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ORIGINAL RESEARCH

Exercise Testing in Severe Emphysema: Association with Quality of Life and Lung Function

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Abstra

Six-minu) are used to evaluate these tests as well a advanced emph physema Treat 218 individu ed. Predicte ns. Correlati etermine the asso rcise measure er (r = 0.57, p < 0.00 than on the correlation with measures of QOL, but maximum exercise capacity was better correlated with lung function measures than 6-minute walk distance. After adjustment, 6MWD had a slightly greater association with total SGRQ score than maximal exercise (effect size 0.37 ± 0.04 vs. 0.25 ± 0.03 %predicted/unit). Despite advanced emphysema, patients are able to maintain 6MWD to a greater degree than maximum exercise capacity. Moreover, the 6MWT may be a better test of functional capacity given its greater association with QOL measures whereas CPX is a better test of physiologic impairment.

Key words: :

Emphysema | Lung diseases | obstructive | Exercise tests | Quality of life | Clinical trial | multicenter studies

INTRODUCTION

The 6-minute walk test (6MWT) measures the distance that an individual can walk in 6 minutes (6-minute walk distance, 6MWD) and was designed as a submaximal exercise test to re ... rently it is widely u ... f mortality ([2], [3]) ... l resources and emp ... y exercise testing (... ce and provides ... h as maximu ... ([4]).

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In general, measures of lung function have limited ability to predict exercise capacity in an individual. The forced expiratory volume in 1 second (FEV_1) is the most widely used lung function measurement to determine disease severity in COPD. However, a limitation of the FEV_1 is that it does not directly reflect the degree of static and dynamic hyperinflation in an individual with COPD. Recently, the development of dynamic hyperinflation with an increase in end-expiratory lung volume has been correlated with exercise limitation due to dyspnea ([7], [8], [9]). As inspiratory capacity (IC) is inversely related to end-expiratory lung volume, it is useful as a marker for lung hyperinflation. Reduced IC and IC/TLC ratio have been associated with poorer exercise performance and survival in COPD ([7], [10], [11]). Because of its relationship with dynamic hyperinflation, IC might be a better predictor of maximal exercise performance in COPD than FEV_1, but it is not known whether IC is a useful predictor of performance of the six-minute walk test.

The National Emphysema Treatment Trial (NETT) was a multicenter clinical trial comparing lung volume reduction surgery to medical treatment in individuals with advanced emphysema ([12]). During a comprehensive baseline evaluation, participants performed both 6MWT and CPX along with measures of lung function and quality of life. Using physiologic data collected during screening for the NETT, we compared these two types of exercise tests in individuals with advanced emphysema to determine the degree c [...] the CPX had a better [...] rrelate better w [...] unction measure [...] both forms of exerci [...]

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smoking for four months prior to baseline screening and be free from severe co-morbid conditions. The trial design and main results have been previously published ([12], [13]). The research protocol was approved by the Institutional Review Boards of all participating institutions, and informed consent was obtained from participants prior to randomization.

Procedures

During the baseline evaluation and prior to initiation of pulmonary rehabilitation and randomization, participants performed a 6MWT and a maximum cycle ergometry exercise test within a 6-week period. Prior to the 6MWT, a treadmill test at 1-2 mph was performed to determine supplemental oxygen requirements during testing. The 6MWT was performed using a standard protocol using scripted prompts at 1-minute intervals. If oxygen supplementation was required during testing, a staff member walked behind the participant to carry the oxygen. Course layout and length varied by participating institution. Maximum walking distance, expressed as a percent predicted ([14]), was used for analysis.

Maximum symptom-limited CPX was performed on a bicycle ergometer with an increase in workload of either a 5 or 10 Watts at 1-minute intervals, based on the participant's maximum voluntary ventilation. Participants breathed 30% oxygen during the test ... ium
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Statistical analysis

Baseline characteristics are presented as means and standard deviations for continuous variables and as frequencies and percentages for categorical variables. Scatter plots and Pearson correlation coefficients were used to determine the association between lung function, QOL scores, and exercise measures. Correlation coefficients were compared using the method of Meng et al. ([22]). Univariate regression models were developed for 6MWD and maximum work with SGRQ and FEV_1 in individual models. Multivariable linear regression models were then developed in a stepwise manner to estimate the magnitude and statistical confidence of the effect of FEV_1 and SGRQ Total Score on 6MWD and maximum exercise capacity, adjusting for age, gender, height, and weight. In order to use a similar metric for both 6MWD and maximum exercise capacity, both were analyzed as the percent of predicted value, calculated from literature values ([14], [15]). All statistics were performed using STATA software, version 8.2 (Stata Corporation; College Station, TX; 2004). P-values of less than 0.05 were considered statistically significant.

Results

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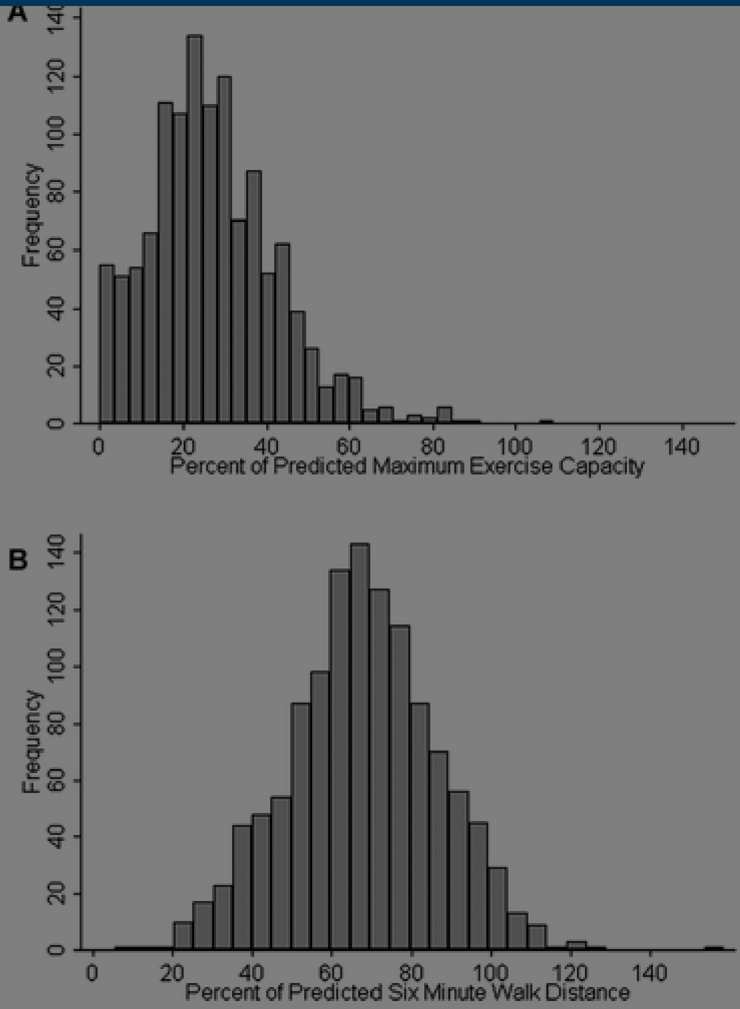

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Figure 2 Scatter plots of maximum exercise capacity (Watts) and 6-minute walk distance … tests are correlate…

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Table 1 Participant characteristics (N = 1218)

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Impairment in maximum exercise capacity was greater than the 6-minute walk distance compared to reference values (27.6 ± 16.8% predicted vs. 67.9 ± 18.9% predicted, $p < 0.001$). Moreover, the range of 6-minute walking distance was narrower and was more symmetrically distributed than maximum exercise capacity. The greater impairment in CPX compared to 6MWT is further illustrated by the fact that only 12 participants (1.0%) had a maximum exercise capacity greater than 80% predicted. In contrast, 308 (25.3%) of the study group had a 6-minute walk distance that was greater than 80% predicted. Alternatively, 34% of individuals had a maximum exercise capacity less than 20% predicted compared to only 2 (0.2%) of individuals who had a 6MWD less than 20% predicted. Additionally, 4.8% were unable to perform more than 5 watts of exercise compared to only 1.2% of the subjects who could walk no more than 500 feet, values that have previously been associated with poorer outcomes in COPD ([3], [23]).

The correlations between 6MWD, exercise capacity, and measures of pulmonary function are shown in Table 2 and Figure 3A and Figure 3B. The best correlates of exercise ... al, maximum exercise ... than was the 6MW... tion as FEV_1 with 6M... 0.65). The partial c... d for age gender, ... for maximu... etween SGRQ a... SGRQ and max...

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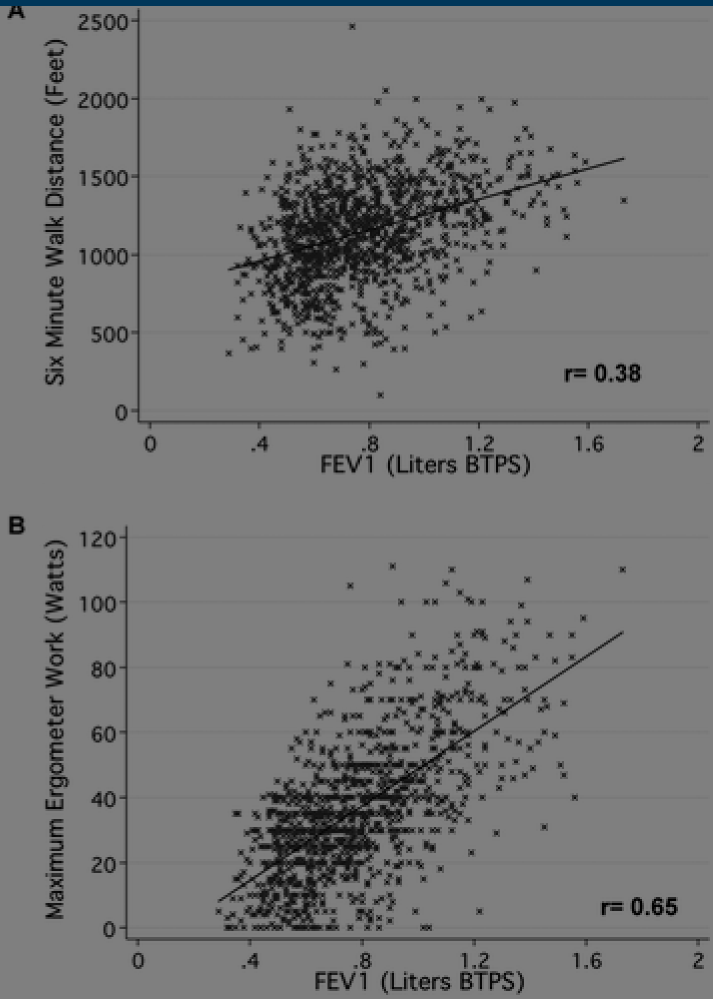

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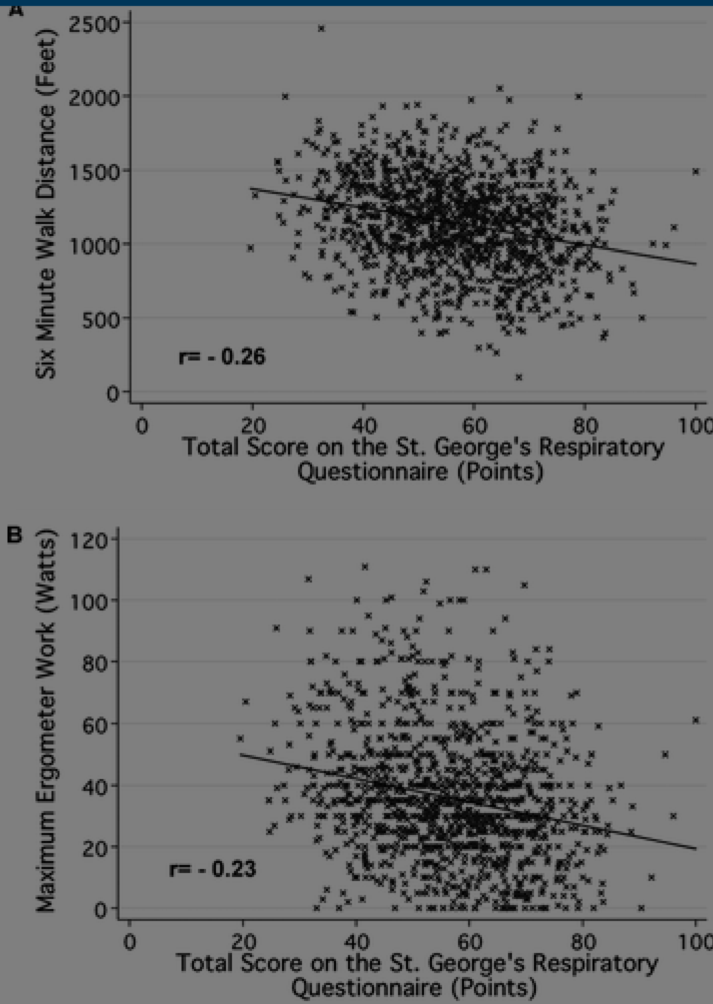

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In order to determine the relationships between the 6MWD and CPX with measures of
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DISCUSSION

This study demonstrates that 6MWD and CPX, although significantly correlated, measure somewhat different domains of exercise performance in individuals with advanced emphysema. When results are expressed as percent of predicted, these individuals with severe emphysema have less impairment of the 6MWD than impairment of maximum exercise capacity. Indeed, despite a mean FEV_1 % predicted of 26.9%, participants achieved a mean of 68% predicted 6MWD and had remarkable preservation of their endurance given the degree of lung function impairment. Individuals with COPD, in general, exercise at a higher fraction of their maximum exercise capacity than normal individuals ([24]). Thus, we interpret these findings to indicate that individuals with severe lung function impairment can maintain walking distance through the use of submaximal ventilation that approaches but does not exceed their maximum sustainable ventilation. This is analogous to the relative preservation of submaximal exercise capacity relative to maximum exercise capacity that is seen in elderly individuals ([25]).

Performance on both exercise tests is correlated with ventilatory impairment indicated by standard lung function tests, particularly the $FEV_1$and IC. However, maximum
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hypoxemia, we might have found better correlation of exercise capacity with diffusing capacity ([29]).

In univariate analysis, both the 6MWT and CPX were similarly correlated with quality of life measures as has been reported previously in the NETT population ([30]). Presumably, the impact of disease on daily activities is more closely related to the submaximal exercise of the 6MWT than by maximum exercise tests. Previously, the NETT investigators have reported that the SOBQ was slightly better in predicting both maximum exercise capacity and 6MWD than the SGRQ ([30]). However, both SOBQ and SGRQ were well correlated with each other ($r = 0.67$, $p < 0.0001$) suggesting that they measure similar features of the impact of respiratory disease. In contrast, the generic health-related QOL instrument, the SF-36 physical component summary, did not have a strong association with either exercise test.

Previous studies that have directly compared the measurement properties of the 6MWT and the CPX have shown variable results ([6]). There is a significant correlation between maximum oxygen consumption and 6MWD ($r = 0.51$) ([31]) and between maximum oxygen consumption and maximum work ($r = 0.58–0.81$) ([5], [32]). However, few studies have directly compared the results of the 6MWT and the CPX to their relationship with lung function and QOL measures. Wijkstra, et al, showed no significant difference in the correlation of lung function (FEV_1, RV, D_{LCO}) with the CPX
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One of the strengths of this study is that it represents a large group of individuals with lung disease well-characterized as emphysema. Because the study was done at 17 clinical centers, it is likely to be more generally representative than studies done at a single center. However, we are cautious about extending the results from this study to those with less severe COPD as the study population was limited to a narrow range of individuals with severe or very severe emphysema who were participating in a trial of lung volume reduction surgery. In addition, the CPX was performed while individuals were receiving 30% inspired oxygen, which is not a standard practice. Delivery of a fixed concentration of oxygen may not be feasible in many laboratories, and some individuals may have better maximum exercise performance while performing CPX on oxygen.

In conclusion, we have found that the 6MWT and CPX, although correlated with each other, measure different aspects of exercise capacity. The CPX better reflects aspects of both lung function and is more severely impaired by emphysema, whereas the 6MWT is more closely related to functional impairment in activities of daily life and is less impaired in severe emphysema.

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