ABSTRACT

Objectives: To evaluate the utility of handgrip strength cut-offs for the identification of weakness and Instrumental Activities of Daily Living (IADL) disability in elderly people with neurocognitive disorders. Methods: Cross-sectional study of community-dwelling elderly individuals with Alzheimer’s disease (AD, n = 40) and mild cognitive impairment (MCI, n = 22); healthy individuals (n = 36) were recruited as controls. Handgrip cut-offs included European Working Group for Sarcopenic Older People (EWGSOP2), Cardiovascular Healthy Study (CHS) and the Frailty in Brazilian Older People Study from Rio de Janeiro (FIBRA RJ) cut-offs. Handgrip strength indexes were calculated by dividing handgrip strength values by cut-off values and the weakness prevalence for each cut-off value was compared among groups. Correlation analyses were employed to evaluate the relationship between Lawton Scale and handgrip strength (crude value and indexes). Results: All handgrip strength indexes were lower in the AD group (p < 0.05), whereas the prevalence of weakness was significantly higher in the AD group only when the CHS cut-off was applied (AD = 47.5%, MCI and control = 18.2%, p < 0.01). Significantly positive correlations were identified between the Lawton ADL scale and handgrip indexes for all cut-offs (p < 0.05), but not between Lawton scale and crude handgrip (p = 0.75). Conclusions: Only the CHS cut-off allowed proper differentiation of the weakness prevalence between groups. In addition, adjusting handgrip strength values according to cut-offs was necessary to determine the correlation between strength and disability in cognitively impaired elderly individuals.

Keywords
Hand strength, neurocognitive disorders, Alzheimer disease, activities of daily living.
INTRODUCTION

Alzheimer’s disease (AD) represents a major cause of disability, loss of autonomy and increased dependence in the elderly population. Frailty and sarcopenia are both more prevalent among AD patients and are associated with negative outcomes, including the incidence of falls, deterioration of mobility, physical disability, poor quality of life, hospitalization and death. In clinical settings, detection of sarcopenia and frailty is a challenge, but weakness, measured by handgrip strength, is easier to assess and overlaps both concepts. The most recent consensus update by the European Work Group for Sarcopenic Older People (EWGSOP2) highlights the importance of handgrip strength in diagnosing sarcopenia as low handgrip strength is also a clinical marker of poor mobility and a better predictor of clinical outcomes than low muscle mass. There is also a linear relationship between baseline handgrip strength and the incidence of disability in activities associated with daily living (ADL) and premature mortality. Measurement of handgrip strength is simple, quick and inexpensive method, that can be considered as an ecological proxy for both frailty and sarcopenia in primary care.

Handgrip strength is influenced by sociodemographic and lifestyle factors and cut-offs based on large epidemiological studies are needed to identify muscle weakness at the level of the individual. Different handgrip strength cut-off values have been proposed based on frailty and sarcopenia models. While the Cardiovascular Health Study (CHS) established cut-offs according to the 20th percentile of strength for each body mass index (BMI) quartile for both sexes in the general population, EWGSOP2 recommendations focus on European populations and the use of normative references (healthy young adults) with cut-offs usually set at -2 standard deviations compared to the mean reference value. Handgrip strength is also dependent on the integrity of the central nervous system, as suggested by cross-sectional and longitudinal studies that indicated an association between handgrip strength and cognitive decline. However, these studies did not take into account handgrip strength cut-offs to define weakness, using raw handgrip measures and comparing cognition between weaker and stronger groups defined by handgrip strength percentile or standard deviations of handgrip strength values for that specific population. Despite credible evidence for the correlation of handgrip strength with both cognition and functionality, it is crucial to understand the influence of existing cut-offs in patients with cognitive impairment to enable accurate utilization of handgrip strength measurement as a predictor of disability in a clinical context.

Like sarcopenia and frailty, a higher prevalence of weakness in AD patients was expected when analyzing handgrip strength using different cut-offs. Also, sarcopenia is associated with ADL impairment in AD, it is supposed that handgrip strength correlates with disability in cognitively impaired individuals. Adjusting handgrip strength according to cut-off values, which corrects for potential bias, may more accurately reflect the correlation with ADL performance than that provided by the raw measures. Therefore, the objective of this study was to evaluate (1) the ability of handgrip strength...
cut-off values to more accurately identify higher weakness prevalence in community-dwelling older people with cognitive impairment; (2) the correlation of handgrip strength with ADL performance in this population; and (3) the ability of handgrip strength measurements adjusted by cut-off values to provide a more accurate reflection of the association with disability than that provided by the raw values.

**METHODS**

**Study design and participants**

This is a cross-sectional study of community-dwelling elderly individuals with diagnosis of Mild Cognitive Impairment (MCI, n = 22) or mild to moderate AD (n = 40) from the Center of Alzheimer’s Disease of the Psychiatry Institute in the Federal University of Rio de Janeiro (Brazil). Cognitively healthy elderly from community were also recruited as controls (n = 36). Diagnostic assessments were performed by clinical staff, using a structured clinical interview to assess mental disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and Petersen criteria for dementia and MCI, respectively. Exclusion criteria included: illiterate; functional classes III and IV according to the New York Heart Association standards; with mental or physical comorbidities that impaired performance during the tests; severe visual and/or auditory impairments; mixed dementia, with evidence of cerebrovascular infarction in neuroimage; and other comorbid psychiatric disorders, as depression.

Among 41 healthy volunteers, four subjects did not return for evaluation and one was excluded for depression. In the MCI group, two subjects did not return for evaluation, leaving 22 participants. In the AD group, from initial 61 subjects, ten did not return and others were excluded for: advanced dementia, CDR 3 (n = 6), cardiac disease (n = 2), comorbid depression (n = 1), inability to perform handgrip (n = 1) and mixed dementia (n = 1).

This study was approved by the Research Ethics Committee (CAAE) of the Psychiatry Institute in the Federal University of Rio de Janeiro (IPUB-UFRJ), under the registry: 24904814.0.0000.5263 and formed part of a larger research project entitled "Efficacy of physical exercise in the Treatment of Major Depression, Alzheimer’s Disease and Parkinson’s Disease".

**Procedures and measures**

After presenting the details of the study, written informed consent was obtained for all participants. Medication use, physical comorbidities, such as hypertension, diabetes, dyslipidemia, and coronary artery disease, were asked to subjects and their caregivers during anamnesis. ADL performance was assessed through Lawton scale and global cognition was evaluated applying Mini-Mental Statement Exam (MMSE), Verbal Fluency and Clock Drawing Test. Clinical Dementia Rating (CDR) scale was applied to measure the severity of dementia in patients with AD.

Handgrip strength was measured using a digital hand dynamometer (Camry®, model EH 101), with a variation of 0.1 kgf, ranging from 0 up to 90 kgf. Subjects remained standing on the floor, with shoulder adducted, the elbow extended, the forearm in a neutral position, and the wrist extended between 0° and 30° extension. Measurement was performed for both hands, and patients were instructed to grip the dynamometer with maximum strength in response to a voice command. This procedure was repeated three times, with a one-minute rest interval between tests. The highest mean peak value between both hands was then recorded for analysis.

According to the handgrip strength cut-off values proposed by the CHS and the EWGSOP2, patients were classified as “strong” or “weak”. Both handgrip strength cut-off values were chosen for their roles in the most replicated model for physical frailty and sarcopenia, respectively. With the aim of determining handgrip strength cut-off values based on the local population, we also adopted cut-off values suggested by the Frailty in Brazilian Older People Study from Rio de Janeiro (FIBRA RJ). All cut-offs are shown in table 1.

To facilitate comparisons among different cut-off values, an index was calculated by dividing the raw handgrip strength value by the corresponding cut-off value for each patient.

**Table 1. Handgrip Cut-offs proposed by EWSOP2 consensus and CHS and FIBRA RJ studies**

| EWGSOP2 | CHS   | FIBRA RJ |
|---------|-------|----------|
| **Male** |       |          |          |
| BMI ≤ 24 | ≤ 29 | BMI ≤ 23 | < 17.33  |
| 27       | BMI 24.1-26 ≤ 30 | BMI 23-28 | < 24.93  |
| BMI 26.1-28 ≤ 30 | BMI 28.1-30 | BMI 28.1-30 | < 28.27  |
| BMI > 28 ≤ 32 | BMI > 30 | BMI > 30 | < 18     |
| **Female** |     |          |          |
| BMI ≤ 23 | ≤ 17 | BMI ≤ 23 | < 12.87  |
| 16       | BMI 23.1-26 ≤ 17.3 | BMI 23-28 | < 14.27  |
| BMI 26.1-29 ≤ 18 | BMI 28.1-30 | BMI 28.1-30 | < 10.53  |
| BMI > 29 ≤ 21 | BMI > 30 | BMI > 30 | < 16.4   |

Note: EWGSOP2: European Work Group for Sarcopenic Older People 2; CHS: Cardiovascular Health Study; FIBRA RJ: Frailty in Brazilian Older People Study from Rio de Janeiro. BMI: Body Mass index, kg/m²; Handgrip, Kg.

**Statistical analyses**

Descriptive analysis of the demographic data was conducted. To verify normality and homoscedasticity, Kolmogorov-Smirnov and Levene were applied, respectively. Demographic characteristics, neuropsychological variables, Lawton scale, and handgrip indexes were compared among groups using ANOVA or Kruskal-Wallis test. Bonferroni and Tamhane’s T2 post hoc analyses were performed to parametric and non-parametric variables, respectively. For assessing differences among weakness prevalence in healthy, MCI, and AD groups, chi-squared test was used. Correlation analyses were
employed to evaluate the relationship between Lawton scale and handgrip strength (crude value and indexes). All statistical analyses were performed using SPSS® version 19.0 and STATA® version 11.0. p ≤ 0.05 was considered to indicate statistical significance.

RESULTS

Descriptive analysis is showed in table 2. There were no significant differences among groups for age and BMI. As expected, cognitive tests and functionality were significantly lower in AD group, compared to MCI and healthy controls. AD patients used more medication, although comorbidity prevalence was similar for hypertension, diabetes and stable coronary artery disease among groups. Dyslipidemia was more prevalent in the AD group and scholarship was also significantly lower among AD patients.

Handgrip indexes were statistically lower in the AD group for all cut-off values. However, post hoc analyzes only showed significantly difference between AD and healthy subjects for CHS and EWGSOP2 handgrip indexes. There was no difference in raw handgrip strength among groups.

Comparison of weakness prevalence among groups is shown in figure 1. There was a significantly higher weakness prevalence in AD group (47.5%), compared to MCI and healthy controls. However, there was no significant difference for weakness prevalence among groups when EWGSOP2 and FIBRA RJ cut-off were applied.

Correlation between handgrip strength and Lawton scale in cognitively impaired individuals (MCI and AD) are showed in figure 2. Significantly positive correlations were identified between the Lawton scale and handgrip indexes for all cut-offs, but not between Lawton scale and crude handgrip.

Table 2. Demographic, clinical, functional, cognitive, and strength characteristics by groups

|                        | Healthy (n = 36) | MCI (n = 22) | AD (n = 40) | F/X (p value) | Post Hoc |
|------------------------|-----------------|--------------|-------------|---------------|----------|
| Age (y)\textsuperscript{a} | 74.5 (8.5)      | 75.6 (6.0)   | 78.0 (7.9)  | 1.97 (0.145)  |          |
| Sex                    |                 |              |             |               |          |
| Male (%)               | 16.7            | 36.4         | 47.5        |               |          |
| Female (%)             | 83.3            | 63.2         | 52.5        | 8.15 (0.01)*  |          |
| Marital Status (%)     |                 |              |             |               |          |
| Single                 | 19.4            | 22.7         | 7.5         |               |          |
| Married                | 44.4            | 36.4         | 50          |               |          |
| Divorced               | 13.9            | 18.2         | 7.5         |               |          |
| Widower                | 22.2            | 22.7         | 35          | 6.18 (0.402)  |          |
| Scholarship (y)\textsuperscript{b} | 12 (7)         | 12 (6)       | 9 (7)       | 10.40 (<0.01)** | ADxH*; ADxMCI* |
| BMI (kg/m\textsuperscript{2})\textsuperscript{b} | 25.14 (3.20) | 25.60 (5.84) | 25.21 (4.91) | 1.19 (0.550) |          |
| Comorbidities (%)      |                 |              |             |               |          |
| Hypertension           | 38.9            | 50           | 55          | 2.01 (0.365)  |          |
| Diabetes               | 5.6             | 9.1          | 20          | 3.94 (0.339)  |          |
| Dyslipidemia           | 13.9            | 31.8         | 42.5        | 7.51 (0.023)* |          |
| Coronaropathy          | 2.8             | 13.6         | 7.5         | 2.44 (0.295)  |          |
| Medications (n)\textsuperscript{b} | 2 (2)          | 2.5 (4)      | 4 (5)       | 13.16 (<0.01)** | ADxH** |
| Lawton (score)\textsuperscript{b} | 21 (1)         | 20.5 (1)     | 13 (5)      | 73.13 (<0.01)** | ADxH**; ADxMCI** |
| MMSE (score)\textsuperscript{b} | 29 (3)         | 29 (1)       | 21 (6)      | 61.25 (<0.01)** | ADxH**; ADxMCI** |
| VF (score)\textsuperscript{b} | 18 (10)        | 17 (7)       | 9 (5)       | 36.02 (<0.01)** | ADxH**; ADxMCI** |
| CDT (score)\textsuperscript{b} | 3 (0)          | 2.5 (1)      | 1 (2)       | 35.38 (<0.01)** | ADxH**; ADxMCI** |
| HS (kgf)\textsuperscript{b} | 22.3 (8.8)     | 24.2 (8.2)   | 23.5 (10.5) | 1.38 (0.591)  |          |
| EWGSOP2\textsuperscript{b} index | 1.41 (0.42)   | 1.37 (0.29)  | 1.14 (0.34) | 11.33 (<0.01)** | ADxH** |
| CHSb index             | 1.27 (0.32)    | 1.23 (0.30)  | 1.02 (0.37) | 9.20 (0.01)*  | ADxH*    |
| FIBRA RJ\textsuperscript{b} index | 1.62 (0.44)   | 1.58 (0.42)  | 1.37 (0.45) | 6.07 (0.048)* | p = 0.054 |

Note – H: Healthy; MCI: Mild Cognitive Impairment; AD: Alzheimer’s dementia; BMI: body mass index; MMSE: Mini-Mental State Exam; VF: Verbal Fluency; CDT: Clock Drawing Test; HS: Handgrip Strength. *Parametric variables: mean (std deviation). *Non-parametric variables: median (interquartile range). * p < 0.05. ** p < 0.01.

Figure 1. Comparison of weakness prevalence among Groups, According to Different Handgrip Cut-offs. * p < 0.01.
**DISCUSSION**

In the present study, we evaluated the potential of handgrip strength cut-off values for the identification of weakness and disability in elderly individuals with neurocognitive disorders. Only the CHS cut-off allowed determination weakness prevalence between groups and adjusting handgrip strength by cut-offs was necessary to determine a correlation between strength and disability in cognitively impaired elderly. The CHS cut-off value revealed a significantly lower handgrip strength index and higher weakness prevalence in the AD group, thus corroborating its applicability for detecting weakness in individuals with dementia. The prevalence of weakness in AD assessed using the CHS cut-off (47.5%) was consistent with the reported prevalence of sarcopenia (41%-47%) and frailty (15.7%-48.5%). These results suggest that BMI is an important factor in defining handgrip strength cut-off values when evaluating the weakness of patients with cognitive impairment, since CHS stratifies cut-offs by BMI, whereas EWGSOP2 does not. Although the FIBRA RJ also adjusts handgrip by BMI and sex, cut-off values are lower than the CHS criteria, resulting in misclassification of patients as “strong”.

By calculating handgrip strength indexes, handgrip strength values were adjusted for cut-offs and, consecutively, for sex (EWGSOP2) or sex and BMI (CHS and FIBRA RJ). Handgrip strength indexes facilitated the comparison of cut-off values using a common metric while retaining the ability to analyze strength as a continuous variable, thus allowing quantification of the strength or weakness of individual patients according to different cut-offs. The positive correlation between handgrip strength indexes and ADL performance was observed using all three studied cut-offs, although this correlation was stronger when CHS or EWGSOP2 values were applied. Graphical representation of the distribution of MCI and AD revealed the same tendency in both groups. Although the correlation is considered low, it indicates that strength still plays a role in the ADL performance equation even when cognition is impaired. These results suggest that handgrip strength may also represent an opportune target for the preservation of function in cognitively compromised patients. Furthermore, our results provide the foundation for future interventional studies focusing on improving or maintaining function by increasing strength in MCI and AD patients. Raw handgrip strength did not correlate with ADL performance, suggesting that sex and BMI are important factors for correcting distortions of absolute handgrip strength measurements in patients with cognitive impairment. This highlights the
importance of considering cut-offs when studying the relationship between handgrip strength and ADL function.

Limitations
A cause-effect relationship between strength and functionality cannot be established using a cross-sectional design. Diagnostic components of frailty and sarcopenia were not evaluated, precluding direct comparisons between weakness prevalence and frailty or sarcopenia prevalence. The possibility of direct interference of cognition during the testing process is important issue that should be considered when analyzing strength in AD patients. Due to potential cognitive effects on the measurements, patients with advanced dementia were excluded; therefore, our analysis was focused on patients in the mild and moderate stages. This approach is in accordance with reports showing that handgrip strength is a reliable measure until the moderate stages of cognitive impairment are reached.

Implications
To our knowledge, this is the first study to show that handgrip strength cut-offs are useful for detecting weakness and correlating handgrip to ADL performance in community-dwelling older people with cognitive impairment. These data highlight the relevance of handgrip strength as an additional measure of cognitive decline in the clinical setting. The differences in the handgrip strength cut-off values demonstrated in this study are crucial for guidance in dementia care facilities, where relevant cut-off values are required for interpretation of handgrip strength on individual patient basis.

CONCLUSIONS
Handgrip cut-offs are useful for identifying weakness and correlating strength to disability among community-dwelling elderly patients with cognitive impairment in a clinical setting, although the CHS cut-off is superior for identifying weakness prevalence in mild-to-moderate AD.

INDIVIDUAL CONTRIBUTIONS
All authors substantially contributed to conception, design, analysis and interpretation of data, substantially contributed to drafting the article and revising it critically for important intellectual content; and have given the final approval of the version to be published.

CONFLICT OF INTERESTS
The authors declare that there is no conflict of interest.

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