



Weight-based reference equations for the 6-min walk test can be misleading in obese patients

To the Editor:

A 79-year-old female presented to a hospital-based laboratory for pulmonary function testing and a 6-min walk test (6MWT). The patient's chief complaint was dyspnoea on exertion. The patient was a life-long nonsmoker with a history of interstitial lung disease and morbid obesity (body mass index (BMI) $44.9 \text{ kg}\cdot\text{m}^{-2}$). The patient's baseline spirometry data were within normal limits but the diffusing capacity was moderately reduced (50% of predicted; z-score -4.05) [1, 2].

The patient was given standardised instructions for a 6MWT on a 30-m course [3]. The patient completed the 6MWT but had to take three short breaks due to dyspnoea. The test was performed while the patient breathed air. The baseline/maximum physiological responses to the 6MWT were as follows: heart rate 90/139 beats per min; dyspnoea *via* the Borg scale 0/5; oxygen saturation *via* pulse oximetry: 0.94/0.79 (nadir). The 6-min walk distance (6MWD) was 228 m, above the lower limit of normal (LLN) (139 m), and 82% of the predicted value according to the reference equation published by ENRIGHT and SHERRILL [4] for females: $(2.11 \times \text{height}_{\text{cm}}) - (2.29 \times \text{weight}_{\text{kg}}) - (5.78 \times \text{age}) + 667 \text{ m}$. However, ENRIGHT and SHERRILL [4] excluded healthy subjects with a BMI $>35 \text{ kg}\cdot\text{m}^{-2}$, and the median BMI in their female cohort was $25.5 \text{ kg}\cdot\text{m}^{-2}$ (95th percentile: $32.4 \text{ kg}\cdot\text{m}^{-2}$). The calculation of the predicted 6MWD in this case was made using the patient's measured weight of 122.5 kg. Because the patient's weight did not fit the reference equation range, the predicted and LLN values were low enough to produce a false normal result. When the percentage of predicted and LLN were recalculated using the patient's ideal body weight, 57.1 kg, the walked distance fell below the LLN (289 m) and was only 53% of predicted. CAPODAGLIO *et al.* [5] published a 6MWT reference equation derived from obese subjects (BMI $>30 \text{ kg}\cdot\text{m}^{-2}$). Applying this equation to the patient's data indicated that the 6MWD was 51% of predicted. The reference equation that may fit this patient best was published by HILL *et al.* [6], which did not include weight and was derived from an older cohort. When this equation was applied, the 6MWD was 42% of predicted; therefore, weight and age may have affected the results according to ENRIGHT and SHERRILL [4] (age 79 years was the 95th percentile) and CAPODAGLIO *et al.* [5] (studied subjects 20–60 years old). A result similar to HILL *et al.* [6] was found when using the reference equation by BRITTO *et al.* [7], which uses age, sex, height and change in heart rate to calculate the 6MWD (table 1). In this obese patient, using a reference equation derived from normal-weight subjects (that includes a coefficient for weight) to calculate the predicted 6MWD yielded values that were not reflective of the clinical picture of reduced exercise tolerance. Interestingly, if this patient lost 20 kg and increased the 6MWD by 30 m, the percentage of predicted according to ENRIGHT and SHERRILL [4] would fall to 79%.

The 6MWT is a widely used test in patients with chronic lung disease. The 6MWD may detect disease progression as well as assess response to treatment and risk of hospitalisation and death. The Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints study found that a 6MWD $\leq 334 \text{ m}$ in patients with COPD is associated with a higher risk of mortality [8]. When assessing longitudinal changes, the minimal important distance for a change in the 6MWD for all patients with chronic lung disease has



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Weight-based reference equations for the 6-min walk test can produce normal results despite poor performance. Using ideal body weight- or non-weight-based reference equations for the 6-min walk test may produce more clinically meaningful results. <https://bit.ly/2wE9Sdn>

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TABLE 1 Walked distance from a 6-min walk test

Total distance m	228
ENRIGHT and SHERRILL [4] equation using measured weight, 122 kg	
LLN m	139
Predicted m	278
% predicted	82
ENRIGHT and SHERRILL [4] equation using ideal body weight, 57.1 kg	
LLN m	289
Predicted m	428
% predicted	53
Equation derived from obese subjects by CAPODAGLIO <i>et al.</i> [5]	
Predicted m	448
% predicted	51
Non-weight based equation by HILL <i>et al.</i> [6]	
Predicted m	536
% predicted	42
Non-weight based equation by BRITTO <i>et al.</i> [7]	
Predicted m	523
% predicted	44

LLN: lower limit of normal.

been estimated to be 30 m [3, 9]. There are numerous reference equations from which to choose to compare recorded 6MWD to a predicted value and LLN [10]. ANDRIANOPOULOS *et al.* [10] compared 21 reference equations for the 6MWD in COPD patients to the reference equations published by TROOSTERS *et al.* [11]. 16 out of the 21 equations, including those of ENRIGHT and SHERRILL [4], produced lower predicted values in patients with a BMI ≥ 30 kg·m⁻². A smaller discordant effect was found in underweight patients.

While reference equations for the 6MWD in obese patients have been published [5], it is unclear whether reduced 6MWD due to obesity and its comorbidities should ever be considered normal. Indeed, DONINI *et al.* [12] found that obesity was associated with a greater frequency of patients having to rest during the 6MWT, which might not be considered normal. However, in this case, a reference equation derived from an obese cohort was able to discriminate between otherwise healthy obese subjects and this obese patient with interstitial lung disease. Reference equations for the 6MWT that include body weight as a coefficient should be used with caution in obese patients and research subjects. When using a 6MWT reference equation that does include body weight, the patient's weight must fit into the range used to produce the equation. If the patient's weight is outside of the range in the reference equation, using ideal rather than actual body weight or an equation that does not include weight [6, 7] may produce more clinically meaningful results.

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