The Paradox of Obesity in Patients with Chronic Obstructive Pulmonary Disease

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Patients with chronic obstructive pulmonary disease (COPD) often exhibit dyspnea on exertion, manifested by reduced exercise capacity (EC), diminished physical activity (PA), and impaired quality of life (QOL). Comorbidities are common in patients with COPD, including cardiovascular disease, neuropsychiatric diseases, and metabolic disorders. These comorbidities may exacerbate to persistent smoking, sedentary lifestyle, and less desire to engage in PA, and they may accentuate systematic inflammation and heighten risks of emergency healthcare use (1). Of these, obesity (defined as body mass index [BMI] greater than 30 kg/m^2) affects 54% of patients with COPD in the United States at a relatively young age, and it elevates the risk of functional limitations (2). However, BMI is a crude (i.e., inexact) measure because it does not consider body composition (e.g., the amount of metabolically and functionally active fat-free mass [FFM] rather than body weight or fat mass [FM]); yet, obesity is positively (surprisingly) related to survival in patients with COPD (3).

The determination of body composition is of high importance in the management of patients with COPD. Low FFM in patients with COPD was associated with muscle weakness, decreased exercise tolerance, poor prognosis, and impaired QOL (4, 5). The most accurate method to diagnose FFM and FM is magnetic resonance imaging, which is costly to use in routine clinical practice. Bioelectrical impedance analysis (BIA), a relatively cheap and portable tool, can determine FFM depletion and FM in patients with COPD (6, 7). However, BIA in patients with COPD often overestimates FM and FFM at various degrees of Global Initiative for Chronic Obstructive Lung Disease severity (3, 8, 9). In recent years, dual-energy X-ray absorptiometry (DEXA) has been used because it provides better accuracy, reproducibility, and assessment of regional body composition with high precision compared with bedside BIA (8). However, DEXA has been used in a limited way in patients with COPD to explore the relationships of FM and FFM with EC and PA, respectively.

Set against this backdrop, in this issue of the *Journal*, Wan and colleagues (pp. 1669–1676) report their findings using DEXA to assess body composition (FFM and FM) in relation to EC and PA in patients with COPD and only moderate airflow obstruction (10). The authors conducted this elegant observational study in a predominantly male (94%), elderly (mean age, 70 yr) population of veterans with COPD. EC was measured using the 6-minute-walk test, and PA was assessed using the self-reported Community Health Activities Model Program for Seniors Physical Activity Questionnaire. Participants underwent whole-body DEXA to obtain total body mass, regional (arms, legs, and trunk) FM, FFM (lean mass), and bone mineral content. In addition, the authors obtained sociodemographic characteristics and, in addition to BMI categories of overweight and obesity, assigned categories of overweight and obesity by FM index (>6 kg/m^2 and >9 kg/m^2 for males and >9 kg/m^2 and >13 kg/m^2 in females, respectively) (11). In addition, sarcopenia was defined as appendicular skeletal muscle (ASM)-to-weight ratio (which considers both lean muscle and fat muscle) <7.26 kg/m^2 (males) and <5.50 kg/m^2 (females). The findings indicate that increased FM index was inversely related to EC and PA, whereas lean mass was not significantly related to EC or PA. Furthermore, ASM was moderately associated with EC and PA.

How do these findings increase our understanding for research and clinical practice in this area? First, Wan and colleagues should be congratulated for this intriguing piece of work. Their detailed analytic plan shows that DEXA should be considered as a diagnostic tool to determine both FFM (lean muscle) and FM. Second, FM was associated with reduced EC and low PA. This observation highlights the importance of periodically monitoring obese patients with COPD (especially with elevated FM) with 6-minute-walk tests or other exercise tests to identify further deterioration and then intervene to reduce disability. Most important, such interventions can include appropriate counseling and referral of obese patients with COPD to nutrition experts and encouragement of patients to engage in a moderate- to high-intensity exercise resistance circuit training program in a local gymnasium. Recently, a 12-week progressive resistance exercise program effectively reduced FM and increased FFM in obese men and women (12). Third, the obesity prevalence in the studied male population was greater than 40% using BMI, greater than 75% using percentage of FM, and 60% by FM index. Eleven subjects (11%) were classified as sarcopenic on the basis of ASM index. This further highlights the importance of DEXA screening in primary care and healthcare prevention programs and education of the public to engage in a physical exercise program according to the American College of Sports Medicine criteria (30 min/d, 5 d/wk). For patients with COPD, a regular walking exercise program should represent a minimum target to achieve in their daily activities. In addition, it is always a worthy endeavor to refer patients with COPD to a pulmonary rehabilitation program after hospital discharge after an

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acute exacerbation of COPD and thereby also reduce the impact of obesity in patients with COPD.

However, a number of caveats within this study require further consideration. First, the studied population comprised predominantly male patients with moderate COPD. This may hamper generalizability to women with COPD and to patients with mild or severe COPD. Therefore, it is important to replicate the findings of this study prospectively with balanced sex distribution and a wide range of respiratory impairment (from mild to severe COPD) using disease-specific disability measures (13) and in other (nonveteran) healthcare settings. Second, expense may preclude employing DEXA for routine clinical care, depending on healthcare coverage of patients. Third, the relatively low correlation between FM and EC in this cross-sectional study may represent underpowering ($n = 98$) of a relationship potentially quite relevant to clinical practice. Fourth, the exact mechanism of how excess FM was associated with reduced PA and EC remains unclear. One potential explanation might be that obese patients have elevated symptoms of joint pain, reduced gait speed, low caloric expenditure, and less engagement in weekly moderate exercise activities compared with nonobese counterparts, as shown in the supplementary figures and tables. Future studies might consider whether reducing FM with interventions such as nutritional counseling and moderate- to high-intensity exercise resistance circuit training programs might improve outcomes in patients with COPD.

A recent critical review showed that obesity appeared to be protective, reducing premature all-cause or COPD-related mortality in patients with very severe COPD (3). In contrast, obesity was related to a 20–34% increase in the relative risk of all-cause mortality in mild to moderate COPD (14). DEXA measurements of FM and FFM across a broad patient population, with COPD ranging from mild to severe and including larger numbers of women, might help to reconcile these seemingly paradoxical observations.

Certainly, the present results provide novel insights and promising findings for tackling obesity in patients with COPD. Previous uncontrolled and cross-sectional studies showed that pulmonary rehabilitation of patients with COPD improved EC and QOL with similar magnitude in patients with and without FFM depletion (6, 7). Thus, future prospective studies may focus on randomized controlled trials and long-term follow-up to show the efficacy of a moderate- to high-intensity exercise resistance circuit training program or pulmonary rehabilitation, in concert with nutritional counseling, in improving both the FM and ASM of patients with COPD. ■

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