# Reference equations for quadriceps strength, endurance and power: a multicentre study

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**Using readily accessible clinical variables, reference equations for quadriceps strength, endurance and power were developed. In COPD, all muscle properties were associated with functional status, supporting the construct validity of these equations.** https://bit.ly/3pm6or5

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## Abstract

***Introduction*** The lack of reference values of lower-limb muscle function hinders the clinical recommendations of its measurement in patients with COPD. Therefore, this study aimed to develop reference equations to predict reference values for quadriceps strength, endurance and power and evaluate their construct validity in patients with COPD.

***Methods*** Quadriceps strength, endurance and power were assessed in 158 healthy individuals and 87 patients with COPD. In addition, patients with COPD performed a 6-min walk test (6MWT) and a 1-min sit-to-stand test (1STS). Multiple linear regressions were performed to develop reference equations. The proportion of patients with COPD with reduced quadriceps function was determined, and correlations between quadriceps strength, endurance and power expressed in percentage of predicted values and 6MWT and 1STS performance were used to document the construct validity of the reference equation.

***Results*** Except for quadriceps isometric endurance, the proposed reference equations explained 50–70% of the variance of the quadriceps properties in healthy individuals. All quadriceps properties were systematically reduced in a large proportion of patients with COPD compared to healthy individuals. Correlation coefficients between quadriceps properties expressed in percentage of predicted values and 6MWT and 1STS performance ranged between 0.28 and 0.49 (all $p<0.05$).

***Conclusion*** In healthy individuals, age, sex, height and body mass index explained 50–70% of the variance of quadriceps strength, endurance and power. When expressed in percentage of predicted values, these quadriceps properties correlated with 6MWT and 1STS performance, suggesting construct validity of the reference values in patients with COPD.

## Introduction

Limb muscle dysfunction is a common extrapulmonary consequence of COPD, negatively impacting physical activity, exercise tolerance and survival [1–4]. Limb muscle dysfunction is present in up to one-third of all patients with COPD; it can be seen in patients with mild airflow limitation, but its prevalence increases in more advanced disease [1, 2]. Although limb muscle dysfunction can be present in both upper and lower limbs, the quadriceps is more affected compared to the upper limb muscles, and is the most critical locomotor muscle [1].

At a functional level, quadriceps dysfunction is evidenced by reduced strength, endurance and power [1, 2, 5–7]. Muscle strength, endurance and power are defined as the muscle's ability to generate force, sustain or repeat a specific task over time, and produce a certain amount of force in a short period of time, respectively [5, 8–10]. The negative impact of reduced quadriceps strength on several clinical outcomes such as exercise tolerance [11, 12], functional capacity [13], daily life activity [14], mortality [15], healthcare service use [16] and health-related quality of life [17] is well established in patients with COPD. In addition, quadriceps endurance correlates more closely with functional capacity and daily activities than muscle strength [18, 19] and muscle power has been associated with better preserved functional capacity and the ability to carry out light-intensity daily life activities in older men with COPD [20].

Based on the relevance of reduced quadriceps function in patients with COPD [11, 12, 17], it has been suggested that the assessment of quadriceps function should be part of the routine clinical evaluation of patients with COPD [1, 21]. However, there are several obstacles to this practice, including the lack of consensus on the use of available reference equations for quadriceps strength [2, 15, 22–25], the absence of reference equations for quadriceps endurance and power, and the fact that the construct validity of the reference equations for quadriceps strength has not been documented in patients with COPD.

To address these issues, the aims of this international and multicentre study were to 1) develop reference equations to obtain reference values for quadriceps strength, endurance and power in healthy individuals; 2) test the reference equations in patients with COPD to establish the prevalence of reduced quadriceps strength, endurance and power in this population; and 3) explore the construct validity of the proposed equations by evaluating the relationships between quadriceps function and functional capacity in patients with COPD. Our goal was to promote the implementation of quadriceps assessment of patients with COPD in the context of pulmonary rehabilitation and clinical exercise testing.

## Methods

### *Study design and participants*

This cross-sectional, multicentre study took place in Quebec City (QC, Canada), Umeå (Sweden) and Diepenbeek (Belgium). The respective local ethics committees approved this research (Quebec City, Canada: CÉR 21785; Umea, Sweden: DNR 2015/426-31, 2020-06881; Diepenbeek, Belgium: B9115201941687), and all assessment procedures were standardised across the three centres. Healthy individuals aged between 40 and 89 years were recruited for this study. Potential study participants were identified from respective local research databases and local advertisements. The following exclusion criteria were applied: 1) known chronic diseases that could affect muscle function, such as ischaemic heart disease, heart failure, respiratory disorders, any cancer, diabetes, neurological or orthopaedic conditions; 2) use of statins; 3) use of systemic corticosteroids (oral or injection) within 3 months of study enrolment; and 4) participation in a structured exercise programme aimed at reaching fitness-related goals. Patients with COPD of a similar age span to healthy individuals were also enrolled in this study. These patients were recruited from ambulatory clinics of the participating centres. The same exclusion criteria were applied, except for the presence of COPD, which was defined by a smoking exposure of ⩾10 pack-years and related symptoms in the presence of mild to severe airflow limitation confirmed *via* spirometry according to the Global Initiative for Chronic Obstructive Lung Disease classification [26]. In addition, patients with COPD were stable (no COPD exacerbation during the 6 weeks before study enrolment) and had not been involved in a rehabilitation programme in the 6 months before study enrolment. All study participants provided written informed consent.

### *Procedures*

Muscle testing was completed in a single visit. After anthropometric measurements (body weight and height) and spirometry [27], isometric strength (strength$_{ISOM}$), isometric endurance (endurance$_{ISOM}$), isotonic endurance (endurance$_{ISOT}$), isokinetic endurance (endurance$_{ISOK}$), and isokinetic power (power$_{ISOK}$) of the dominant leg were evaluated using a computerised dynamometer (System Pro 3 or 4; Biodex Medical Systems, Shirley, NY, USA). The protocols used have shown their reliability and feasibility in patients with COPD [8, 28, 29] and are described in details in the supplementary material. In addition, patients with COPD were asked to complete a second visit during which functional exercise capacity was assessed using the 6-min walk test (6MWT) and the 1-min sit-to-stand test (1STS). Both tests were performed according to recommended guidelines [30, 31], as decribed in the supplementary material.

### *Statistical analysis*

Descriptive data were expressed as mean±SD or frequency (proportion). Multiple linear regression analyses were performed to establish reference equations in healthy individuals with strength$_{ISOM}$, endurance$_{ISOM}$, endurance$_{ISOT}$, endurance$_{ISOK}$ and power$_{ISOK}$ as dependent variables and readily accessible individual characteristics (age, sex, height and body mass index (BMI)) as independent variables. A separate regression analysis was done for each dependent variable. Continuous variables were checked for the assumption of linearity using graphical representations. Model selection was based on a hierarchical approach that, for any interaction term in the statistical model, contains the main effects. With four independent variables (main effects) and 2×2 interaction terms, 96 statistical models were investigated. The final models retained were those with the lowest Akaike information criterion. Model fit statistics and diagnostic statistics were used for assessing the fit and the adequacy of the models. Since no corelation was found between independent variables, collinearity was not an issue. The normality assumption was verified using Shapiro–Wilk tests on error distribution from the statistical models. Predicted values were computed from these reference equations for each quadriceps property in patients with COPD. The lower limit of normal (LLN) at the 5th percentile was used as a primary threshold to assess the presence of reduced quadriceps strength, endurance and power in patients with COPD [2, 24]. LLN was calculated according to the method previously published by Trethewey *et al.* [24]. For comparative purposes, the proportion of patients with COPD whose measures of quadriceps function were <80% predicted is also reported in the supplementary material. Pearson correlations were used to evaluate associations between quadriceps properties and functional exercise capacity results in patients with COPD. Correlation coefficients (r) were interpreted in the range of <0.10 considered trivial, 0.10–0.29 small, 0.30–0.49 moderate, 0.50–0.69 large, 0.70–0.90 very large and >0.90 extremely large [32]. Previous investigators have developed reference equations for quadriceps strength [16, 24, 25]. To evaluate to which extent these equations apply to our control population, they were used to derive predicted quadriceps strength in the healthy subjects of the present study. All statistical analyses were performed using SAS (version 9.4; SAS Institute, Cary, NC, USA), and a p-value of <0.05 was considered statistically significant. The study sample size was established to obtain sufficient number of participants relative to the pre-specified number of covariates and to reduce the problem of overfitting [33]. Using a shrinkage factor of 0.98 and up to four covariates to build the statistical models, it was estimated that 139 participants were required. Considering a dropout rate of 10%, 158 healthy individuals were enrolled.

## Results

The sample for this study was 158 healthy individuals (67 in Quebec City, 68 in Umeå and 23 in Diepenbeek), and 87 patients with COPD (54 in Quebec City and 33 in Umeå) including 72 who had been recruited for another study [34] and 15 specifically recruited for the present study. Characteristics of study participants are shown in table 1. Although patients with COPD, on average, were slightly older than the healthy individuals ($p<0.0001$), their age span was similar to that of healthy individuals (ranging from 51 to 88 years). All quadriceps functions were reduced in patients with COPD compared to healthy individuals ($p<0.0001$).

Reference equations of quadriceps function developed in healthy individuals are shown in table 2. Suggested models using age, sex, height and BMI as independent variables explain 69%, 5%, 48%, 71% and 69% of the variance in $\text{strength}_{ISOM}$, $\text{endurance}_{ISOM}$, $\text{endurance}_{ISOT}$, $\text{endurance}_{ISOK}$ and $\text{power}_{ISOK}$, respectively. Considering that only 5% of $\text{endurance}_{ISOM}$ could be explained by the model, this quadriceps property was excluded from further analysis.

Identity plots of measured and predicted values of quadriceps $\text{strength}_{ISOM}$, $\text{endurance}_{ISOT}$, $\text{endurance}_{ISOK}$ and $\text{power}_{ISOK}$ in patients with COPD are presented in figure 1. These quadriceps properties were systematically reduced compared to the predicted values derived from healthy individuals, indicating impaired quadriceps function in patients with COPD.

Graphical representations of $\text{strength}_{ISOM}$, $\text{endurance}_{ISOT}$, $\text{endurance}_{ISOK}$ and $\text{power}_{ISOK}$ as a function of age in healthy men and women are provided in figure 2. $\text{Strength}_{ISOM}$, $\text{endurance}_{ISOK}$ and $\text{power}_{ISOK}$ all were negatively associated with age (r-values ranging from −0.53 to −0.72, $p<0.0001$) and were higher in men than women ($p<0.0001$). $\text{Endurance}_{ISOM}$ and $\text{endurance}_{ISOT}$ showed a small-to-moderate correlation to age and sex (r-values ranging from −0.24 to −0.40, $p<0.05$), except for $\text{endurance}_{ISOM}$ in men which was not correlated to age ($r=0.11$, $p=0.3$).

The distribution of patients with COPD presenting reduced quadriceps function according to the LLN threshold is provided in figure 3. $\text{Strength}_{ISOM}$, $\text{endurance}_{ISOT}$, $\text{endurance}_{ISOK}$ and $\text{power}_{ISOK}$ were reduced below the 5th percentile of normal in 14%, 43%, 26% and 36% of the patients with COPD, respectively.

$\text{Strength}_{ISOM}$, $\text{endurance}_{ISOK}$ and $\text{power}_{ISOK}$ predicted values were moderately correlated (r-values ranging from 0.30 to 0.49, $p<0.05$) with 6-min walk distance (6MWD) and 1STS. $\text{Endurance}_{ISOT}$ only correlated with 1STS (table 3).

Comparisons between ours and three previously published reference equations for isometric strength using comparable methodology are shown in table 4. Mean differences between the measured values in healthy

**TABLE 1** Participant characteristics

| | Healthy | COPD | p-value |
|---|---|---|---|
| **Participants** | 158 | 87 | |
| **Age, years** | 62±12 | 69±7 | **<0.0001** |
| **Female** | 83 (53) | 34 (39) | **0.046** |
| **Height, m** | 1.69±0.08 | 1.67±0.09 | 0.05 |
| **Weight, kg** | 74.4±14.7 | 75.5±16.5 | 0.06 |
| **BMI, kg·m$^{-2}$** | 25.8±4.0 | 26.9±4.6 | 0.07 |
| **FVC, % pred** | 114±15 | 98±21 | **<0.0001** |
| **$FEV_1$, % pred** | 108±14 | 59±20 | **<0.0001** |
| **$FEV_1$/FVC, %** | 77±5 | 47±12 | **<0.0001** |
| **GOLD classification** | NA | | NA |
| 1 | | 16 (18) | |
| 2 | | 42 (48) | |
| 3 | | 18 (21) | |
| 4 | | 11 (13) | |
| **Quadriceps properties** | | | |
| $Strength_{ISOM}$, N·m | 169.0±58.7 | 138.5±47.8 | **<0.0001** |
| $Endurance_{ISOM}$, s | 58±27 | 49±22 | **0.005** |
| $Endurance_{ISOT}$, N·m × reps | 1922±1503 | 1014±550 | **<0.0001** |
| $Endurance_{ISOK}$, J | 2543.2±812.4 | 1928.3±746.0 | **<0.0001** |
| $Power_{ISOK}$, W | 86.9±29.1 | 59.7±21.5 | **<0.0001** |
| **Functional exercise capacity** | | | |
| 6MWD, m | NA | 473±115 | NA |
| 1STS, reps | NA | 23±7 | NA |

Data are presented as n, mean±SD or n (%), unless otherwise stated. Bold type represents statistical significance. BMI: body mass index; FVC: forced vital capacity; $FEV_1$: forced expiratory volume in 1 s; GOLD: Global Initiative for Chronic Obstructive Lung Disease; $strength_{ISOM}$: quadriceps isometric strength; $endurance_{ISOM}$: quadriceps isometric endurance; $endurance_{ISOT}$: quadriceps isotonic endurance; reps: repetitions; $endurance_{ISOK}$: quadriceps isokinetic endurance; $power_{ISOK}$: quadriceps isokinetic power; 6MWD: 6-min walk distance; 1STS: 1-min sit-to-stand test; NA: not applicable.

individuals of the present study and predicted values from three previously published reference equations indicated a systematic underestimation of quadriceps isometric strength in healthy controls by the previously published reference equations.

## Discussion

This study provides reference equations generated from a cohort of healthy individuals that explain ∼70% of the variance in quadriceps $strength_{ISOM}$, $endurance_{ISOK}$ and $power_{ISOK}$, and 48% of the variance for $endurance_{ISOT}$. Using the LLN as a threshold to assess reduced quadriceps function, 14%, 43%, 26% and 36% of patients with COPD presented a reduction in $strength_{ISOM}$, $endurance_{ISOT}$, $endurance_{ISOK}$ and $power_{ISOK}$, respectively. The observed correlations between quadriceps properties and functional exercise capacity results supported the construct validity of the reference equation. Moreover, the strength and the direction of these correlations are similar to direct measures of quadriceps function previously reported in COPD [34].

**TABLE 2** Reference equations of quadriceps function in healthy individuals

| | Equations[#] | Adjusted $R^2$ | p-value | SEE |
|---|---|---|---|---|
| **$Strength_{ISOM}$, N·m** | Y = −982.2 + 12.6(age) − 50.5(sex) + 742.7(height) + 1.6(BMI) − 8.6(age×height) | 0.69 | <0.0001 | 32.16 |
| **$Endurance_{ISOM}$, s** | Y = 92.6 + 0.3(age) − 23.1(sex) − 2.0(BMI) − 0.8(age×sex) + 2.8(sex×BMI) | 0.05 | 0.03 | |
| **$Endurance_{ISOT}$, N·m × reps** | $Y = e^{(5.13-0.01(age) - 0.42(sex) + 1.86(height))}$ | 0.48 | <0.0001 | 0.38 |
| **$Endurance_{ISOK}$, J** | Y = −454.6 − 43.9(age) − 1931.7(sex) + 3256.4(height) + 20.1(BMI) + 21.8(age×sex) | 0.71 | <0.0001 | 433.43 |
| **$Power_{ISOK}$, W** | Y = −3.3 − 1.6(age) − 71.1(sex) + 103.5(height) + 1.0(BMI) + 0.8(age×sex) | 0.69 | <0.0001 | 16.11 |

SEE: standard error of the estimate; $strength_{ISOM}$: quadriceps isometric strength; $endurance_{ISOM}$: quadriceps isometric endurance; $endurance_{ISOT}$: quadriceps isotonic endurance; reps: repetitions; $endurance_{ISOK}$: quadriceps isokinetic endurance; $power_{ISOK}$: quadriceps isokinetic power; BMI: body mass index. [#]: units are age (years), sex (male=0), height (m), BMI (kg·m$^{-2}$).

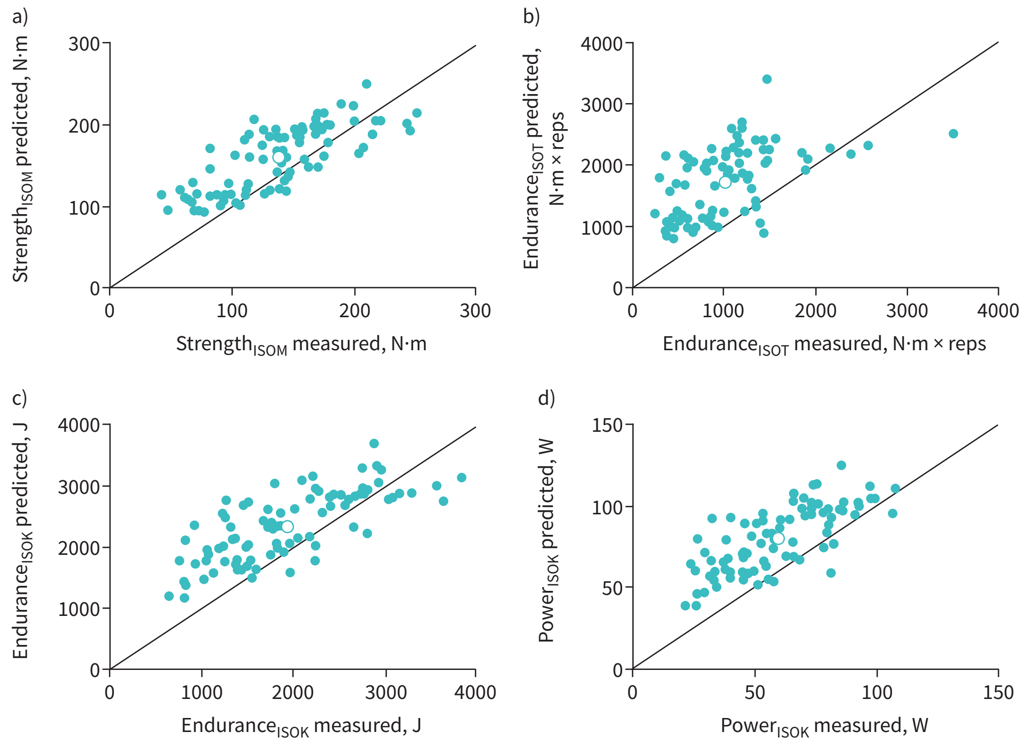


FIGURE 1 Identity plots of measured and predicted quadriceps a) isometric strength (strength$_{ISOM}$), b) isotonic endurance (endurance$_{ISOT}$), c) isokinetic endurance (endurance$_{ISOK}$) and d) isokinetic power (power$_{ISOK}$) in patients with COPD. The black lines represent the identity lines, and the open circles represent the mean. Reps: repetitions.

Possible predictors of quadriceps properties were chosen according to prior studies [2, 16, 24, 25, 35], but also by considering their availability in clinical settings. Age, sex, height, weight, BMI and fat-free mass (FFM) were previously used to predict quadriceps function [2, 16, 24, 25, 35]. In the current study, age, sex, height and BMI turned out to be excellent predictors of strength$_{ISOM}$, endurance$_{ISOK}$ and power$_{ISOK}$, explaining ∼70% of their total variance and 48% of the total variance of endurance$_{ISOT}$. However, these variables poorly predicted endurance$_{ISOM}$. Although we do not have a clear explanation for the lack of predictability of endurance$_{ISOM}$, other variables that have not been measured in this study, such as motivation or neuromuscular recruitment, could be better predictors than the independent variables presented in this article. Alternatively, endurance$_{ISOK}$ measured at an angular velocity of 90°·s$^{-1}$ could be highly dependent on muscle strength, perhaps explaining that the prediction model for this variable performed as well as that of quadriceps strength.

A few reference equations have been proposed for quadriceps strength [2, 16, 22, 24, 25] and power [22], but none for quadriceps endurance. Some incorporated FFM from bioelectrical impedance [2], which is not routinely available. In this study, we suggest, for the first time, a multicentre approach to determine reference values for three quadriceps properties which should help in their generalisability and thus their clinical applicability. When applying three previously proposed reference equations for quadriceps isometric strength developed with a similar methodology [24, 25] in the healthy subjects involved in the present study, we found a systematic underestimation of strength$_{ISOM}$ using previously proposed equations. The reasons for this are not entirely clear, but could be related to differences in characteristics of the population across studies and to subtle and unaccounted methodological differences. Considering the discrepancy between ours and others predictive models, it would be informative to study their behaviour in other cohorts of healthy individuals to assess their respective external validity. The implication of this discussion is that the applicability of a set of reference equations for quadriceps function should be tested locally in a sample of individuals thought to be representative of the local population prior to using them routinely.

According to the identity plots, quadriceps strength$_{ISOM}$, endurance$_{ISOT}$, endurance$_{ISOK}$ and power$_{ISOK}$ in patients with COPD were systematically lower than their corresponding predicted values. Although this

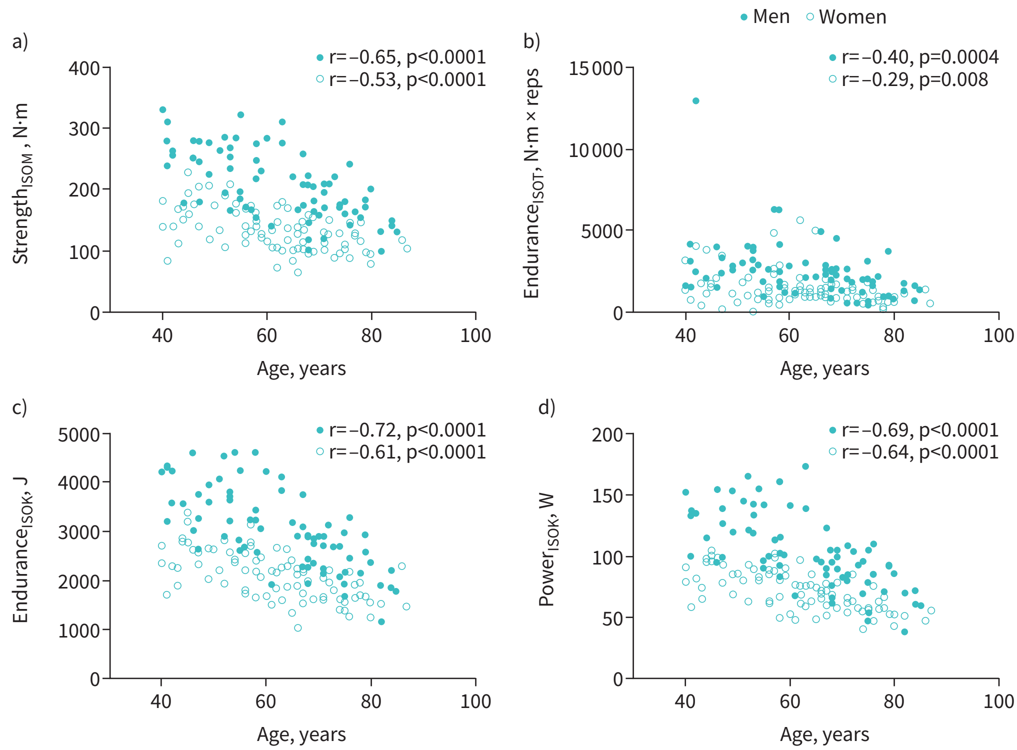


FIGURE 2 Quadriceps a) isometric strength (strength$_{ISOM}$), b) isotonic endurance (endurance$_{ISOT}$), c) isokinetic endurance (endurance$_{ISOK}$) and d) isokinetic power (power$_{ISOK}$) as a function of age in healthy men and women. Reps: repetitions.

finding is expected, given that quadriceps dysfunction is common in patients with COPD [1, 2, 5, 7], it also indicates that mechanisms other than ageing or sex-based differences are responsible for the loss in muscle function in COPD. In our study, BMI or height were used as crude estimates of muscle mass. It

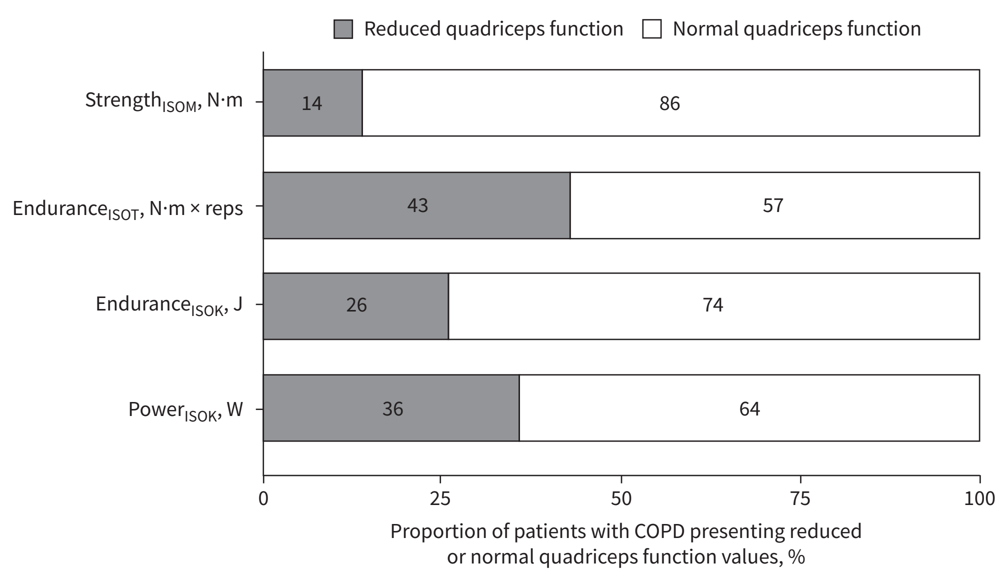


FIGURE 3 Proportion of patients with COPD with reduced quadriceps isometric strength (strength$_{ISOM}$), isotonic endurance (endurance$_{ISOT}$), isokinetic endurance (endurance$_{ISOK}$) and isokinetic power (power$_{ISOK}$) according to the lower limit (5th percentile) of normal. Reps: repetitions,

**TABLE 3** Results of the correlation analyses between quadriceps isometric strength (strength$_{ISOM}$), isotonic endurance (endurance$_{ISOT}$), isokinetic endurance (endurance$_{ISOK}$) and isokinetic (power$_{ISOT}$) power and functional exercise capacity in patients with COPD

| | 6MWD, m | | 1STS, reps | |
|---|---|---|---|---|
| | r | p-value | r | p-value |
| **Strength$_{ISOM}$, % pred** | 0.37 | 0.0004 | 0.30 | 0.005 |
| **Endurance$_{ISOT}$, % pred** | 0.19 | 0.07 | 0.28 | 0.008 |
| **Endurance$_{ISOK}$, % pred** | 0.46 | <0.0001 | 0.49 | <0.0001 |
| **Power$_{ISOK}$, % pred** | 0.44 | <0.0001 | 0.49 | <0.0001 |

6MWD: 6-min walk distance; 1STS: 1-min sit-to-stand test; reps: repetitions.

can be argued that more precise estimations of muscle mass with techniques such as bioelectrical impedance or dual-energy X-ray absorptiometry scan could have improved the prediction of quadriceps function in patients with COPD. Additionally, Trethewey *et al.* [24] reported that the addition of FFM did not affect the total variance of the prediction in healthy individuals. Still, when applied to patients with COPD, the predictive model was somewhat improved by incorporating this variable, which is consistent with the observation that muscle atrophy contributes to quadriceps weakness in patients with COPD [36]. Hypoxaemia could also influence muscle properties, since it has been linked with reduced quadriceps endurance in patients with COPD [37]. COPD exacerbations might also be a predictor of muscle function, since a reduction in muscle strength is often observed during hospitalisation [38]. Irrespective of the underlying mechanisms for quadriceps dysfunction, the reference values for quadriceps that we report herein based on variables that are readily available to clinicians should help interpret measurements of quadriceps function in individual patients with COPD.

Using the LLN threshold (below the 5th percentile of normal), we found that quadriceps strength$_{ISOM}$, endurance$_{ISOT}$, endurance$_{ISOK}$ and power$_{ISOK}$ were reduced in 14%, 43%, 26% and 36% of patients with COPD, respectively. Although these proportion are somewhat different from those previously reported [1, 2, 5, 7], they are consistent with the notion that quadriceps endurance and power are more affected than strength in COPD [1, 5, 7]. Discrepancies in the prevalence rates of impaired quadriceps function across studies can be explained by the fact that there is no agreement on how to define the presence or absence of reduced quadriceps function [23]. Some studies used the percentage of predicted values [11, 16, 22] to establish the presence of reduced quadriceps function while others, similar to us, use the more conservative LLN approach [2, 24]. We decided to use the LLN approach because it is used in many medical fields such as pulmonary function interpretation, and hypertension diagnosis in children and adolescents [39, 40]. However, for comparative purposes, we also presented the prevalence rates of reduced quadriceps function among our population according to the percentage of predicted values (supplementary material).

**TABLE 4** Comparison of quadriceps isometric strength in healthy individuals measured in the current study with predicted values derived herein, the NIMS Database Consortium [25], Trethewey *et al.* [24] and Decramer *et al.* [16]

| | | Present study | | NIMS Database Consortium [25] | | Trethewey *et al.* [24] | | Decramer *et al.* [16] | |
|---|---|---|---|---|---|---|---|---|---|
| | Measured value | Predicted value | Measured − predicted value | Predicted value | Measured − predicted value | Predicted value | Measured − predicted value | Predicted value | Measured − predicted value |
| **Participants** | | 158 | | 469 | | 175 | | NA | |
| **Quadriceps isometric strength, kg** | 56.9±18.9 | 56.7±14.9 | −0.2±10.9 | 35.6±10.7 | 21.3±13.4 | 37.1±11.4 | 19.8±13.4 | | |
| **Quadriceps isometric strength, N·m** | 169.0±58.7 | 168.8±48.1 | −0.2±32.7 | | | | | 145.3±53.3 | 23.7±36.8 |

Data are presented as n or mean±SD. NIMS: National Isometric Muscle Strength; NA: not available.

The observed correlations between $\text{strength}_{\text{ISOM}}$, $\text{endurance}_{\text{ISOT}}$, $\text{endurance}_{\text{ISOK}}$ and $\text{power}_{\text{ISOK}}$ with functional exercise capacity as evaluated by the 6MWD and 1STS support the construct validity of the proposed reference equations, and are not different from previously reported direct measurements of these quadriceps properties and functional tests in COPD [22]. Furthermore, the strength of the associations between $\text{endurance}_{\text{ISOK}}$ and $\text{power}_{\text{ISOK}}$ when derived from the proposed equations and functional exercise capacity was somewhat greater than for $\text{strength}_{\text{ISOM}}$, supporting the clinical relevance of assessing dynamic rather than static muscle properties in patients with COPD from a functional perspective [9, 34].

### *Clinical implications*

The proposed reference equations and reference values proposed in the current trial will facilitate implementation of quadriceps function assessment of patients with COPD. It will enable clinicians to identify patients presenting quadriceps dysfunction and its magnitude and, therefore, are at further risk of poor functional status and adverse clinical outcomes. Such measurements should also offer an opportunity for personalised interventions, as patients with reduced quadriceps function could be targeted for specific rehabilitative or nutritional therapies. For example, identifying quadriceps weakness as the primary muscle deficit in an individual would lead to recommending strengthening muscle exercises. In turn, if the primary limitation was poor muscle endurance, a programme of low-intensity muscle exercises with a high number of repetitions would be a preferable approach [41]. A thorough assessment of quadriceps function is necessary to identify which muscle property(ies) should be targeted in a rehabilitation programme and therefore to prescribe a specific training regimen.

### *Strength and limitations*

One strength of this study is the multicentre design which provides a varied sample for both populations of healthy individuals and patients with COPD, allowing for a good external validity and generalisability of the findings. Another strength is that the study procedures relied on validated protocols and were standardised across centres. Furthermore, we document for the first time the construct validity of the reference equations, which is supported by the existing correlations between quadriceps properties expressed in percentage of predicted values and functional exercise capacity of similar magnitude as previously reported from direct measures [22]. These findings reinforce the clinical relevance of the quadriceps function assessment and should facilitate its incorporation into patient care.

This study presents some limitations. First, the healthy individuals were not recruited by random sampling and as such may not be fully representative of the general population. Second, even though disease severity was different across patients with COPD, the majority presented less advanced disease and a well-preserved functional exercise capacity. Therefore, caution should be taken before generalising these study findings to patients with advanced COPD and/or markedly impaired functional exercise capacity. Thirdly, a computerised dynamometer was used to assess dynamic quadriceps properties, but its availability may be limited in clinical settings considering its cost and requirement for relatively large storage room. Thus, there are opportunities for the development of simpler measuring tools such as using weight machines for isotonic testing or a fixed handheld dynamometry for isometric testing, the latter has shown excellent correspondence with those obtained from a computerised dynamometer [9]. We did not consider other variables beside age, sex, height and BMI in the prediction models. This decision was based on the objective of providing simple reference equations that could be easily implemented in clinical practice.

### *Conclusion*

In healthy individuals, age, sex, height and BMI explained ∼50–70% of the total variance in isometric strength, isotonic endurance, isokinetic endurance and power of the quadriceps. When applying these reference equations in patients with COPD, we found that a significant quadriceps dysfunction was observed in a large proportion of patients with COPD and varied according to the quadriceps properties, with endurance and power being more affected than strength. Quadriceps function of patients with COPD was moderately correlated with 6MWT and 1STS performance, suggesting the construct validity of the reference values in this population.

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