Predicting Oxygen Uptake for Men and Women With Moderate to Severe Chronic Obstructive Pulmonary Disease

Rick Carter, PhD, MBA, David B. Holiday, PhD, James Stocks, MD, Carol Grothues, PhD, Brian Tiep, MD

ABSTRACT. Carter R, Holiday DB, Stocks J, Grothues C, Tiep B. Predicting oxygen uptake for men and women with moderate to severe chronic obstructive pulmonary disease. Arch Phys Med Rehabil 2003;84:1158-64.

Objective: To develop regression equations for estimating peak oxygen consumption ($\dot{V}O_2$) for men and women with moderate to severe chronic obstructive pulmonary disease (COPD) from the 6-minute walk test (6MWT).

Design: Multivariate analysis of patient pulmonary function and exercise gas exchange indices to 2 outcomes for the 6MWT (distance ambulated, calculated work [$6M_{WORK}$]).

Setting: A university hospital and clinics.

Participants: A total of 124 patients (90 men 34 women; age range, 45–81y), from the community, with moderate to very severe COPD. Forced expiratory volume in 1 second (FEV_1) ranged from .70 to 2.79L/min, forced vital capacity (FVC) ranged from 1.73 to 5.77L, and FEV_1/FVC ranged from 24% to 69%. All patients were in stable condition at the time of testing and were on a stable drug regimen.

Interventions: Not applicable.

Main Outcome Measures: Pulmonary function testing was completed according to American Thoracic Society criteria. Cycle ergometry with gas exchange, by using a ramp protocol, was completed. The 6MWT was done in the hospital corridor, with distances recorded after each minute. Work capacity by each method was reduced from the normal predicted.

Results: Peak oxygen uptake ($\dot{V}O_2$) averaged 1184±302mL/min for men and 860±256mL/min for women (58%, 68% of predicted, respectively). Ventilatory reserve was limited at an achieved peak ventilation ($\dot{V}E$) of 79.9%±19.1% of predicted. Borg scores for dyspnea and leg fatigue were equivalent for each test modality, with leg fatigue being slightly higher for each gender. $6M_{WORK}$ for the 6MWT was the strongest independent predictor of peak $\dot{V}O_2$ ($r=.81$, $P<.0001$), whereas that for distance ambulated was correlated at r equal to .54 ($P<.0001$). This is a 36% improvement in the variance accounted for by the application of $6M_{WORK}$ as the outcome for the 6MWT. Generalized regression modeling was then used to develop equations for the estimation of peak $\dot{V}O_2$ for the 6MWT. Additional variables included in the model were diffusing capacity of lung for carbon dioxide, FVC, maximal inspiratory pressure, weight (in kilograms), and age, with their appropriate interactions. This derived regression model accounted for 79% on the variance for estimation of peak $\dot{V}O_2$ in the patients studied.

Conclusion: Peak $\dot{V}O_2$ can be estimated for men and for women by using the generalized equations presented. The calculation of $6M_{WORK}$ is an improvement over distance ambulated as the 6MWT outcome. These data build on the existing body of knowledge for the 6MWT and extend its application for patients with COPD. Knowledge of the peak $\dot{V}O_2$ can be used for patient assessment, serial monitoring, evaluating disability, and as a common index of function across modalities. The calculation of $6M_{WORK}$ outperformed distance ambulated and is easily converted to other indices of caloric expenditure that are commonly used in the laboratory and clinical settings.

Key Words: Exercise test; Functional residual capacity; Pulmonary disease; chronic obstructive; Quality of life; Rehabilitation; Walking; Work capacity evaluation.

CHRONIC DISEASE PROGRESSION promotes a loss in functional capacity, negatively impacting activities of daily living (ADLs), occupation, and numerous quality-of-life (QOL) issues.[1,2] For patients with chronic obstructive pulmonary disease (COPD), dyspnea on exertion is a sentinel event, indicating a loss in pulmonary function and work capacity. As the disease progresses, medical attention is sought, and treatment strategies are offered to counter the signs, symptoms, and physiologic changes responsible for dyspnea and reduced work capacity.

Assessment of patient status and response to treatment is paramount in today's health care environment. Many options exist, but the need for a simple, quality, and cost-effective functional evaluation method with widespread application for various disease processes is needed. Current methodologies range from the sophisticated laboratory stress testing approaches, to observing individuals engaged in activity, to questionnaires completed during interviews or by the patient.[3,4] Access to laboratory assessments can be limited by the availability of equipment and experienced laboratory staff. Cost is another consideration.

Assessment of cardiopulmonary function and peak oxygen uptake (peak $\dot{V}O_2$) during exercise stress reveals valuable insights with respect to the disease process and limitations imposed.[5] Furthermore, these data are routinely used to initiate specific therapeutic interventions and to establish training parameters for many patient cohorts. These same tests are routinely used to monitor the impact of therapy over time. Yet, there is a need for a simple and widely applicable test that can monitor changes in function and deliver data that are comparable and meaningful.

Functional status evaluations can be approached from a less costly, less time-consuming, and wider patient-acceptance perspective, yielding a broadened application of the methodology. Because the ability to ambulate independently is reflective of function, assessment of walk performance by using walk tests

From the University of Texas Health Center, Tyler, TX (Carter, Holiday, Stocks, Grothues); and Pulmonary Care Continuum, Irwindale, CA (Tiep).

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Reprint requests to Rick Carter, PhD, MBA, Center for Clinical Research, University of Texas Health Center, 11937 US Hwy 271, Tyler, TX 75708, e-mail: *Rick.Carter@uthct.edu*.

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Table 1: Demographic Characteristics by Sex for the COPD Patients Studied

Variable	Men	Women
Age (y)	66.9±6.9	66.5±8.3
Weight (kg)	85.2±14.7	69.3±18.2
Height (cm)	175.5±7.4	161.7±5.9
BMI (kg/m^2)	27.3±4.6	26.4±6.7
% fat (%)	24.9±9.2	29.6±10.3
LBW (%)	74.9±9.3	69.4±10.0
Smoking history (pack years)	66.4±30.9	47.9±37.7

NOTE. Values are mean ± SD.
Abbreviations: BMI, body mass index; LBW, lean body weight as a percentage.

should be considered. The 2-, 6-, and 12-minute walk tests have been advocated and refined in the last decade as an alternative to the more elaborate methodologies available.[6-8] The 6-minute walk test (6MWT) has emerged as a common approach, and recent normative data have extended its application.[9-11] When administered by using a standardized format, the 6MWT has shown good validity, reliability, and responsiveness to change.[9]

Because the 6MWT is routinely used to estimate function in patients with COPD, there is need for additional data linking the 6MWT performance to peak V_{O_2} and other selected physiologic measures of gas exchange. In additional, walk distance may not be the best 6MWT outcome for the assessment of function. We and others suggest an index of work—in this application $6M_{WORK}$=6-minute walk distance×body weight—that accounts for differences in body weight and is more precisely related to the bioenergetics of movement.[12] And last, no study has investigated the gender influence in concert with varying levels of airway obstruction on function and the prediction of peak V_{O_2} for the 6MWT. Our working hypothesis was that differences in peak V_{O_2} would be observed for each sex and that the derived gender-specific peak V_{O_2} prediction equation would be superior to an equation ignoring sex. Furthermore, by application of the work calculation for the 6MWT outcome, the predictive capability of peak V_{O_2} will be enhanced for univariate and multivariate models. If these hypotheses are confirmed, the utility of the 6MWT will be improved, data variance will be reduced, and the precision of the technique will be strengthened.

METHODS

Study Sample

Ninety men and 34 women between the ages of 45 and 79 years, with moderate to very severe COPD, as judged by indices of pulmonary function, agreed to participate in this trial. Each patient was fully informed of the nature of the study and signed an informed consent consistent with the standards of the institutional review board. All patients were on a stable treatment program and had not been previously enrolled in a pulmonary rehabilitation program. Those patients who were smoking were referred to a smoking cessation program. Exclusionary criteria included a restrictive lung process, or heart, circulatory, renal, metabolic, or neurologic processes that would contraindicate engagement in exercise training. Group mean ± standard deviation (SD) demographic characteristics can be found in table 1.

Pulmonary Function

Maximal forced expiratory flow-volume loops were performed by using a rolling-seal spirometer (Vmax 20C[a]). Lung volumes were measured with a body plethysmograph (Vmax 22, AutoBox[a]), and diffusing capacity of the lung for carbon monoxide (DLCO) was measured by the single-breath technique of Jones and Mead[13] by using a SensorMedics system (Vmax 22, AutoBox). The normalized data from Crapo et al[14] were used for spirometric measurements, whereas predicted lung volumes were derived from the equations of Goldman and Becklake[15] (for women) and of Boren et al[16] (for men). Prediction of DLCO was made using the data of Make et al.[17] All values reported for pulmonary function testing were obtained postbronchodilation, using albuterol via a metered-dose inhaler. Albuterol was administered as follows: 1 puff was followed by a second puff 10 minutes later, which was followed by an additional 10 minutes of waiting before performing the postbrochodilator spirometry. Pulmonary function testing was performed by using the standards outlined by the American Thoracic Society (ATS).[18] The best flow-volume loop was used in the final analysis of the data. All calculations were performed by using automated processors interfaced with the measuring instruments. Severity was defined according to ATS criteria.[19]

The 6MWT

We conducted the 6MWT as described by Guyatt et al.[20] A straight hospital corridor of 30.5m (100ft) was marked by colored tape. The corridor was paved with 1×1 ft tile squares, and the data were recorded to the nearest foot of distance completed. Patients were instructed to walk from end to end at their own pace, while attempting to cover as much distance as possible in the allotted 6 minutes. Arterial oxygen saturation by noninvasive oximetry (Sp_{O_2}) was continuously monitored. Patients (n=9) who were known to desaturate during exercise were prescribed supplemental oxygen at a liter flow sufficient to maintain the Sp_{O_2} at 90% or above. The research assistant rolled a portable oxygen cylinder behind the patient during the walk. All patients were encouraged to walk as briskly and as far as possible by the attending research assistant. Patients were allowed to stop and rest, as necessary, but were encouraged to proceed with the walk on recovery. A research assistant timed the walk and recorded the distance ambulated to the nearest foot for each minute of walking completed.

Exercise Gas Exchange

A cycle ergometry was used to impose the required workload 30 minutes after administration of bronchodilator therapy. Each patient was prepared for testing after a detailed explanation of the procedure was delivered and discussed. Electrocardiogram electrodes were positioned on the thorax by using a standard 12-lead configuration. The patient then sat on the ergometer, and seat height was adjusted to full knee extension. The mouthpiece was placed in the patient's mouth, and the nose clip was secured to prevent air leaks. The technician observed the end-tidal carbon dioxide values; when stabilized, a 3-minute resting baseline gas was collected. Each subject was instructed to use specific hand signals during the test. Gas exchange data were collected and analyzed with a Medical Graphics CPX-D[b] gas exchange system after volume and gas calibration by using known quantities. After testing, the data were analyzed, a printed copy was obtained, and the data were stored electronically for future reference. Normal predicted values were computed according to the method of Wasserman et al.[21]

Ramp-Cycle Ergometry

Ramp-cycle ergometry was used as the workload forcing pattern for each patient. This method was selected to maximize

Table 2: Indices of Pulmonary Function, Peak Work Performance, and Gas Exchange by Sex

Variable	Men	% Predicted	Women	% Predicted	*P* Value
FEV_1 (L)	1.44±0.44	45.0±12.6	1.08±0.26	48.4±12.1	.0001
FVC (L)	3.59±0.81	84.0±16.3	2.35±.44	80.2±12.7	NS*
DLCO ($mL \cdot min^{-1} \cdot mmHg^{-1}$)	14.71±6.10		10.34±3.90		.0004
MIP (cmH_2O)	68.26±22.44		52.17±18.24		.0006
Exercise time (min)	9.77±2.64		7.66±2.10		.0001
Work (W)	69.0±25.3		48.7±18.9		.0001
Vo_2 (mL/min)	1183.8±302.1	58.0±11.4	860.3±256.4	68.2±14.9	.0001
$\dot{V}co_2$ (mL/min)	1153.3±349.8		830.5±281.2		.0001
$\dot{V}E$ (L)	42.6±11.9	80.8±19.2	31.1±8.1	77.5±17.4	.0001
RR (breaths/min)	30.7±5.7		33.4±7.0		.0289
VT (mL)	1424.6±370.3		947.0±229.1		.0001
VDS/VT (%)	.29±.05		.31±.05		.0230
Sao_2 (%)	95.6±3.6		95.8±3.3		NS*
HR (bpm)	118.3±19.3		113.5±14.4		NS*
SBP (mmHg)	164.4±22.2		156.2±19.4		NS*
DBP (mmHg)	81.4±9.3		77.5±7.9		.0284

NOTE. Values are mean ± SD.
Abbreviations: DBP, diastolic blood pressure; HR, heart rate; MIP, maximal inspiratory pressure; NS, not significant; RR, respiratory rate; Sao_2, noninvasive oxygen saturation; SBP, systolic blood pressure; $\dot{V}co_2$, carbon dioxide production; VDS/VT, dead space to tidal volume ratio; $\dot{V}E$, minute ventilation; VT, tidal volume.
* $P<.05$.

gas exchange data, to ensure a quality effort, and to limit test duration to around 10 minutes. Ramp workload increments were determined by using the patient's age, reported home activities, and measured pulmonary function data.[21] Peak ventilatory capacity was estimated according to the method of Carter et al.[22] Once the ramp workload was selected (typically between 10–30W), the computer was programmed to deliver a patient-specific ramp workload after 3 minutes of resting data collection and 1 minute of zero load cycling. Each patient peddled to his/her limit of effort. If a patient was stopped by the technician, he/she was either retested at a later time or excluded from the analysis. Criteria for terminating testing included an arrhythmia contraindicating further testing, ST-T wave changes suggesting ischemia, a significant decrease in blood pressure with increasing workload (>20mmHg), patient confusion, or equipment problems. Gas exchange data were obtained as outlined previously.

Statistical Analysis

All statistics were generated by using the Statistical Analysis System, version 8e (PC-SAS[c]). Demographic statistics were generated for the variables of interest and expressed as the mean ± SD. Regression techniques were used to explore relationships among the variables under study. First, we used stepwise and maximum R^2 improvements for identifying variables that would contribute to the prediction of peak Vo_2 for each sex separately. All potentially important variables were allowed in the initial phase, including age, body weight, forced expiratory volumn in 1 second (FEV_1), forced expiratory volume (FVC), FEV_1/FVC, peak expiratory flow, maximal voluntary ventilation, residual volume (RV), total lung capacity (TLC), alveolar ventilation, vital capacity, RV/TLC, lung diffusion capacity for carbon monoxide (DLCO), lung diffusion for carbon monoxide corrected for alveolar ventilation, walk distance, and walk work. Any variable that was deemed important in the best models for either sex was retained for further analysis in a generalized regression model—that is, one in which sex was incorporated as an interaction variable. This was accomplished by standard coding techniques, in which sex was coded as 0 for men and 1 for women. The product of the coded sex and each potentially important variable was included in the generalized model to afford the ability to test for additional parameters, which could significantly modify the intercept and/or slope parameters for each of the variables retained after the first pass.

We used backward elimination principles for model building, starting with a full model and removing variable(s) sequentially. We examined the *P* values (for deletion) manually, because automated variable selection would not necessarily take into account the significance of the variable for both sexes at the same time. A variable (with the highest nonsignificant *P* value) was eliminated by using the partial F test if both of its slope terms (men, women) were not significant by using a more liberal level of significance of .15 to .20 (this is similar to the defaults SAS[c] uses in Proc Reg). If the interaction term for women was significant, the corresponding male term was also retained, even if not significant, because the data were dominated by men (approximately 67% men vs 33% women). The elimination procedure was continued until a model was obtained where all β weights in the model were significant at the usual level (.05), with the potential exceptions noted earlier. This method could yield a model with a common coefficient for some variables and an adjusted coefficient for other predictors when a significant gender interaction was deemed present, while maintaining sufficient error degrees of freedom. The rationale for this procedure was to gain insight into the differences between the sexes, while controlling the models for similar variables, even though further interpretability was not guaranteed.

RESULTS

Work capacity for each sex was reduced from the normal predicted. Selected indices of peak exercise capacity and gas exchange are shown in table 2. The mean cycle exercise duration for men was 9.77±2.64 minutes; that for women was 7.66±2.10 minutes ($P<.0001$). Their corresponding peak Vo_2 was 1183.8±302.1mL/min and 860.3±256.4mL/min for men and women, respectively ($P<.0001$). Peak ventilation averaged 42.6±11.9L for men and 31.1±8.1L for women ($P<.0001$),

Table 3: Results of the 6MWT by Sex

Variable	Men	Women	*P* Value
Minute 1 (ft)	241.8±38.9	222.0±34.6	<.0100
Minute 2 (ft)	235.4±41.3	205.7±38.3	<.0004
Minute 3 (ft)	224.9±50.7	194.0±57.0	<.0043
Minute 4 (ft)	222.5±49.3	193.8±54.4	<.0060
Minute 5 (ft)	218.5±53.1	194.7±43.9	<.0221
Minute 6 (ft)	224.3±46.6	196.5±51.8	<.0050
6MWT (ft)	1367.5±259.3	1206.6±257.7	<.0026
Work	35,370.2±9482.8	25,643.4±9080.7	<.0001

NOTE. Values are mean ± SD. Work is expressed as the product of 6MWT distance in meters by individuals' body weight in kilograms.

which showed little ventilatory reserve in either group ($\dot{V}$E reserve, 20.1%±19.1% of predicted).

All patients completed the 6MWT. Distance covered for each minute as well as the total distance covered in the allotted 6-minute period was recorded to the nearest foot. These data are presented in table 3. On average, men were able to cover greater distances then were women for each minute of the 6MWT. The total 6MWT distance was then compared with that predicted by Enright and Sherrill.[23] Men were able to achieve 78.6%±14.6% of the age/gender-specific predicted distance, whereas women obtained 79.9%±17.5% of the predicted distance. Percentage predicted walk distance ranged from 36% to 118% for men and 39% and 121% for women.

We then calculated work for the 6MWT after conversion of distance in feet to meters where $6M_{WORK}$=body weight in kilograms×distance in meters. Distance covered during the 6MWT and $6M_{WORK}$ correlated with measures of pulmonary function and gas exchange measures. We found an increase in the magnitude of the correlations for $6M_{WORK}$ as compared with walk distance (figs 1, 2). This simple calculation improved the overall correlation to measured peak $\dot{V}O_2$, as well as that for each sex (figs 3–6).

Next, we examined Borg scores for dyspnea and leg fatigue at peak exercise by gender for ergometry and the 6MWT. For each sex, there was a tendency for the leg fatigue scores to be slightly, but not significantly (*P*>.05), higher than mean dyspnea scores. This pattern was consistent for each modality.

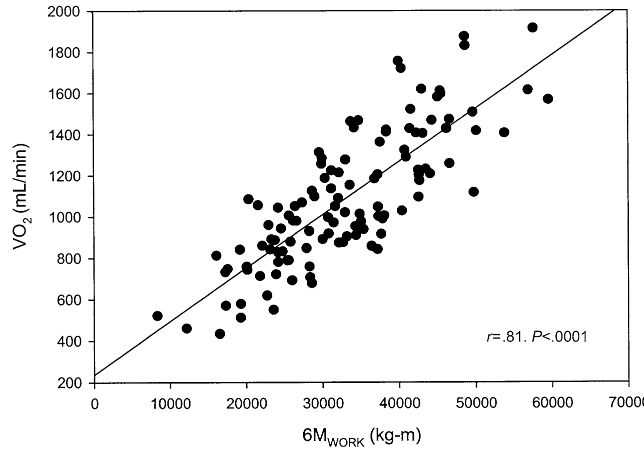

Fig 2. Scatterplot of peak $\dot{V}O_2$ to 6MWT work for the entire group.

There were no significant differences observed for dyspnea or leg fatigue Borg scores between modalities (*P*>.05).

Regression techniques were used to identify pulmonary function and gas exchange variables that correlated with 6MWT performance. These variables were used in a generalized regression model to predict absolute $\dot{V}O_2$ (mL/min) for men and women. The derived regression equations from the generalized gender model accounted for more than 79% of the variance in peak $\dot{V}O_2$, and these specific gender-based equations are presented in table 4.

On inspection of the resulting equations, work for the 6MWT was superior to the total distance walked and was highly significant for each sex (*P*<.0001). Other variables deemed important in the equation were DLCO, FVC, maximal inspiratory pressures (MIPs), weight (in kilograms), and age. It is important to note that the coefficients applied to each variable entered into the equation could differ by sex. These differences are the result of the computed interaction effects of sex on the model.

DISCUSSION

The importance of exercise testing in patients with COPD is well documented.[24-26] Assessment of exercise capacity assists

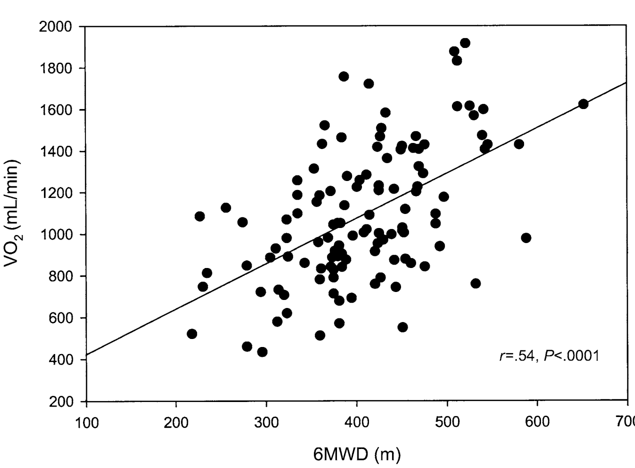

Fig 1. Scatterplot of peak $\dot{V}O_2$ to total 6-minute walk distance (6MWD) for the entire group.

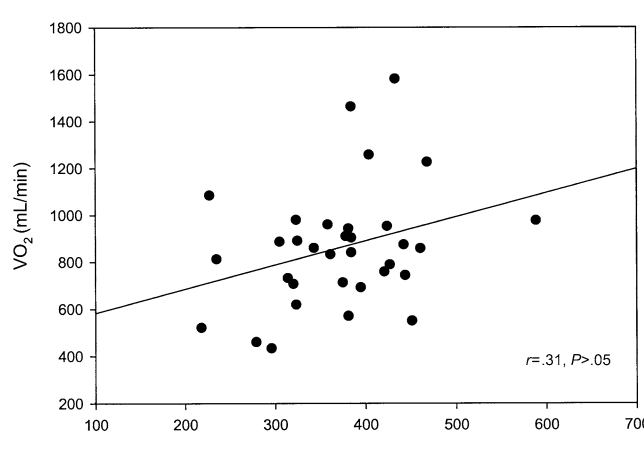

Fig 3. Scatterplot of peak $\dot{V}O_2$ to total walk distance for women.

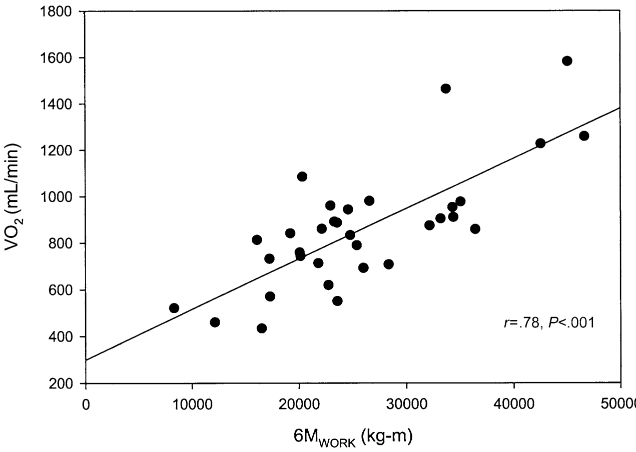

Fig 4. Scatterplot of peak Vo_2 to $6M_{WORK}$ for women.

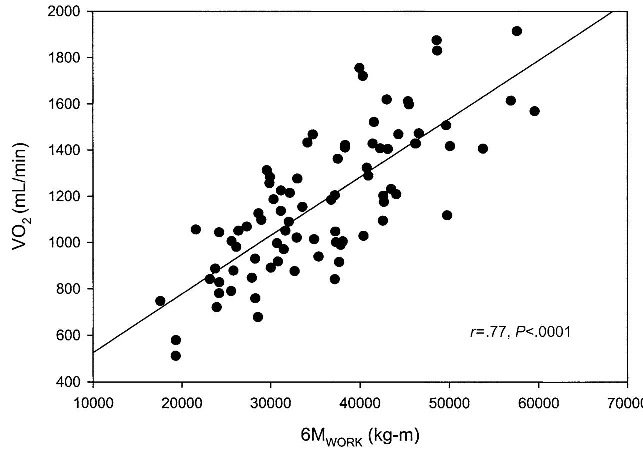

Fig 6. Scatterplot of peak Vo_2 to $6M_{WORK}$ for men.

in the differential diagnosis; assessment of functional capacity delineates the impact of dyspnea on daily function and derives training guidelines for those individuals wishing to enter self-directed or center-sponsored rehabilitation programs. Functional performance is also tightly coupled with indices of QOL, which may have a direct or indirect impact on the patient's ability to cope with the disease process and to remain independent.[27] The 6MWT offers an opportunity to evaluate patients in a timely, practical, and economically advantageous manner. Furthermore, the 6MWT can be administered in a number of settings, and patients do not object to repeat testing over time, which is essential for an understanding of disease progression or changes resulting from medical interventions. We now present regression models that allow the evaluator to estimate peak Vo_2 for men and for women patients with COPD, and this knowledge will impact favorably on the utility of the 6MWT.

In our study, the distance walked in 6 minutes was not the best predictor for peak Vo_2; rather, it was the calculation of work (ie, distance walked in meters×weight in kilograms). For men, the correlation between peak Vo_2 and walk distance was r equal to .53 ($P<.0001$), and a respectable improvement was obtained when correlated to work ($r=.76$, $P<.0001$). A similar trend was noted for women ($r=.31$, $P>.05$; $r=.65$, $P<.0001$, respectively). This finding is supported by some studies[12] but not by others.[28,29] We suggest that 6MWT work should be used as an outcome for the 6MWT, for several reasons. First, work accounts for differences in body weight that significantly impact the amount of energy expenditure required to move a body on a level surface. This energy requirement is tightly coupled with the ability of the patient to increase ventilation through increases in tidal volume and respiratory rate. These changes impact significantly on gas exchange and, thus, the ability of the system to deliver oxygen to the active muscle. Second, the use of work for the 6MWT outcome is in keeping with other routinely used laboratory indices for measuring exercise or functional performance.[30] For example, cycle ergometer performance is routinely expressed in units of kilograms per meter per minute or as calories expended. Last, the calculated work in kilograms per meter can be converted to other indices of caloric expenditure and, thus, represents a common platform for all individuals and functional performance evaluations. This application will make it easier for data to be compared across modalities.

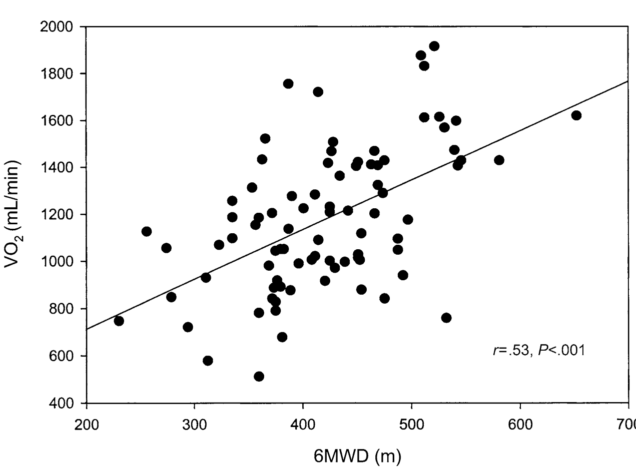

Fig 5. Scatterplot of peak Vo_2 to total walk distance for men.

By using regression analysis, we identified anthropometric and physiologic variable that can influence a patient's ability to engage in physical work. The addition of DLCO, FVC, MIPs, weight, and age improved the predictability of the model from an R^2 equal to .42 to slightly greater than 79%. This is a substantial increase in variance accounted for by the model. Our noted standard error of the estimate was 154.31mL/min. We and others have found that DLCO is a significant variable for estimating Vo_2 as well as functional performance.[29] This

Table 4: Regression Models for Estimating Peak Vo_2 From the 6MWT Distance

Male Regression Model	Female Regression Model
Vo_2=299.76	Vo_2=655.36
+(0.013×work)	+(0.013×work)
+(19.11×DLCO)	+(7.8×DLCO)
+(66.73×FVC)	+(−153.67×FVC)
+(−0.71×MIP)	+(4.59×MIP)
+(2.55×wt)	+(2.55×wt)
+(−4.44×age)	+(−4.44×age)

NOTE. Each equation is presented vertically, with each variable entered on a separate line. Vo_2 is in milliliters per minute. SEE=154.31, R^2=.7930.
Abbreviations: wt, weight; SEE, standard error of the estimate.

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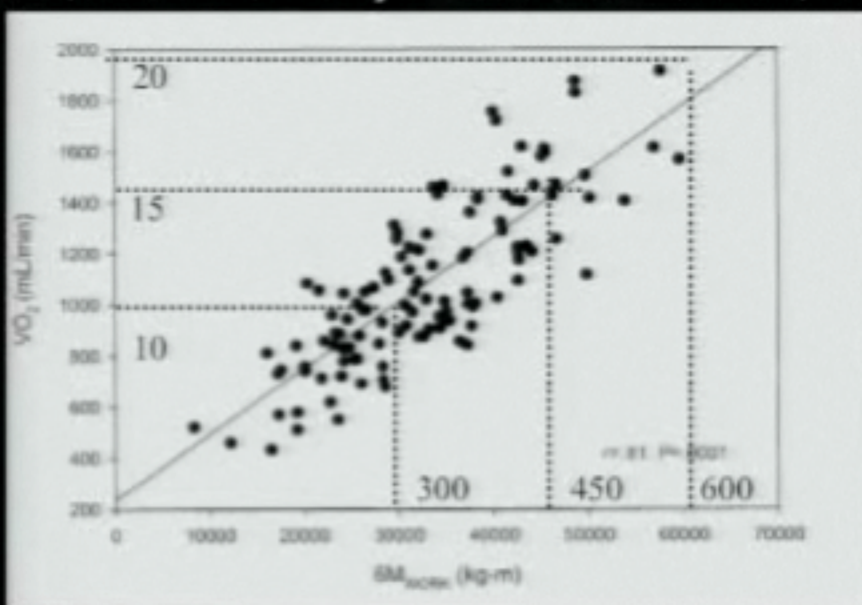

(100 kg. Patient)

VO2max = 6MWTdist.(M)/30

(450M = 15 ml/kg/min)

represents the lung's ability to exchange respiratory gases between the alveolus and the pulmonary circulation. The lower the DLCO, the greater the destruction in the lung. A low DLCO indicates the inability to effectively transfer oxygen from the lung to the circulation and, thus, constrains oxygen transport to the metabolically active cell. Bioenergetics for active muscle shifts from an aerobic to an anaerobic pathway of limited capacity. This hampers the ability of the individual to function, with resulting decreases in ADLs with an accentuated dyspnea response.

Other measures of pulmonary function have been shown to be predictive, as well. FVC has been identified in several studies.[29,31] The mathematical selection of FVC over FEV_1 may be partially explained by the range of airway obstruction included in the study. Alternatively, airway obstruction may account for only part of the pulmonary function influence on functional performance, whereas FVC accounts for airway obstruction through its correlation with the FEV_1, and changes in vital capacity may represent additional changes in lung function not accounted for by the FEV_1 (muscle strength, overall lung capacity, volume shifts, patient effort).

MIP was significantly related to the predictive capacity of the model. MIP is an index of respiratory muscle function and, thus, is a surrogate for overall muscle function.[32-34] Therefore, 2 possible impacts exist for MIPs being included in the model. The first is that it is directly representative of respiratory muscle function. In patients with COPD, there is a shift in lung volumes to higher levels of air trapping, which increases the work of breathing. These changes influence nutrient intake through an increase in dyspnea. As a result, the respiratory muscles work harder, and, over time, their nutrient balance is compromised and their efficiency diminished.[35] Thus, when faced with increased demand, the bioenergetic systems are limited, and muscle fatigue may present even under modest load increase requirements. This is compounded by an upward shift in functional residual capacity during exercise, which further stresses the ability of the respiratory pump to keep pace with demand. The patient-centered consequence of these shifts results in a heightened perception of dyspnea and limited functional ability. From a more global perspective, MIPs are also correlated with overall muscle function.[36] Thus, when muscles of locomotion are recruited, their ability to respond to the heightened demand may be limited, thereby limiting performance.

Age and body weight also entered the regression model. These variables are known to influence work performance. It is well established that as an individual ages, after the second or third decade of life, functional capacity diminishes.[37] This is true for sedentary and trained individuals alike. However, trained individuals start at a much higher level of functional capacity, and thus the loss does not impact ADL function as much as that for sedentary individuals. When normal aging is confounded with development of chronic disease, there is an accentuated rate of decline. This is especially true for patients with COPD.[36] For example, a COPD patient's age is associated with a significant smoking history, progressive movement toward a sedentary lifestyle, and declining lung function. Each of these variables can independently reduce exercise ability, and, collectively, they constrain functional capacity at the lowest levels of function. Increased body weight is associated with overeating, consumption of excess kilocalories and sedentary living. Excess body weight can increase the work of breathing and reduce exercise capacity. When these changes accompany a loss in lung function, exercise capacity is further compromised. Thus, it is not surprising that body weight is included.

From our regression modeling, we observed some interesting gender interactions. There were significant gender by variable interactions for DLCO, FVC, and MIPs. For women, the parameter estimates for DLCO and FVC were negative, whereas that for MIPs was positive compared with the male model. We do not know why these differences exist, but they may be related to the range of airway dysfunction studied or perhaps to the ability of each sex to perform exercise. Furthermore, the coefficients themselves must be viewed in the context of the other variables allowed in the particular model, because multicolinearity could cloud their interpretation. We[38] have previously shown differences in work performance for men and women. Although the underlying mechanisms may be elusive, the impact is substantial and, thus, separate equations should be used for the prediction of peak $\dot{V}O_2$.

CONCLUSION

No studies could be found that evaluated the relationship of the 6MWT (distance ambulated, calculated work) to peak $\dot{V}O_2$ for men and women with COPD. This study showed that the work calculation is an improved index as an outcome for the 6MWT. We showed that a generalized regression equation for estimation of peak $\dot{V}O_2$ for the 6MWT exists for men and women with moderate to very severe COPD. In addition to walk work, DLCO, FVC, MIPs, weight, and age were included in the model. The resulting model accounted for 79% of the variance in peak $\dot{V}O_2$. This model appears to be practical and is easy to calculate. These new data add to the utility of the 6MWT and, given its ease of administration and its time and cost effectiveness, the applicability of the 6MWT is expanded as an alternative when formal tests of exercise capacity and gas exchange are unavailable or impractical. With this new knowledge, investigators will be able to estimate functional capacity with greater precision. The estimation of peak $\dot{V}O_2$ may then be used for exercise prescription or for evaluating a therapeutic intervention. These same models also have application for quantification of function and for judging the level of functional impairment or disability present. Further studies are recommended to extend and validate the findings presented.

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