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Functionally Relevant Cut Point for Isometric Quadriceps Muscle Strength in Chronic Respiratory Disease

To the Editor:

The recently updated American Thoracic Society/European Respiratory Society statement on limb muscle dysfunction in chronic obstructive pulmonary disease (COPD) (1) highlighted important clinical implications of quadriceps muscle weakness, including reduced exercise tolerance (2), sarcopenia (3), and increased mortality (4). Quadriceps weakness is present in more than a quarter of stable outpatients with COPD, including those with only mild abnormalities in spirometry (5). Although quadriceps muscle strength can be readily measured by volitional and nonvolitional techniques in the research setting, none have been incorporated into clinical practice. The American Thoracic Society/European Respiratory Society statement suggests that isometric quadriceps maximal voluntary contraction (QMVC) shows the most potential for being "implemented in clinical practice to provide reliable and reproducible measurements" (1). Although normal values for QMVC have been described (5), clinically relevant cut points have not been determined. This is important, as the relationship between QMVC and functional performance is not linear (6). With several putative anabolic agents entering phase 2 and phase 3 studies, there is a need to validate outcome measures that can directly assess the effects of interventions of lower limb muscle strength. The aim of the current study was to determine and validate sex-specific QMVC cut points to provide clinical context for clinicians and patients.

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Participants were recruited from respiratory and pulmonary rehabilitation assessment clinics at Harefield Hospital, London, United Kingdom. Inclusion criteria for the derivation cohort included age older than 35 years, a diagnosis of COPD according to Global Initiative for Chronic Obstructive Lung Disease criteria (7), and stable state (no exacerbation requiring change of medication within the previous 4 weeks). Exclusion criteria included a predominant joint or neurological limitation to standing or walking.

QMVC of the dominant leg was measured using a specially adapted chair and strain gauge (8), with hips and knees at 90° flexion, and was recorded as the maximal force that could be sustained over the course of 1 second. The best of three reproducible maneuvers was reported. QMVC was also normalized to weight (kilograms), body mass index (kilograms/meters squared), height (meters), and height squared (meters squared). As the ability to stand from a sitting position is fundamental to functional independence, we anchored QMVC measurements to sit-to-stand ability. Participants sitting, with upper limbs folded, on a straight-backed armless chair with floor to seat height of 48 cm, were instructed to stand up, all the way, without using the upper limbs. This was performed by an assessor blinded to QMVC measurements. Other assessments included comorbidity burden using the COPD-specific comorbidity test index (9), Medical Research Council dyspnea score, incremental shuttle walk, and COPD Assessment Test (10).

Men and women were analyzed separately. We plotted receiver operating curves and calculated area under the curve for raw and normalized QMVC values that best identified patients who were unable to stand from a sitting position, giving equal weighting to sensitivity and specificity.

A total of 437 patients with COPD were recruited (277 men, 160 women), with a mean age of 70 years (standard deviation, 10 years); FEV_1, 47% predicted (standard deviation, 19% predicted); FEV_1/FVC ratio, 0.48 (standard deviation, 0.12); Medical Research Council dyspnea score, 3.2 (standard deviation, 1.1); body mass index, 27.1 kg/m^2 (standard deviation, 5.9 kg/m^2); COPD-specific comorbidity test score, 1.4 (standard deviation, 2.0); incremental shuttle walk, 236 m (standard deviation, 154); COPD Assessment Test score, 21.0 (standard deviation, 8.0); and QMVC, 25.7 kg (standard deviation, 10.3 kg; men, 29.5 kg [standard deviation, 9.6 kg], and women, 19.0 kg [standard deviation, 7.7 kg]). Twenty-three women and 26 men were unable to stand unaided (14 and 9%, respectively); two of the men were receiving long-term systemic corticosteroids. Table 1 describes the clinical characteristics of those who could and those who could not stand unaided. Table 2 shows the area under the curve, sensitivity, and specificity for sex-specific cut points for raw and normalized QMVC values in predicting failure to stand in patients with COPD. QMVC normalized to height squared produced the highest area under the curve, with 8.30 and 5.99 kg/m^2 identified as the cut points for men and women that best identified failure to stand.

To validate these results, we recruited a separate cohort of 208 patients (98 men, 110 women) with non-COPD chronic respiratory disease (62 patients with asthma, 61 with bronchiectasis, 76 with interstitial lung disease, and nine with extrathoracic restriction) from outpatient respiratory clinics. Baseline characteristics were mean age, 68 years (standard deviation, 12 years); FEV_1, 68% predicted (standard deviation, 24% predicted), FEV_1/FVC ratio, 0.73 (standard deviation, 0.13); Medical Research Council dyspnea score, 3.0 (standard deviation, 1.0); body mass index, 28.5 kg/m^2 (standard deviation, 5.8 kg/m^2), incremental shuttle walk, 285 m

Table 1. Comparison of Clinical Characteristics in Patients with Chronic Obstructive Pulmonary Disease Who Were Able and Unable to Stand Unaided from the Sitting Position

	Able to Stand	Unable to Stand	*P* Value
Age, yr	69 (10)	75 (9)	0.0002
Sex, M:F	251:137	26:23	0.12
Smoking, pack-years	41 (25)	47 (38)	0.16
BMI, kg/m^2	27.3 (5.8)	25.4 (6.4)	0.03
FEV_1, % predicted	47 (19)	42 (19)	0.10
MRC	3.2 (1.1)	3.9 (1.0)	<0.0001
ISW, m	255 (151)	88 (84)	<0.0001
COTE	1.3 (2.0)	1.9 (2.2)	0.05
CAT	20.2 (7.9)	23.3 (9.5)	0.01
QMVC, kg	26.7 (10.2)	17.9 (7.0)	<0.0001

Definition of abbreviations: BMI = body mass index; CAT = Chronic Obstructive Pulmonary Disease Assessment Test; COTE = chronic obstructive pulmonary disease–specific comorbidity test; ISW = incremental shuttle walk; MRC = Medical Research Council dyspnea score; QMVC = quadriceps maximum voluntary contraction.
Data are mean (SD) except where otherwise indicated.

(standard deviation, 202); COPD Assessment Test, 19.0 (standard deviation, 7.7); and QMVC, 23.1 kg (standard deviation, 9.5 kg). The derived cut points from the COPD cohort had a sensitivity and specificity of 73 and 78% for men and 76 and 75% for women in predicting failure to stand in the validation cohort, similar to the results from the derivation cohort.

To our knowledge, this study involving two large cohorts is the first to report clinically relevant cut points for isometric QMVC in COPD and chronic respiratory disease. Maintenance of the ability to perform a sit-to-stand maneuver is a key factor in retaining functional independence: it is required for basic daily activities such as getting in and out of a standard height chair or a lower-height surface such as a bathtub, bed, or toilet. In community-dwelling elderly people, the inability to complete a sit-to-stand maneuver is associated with greater disability and mortality (11). The identification of this clinically relevant threshold provides clinical context to clinicians interpreting QMVC measurements and may be used to determine meaningful effect of interventions (e.g., exercise, pharmacological) on lower limb muscle dysfunction, as well as enable stratification of patients for randomized controlled trials aimed at preventing loss of independence. Further studies are required to determine the psychometric properties of QMVC.

Quadriceps strength is not the only predictor of the ability to stand (6). Factors such as core stability, functional range of motion at the hips and knees, balance, and cognitive integration of sensory and mechanoreceptors are known determinants of sit-to-stand ability. Despite this, our analysis revealed that QMVC normalized to height had an accuracy of 80% in determining the ability to stand from a sitting position.

In older adults, cut points for quadriceps strength have been identified to determine sit to stand, stair climb, and walking ability (12) and to predict subsequent mobility decline (13, 14). No directly comparable values are available as a result of differences in measurement techniques, equipment, and outcomes, although the sensitivity and specificity values for predicting functional performance are consistently high (>0.70). In this letter, we have validated our cut points in a separate cohort of chronic respiratory disease patients.

In summary, we have determined that cut points of 5.99 kg/m^2 for women and 8.30 kg/m^2 for men for QMVC normalized to height squared are functionally relevant. These thresholds provide

Table 2. Sex-Specific Cut Points for Quadriceps MVC Strength in Predicting Failure to Stand in Patients with Chronic Obstructive Pulmonary Disease

	Inability to Stand				
	Cut Point	AUC	*P* Value	Sensitivity *(%)*	Specificity *(%)*
Females					
QMVC	14.8	0.80	<0.001	72	74
QMVC/BMI	0.62	0.74	<0.001	70	70
QMVC/weight	0.24	0.74	<0.001	74	70
QMVC/height	9.45	0.80	<0.001	71	70
QMVC/height^2	5.99	0.80	<0.001	73	74
Males					
QMVC	25.3	0.76	<0.001	69	69
QMVC/BMI	0.96	0.76	<0.001	72	73
QMVC/weight	0.33	0.81	<0.001	73	73
QMVC/height	14.76	0.78	<0.001	69	69
QMVC/height^2	8.30	0.81	<0.001	73	73

Definition of abbreviations: AUC = area under the curve; BMI = body mass index; MVC = maximum voluntary contraction; QMVC = quadriceps maximum voluntary contraction.

added clinical context to QMVC measurements in chronic respiratory disease, which may encourage adoption into routine clinical practice. ■

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Sedation Options for Endobronchial Ultrasound–guided Transbronchial Needle Aspiration

To the Editor:

As an early user of endobronchial ultrasound (EBUS) (1, 2), and the first physician in Pittsburgh, Pennsylvania, to perform the procedure, who does not have general anesthesia available for bronchoscopies, I found the study by Casal and colleagues very illuminating (3). As I taught many of the pulmonologists and thoracic surgeons currently using EBUS at the University of Pittsburgh Medical Center, I believe another important reason for using general anesthesia for advanced bronchoscopy procedures, including EBUS, is for teaching purposes. Although I also believe EBUS should only be taught to experienced bronchoscopists (not first-year fellows), I have found that much of the sedation time can be used up while trainees try to pass the EBUS bronchoscope through the vocal cords. This obviously leaves less time for the most important parts of the procedure: learning imaging and anatomical landmarks and tissue acquisition. This can be avoided with general anesthesia, leaving plenty of time in the lower airways for ultrasound and tissue acquisition. After reading the

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