Original Study

Combined Reduced Forced Expiratory Volume in 1 Second (FEV1) and Peripheral Artery Disease in Sedentary Elders With Functional Limitations

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A B S T R A C T

Objectives: Because they are potentially modifiable and may coexist, we evaluated the combined occurrence of a reduced forced expiratory volume in 1 second (FEV1) and peripheral artery disease (PAD), including its association with exertional symptoms, physical inactivity, and impaired mobility, in sedentary elders with functional limitations.

Design: Cross sectional.

Setting: Lifestyle Interventions and Independence in Elder (LIFE) Study.

Participants: A total of 1307 sedentary community-dwelling persons, mean age 78.9, with functional limitations (Short Physical Performance Battery [SPPB] <10).

Measurements: A reduced FEV1 was defined by a z-score less than –1.64 (<lower limit of normal), whereas PAD was defined by an ankle-brachial index less than 1.00. Exertional dyspnea was defined as moderate to severe (modified Borg index) immediately after a 400-meter walk test (400MWT). Exertional leg symptoms were established by the San Diego Claudication Questionnaire. Physical inactivity was evaluated by percent of accelerometry wear-time with activity less than 100 counts per minute (top quartile established high sedentary time). Mobility was evaluated by the 400MWT (gait speed <0.8 m/s defined as slow) and SPPB (<7 defined moderate-to-severe mobility impairment).

Results: A combined reduced FEV1 and PAD was established in 6.0% (78/1307) of participants. However, among those who had a reduced FEV1, 34.2% (78/228) also had PAD, whereas 20.8% (78/375) of those who had PAD also had a reduced FEV1. The 2 combined conditions were associated with exertional dyspnea (adjusted odds ratio [adjOR] 2.59 [1.20–5.60]) and slow gait speed (adjOR 3.15 [1.72–5.75]) but not with exertional leg symptoms, high sedentary time, and moderate-to-severe mobility impairment.
Older persons are at risk of having respiratory disease, a consequence of frequent exposures to tobacco smoke, respiratory infections, air pollutants, and occupational dusts, and of an age-related vulnerability for developing disease. The diagnosis of respiratory disease is often based on spirometric measures, including a reduced forced expiratory volume in 1-second (FEV1). Because it predicts the maximal attainable ventilation during exercise, a reduced FEV1 can lead to exercise intolerance and exertional dyspnea.

The risk of peripheral artery disease (PAD) also increases in older age. For example, the prevalence of PAD increases exponentially across groups aged 40 years and older, doubling each decade for most ethnicities. PAD increases the risk of having lower-extremity functional impairment, including exertional leg symptoms and exercise intolerance. Because it is associated with tobacco smoke, PAD may coexist with a reduced FEV1.

Older age is additionally characterized by sedentary status and functional limitations. Previous work has shown that only 17.4% of Americans aged 75 or older reported any regular leisure-type physical activity, and that 53.4% of community-dwelling elders who reported no disability had functional limitations (Short Physical Performance Battery [SPPB] <10). Importantly, older persons who are sedentary and have functional limitations are at increased risk of future disability, and hence represent a highly vulnerable population wherein identifying potentially modifiable factors has strong clinical relevance.

Although previous work has shown that a reduced FEV1 and PAD may coexist, study populations were limited to those who had chronic obstructive pulmonary disease or had undergone major vascular surgery. As a result, the combined prevalence of a reduced FEV1 and PAD, including its clinical relevance, remains to be established in sedentary elders with functional limitations. Accordingly, and because they are potentially modifiable, we have evaluated the combined occurrence of a reduced FEV1 and PAD, including cross-sectional associations with exertional symptoms, physical inactivity, and impaired mobility in a large sample of sedentary community-dwelling elders with functional limitations (SPPB <10), that is, Lifestyle Interventions and Independence for Elders (LIFE) Study. At baseline, the LIFE Study administered validated questionnaires of exertional dyspnea and leg symptoms, as well as recorded objective measures of physical activity and mobility, spirometry (FEV1), and ankle-brachial index (ABI). In addition, the LIFE Study has evaluated the FEV1 as a z-score, providing a more age-appropriate method for defining the lower limit of normal (LLN) than the current standard. In particular, an FEV1 z-score less than −1.64 (<LLN) is likely to establish respiratory disease because it rigorously accounts for age-related changes in lung function, including variability in spirometric performance.

**Methods**

**Study Population**

The LIFE Study is a multicenter randomized controlled trial designed to compare a moderate-intensity physical activity program with a successful aging health education program in 1635 sedentary community-dwelling persons aged 70 to 89. The study design has been described in detail elsewhere. In brief, eligibility criteria included low physical activity and functional limitations (SPPB <10), but participants were otherwise nondisabled (able to walk 400 meters in ≤15 minutes without assistance). The institutional review boards of the 8 participating centers approved all study procedures. The present study reports on the baseline evaluation of participants who had valid measurements for both FEV1 and ABI (described later in this article). The LIFE study was conducted in accordance with the amended Declaration of Helsinki. Written informed consent was obtained from all patients.

**Demographic and Clinical Characteristics**

The baseline characteristics included age, sex, ethnicity, body mass index (BMI), smoking status, chronic conditions, and health status. Chronic conditions were self-reported and physician-diagnosed, and included hypertension, diabetes mellitus, symptomatic arthritis, chronic lung disease, coronary artery disease, stroke, hip fracture, and heart failure. To assess health status, participants were asked, “Would you say your health in general is excellent, very good, good, fair, or poor?” Reduced health was defined as a rating of “fair-to-poor.”

**Exertional Dyspnea and Leg Symptoms**

The modified Borg index is a multilevel scale that evaluates dyspnea after a physical activity: the higher the Borg, the more severe the dyspnea. Using this scale immediately after a 400-meter walk test (400MWT; described later in this article), dyspnea was categorized as none to just-noticeable (Borg <1), mild (Borg 1 and 2), and moderate-to-severe (Borg >2).

Exertional leg symptoms were established by a “yes” response to the following question from the San Diego claudication questionnaire: “Do you get pain in either leg or either buttock when walking?” We chose not to categorize further by intermittent claudication because only 20 (1.5%) participants who completed the questionnaire had this symptom. Although intermittent claudication is considered the most classic manifestation of PAD, most men and women with PAD do not have classic intermittent claudication symptoms.

**Spirometry**

The spirometric protocol involved at least 3 trials of a forceful exhalation maneuver, starting from maximal inspiration and concluding with a 6-second end-of-test criterion. The FEV1 was recorded as the highest value achieved during the spirometric trials that had attained a quality grade C or higher for FEV1. Of the 1635 LIFE participants, 1362 (83.3%) achieved a valid FEV1. For comparisons between measured and predicted FEV1 values, we used reference equations from the Global Lung Function Initiative (GLI). Using the GLI reference equations, z-scores for FEV1 were calculated for each participant, with a z-score of −1.64 defining the LLN as the fifth percentile of the distribution. Hence, participants were classified as having a reduced FEV1 if the z-score was less than −1.64.

**PAD**

The presence or absence of PAD was established by the leg with the lower ABI, measured after the participant rested supine for 5 minutes and using a handheld Doppler probe to obtain systolic
pressures at the right brachial artery, right posterior tibial artery, left posterior tibial artery, and left brachial artery in the order listed.24 Pressures were repeated in reverse order. The ABI was calculated for each leg by averaging the 2 posterior tibial artery pressures and dividing them by the average of the 4 brachial artery pressures.

To optimize the available number of outcomes for analyses, we established the presence and absence of PAD based on an ABI lower than 1.00 and 1.00 to 1.40, respectively.25 An ABI lower than 1.00 included both definite and borderline PAD.24,25 In sensitivity analysis, however, we also used an ABI lower than 0.90 and 0.90 to 1.40 to establish the presence and absence of definite PAD, respectively.24,25 Of the 1635 LIFE participants, 1566 (95.8%) achieved a valid ABI.

Physical Inactivity and Mobility Impairment

Physical inactivity was established by accelerometry, using the ActiGraph GT3X and ActiLife software (version 5) (ActiGraph LLC, Pensacola, FL), over a planned 7-day monitoring period. Briefly summarized, after dressing each morning, participants placed the accelerometer on their right hip (waistline belt), thereafter removing the monitor just before going to bed at night. Sedentary time was defined by percentage of accelerometer wear-time with activity fewer than 100 counts per minute, averaged across days.26 Participants who were in the top quartile of sedentary time were classified as having high sedentary time.

Mobility measures included the 400MWT and the SPPB.16 The 400MWT was completed at the participant’s usual walking pace over a 40-meter course. A gait-speed of less than 0.8 m/s was operationalized as slow.27 The SPPB is a summary performance measure consisting of time to walk 4 meters at usual pace, time to complete 5 chair stands, and 3 increasingly difficult standing balance maneuvers.11 An SPPB of 7 or lower was selected to identify participants as having moderate-to-severe mobility impairment (relative to scores of 8 and 9, which were considered mild mobility impairment).13

Statistical Analysis

The baseline clinical characteristics, including exertional dyspnea and leg symptoms, were summarized as means accompanied by SDs or as counts accompanied by percentages. Similarly, the FEV1, ABI, and measures of physical inactivity and mobility also were summarized, first as continuous variables and then as dichotomous variables.

Next, we evaluated the associations of a combined reduced FEV1 and PAD on exertional dyspnea and leg symptoms, high sedentary time, slow gait speed, and moderate-to-severe mobility impairment, respectively, by calculating odds ratios and 95% confidence intervals using logistic and multinomial logistic regression models (a multinomial model was required for the 3-level dyspnea variable). In these analyses, the reference group included a normal FEV1 without PAD, (2) reduced FEV1 without PAD, and (3) reduced FEV1 with PAD. Covariates in the adjusted models included age, height, sex, race, BMI, smoking, chronic conditions (number and type), fair-to-poor health status, and LIFE Study site. In sensitivity analysis, these same associations were evaluated using an ABI lower than 0.90 and 0.90 to 1.40 to establish the presence or absence of PAD.

All statistical analyses were performed using SAS v9.3 (SAS, Inc, Cary, NC), and assuming a Type 1 error rate of 0.05.

Results

Of the 1635 LIFE participants, 1307 (79.9%) had a valid FEV1 and ABI. Table 1 summarizes the clinical characteristics of the analytical sample. The mean age was 78.8; 68.3% were women and 75.8% were white. The mean BMI was 30.3 kg/m². A smoking history was reported by 48.1% (former and current smokers). The mean number of chronic conditions was 1.5, with the 5 most frequent being hypertension, diabetes mellitus, symptomatic arthritis, chronic lung disease, and coronary artery disease. A reduced health status was reported by 34.5%. Exertional dyspnea was reported as mild by 34.4% and moderate-to-severe by 31.0%; exertional leg symptoms were reported by 25.4.

Of the 1635 LIFE participants, 328 (20.1%) were excluded from the analytical sample because they did not have a valid FEV1 and ABI. In comparison with participants in the analytical sample, those who were excluded were less likely to be women (62.5% vs 68.3%; P = .045) and had a higher prevalence of coronary artery disease (11.1% vs 7.1%; P = .019). There were no significant differences according to age, ethnicity, BMI, smoking status, number of chronic conditions, health status, or exertional symptoms.

Table 2 summarizes the FEV1 and ABI, including the FEV1/ABI groups. A reduced FEV1 and PAD were established in 17.4% and 28.7%, respectively, with 6.0% having both conditions. However, among participants who had a reduced FEV1, 34.2% (78/228) also had PAD, whereas 20.8% (78/375) of those who had PAD also had a reduced FEV1. Table 2 additionally summarizes measures of physical inactivity and mobility. Physical inactivity, defined by sedentary time, was observed during 77.0% of accelerometer wear time. A slow gait speed was present in 43.2% of participants and moderate-to-severe mobility impairment in 44.7%. These features did not differ between participants who were included versus excluded from the analytic sample.
Reduced FEV1 with and without PAD was strongly associated with exertional leg symptoms (77.0%), exertional dyspnea (31.0%), and moderate-to-severe mobility impairment, respectively. The reference and comparison groups were the same as described in Table 3. In adjusted models, significant differences were found across the 3 comparison groups for slow gait speed (P < .001), but not for high sedentary time (P = .127) or moderate-to-severe mobility impairment (P = .087). In particular, a reduced FEV1 with PAD was strongly associated with slow gait speed, yielding an adjOR of 3.15 (1.72–5.75); this effect was additive, rather than multiplicative (P value for interaction was .452). In contrast, PAD with a normal FEV1 and reduced FEV1 without PAD yielded adjORs for slow gait speed of only 1.57 (1.11–2.24) and 1.50 (0.99–2.27), respectively. In sensitivity analysis, results were comparable when using an ABI lower than 0.90 (rather than < .10) for establishing PAD (Appendix A).

Table 4 shows the associations of a combined reduced FEV1 and PAD on high sedentary time, slow gait speed, and moderate-to-severe mobility impairment, respectively. The reference and comparison groups were the same as described in Table 3. In adjusted models, significant differences were found across the 3 comparison groups for slow gait speed (P < .001), but not for high sedentary time (P = .127) or moderate-to-severe mobility impairment (P = .087). In particular, a reduced FEV1 with PAD was strongly associated with slow gait speed, yielding an adjOR of 3.15 (1.72–5.75); this effect was additive, rather than multiplicative (P value for interaction was .452). In contrast, PAD with a normal FEV1 and reduced FEV1 without PAD yielded adjORs for slow gait speed of only 1.57 (1.11–2.24) and 1.50 (0.99–2.27), respectively. In sensitivity analysis, results were comparable when using an ABI lower than 0.90 (rather than < .10) for establishing PAD (Appendix A).

Discussion

In a large sample of sedentary community-dwelling elders with functional limitations, a reduced FEV1 and PAD were prevalent (17.4% and 28.7%, respectively), with 6.0% of participants having both conditions. Similarly, prevalence rates were high for moderate-to-severe exertional dyspnea (31.0%), exertional leg symptoms (25.4%), slow gait speed (43.2%), and moderate-to-severe mobility impairment (44.7%), and most physical activity was spent in the sedentary range (77.0% of accelerometer wear time).

In models adjusted for multiple potential confounders, we also found that a combined reduced FEV1 and PAD increased significantly the odds of having slow gait speed by 215%, but not the odds of having exertional leg symptoms, high sedentary time, or moderate-to-severe mobility impairment. Although a combined reduced FEV1 and PAD increased significantly the odds of having moderate-to-severe exertional dyspnea by 159%, the association was only significant for reduced FEV1 alone, and not for PAD alone. Last, in sensitivity analysis, these results were comparable when using an ABI lower than 0.90 (rather than < .10) for establishing PAD.

Our results suggest that the combined occurrence of reduced FEV1 and PAD has clinical relevance among sedentary community-dwelling older persons, for at least 2 reasons. First, although seemingly modest, the prevalence of these combined conditions was nonetheless similar to that of coronary artery disease, stroke, and heart failure in the LIFE Study (6.0% vs 7.1%, 6.5%, and 4.2%, respectively). Second, these combined conditions had a strong association
With slow gait speed, previous work has shown that slow gait speed in older persons is strongly associated with adverse outcomes, including falls, cognitive impairment, disability, institutionalization, and mortality. The effect of a combined reduced FEV1 and PAD on slow gait speed was additive, not multiplicative (P value for interaction was .452). Namely, the odds ratios of having slow gait speed for a combined reduced FEV1 and PAD was similar to adding together the odds ratios from reduced FEV1 alone and PAD alone. An additive effect is especially meaningful when 2 conditions frequently coexist. In particular, among LIFE participants who had PAD based on ABI lower than 1.00, we found that 20.8% also had reduced FEV1 (Table 2). Conversely, among those who had reduced FEV1, 34.2% also had PAD based on ABI lower than 1.00 (Table 2). These prevalence rates were comparable when using an ABI lower than 0.90 (rather than <1.00) for establishing PAD (Appendix A, Table 2A).

Future work should evaluate the mechanisms that underlie the association of a combined reduced FEV1 and PAD on slow gait speed. One potentially modifiable mechanism may relate to exercise intolerance that is due to multiple types of cardiopulmonary disease. LIFE participants, for example, frequently reported a smoking history and other cardiovascular risk factors (hypertension, diabetes, and obesity), as well as chronic lung disease and other types of cardiovascular disease (coronary artery disease, stroke, and heart failure).

Although strongly associated with slow gait speed, a combined reduced FEV1 and PAD was not significantly associated with other measures of mobility (moderate-to-severe mobility impairment), or associated with physical inactivity (high sedentary-time). These results suggest that, among sedentary older persons, a reduced FEV1 and PAD are likely to jointly affect endurance (slow gait speed was determined during the 400MWT), but not measures that require a short walking distance (moderate-to-severe mobility impairment was based on the SPPB, which included only 4 meters of walking) or establish very low levels of physical activity (high sedentary-time).

With regard to exertional symptoms, we found that a combined reduced FEV1 and PAD increased significantly the odds of having moderate-to-severe exertional dyspnea but the association was entirely due to a reduced FEV1, and not PAD. These results were comparable regardless of whether the ABI threshold was 1.00 and 0.90, suggesting that PAD may not be an important contributor to exertional dyspnea in older persons. Because it impairs walking ability, PAD may limit exercise to a low workload that is otherwise insufficient to increase ventilatory demand to levels that would lead to dyspnea. Nonetheless, future work should evaluate whether dyspnea limits the therapeutic response to a moderate-intensity physical activity program among participants who have PAD. We posit that, in contrast to the 400MWT, which is performed at the participant’s usual pace, a moderate-intensity physical activity program may increase ventilatory demand in PAD (higher exercise workloads may increase CO2 flux due to bicarbonate buffering of an earlier lactate threshold).

We also found that the combined occurrence of reduced FEV1 and PAD was not associated with exertional leg symptoms, regardless of whether the ABI threshold was 1.00 and 0.90. However, among participants who had PAD alone, the adjOR of having exertional leg symptoms increased from 0.98 (0.67–1.44) to 1.43 (0.87–2.35) when the ABI threshold was reduced from 1.00 to 0.90, respectively (Table 3 and Appendix A [Table 3A]). Future work should evaluate whether progressively lower ABI thresholds increase the association with exertional leg symptoms (and dyspnea) among participants who have both a reduced FEV1 and PAD. If not, an alternative explanation is that a reduced FEV1, with or without exertional dyspnea, may limit exercise to a workload that is insufficient to lead to leg symptoms.

The present study has 2 major strengths. First, it evaluated a highly vulnerable population of older persons whose sedentary status and functional limitations increase the risk of future disability. Second, it evaluated objective measures of physical inactivity, performance-based mobility, lung function, and PAD, as well as a validated rating of exertional dyspnea based on the 400MWT. Lung function was additionally based on a novel, more age-appropriate method for reporting the FEV1, not previously evaluated regarding the combined occurrence of a reduced FEV1 and PAD.

We acknowledge, however, at least 2 potential study limitations. First, we excluded from analysis 16.7% of participants who had not achieved an acceptable FEV1. Previous work has shown that an acceptable spirometric test may be difficult to perform among older persons who are physically frail and, as a result, these same individuals also may be sedentary and have impaired mobility. Nonetheless, participants who were excluded had a similar sedentary time, frequency of having a slow gait speed, and SPPB score as those in the analytical sample. Second, because the LIFE Study included only individuals who had low levels of physical activity and functional limitations, the range of scores on measures of physical activity and mobility was constrained. These 2 limitations likely attenuated the associations of interest. Importantly, on completion of the LIFE randomized controlled trial, we will evaluate longitudinally the association of a combined reduced FEV1 and PAD with exertional dyspnea and leg symptoms, physical inactivity, and mobility, as well as evaluate the effects of increased physical activity on these same associations.

In conclusion, among sedentary community-dwelling elders who have functional limitations, we found that the prevalence of a
combined reduced FEV1 and PAD was modest but nonetheless strongly associated with slow gait speed (a frailty indicator that confers an increased risk of deleterious outcomes) and moderate-to-severe exertional dyspnea.

Research investigators for the LIFE Study group are listed in Appendix B.

Supplementary Data

Supplementary data related to this article can be found at 10.1016/j.jamda.2014.05.008.

References