Influence of muscle mass in the assessment of lower limb strength in COPD: validation of the prediction equation

ABSTRACT

Absence of established reference values limits application of quadriceps maximal voluntary contraction (QMVC) measurement. The impact of muscle mass inclusion in predictions is unclear. Prediction equations encompassing gender, age and size with (FFM+) and without (FFM−), derived in healthy adults (n=175), are presented and compared in two COPD cohorts recruited from primary care (COPD-PC, n=112) and a complex care COPD clinic (COPD-CC, n=189). Explained variance was comparable between the prediction models (R2: FFM+: 0.59, FFM−: 0.60) as were per cent predictions in COPD-PC (88.8%, 88.3%). However, fat-free mass inclusion reduced the prevalence of weakness in COPD, particularly in COPD-CC where 11.9% fewer were deemed weak.

INTRODUCTION

Measurement of lower limb muscle strength is valuable in the clinical management of patients with COPD. Muscle weakness is common, independently relates to mortality and morbidity and is modifiable by exercise rehabilitation and potentially anabolic drug therapy.[1–4] Assessment of lower limb strength can be easily and reproducibly performed in clinical settings through quadriceps maximal voluntary contraction (QMVC) measurement. Establishment of reference ranges in healthy adults is required to identify weakness to assist decisions regarding therapies and assess outcomes in both clinical and research settings.[1 5] Prediction equations previously used to study strength in COPD populations have included fat-free mass (FFM) thereby incorporating a measure of muscle mass. The inclusion of FFM may underestimate the prevalence of muscle weakness, particularly in populations where muscle mass is frequently low, as in COPD.[2] We aimed to examine the influence of muscle mass measurement on prediction equations for QMVC by determining the prevalence of weakness in two separate COPD cohorts using prediction equations with and without fat-free mass derived from healthy subjects.

METHODS

Prediction equations were derived using multiple linear regression from an existing cohort of healthy adults (HC). Age, gender, weight and height were entered in the first model. A whole-body measure of FFM was added for the second. The derived equations were used to calculate individual per cent predicted (%pred) values of QMVC in two COPD cohorts: one recruited from primary care (COPD-PC) and the other from a complex care COPD outpatient clinic (COPD-CC). The lower limit of normal was used as a threshold for the presence of weakness. A further description of the participants, measurements and analysis is provided in the online supplementary file 1.

RESULTS

One hundred and seventy-five HC participants were included and 301 patients with COPD (n=112, COPD-PC; n=189, COPD-CC). Baseline characteristics can be found in the table S1 in the online supplementary file 1.

Prediction models derived from healthy subjects

Model without FFM (FFM−)

QMVC = (−0.318 × A) + (13.138 × G) + (0.245 × W) + (29.781 × H) −18.072

QMVC (kg), A = age (years) G = gender: (F = 0), W = weight (kg), H = height (m)

R = 0.773, R^2 = 0.598, SEE: 8.86, p≤0.005

Model including FFM (FFM+)

QMVC = (−0.320 × A) + (10.670 × G) + (0.566 × FFM) + 20.952

FFM = fat-free mass (kg)

R = 0.770, R^2 = 0.585, SEE = 8.90, p≤0.005

Application of the prediction equations in patients with COPD

The predicted values for QMVC using the FFM− and the FFM+ model in the two COPD cohorts were calculated. Individual measured values were then compared with respective predictions as percentages to yield the %pred value for both models in all cohorts, presented in table 1.

QMVC weakness

The number and proportion of each cohort classified as weak is presented in table 1.

The FFM− model increased the percentage defined as weak (3.6% increase in COPD-PC and 11.9% in COPD-CC) compared with the FFM+ model.

The distribution of the standardised residuals calculated using the FFM− and FFM+ equations for the HC, primary care and complex care COPD cohorts in relation to the threshold of weakness are shown in figure 1.

DISCUSSION

We present two prediction equations for QMVC that estimate the presence of lower limb muscle weakness, one including and one without muscle mass (estimated using whole body measures of FFM). In healthy adults, inclusion of FFM did not affect explained variance of the prediction. However, when applied to COPD cohorts, there was a difference in the assessment of weakness between the two equations, which was amplified in those with more severe disease.

While percentage predicted values were similar in the primary care COPD (COPD-PC) cohort using both equations there was a marginally greater number classed as weak with the FFM− model. A larger difference occurred between models in the complex care cohort (COPD-CC). Using the FFM+ model, %pred values were higher and fewer were assigned as weak (table 1 and figure 1). This results from the partial adjustment for the lower muscle mass associated with more severe disease by the inclusion of FFM in the prediction equation. Where muscle mass is not abnormally low within the COPD-CC, the difference in the classification of weakness between the models is reduced (details of this subanalysis are supplied in

Table 1 Quadriceps maximal voluntary contraction (QMVC) values expressed as per cent predicted (%pred) values and number classed as weak using the FFM− and FFM + models for the COPD cohorts

	Primary care COPD, n=112	Complex care COPD, n=189
FFM− model %pred QMVC	88.3 (23.6)	54.0 (16.4)
Number classed as weak (%)	17 (15.2)	101 (53.4)
FFM+ model %pred QMVC	88.8 (22.4)	59.2 (17.8)
Number classed as weak (%)	13 (11.6)	78 (41.3)

Mean values and SD of measured QMVC presented as %pred and the number in each cohort classed as weak using the FFM− and FFM+ models.
FFM+, fat-free mass model; FFM−, model without fat-free mass; n, number in each group.

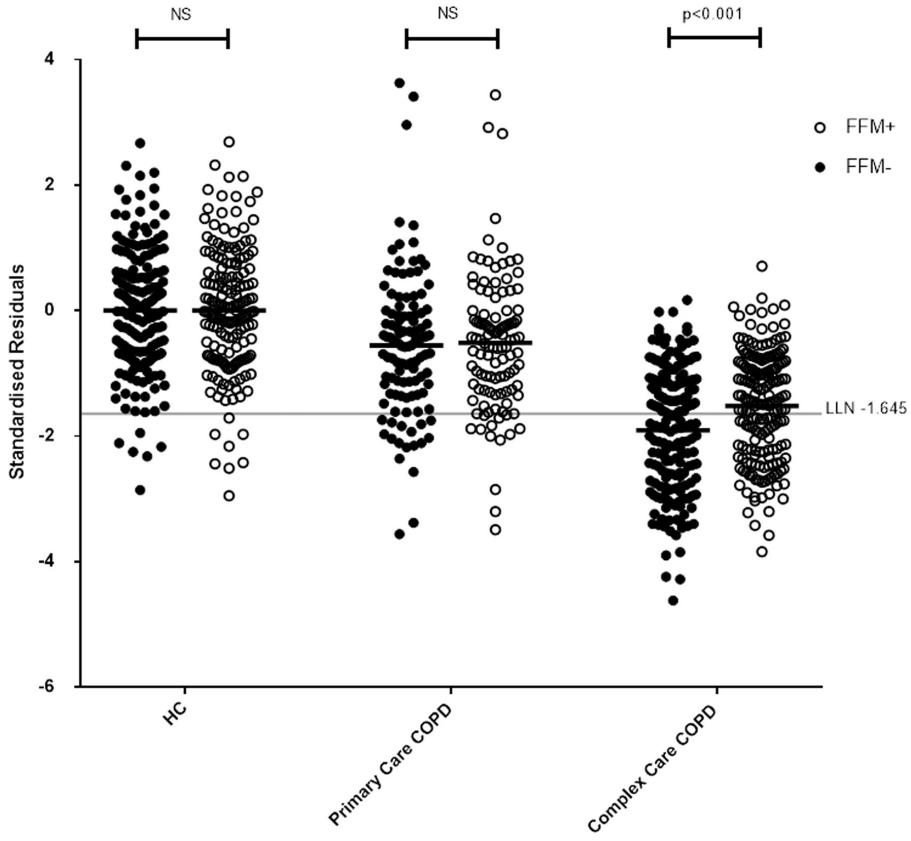

Figure 1 The distribution of the standardised residuals calculated using the FFM– and FFM+ equations for the HC, primary care and complex care COPD cohorts. The lower limit of normal (LLN) threshold for weakness is shown as a grey horizontal line. Those below this line are classed as weak. Mean value for each group is shown as a solid black line. The significance of the difference between the standardised residuals for the models in each cohort is indicated above the respective columns. FFM–, model without fat-free mass; FFM+, fat-free mass included model; HC, healthy controls; NS, non-significant.

the online supplementary file 1).

The prevalence and magnitude of muscle weakness observed and the finding that this occurred in milder disease (managed in primary care) but was more pronounced in those with more severe COPD are consistent with other reports.[2 4 6] Previous reference equations for QMVC have variably included muscle mass.[2 4] A negligible difference in predictions with the inclusion of muscle mass in healthy subjects was reported in an examination of isokinetic muscle strength.[7] A comparison of different reference equations for muscle strength in patients with COPD, one including FFM, demonstrated differences between them.[8] We advance previous studies by directly comparing how model components influence predictions by using the same healthy cohort to derive equations and applying them to separate COPD cohorts of differing severities, from different healthcare sectors. We have identified statistical thresholds of 'normality' for muscle strength both in absolute terms and relative to an individual's muscle mass. The prediction does not encompass regional differences in muscle mass that might be important in some patients with COPD and clearly has relevance to the prediction of QMVC, a measure of regional muscle function. The impact of the identification of muscle weakness using this method on treatment stratification (eg, for local muscle reconditioning or whole body anabolic therapies) requires further investigation.

We acknowledge some limitations. Different methods were used to measure FFM in the two COPD cohorts, which could affect the predicted values but would have minimal effect on comparison of the prediction models.[9] The functional and prognostic relevance of the identified lower limit of normal for muscle strength requires confirmation through linkage with outcomes such as functional status and mortality.

Proximal lower limb muscle dysfunction has significant implications for mortality, morbidity and healthcare utilisation in COPD.[4] Measurement is important in clinical assessment with the potential to aid targeting of therapeutic interventions such as strength training, nutritional support and anabolic drug therapy, availability of accessible reference values for interpretation will assist implementation.[1 10]

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