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ORIGINAL ARTICLE

Use of different reference values for handgrip strength in individuals with COPD: analysis of agreement, discriminative capacity, and main clinical implications

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Study carried out in the Laboratório de Pesquisa em Fisioterapia Pulmonar —LFIP — Hospital Universitário, Universidade Estadual de Londrina, Londrina (PR) Brasil.

ABSTRACT

Objective: To identify reference values for handgrip strength through a literature search and compare the agreement of reference values from Brazil with others for handgrip strength in a sample of COPD patients in Brazil, as well as to determine which set of reference values is more discriminative regarding differences in clinical characteristics between individuals with low handgrip strength and normal handgrip strength. **Methods:** To identify reference values for handgrip strength, a literature search was performed; a retrospective cross-sectional analysis of baseline-only data from two unrelated studies was then performed. Individuals were evaluated for handgrip strength, peripheral muscle strength, respiratory muscle strength, pulmonary function, body composition, exercise capacity, dyspnea, and functional status. **Results:** Of the 45 studies that were initially selected, 9 met the criteria for inclusion in the analysis, which included 99 COPD patients in Brazil (52% of whom were male with GOLD stage II-IV COPD). The prevalence of low handgrip strength varied across studies (from 9% to 55%), the set of reference values for handgrip strength in a sample of individuals in Brazil having classified 9% of the study sample as having low handgrip strength. The level of agreement between the reference values for a sample of individuals in Brazil and the other sets of reference values varied from weak to excellent. The reference values for a sample of individuals in Brazil showed the highest number of significantly different characteristics between individuals with low and normal handgrip strength. **Conclusions:** The level of agreement between national and international sets of reference values for handgrip strength varied from weak to excellent in COPD patients in Brazil. Reference values for handgrip strength with higher discriminative capacity are not necessarily those that identify more individuals as having low handgrip strength.

Keywords: Pulmonary disease, chronic obstructive; Hand strength; Muscle weakness; Muscle strength; Reference values.

INTRODUCTION

Handgrip strength has been described as an important prognostic factor, moderately strongly associated with mortality in the general population and in individuals with COPD.[1,2] Handgrip strength reflects well overall peripheral muscle strength in individuals with COPD,[3] and assessment of muscle strength in this population is common and highly encouraged because muscle dysfunction is expected as a systemic manifestation of the disease.[4] Reference values or prediction equations are useful tools to identify the presence of abnormal muscle function while accounting for differences in individual characteristics because muscle strength is somehow associated with such characteristics.[4] Correct identification of individuals with peripheral muscle weakness is essential so that those at risk can be referred for specific treatment.[5]

Since the publication of reference values for handgrip strength by Mathiowetz et al.[6] in 1985, various studies have reported normative data for handgrip strength. Normative ranges, cutoff points, and reference equations are available in the literature,[7-9] but there are differences across studies regarding age ranges and methods. In addition to population-based characteristics, technical issues such as patient positioning for assessment, the instrument used for assessment, the hand selected for assessment, and the number of attempts should be taken into consideration when choosing the most suitable reference values.[10]

The objectives of this study were threefold: to identify reference values for handgrip strength through a literature search; to determine the level of agreement between a set of reference values for handgrip strength from Brazil[11] and other sets of reference values for handgrip

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strength in a sample of COPD patients recruited in Brazil; and to determine which set of reference values is more discriminative regarding differences in clinical characteristics between individuals with low handgrip strength and normal handgrip strength.

METHODS

This was a retrospective cross-sectional study of baseline-only data from two unrelated studies: a previous study conducted by our research group[12] and an as yet unpublished study by our research group (NCT03127878, approved by the local research ethics committee [Protocol no. 1.730.247]). Data from the two studies were collected between 2006 and 2019 in the Laboratory of Research in Respiratory Physiotherapy at the State University of Londrina, located in the city of Londrina, Brazil. The inclusion criteria for the two studies were as follows: a clinical diagnosis of COPD in accordance with the GOLD criteria[13]; clinical stability, without infections or exacerbations in the previous month; no severe/unstable cardiac disease; and no orthopedic, neurological, or muscular impairment that could hinder the assessments. Participants were evaluated for handgrip strength, peripheral muscle strength (quadriceps, biceps, and triceps muscle strength), respiratory muscle strength, pulmonary function, body composition, exercise capacity, dyspnea, and functional status. All participants gave written informed consent prior to inclusion in the study.

Literature search

A literature search was undertaken in order to identify studies for analysis. Studies reporting reference values and/or prediction equations for handgrip strength were retrieved from the MEDLINE (PubMed) database on September 13, 2021. The search strategy and process of article selection are described in detail in the supplementary material.

Handgrip strength assessment

Handgrip strength was assessed for both hands with the use of a validated hydraulic hand dynamometer (SH50011; Saehan Corporation, Changwon, South Korea),[14] with the patient in a seated position with unsupported arms, shoulders in a neutral position along the body, elbows flexed to 90°, and wrists in a neutral position. Three maximal attempts were made for each hand, with 3 s of contraction and 30 s of rest between attempts; the highest value for each hand was used in the analysis.[15] Right- or left-hand dominance was self-reported.

Other assessments

Quadriceps, biceps, and triceps muscle strength was assessed by the one-repetition maximum test; pulmonary function was assessed by spirometry; body composition was assessed by bioelectrical impedance analysis and an equation proposed by Rutten et al.[16]; and exercise capacity was assessed by the six-minute walk test. All assessments were performed as previously described.[3]

Respiratory muscle strength was assessed by measuring maximum respiratory pressures (MIP and MEP) with a digital manometer (MVD 300; Globalmed, Porto Alegre, Brazil), in accordance with recommendations by Black & Hyatt[17] and population-specific reference values.[18] Dyspnea during activities of daily living and functional status were respectively assessed by the Portuguese-language versions of the Medical Research Council scale[19] and the London Chest Activity of Daily Living scale.[20] In addition, the BODE index[21] and the Age, Dyspnea, and airflow Obstruction (ADO) index[22] were calculated.

Statistical analysis

All statistical analyses were performed with the IBM SPSS Statistics software package, version 22.0 (IBM Corporation, Armonk, NY, USA) and Epidat, version 3.1 (*Dirección Xeral de Saúde Pública de la Consellería de Sanidade*, *Xunta de Galicia*, Santiago de Compostela, Spain). The normality of the data distribution was examined with the Shapiro-Wilk test. Normally distributed data were described as mean ± standard deviation, and non-normally distributed data were described as median (IQR). Individuals were classified as having normal or reduced handgrip strength in accordance with different sets of reference values, on the basis of the limits proposed by the authors of each study or the number of SDs below the mean and specific for each group of individuals (classified by sex, age, and height in some cases), with the limit of 2 SDs[23] or the 5th percentile if values of mean ± SD were not available. The level of agreement between sets of reference values was determined by calculating the kappa statistic, being classified as weak (< 0.20), fair (0.21-0.40), moderate (0.41-0.60), excellent (0.61-0.80), or almost perfect (0.81-0.99).[24] For comparison of clinical characteristics between individuals with normal and reduced handgrip strength (in accordance with each set of reference values), the Student's t-test or the Mann-Whitney test was used depending on the normality of the data distribution. A value of $p < 0.05$ was considered statistically significant for all analyses.

RESULTS

Thirty-seven studies were selected from a total of 895 articles retrieved from the MEDLINE (PubMed) database. An additional 8 were retrieved by manual search, adding up to a total of 45 studies. Of those, 9 were selected for analysis.[6,11,25-31] The selection process is shown in detail in Figure 1. Table 1 shows the characteristics of the 9 studies selected for analysis. The studies reported normative ranges for handgrip strength by sex and age, at least. General characteristics of the 36 studies that were not included in the analysis are shown in Table S1, including the reasons for not including them in the analysis (differences regarding

the assessment of handgrip strength and the lack of a representative sample, in most cases).

Table 2 describes the sample characteristics. Ninety-nine individuals with COPD were included in the analysis. Of those, 52% were men with moderate to very severe airflow obstruction and relatively preserved exercise capacity. As can be seen in Figure 2, the prevalence of low handgrip strength ranged from 9% in studies conducted in Brazil[11] and the UK[30] to 55% in a multinational study conducted in the USA, Australia, Canada, the UK, and Sweden.[25] Table 3 shows the kappa statistics for the level of agreement between the set of reference values for a sample of adults and elderly individuals in Brazil[11] and the other sets of reference values.[6,25-31] The values varied considerably, ranging from as low as 0.1481 in the multinational study[25] to as high as 0.7963 in a study conducted in Korea.[29] Table S2 shows the level of agreement among all sets of reference values except the one for a sample of adults and elderly individuals in Brazil,[11] the kappa values having also varied widely (from 0.02 to 0.90).

A comparison of individuals with normal handgrip strength and those with low handgrip strength in accordance with each set of reference values was performed in order to find meaningful clinical differences between these two groups (Table 4). The reference values for a sample of adults and elderly individuals in Brazil[11] had a high number of variables showing statistical differences between groups (15 of 19 variables), with all of the variables showing better results for individuals with normal handgrip strength. Differences were found regarding peripheral muscle strength, exercise capacity, body composition, dyspnea, functional status, the BODE index, and the ADO index (Table 4). In a study conducted in the Netherlands,[28] the number of variables showing statistical differences was the same as that in the study conducted in Brazil.[11] However, in the former study,[28] 32% of the individuals were classified as having low handgrip strength, whereas, in the latter,[11] 9% were classified as having low handgrip strength (Figure 2), the level of agreement between the two being low (0.3463; Table 3).

DISCUSSION

In the present study, we analyzed 9 different sets of reference values for handgrip strength. The proportion of COPD patients classified as having low handgrip strength varied substantially across studies, from 9% to 55%. Weak to excellent agreement was observed between reference values for a sample of adults and elderly individuals in Brazil[11] and those for individuals in other countries when classifying individuals with COPD as having low or normal handgrip strength. The reference values that revealed the highest prevalence of individuals with low handgrip strength did not necessarily show better discriminative capacity than did the other sets of values; that is, a greater number of significant differences in clinical characteristics between individuals with normal and low handgrip strength. The reference values proposed by Amaral et al.[11] were found to be the most discriminative when applied to a sample of individuals with moderate to very severe COPD in Brazil, together with the reference values proposed by Peters et al.,[28] although the level of agreement between the two sets of reference values was not good. This indicates that the reference values for handgrip strength with the highest discriminative capacity to identify individuals with worse clinical characteristics are not necessarily the same as those that identify the highest number of individuals as having low handgrip strength. These results also indicate that, although handgrip strength might be a good reflection of peripheral muscle strength,[32] it does not necessarily indicate worse clinical characteristics in a broader sense.

One hypothesis as to why the reference values for a sample of adults and elderly individuals in Brazil[11] classified considerably fewer individuals as having low handgrip strength in comparison with other sets of reference values is that the aforementioned reference values[11] were derived from individuals in a single state in northern Brazil, whereas our study sample comprises individuals in a single state in southern Brazil. Brazil is a very large country, with marked differences in population characteristics across regions (especially between the northern and southern regions of the country), and this might have affected the representativeness of the reference values. In countries of continental dimensions, as in the present case, multicenter samples are more likely to be representative of the population as a whole. In addition, the reference values that showed the lowest level of agreement with the reference values for a sample of adults and elderly individuals in Brazil[11] were those from a multinational study by Bohannon et al.,[25] who investigated independent samples of individuals in countries in various continents. However, all of the countries involved were well-developed countries. According to Dodds et al.,[33] normative values for handgrip strength derived from individuals in developing regions are considerably lower than those derived from individuals in developed regions. Although Bohannon et al. argue that there is homogeneity across studies,[25] reference values derived from individuals in developed countries can overestimate the number of individuals with lower handgrip strength in developing countries[33] and lead to a very low level of agreement.

Reference values derived from individuals in developed countries such as the USA, Australia, and the UK[6,27,30] are expected to classify a higher number of individuals as having low handgrip strength because the normal values for individuals in developed countries are greater than those for individuals in developing countries, such as Brazil. Factors other than the country of origin might explain this difference in handgrip strength, including genetic factors; body size and composition[33]; comorbidities; and nutritional status.

Table 1. Characteristics of the nine studies included in the analysis.

Study	Sample Age range, years	Country	Reference values	Method of handgrip strength evaluation	Criteria used in order to identify reduced handgrip strength
Amaral et al.[11]	n = 1,462 18-102	Brazil	Stratified by sex and age (10-year age groups)	Position in accordance with the ASHT recommendations; measurements were performed with the patient in a seated position, with the elbow at 90° and the handle adjusted to the second position; a familiarization with the instrument was allowed; the procedure was performed three times for each hand alternately, with an interval of 1-min between measurements; a hydraulic hand dynamometer (SH50011; Saehan Corporation, Changwon, South Korea) was used; values were expressed in kg; the highest handgrip strength value for each hand was used.	2 SDs below the mean and group-specific (by sex and age)
Bohannon et al.[25]	n = 3,317 20-75[a]	USA, Australia, Canada, UK, and Sweden	Stratified by sex and age (5-year age groups)	Position in accordance with the ASHT recommendations; a Jamar dynamometer (Patterson Medical/Sammons Preston, Bolingbrook, IL, USA) was used. Most of the studies included in the meta-analysis used the mean of three trials and assessed both hands.	Values below the 5th percentile and group-specific (by sex and age)
Frederiksen et al.[26]	n = 8,342 45-102	Denmark	Stratified by sex, height (5-cm height groups), and age (5-year age groups)	Measurements were performed in a series of three measurements with the elbow at 90° and the upper arm tight against the trunk; a Smedley dynamometer (TTM, Tokyo, Japan) was used; the width of the handle was adjusted to fit the hand size; the second phalanx should rest against the inner stirrup; three trials were performed for each hand, with each hand in two cohorts of the study and three trials for the preferred hand in the other study cohort; values were expressed in kg.	2 SDs below the mean and group-specific (by sex, height, and age)
Massy-Westropp et al.[27]	n = 2,629 20-70	Australia	Stratified by sex and age (10-year age groups)	Measurements were performed with the patient in a seated position, with the elbow by the side and flexed to right angles, as well as with a neutral wrist position; the dynamometer handle was on position II, and there was provision of support underneath the dynamometer; a Jamar dynamometer (Patterson Medical/Sammons Preston) was used; three trials were performed for each hand; the mean value for each hand was used.	2 SDs below the mean and group-specific (by sex and age)
Mathiowetz et al.[6]	n = 628 20-94	USA	Stratified by sex and age (5-year age groups, the eldest individuals being > 75 years of age)	Measurements were performed with the patient in a seated position, with shoulders adducted and neutrally rotated, elbows flexed at 90°, forearms in a neutral position, and wrists between 0° and 30° of dorsiflexion and between 0° and 15° of ulnar deviation; a Jamar dynamometer (Patterson Medical/Sammons Preston) was used, being set at the second handle position for all individuals; three successive trials were performed for each hand; values were expressed in pounds; the mean of three trials was used.	2 SDs below the mean and group-specific (by sex and age)

Continue...▶

Table 1. Characteristics of the nine studies included in the analysis. (Continued...)

Study	Sample Age range, years	Country	Reference values	Method of handgrip strength evaluation	Criteria used in order to identify reduced handgrip strength
Peters et al.[28]	n = 720 20-96	The Netherlands	Stratified by sex and age (10-year age groups)	Position in accordance with the ASHT recommendations; a Jamar dynamometer (Patterson Medical/Sammons Preston) was used; three trials were performed for each hand; the mean value for each hand was used.	Values below the 5th percentile and group-specific (by age and sex)
Shim et al.[29]	n = 366 13-77	Korea	Stratified by sex and age (10-year age groups)	Measurements were performed with the patient in a seated position, with the shoulders adducted and neutrally rotated, the elbows flexed at 90°, the forearms in a neutral position, and the wrists between 0° and 30° of flexion and between 0° and 15° of ulnar deviation; a Jamar hand dynamometer (Patterson Medical/Sammons Preston) was used; three consecutive trials were performed for each hand, 1 min apart; values were expressed in kg.	2 SDs below the mean and group-specific (by sex and age)
Spruit et al.[30]	n = 224,852 39-73	UK	Stratified by sex, height (5-cm height groups), and age (5-year age groups)	Measurements were performed with the patient in a seated position, with the elbow of the arm holding the dynamometer against the side of the patient and bent to a 90° angle, the forearm pointing forward, and the thumb in the uppermost position; the wrist was straight so that the hand was either pointing forward or bent slightly outward; a Jamar hydraulic hand dynamometer (Patterson Medical/Sammons Preston) was used; three trials were performed for each hand; values were expressed in kg.	Values below the 5th percentile and group-specific (by sex, height, and age)
Werle et al.[31]	n = 1,023 18-96	Switzerland	Stratified by sex and age (5-year age groups, the eldest individuals being > 85 years of age)	Position in accordance with the ASHT recommendations; a Jamar dynamometer (Patterson Medical/Sammons Preston) was used and set at the second handle position; both hands were assessed; the mean of three trials was used; values were expressed in kg.	2 SDs below the mean and group-specific (by sex and age)

ASHT: American Society of Hand Therapists. [a]The eldest individuals were at least that age. Beyond that, the maximum age was not clear.

Table 2. Characteristics of the study sample (N = 99).[a]

Variable	Result
Age, years (min-max)	65 ± 8 (47-89)
Height, m	1.58 [1.52-1.67]
Weight, kg	70 ± 17
BMI, kg/m^2	27 ± 6
GOLD stage II/III/IV COPD, n (%)	39/45/15 (39/46/15)
FEV_1, L	1.19 [0.81-1.53]
FEV_1, % predicted	46 ± 15
FVC, L	2.33 [1.91-2.99]
FVC, % predicted	74 ± 20
FEV_1/FVC	51 ± 13
Handgrip strength, kg	26 ± 10
Quadriceps muscle strength, kg	17 [9-23]
Biceps muscle strength, kg	12 [10-15]
Triceps muscle strength, kg	14 [11-17]
Six-minute walk distance, m	453 [388-500]
Six-minute walk distance, % predicted	85 [72-95]
MIP, cmH_2O[a]	74 ± 25
MIP, % predicted[a]	81 ± 26
MEP, cmH_2O[a]	101 ± 32
MEP, % predicted[b]	111 ± 36
Fat-free mass, kg[c]	46 ± 10
Fat-free mass, % of body weight[c]	66 [60-72]
Fat-free mass index, kg/m[c]	18 ± 3
Fat mass, kg[c]	23 ± 10
Fat mass, % of body weight[c]	34 [27-39]
MRC scale score	3 [2-4]
LCADL scale - total[b]	23 [18-30]
LCADL - self-care	6 [5-8]
LCADL - domestic	9 [5-13]
LCADL - physical	4 [3-5]
LCADL - leisure	4 [3-6]
BODE index	3 [2-5]
ADO index	4 [4-6]

LCADL: London Chest Activity of Daily Living; MRC: Medical Research Council; and ADO: Age, Dyspnea, and airflow Obstruction. [a]Values expressed as mean ± SD or median [IQR], except where otherwise indicated. [b]n = 96. [c]n = 97.

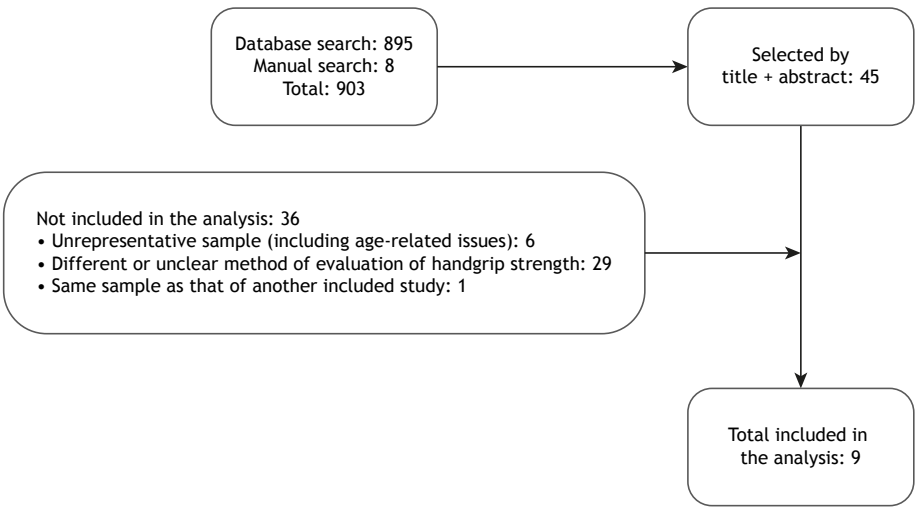

Figure 1. Flow chart of study selection for inclusion in the analysis.

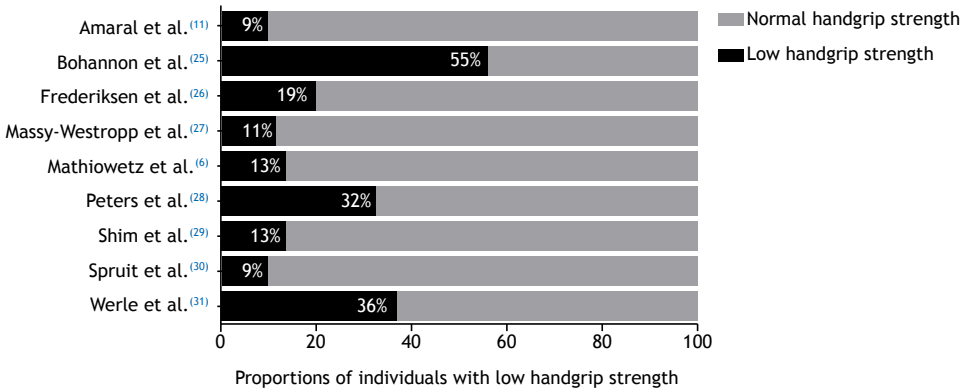

Figure 2. Proportions of individuals classified as having low handgrip strength in accordance with different sets of reference values.

Table 3. Level of agreement between a set of reference values proposed by Amaral et al.[11] for a sample of adults and elderly individuals in Brazil and other sets of reference values when classifying individuals with COPD in Brazil as having low handgrip strength.

Amaral et al.[11] vs.	Kappa statistic
Bohannon et al.[25]	0.1481
Frederiksen et al.[26]	0.4913
Massy-Westropp et al.[27]	0.7778
Mathiowetz et al.[6]	0.6944
Peters et al.[28]	0.3463
Shim et al.[29]	0.7963
Spruit et al.[30]	0.7090
Werle et al.[31]	0.2979

Discrepancies in the proportions of individuals with low handgrip strength in accordance with reference values for different populations might also have been due to the population profile, with different occupational physical demands, activities of daily living, and leisure activities,[34] for example. This profile can vary depending on the country or region of origin, as well as on how recent the reference values are.[34] This is due to the fact that many influencing characteristics can change over the decades, and this might explain the finding that most of the sets of reference values that had a lower level of agreement with the reference values for a sample of adults and elderly individuals in Brazil[11] originated from studies[25,26,31] published prior to most of the studies presenting sets of reference values that had a higher level of agreement[29,30] with those for the sample in Brazil,[11] with the exception of the reference values derived from individuals in the USA, proposed by Mathiowetz et al.[6]

All of the aforementioned factors can lead to underestimation or overestimation of a sample analyzed in accordance with reference values based on different population characteristics and time frames. Regardless of differences in the proportions of individuals classified as having reduced handgrip strength, reference values should be discriminative. Despite having classified fewer individuals as having reduced handgrip strength, the reference values for the sample in Brazil,[11] together with those proposed by Peters et al. in the Netherlands,[28] showed the highest discriminative capacity regarding differences in clinical variables between individuals with normal handgrip strength and those with reduced handgrip strength. Furthermore, the classifications made by the Brazilian reference values[11] and the Dutch reference values[28] were the only ones that showed differences in dyspnea and functional status between individuals with normal handgrip strength and those with low handgrip strength, with the Brazilian reference values[11] also showing differences regarding other London Chest Activity of Daily Living scale domains and the ADO index. These results constitute further evidence of the discriminative capacity of these sets of reference values, suggesting that they were an appropriate choice for use in the present sample. Moreover, the fact that these two sets of reference values had similarly high discriminative capacity suggests that, in the absence of national, population-specific reference values, there might be an acceptable alternative, i.e., reference values for a population whose characteristics more closely resemble those of the sample to be assessed and/or reference values that have similar discriminative capacity.

All of the studies analyzed in the present study provided reference values in table format, stratified at least by sex and age, showing values of mean ± SD,[6,11,26,27,29,31] mean and 95% CI,[25] or 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles.[30] Three sets of reference values[25,28,30] were developed on the basis of the lower limit of the confidence interval (5th percentile) rather than 2 SDs.[6,11,26,27,29,31] It is of note that two of the sets of reference values on the basis of which the prevalence of low handgrip strength was highest[25,28] were developed on the basis of the lower limit (5th percentile). Therefore, we speculate that reference values developed on the basis of the lower limit of the confidence interval constitute another factor leading to a difference in prevalence between the reference values proposed by Peters et al.[28] and those proposed by Amaral et al.,[11] despite a clear similarity in discriminative capacity between these two sets of reference values.

Table 4. Comparison between individuals with normal handgrip strength and those with low handgrip strength in accordance with each set of reference values.

Variable	Amaral et al.[11]		Bohannon et al.[25]		Fredericksen et al.[26],b	
	Normal handgrip strength (n = 90)	Low handgrip strength (n = 9)	Normal handgrip strength (n = 44)	Low handgrip strength (n = 55)	Normal handgrip strength (n = 66)	Low handgrip strength (n = 16)
Quadriceps muscle strength, kg	17 [10-24]	9 [3.25-11.75]*	20 [16-29]	12 [7-18]*	18 [11.35-24]	8 [5-17.75]*
Biceps muscle strength, kg	15.5 [10-15]	2.5 [1.75-7.75]*	12.5 [10-18]	12 [10-14]*	12.5 [10-15]	11.5 [3.1-13.9]
Triceps muscle strength, kg	13.5 [11.87-17.75]	5.5 [1.75-10]*	15 [12-20]	12 [10-15]*	13.5 [12-17]	11 [6.515.87]*
Handgrip strength, kg	26 [20.75-34]	10 [4-14.5]*	29 [24-42]	20 [16-28]*	26 [21-36]	24.5 [10-29.5]*
FEV_1, % predicted	46 [35-57]	42 [35-46]	49 [41-63]	43 [31-54]*	47 [35-62]	41 [30-53]
MIP, % predicted	80 [66-98]	66 [57-97]	90 [74-106]	72 [58-92]*	80 [65-99]	66 [57-77]*
MEP, % predicted	107 [89-134]	82 [62-119]	107 [89-133]	108 [83-134]	108 [90-134]	97 [65-124]
6MWD, m	458 [399-506]	345 [237-456]*	465 [404-500]	437 [351-510]	459 [401-506]	415 [258-470]*
6MWD, % predicted	86 [75-96]	60 [43-82]*	87 [79-97]	80 [64-93]*	86 [77-97]	68 [46-84]*
FFMI, kg/m^2	18.09 [16.22-20.82]	16.03 [14.07-17.01]*	19.23 [17.35-21.24]	16.48 [15.38-19.77]*	17.80 [16.06-20.91]	16.26 [15.80-19.78]
FMI, kg/m^2	9.78 [7.12-12.01]	8.35 [5.34-8.02]*	10.23 [7.39-11.82]	8.76 [6.06-11.19]	9.52 [7.00-12.00]	7.45 [4.06-9.87]
MRC scale score	3 [2-4]	4 [3.5-5]*	3 [2-4]	3 [2-4]	3 [2-4]	4 [2.25-4.75]
LCADL scale, total	22 [17-28]	31 [26-42]*	21 [16-28]	23 [20-31]	22 [17-28.75]	23 [18-28.5]
Self-care	5 [5-7]	9 [6.5-10.5]*	5 [5-7]	6 [5-9]	5 [5-7]	6.5 [5-8.75]
Domestic	9 [5-12]	15 [8.5-23.5]*	7 [4-12]	9 [6-15]	8.5 [4.25-13]	7 [4-11.25]
Physical activity	4 [3-5]	5 [4-5]*	4 [3-5]	4 [3-5]	4 [3-5]	4 [3-5]
Leisure	4 [3-6]	6 [4-6.5]	4 [3-5]	5 [4-6]*	4 [3-5]	5 [4-6]
BODE index	3 [2-5]	6 [3-7]*	3 [1-3]	4 [2-6]*	3 [2-4]	4 [3-7]*
ADO index	4 [3-5]	6 [4-7]*	4 [3-5]	5 [4-6]	4 [4-5]	4 [3-7]
	Massy-Westropp et al.[27]		Mathiowetz et al.[6]		Peters et al.[28]	
	Normal handgrip strength (n = 88)	Low handgrip strength (n = 11)	Normal handgrip strength (n = 86)	Low handgrip strength (n = 13)	Normal handgrip strength (n = 67)	Low handgrip strength (n = 32)
Quadriceps muscle strength, kg	17 [10.6-24]	8 [2-11]*	17.5 [11.37-24]	8 [3.5-10.5]*	18 [11-24]	11 [8-17]*
Biceps muscle strength, kg	12.5 [10-15]	3.5 [2-12]*	12.5 [10-15.2]	10 [2-12]*	12 [10-16]	10 [5-12]*
Triceps muscle strength, kg	13.5 [12-18.25]	8 [5-12]*	13.75 [12-18.5]	10 [5.25-12]*	14 [12-19]	11 [7-15]*
Handgrip strength, kg	20 [20.25-34]	11 [4-20]*	26 [21-34]	15 [6.5-19]*	28 [24-36]	18 [14-23]*
FEV_1, % predicted	46 [35-58]	40 [33-46]	47 [36-58]	38 [28-45]*	50 [38-62]	40 [31-46]*
MIP, % predicted	80 [66-99]	73 [53-93]	80 [66-98]	73 [49-97]	88 [67-100]	70 [57-91]*
MEP, % predicted	109 [91-135]	82 [64-101]*	109 [91-135]	82 [66-113]*	114 [95-142]	92 [74-118]*
6MWD, m	457 [398-504]	388 [220-472]	458 [396-506]	428 [244-468]	465 [403-510]	424 [283-465]*
6MWD, % predicted	86 [74-97]	74 [42-82]*	86 [74-97]	76 [43-84]*	88 [77-97]	76 [83-85]*
FFMI, kg/m^2	18.21 [16.30-20.86]	16.03 [14.15-16.70]*	18.48 [16.39-20.96]	16.01 [14.20-16.48]*	18.61 [17.02-21.24]	16.26 [14.42-19.76]*
FMI, kg/m^2	9.78 [7.15-11.99]	6.13 [4.96-8.96]*	9.88 [7.17-12.01]	6.13 [5.22-8.86]*	10.23 [7.20-12.17]	8.49 [5.72-9.88]*
MRC scale score	3 [2-4]	4 [3-4]	3 [2-4]	4 [2.5-4.5]	3 [2-4]	4 [2.5-4]*
LCADL scale, total	22 [17-28.5]	29 [20-42]	22 [17-28]	29 [20.5-42]	21.5 [17-26.7]	28 [20.2-36]*
Self-care	5 [5-7.5]	8 [5-10]	5 [5-7]	8 [5-10.5]	5 [5-7]	6.5 [5-9]
Domestic	9 [5-13]	10 [7-20]	8 [5-13]	10 [8-19]	7 [5-11]	9.5 [6.25-18]*

Continue...▶

Table 4. Comparison between individuals with normal handgrip strength and those with low handgrip strength in accordance with each set of reference values. (Continued...)

Physical activity	4 [3-5]	5 [3-5]	4 [3-5]	5 [3-5]	4 [3-5]	4 [3-5]
Leisure	4 [3-6]	5 [4-6]	4 [3-6]	5 [4-6.5]	4 [3-5]	5 [4-6]
BODE index	3 [2-4]	5 [3-7]*	3 [2-4]	5 [3-7]*	3 [1-4]	4 [3-6]*
ADO index	4 [3-5]	5 [4-6]	4 [3-5]	5 [4-6]	4 [3-5]	5 [4-7]
	Shim et al.[29]		Spruit et al.[30]		Werle et al.[31]	
	Normal handgrip strength (n = 86)	Low handgrip strength (n = 13)	Normal handgrip strength (n = 90)	Low handgrip strength (n = 9)	Normal handgrip strength (n = 63)	Low handgrip strength (n = 33)
Quadriceps muscle strength, kg	17 [10.37-24]	9 [3.5-12.75]*	17 [10-24]	9.50 [4.12-15.75]*	19.5 [14-25.5]	10.75 [6.25-17]*
Biceps muscle strength, kg	12.5 [10-15.25]	3.5 [2-12]*	12.50 [10-15]	3.25 [1.87-13.5]*	12.5 [10-16]	11 [7.37-13.37]*
Triceps muscle strength, kg	13.5 [12-18.5]	8 [3.75-12]*	13.5 [11.75-17]	7 [2.15-17]*	14 [12.5-18.5]	11.5 [8.62-14.75]*
Handgrip strength, kg	26 [21.75-34]	11 [6.5-20]*	26 [20-34]	10 [4-21]*	28 [24-36]	20 [16-27.5]*
FEV_1, % predicted	47 [35-58]	40 [34-46]*	46 [34-57]	43 [37-47]	47 [37-62]	43 [30-54]
MIP, % predicted	80 [66-98]	66 [49-97]	84 [66-99]	57 [68-40]*	86 [68-100]	70 [57-91]*
MEP, % predicted	107 [90-134]	85 [66-119]	107 [87-135]	111 [72-129]	107 [91-135]	108 [83-130]
6MWD, m	459 [401-510]	370 [237-453]*	458 [394-507]	412 [265-467]	461 [400-505]	439 [316-490]*
6MWD, % predicted	86 [75-97]	74 [43-81]*	85.87 [73.94-95.5]	75.32 [49.31-83.01]*	86 [76-97]	79 [58-89]*
FFMI, kg/m^2	18.09 [16.22-20.96]	16.26 [14.62-18.57]*	17.92 [16.15-20.82]	16.26 [14.07-19.69]	18.52 [16.53-21.10]	16.48 [15.66-19.78]*
FMI, kg/m^2	9.67 [7.12-11.85]	8.49 [5.66-9.86]	9.67 [7.03-13.01]	8.49 [5.93-9.33]	9.80 [7.15-12.06]	8.90 [5.92-10.64]
MRC scale score	3 [2-4]	4 [3-4.5]	3 [2-4]	4 [2-4.25]	3 [2-4]	3.5 [2-4]
LCADL scale, total	22 [17-28]	30 [19.5-41]	22 [18-29.25]	26 [16.75-40.5]	22 [17-28]	24 [18-32.5]
Self-care	5 [5-7]	8 [5.5-9.5]	6 [5-8]	6.5 [5-9.5]	5 [5-7.75]	6 [5-9]
Domestic	9 [5-12]	12 [6.5-21.5]	9 [5-13]	9.5 [3.75-20.75]	9 [5-12.75]	9 [5.25-16.5]
Physical activity	4 [3-5]	4 [2-5]	4 [3-5]	4 [3-5]	4 [3-5]	4 [3-5]
Leisure	4 [3-6]	5 [3.5-6]	4 [3-6]	5 [3-6]	4 [3-5]	5 [3.25-6]
BODE index	3 [2-4]	5 [3-7]*	3 [2-5]	4 [2-6]	3 [1-4]	4 [2-6]
ADO index	4 [3-5]	5 [4-6]	4 [4-5]	5 [4-7]	4 [4-5]	4 [3-6]

6MWD: six-minute walk distance; FFMI: fat-free mass index; FMI: fat mass index; MRC: Medical Research Council; LCADL: London Chest Activity of Daily Living; and ADO: Age, Dyspnea, and airflow Obstruction. [a]Values expressed as median [IQR]. [b]n = 82 (i.e., those who fit into the categories of height, sex, and age). *p < 0.05 in comparison with individuals with normal handgrip strength.

The present study has limitations. The retrospective nature of the study did not allow us to analyze adequately studies providing predictive equations, because it was impossible to assess some of the predictive variables in those equations. In addition, we did not evaluate comorbidities. Evaluation of comorbidities could have provided additional information on impaired handgrip strength. Furthermore, characteristics of the study sample resulted in the fact that many studies (80% of the studies that were initially retrieved) were not included in the analysis, because of methodological differences such as very specific populations[35] or a very limited age range.[36] Another limitation is that only one reviewer selected the articles, and this is not the ideal methodological scenario. Moreover, despite the high number of studies retrieved from the literature search, a stricter standardization of handgrip strength assessment might be required in order to allow more comprehensive and reliable comparisons between studies and populations.

In summary, a large number of studies providing reference values were identified through a literature search, and there was large variation in the level of agreement (i.e., from weak to excellent) between national and international sets of reference values for handgrip strength used in order to classify individuals with moderate to very severe COPD as having normal or low handgrip strength. Although the set of reference values for a sample of adults and elderly individuals in Brazil[11] classified fewer individuals as having low handgrip strength than did almost all other sets of values, it was one of the sets with the highest discriminative capacity (showing significant differences in clinical characteristics between individuals with

normal handgrip strength and those with low handgrip strength), together with the set of reference values for individuals in the Netherlands, which classified a higher proportion of individuals as having low handgrip strength. Therefore, reference values for handgrip strength with higher discriminative capacity to identify individuals with worse clinical characteristics are not necessarily those that identify more individuals as having low handgrip strength.

AUTHOR CONTRIBUTIONS

JF, FVCM, and FP: study conception, statistical analysis, and interpretation of results. LCS: drafting and revision of the manuscript. All authors revised and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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