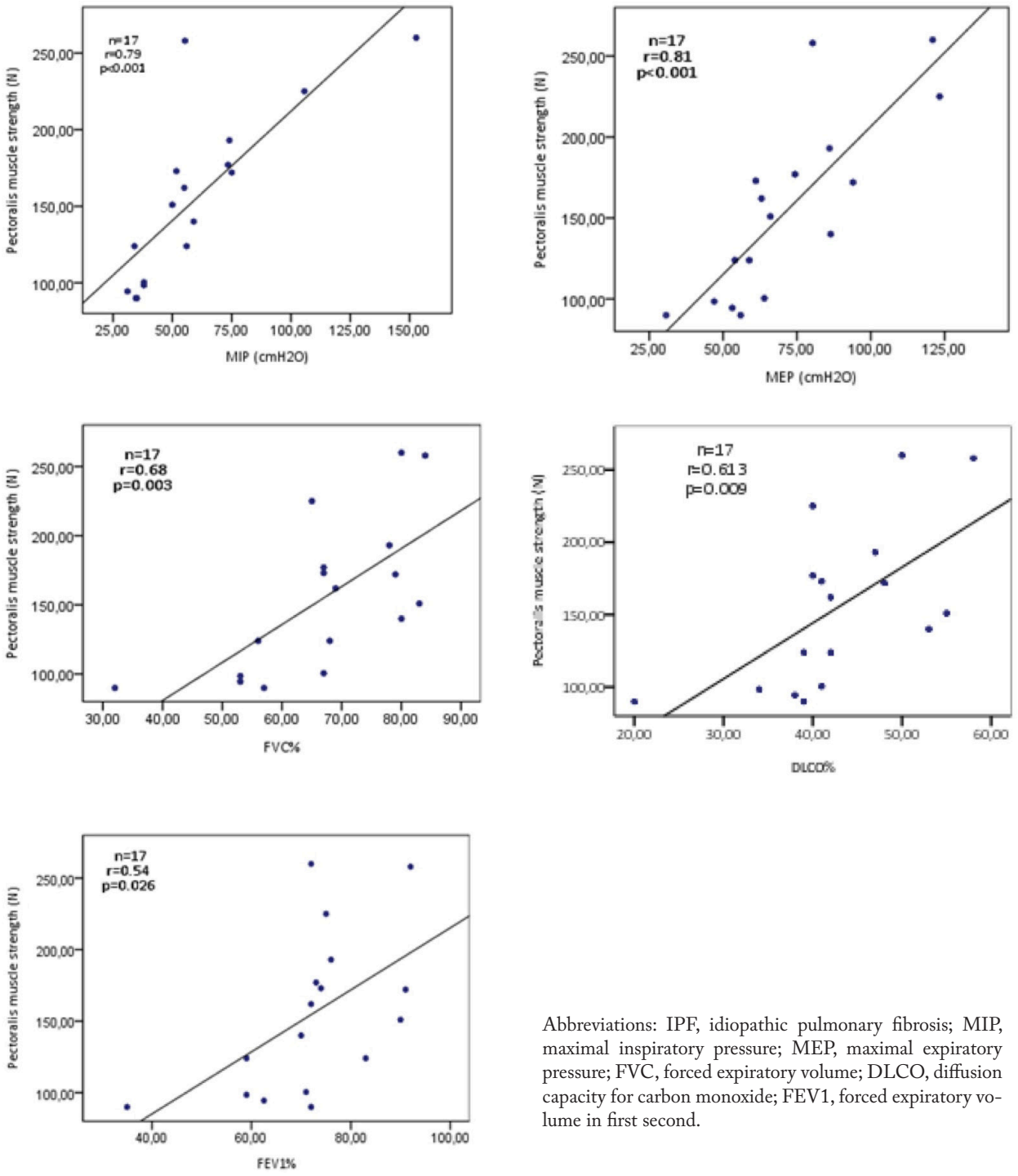
In the patient group, MIP and MEP revealed positive and strong (r=0.79, p< 0.001 and r=0.81, p<0.001, respectively), and FEV_1%, FVC%, DL_{CO}% showed positive and moderate correlations ((r=0.54, p=0.026), (r=0.68, p=0.003) and (r=0.61, p=0.009) respectively) with the pectoralis muscle strength (Figure 1).

The multivariate regression model consisting of the pectoralis muscle strength and the respiratory muscle strength was significant. The model predicted 37% of variance in FVC% but only pectoralis muscle strength was a significant independent predictor for FVC% (ß=0.79, t (15) =2.24, p=0.043). The results of multivariate linear regression analysis are shown in Table 3.

Discussion

This study mainly showed that pectoralis muscle strength was significantly decreased in elderly patients with IPF and pectoralis muscle strength was associated with pulmonary function as well as being an independent predictor for FVC% in this patient group.

Although there are studies showing skeletal muscle strength decreases in patients with IPF, limited data is available about this topic and previous studies focused on lower limb muscles (18,19). To the best our knowledge, this is the first study evaluating thoracic skeletal muscle strength in IPF. Specific muscle force begins to decrease from the age of 60-70 years (20). The present finding of pectoralis muscle weakness in IPF, regardless of aging, may have multifactorial causes such as exercise intolerance, limited activity in daily life, malnutrition, oxidative stress, corticosteroid use and hypoxemia as in other skeletal muscles (21). The pectoralis muscle, as a thoracic skeletal muscle, responsible for horizontal adduction movement in the upper limb and helps ventilation as an accessory respiratory muscle (15). In order to eliminate the effect of abnormal lung mechanics, it is recommended to evaluate the accessory respiratory muscles by a method other than the measurement of



Abbreviations: IPF, idiopathic pulmonary fibrosis; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; FVC, forced expiratory volume; DLCO, diffusion capacity for carbon monoxide; FEV1, forced expiratory volume in first second.

Figure 1. Relationship between pectoralis muscle strength and pulmonary function in patient with IPF

maximal mouth pressure (22). Therefore, we consider that evaluating pectoralis muscle strength in patients with IPF, which is known to increase respiratory workload, is important. Our results provide information about both upper limb and respiratory muscle strength in IPF.

Table 3. Results of multivariate lineer regression of FVC% and independent determinants in patient with IPF

Predictors	Unstandardized		Standardized	P value	R	R^2	Adj. R^2
	B	SE	Beta				
Model 1				0.03*	0.70	0.48	0.37
Constant	37.7	9.7		0.002*			
MIP, cmH2O	-0.17	0.19	-0.38	0.41			
MEP, cmH2O	0.13	0.26	0.24	0.62			
PM (N)	0.19	0.09	0.79	0.04*			

*Statistically significant data.
Abbreviations: SE, standard error; Adj R^2, adjusted R^2; FVC, forced expiratory volume; MIP, maximum inspiratory pressure; MEP, maximum expiratory pressure; PM, Pectoralis muscle strength

The changes in respiratory muscle strength are controversial in patients with IPF (12). Most of the previous studies have not been reported any change in inspiratory muscle strength compared to healthy controls, similar to our results (4,18). In contrast, decreasing maximal inspiratory pressure has also been reported in patients with IPF (23). Walterspecher et al. reported decreased transdiaphragmatic pressure and preserved PImax in 25 patients with interstitial lung disease (ILD) including the IPF subgroup (4). Diaphragm weakness and rapid shallow breathing which are common in IPF increase ventilatory demand and dyspnea sensations (24). The accessory respiratory muscles play the main roles in ventilation when the diaphragm cannot meet ventilatory demand (22). Therefore, the assessment of diaphragm and other respiratory muscles separately becomes important in IPF (12), although measurement of maximal inspiratory and expiratory mouth pressure is a practical and useful method in clinical practice.

In this study, pectoralis muscle strength was correlated with spirometric values at moderate levels and maximal mouth pressures at strong levels. In a previous study, it was reported that horizontal adductor strength may be associated with pulmonary function and measurement of shoulder joint horizontal adductor strength may be an alternative method when the pulmonary function test cannot be performed, especially in elderly individuals (8). Another study was shown that no correlation between proximal shoulder muscle strength and pulmonary function in COPD patients. Shoulder muscle strength was measured by 1 repetition maximum test in that study. 1RM test is performed with shoulder flexion movement in which the middle deltoid muscle plays the main role (25). Ortega et al. were reported that upper limb training which included the butterfly exercise that mainly focuses on the pectoralis major muscle decreased dyspnea in COPD (7). In a study conducted with 15 patients with COPD, inspiratory tidal volume, expiratory tidal volume and minute ventilation increased during horizontal adduction with inspiration when compared to the rest position. Chest wall expansion is more restricted during the horizontal adduction compared the other arm elevation movements. In this case, activation of accessory respiratory muscle is minimized and inspiration movement is directed to diaphragm muscle. Based on these, the addition of horizontal adduction exercise with inspiration to the pulmonary rehabilitation was recommended in patient with COPD (26).

To our researches, the only study investigating the relationship between pulmonary function and skeletal muscles in IPF belongs to Nishiyama et al. The quadriceps muscle strength correlated with vital capacity and total lung capacity in that study (18). On the other hand, on our topic, muscle cross-sectional area studies most of which are retrospectively designed and relatively easy to do have been recently included in the literature. In one of those studies, it was observed that thoracic skeletal muscle cross-sectional area is strongly correlated with mortality and disease severity in patient with ILD (9). The pectoralis muscle cross-sectional area (PM_{CSA}) is associated with MIP value in lung transplant candidates (27). A previous study reported that chest wall muscle mass was lost over time; therefore, the FVC% value decreased independent from disease progression in systemic sclerosis associated with ILD (6). While PM_{CSA} was associated with peripheral muscle strength and dyspnea in ILD, it was also associ-

ated with spirometric values in patients with COPD (10,28). On the other hand, regardless of total muscle mass and percentage of fat it has been demonstrated that IPF severity associated with upper limb muscle strength and physical performance (29). Decreased pectoralis muscle strength could be triggered an increased perception of exertional dyspnea and fatigue, the cardinal signs of IPF, because weakness of pectoralis muscle increases ventilatory demand and overload of the diaphragm (26). There is a moderate-strong correlation between skeletal muscle size and muscle strength in chronic respiratory disease (30). Mendes et al. reported that quadriceps muscle cross-sectional area was correlated with quadriceps muscle strength (r=0.63, p=0.001) and elbow flexor strength was correlated with biceps thickness (r=0.71, p=0.001) in patient with IPF (21). Considering that muscle strength is an indicator of both muscle mass and muscle force (28), the relationship between muscle strength and disease progression may lead to the conclusion that it may also be associated with deterioration in clinical parameters. In this context, we consider that our results are consistent with previous studies; however, further research is required about this topic.

The FVC value is an important spirometric variable in order to determine disease severity and predicted mortality in IPF as a restrictive disease (31). Knowing the components affecting FVC may contribute to establishing a treatment protocol. In our study, pectoralis muscle strength was an only independent predictor of FVC% value in the multivariate linear regression model consisting of pectoralis muscle strength and respiratory mouth pressures. Similar to a previous study (12), although negatively correlated with FVC%, the MIP value wasn't a significant predictor in the model. These results may be explained by several potential mechanisms. In one of them, accessory respiratory muscles play an important role in forced expiration and mainly contribute to FVC measurement, in addition to diaphragm and intercostal muscles becoming active during tidal breathing (6). Another explanation is that in lung diseases while limb muscle dysfunction may also be observed in the early period, respiratory muscle dysfunction generally occurs in the advanced stages of the disease (32). Hence, we may consider pectoralis muscle weakness occurs before respiratory muscle weakness. In a study was reported that 13% of patients with FVC > 90% needed oxygen supplementation (33).When considering that pectoralis muscles are mostly in type 1 fiber (28), weakness of pectoralis muscle may be explained with deoxygenation that seen in patient with mild severity of IPF. Also, corticosteroid drug therapy leads to weakness of peripheral muscle strength in early stage of IPF (34). In this content weakness of pectoralis muscle, which we found in patients with early stage IPF, may be an early indicator of disease progression.

The present study has some limitations. The sample size was relatively small due to the study was conducted in a single center. Our patients had mild-moderate disease severity. Therefore, changes in the pectoralis muscle strength were not shown per disease severity. On the other hand, we showed that pectoral muscle strength was decreased even in the early stage of IPF. The diffusion capacity of lung carbon monoxide values could not be measured in healthy controls therefore was not compared with patient group.

Conclusion

The present study may pioneer evaluation of pectoralis muscle strength. We proved that the pectoralis muscle strength was decreased and it was an independent predictor of FVC% value in patients with IPF. This result will contribute to understanding of skeletal muscle dysfunction and the relationship between skeletal muscle strength and pulmonary function in this population with limited data. Will exercise training programs for the pectoralis muscle may improve lung mechanics and respiratory volume, as in COPD? Further research in which muscle cross-sectional area and muscle strength are evaluated together is needed for more comprehensive investigation of the relationship between pectoralis muscle strength and patient clinical variables, such as exercise capacity, pulmonary function, and health-related quality of life.

Clinical Implication

The pulmonary function test is gold standard for measurement of spirometric value but when the pulmonary function test cannot be measured in cases such

as airway contamination or advanced age of the patient, pectoralis muscle strength test may be use for assessment of pulmonary function with an easy and well tolerated method. Since measurement of pectoralis muscle strength is a low-cost, rapid and clinically beneficial test, it may be beneficial for the patient to use it in geriatric patients and also patients require quicky decision.

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