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ORIGINAL ARTICLE

Handgrip strength as a diagnostic tool for frailty risk in elderly patients with moderate to severe asthma

Ricardo G Figueiredo[1,2], Fernando Holguin[3], Marcia Pizzichini[4], Gabriela P Pinheiro[2,5], Vanessa Arata[6], Maisa F M Leal[2], Cinthia V N Santana[2], Álvaro A Cruz[2,5], José Bessa Júnior[1]

1. Programa de Pós-Graduação em Saúde Coletiva, Universidade Estadual de Feira de Santana – PPGSC-UEFS – Feira de Santana (BA) Brasil.
2. Fundação Programa para o Controle da Asma na Bahia – ProAR – Salvador (BA) Brasil.
3. Division of Pulmonary Sciences and Critical Care, University of Colorado, Aurora (CO) USA.
4. Universidade Federal de Santa Catarina – UFSC – Florianópolis (SC) Brasil.
5. Programa de Pós-Graduação em Ciências da Saúde, Faculdade de Medicina da Bahia, Universidade Federal da Bahia – UFBA – Salvador (BA) Brasil.
6. Departamento de Saúde, Universidade Estadual de Feira de Santana – UEFS – Feira de Santana (BA) Brasil.

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ABSTRACT

Objective: To evaluate handgrip strength (HGS) as a diagnostic tool for frailty risk in elderly patients with asthma, as well as to investigate the prevalence of frailty in this population. **Methods:** This was a cross-sectional study including 96 patients ≥ 60 years of age diagnosed with moderate to severe asthma and treated at a tertiary referral center in Brazil. We measured HGS using a calibrated hydraulic hand dynamometer. We used a frailty scale and the AUC to assess the diagnostic accuracy of the HGS test. **Results:** The median age of participants was 67 years. Most (78%) were women and non-White (91%) of low socioeconomic status. HGS identified those at risk for frailty, with an AUC of 71.6% (61.5-80.4%; $p < 0.002$), as well as a sensitivity of 73.58% and a specificity of 67.53%, on the basis of a cutoff of ≤ 19 kgf. **Conclusions:** HGS appears to be a simple, reliable tool for clinicians to determine frailty risk in older asthma patients in a point-of-care setting.

Keywords: Hand strength; Frailty; Asthma; Aged.

INTRODUCTION

Aging promotes physiological changes related to increased proinflammatory cytokine activity, resulting in peripheral muscle dysfunction and declining lung function.[1] With the global increase in life expectancy, asthma in the elderly has become an emerging public health issue worldwide. Notably, asthma prevalence in this population ranges from 7.0% to 10.6%, with unexpectedly high asthma-related mortality.[2] Elderly asthma patients are also more likely to present with airway remodeling and noneosinophilic asthma, as well as being more likely to have a poor perception of symptoms.[3,4] Accumulating evidence indicates that frailty is a critical prognostic factor in chronic respiratory diseases and impacts asthma control.[5,6] Therefore, assessing frailty risk is critical in the clinical management of elderly asthma patients.

Frailty, a cornerstone in geriatric medicine, is a multidimensional syndrome with complex physical, psychosocial, and economic associations.[7-9] It has been reported that the prevalence of frailty among noninstitutionalized adults ≥ 60 years of age in Brazil is 13.5%.[10] The frailty phenotype, first described by Fried et al.,[11] has a substantial clinical impact because these individuals experience a three-fold increased mortality when compared with robust older adults.[12] Although frail elderly individuals experience several apparent physiological dysfunctions, early recognition of frailty can be challenging. Despite the lack of agreement regarding the best methodology to identify frailty in older adults, several screening instruments have been validated for evaluating frailty risk in clinical practice.[9] The handgrip strength (HGS) test measures the maximum static muscular force of the dominant hand using a dynamometer. Given that muscle strength is a component of the frailty phenotype, HGS has been validated as a reliable tool for frailty syndrome screening in older adults.[13,14] Moreover, HGS is a predictor of a wide range of health outcomes, including mortality, disability, and hospitalization.[15,16]

Frailty is not a static condition and can be modified by targeted clinical interventions. Identifying elderly asthma patients at an increased frailty risk is paramount, given that this condition can increase asthma morbidity.[17-19]

Correspondence to:
Ricardo G Figueiredo. Av. Transnordestina, s/n, CEP 44036-900, Feira de Santana, BA, Brasil.
Tel.: 55 75 3161-8089. E-mail: rgfigueiredo@uefs.br
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We hypothesized that HGS is a reliable and easy-to-use method for frailty risk assessment in older patients with asthma. Moreover, given its ease of use, this tool could be part of a comprehensive evaluation of comorbidities among asthma patients with advanced age.

METHODS

This was a cross-sectional study performed between 2020 and 2021 and designed to evaluate the diagnostic accuracy of HGS for frailty risk assessment in elderly patients with asthma. A consecutive sample of 96 older patients was included in the study (Figure 1). All of the patients were treated at a tertiary outpatient clinic located in the city of Salvador, Brazil. Inclusion criteria were as follows: having been diagnosed with asthma by a chest physician and being ≥ 60 years of age. We excluded former or current smokers with a smoking history > 10 pack-years; patients with other pulmonary diseases or extrapulmonary diseases that could interfere with asthma evaluation; and patients with a history of asthma exacerbation in the week before enrollment.

We collected data on demographic characteristics (age, sex, race, household income, and BMI), as well as clinical data on smoking (current smoking, past smoking, and smoking history, in pack-years), comorbidities, current asthma treatment, medication adherence, inhaler technique, use of oral corticosteroids, history of exacerbations, and history of hospitalizations. The definition of asthma and severity classification followed the 2020 recommendations of the GINA.[20] We objectively assessed inhaler technique errors such as errors in dose preparation, placing the inhaler in the mouth, exhaling normally before use, incorrect inhalation technique, and failure to hold the breath after inhaling.[20] The 5-item Asthma Control Questionnaire was used in order to assess asthma control.[21] Spirometry and flow-volume curves were performed before and after bronchodilator administration, with the use of a computerized spirometer (KoKo PFT, Longmont, CO, USA), in accordance with the American Thoracic Society recommendations.[22]

We evaluated HGS (in kgf) using a calibrated hydraulic dynamometer (Baseline®; Fabrication Enterprises Inc., White Plains, NY, USA).[23] Trained research staff collected three consecutive measurements from the dominant hand, with a minimum interval of 1 min between measurements, with the patient in a sitting position and with the elbow flexed at 90°. The best of the three measurements was used for analysis. The research staff that performed the HGS test was blinded to the frailty status of patients.

To determine the diagnostic accuracy of the HGS test, we used s frailty scale developed by Fried et al., previously translated to Portuguese and validated for use in Brazil.[12] The scale is the instrument of choice for characterizing frailty on the basis of the following clinical criteria: unintentional weight loss, weakness, slow gait speed, self-reported exhaustion, and a low level of physical activity. Unintentional weight loss was defined as self-reported loss of 4.5 kg or 5% of

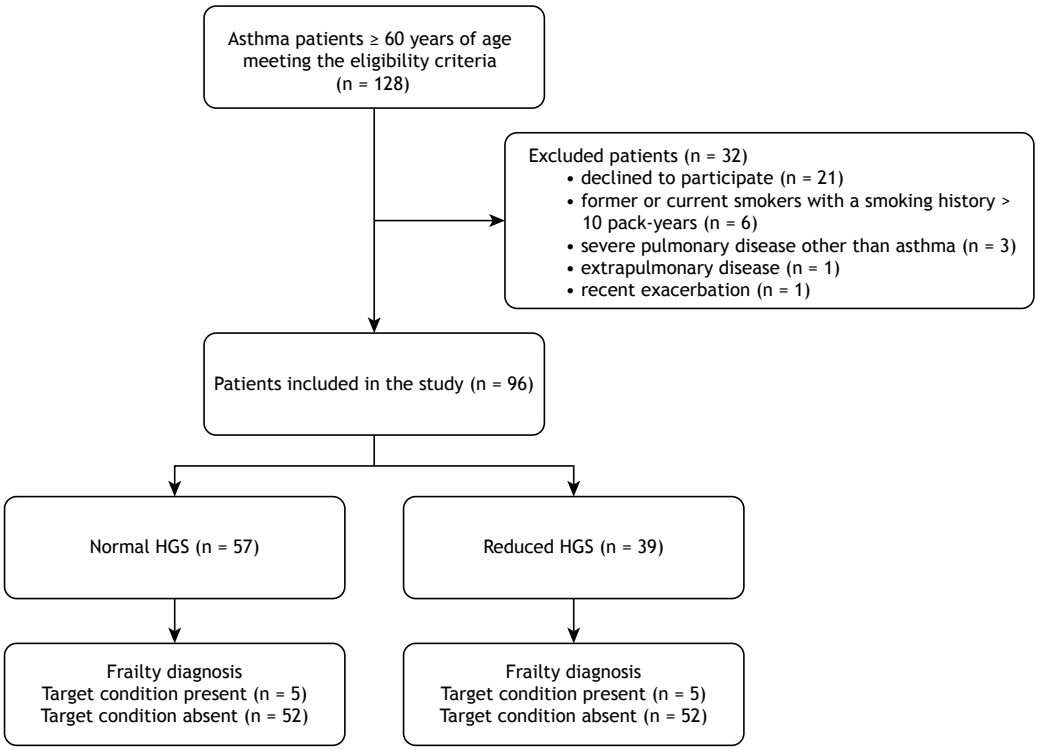

Figure 1. Flow chart of the study population. HGS: handgrip strength.

normal body weight in the last 12 months. Weakness (HGS) was measured with a hand dynamometer on the dominant hand. Muscle weakness was defined by an inability to perform an HGS maneuver or HGS within the lower quintile of the normal range. A stopwatch was used in order to monitor the gait speed over three meters. Slow gait speed was determined on the basis of performance in the highest quintile of time or inability to perform the test. Exhaustion was defined by affirmative responses (most or almost all of the time) to the items on the Center for Epidemiological Studies-Depression Scale. We used the Minnesota Leisure Time Physical Activity Questionnaire in order to assess the level of physical activity. A combination of 3 or more frailty criteria defined frailty; the presence of 1 or 2 frailty criteria characterized prefrail individuals; and the absence of any frailty criteria characterized the nonfrail or robust group.[11]

Likelihood ratios (LRs) are a measure that incorporates both sensitivity and specificity and is used in order to determine the impact of a new diagnostic test on the probability of a disease. The formula for calculating the LR for a positive test result (LR+) is LR+ = sensitivity/(1 − specificity), whereas the formula for calculating the LR for a negative test result (LR−) is LR− = (1 − sensitivity)/specificity. Specifically, we employed LRs to assess the pretest probability for frailty at different proposed cutoff points for HGS, considering the prevalence of the disease in the study population.

The study was conducted in accordance with the 2015 Standards for Reporting of Diagnostic Accuracy Studies guidelines[24] and was approved by the local institutional review board (CAAE no. 3.505.830 - 07/29/2019). All participating patients gave written informed consent. The data obtained were stored in real time on the Research Electronic Data Capture (REDCap; Vanderbilt University, Nashville, TN, USA) platform. We intend to make research data freely available to other researchers (and study participants) upon request.

Statistical analysis

We summarized quantitative variables using medians and interquartile ranges. We expressed categorical and qualitative variables as numbers and proportions. We used the chi-square test in order to compare categorical variables and the Student's t-test or the Mann-Whitney test in order to compare continuous data. To measure the global accuracy of the index test, we used the AUC. An HGS of ≤ 19 kgf was the cutoff point that showed the best diagnostic accuracy. We considered a p value < 0.05 as statistically significant. We conducted the statistical analysis using the GraphPad Prism software, version 9.0.3 (GraphPad Software, Inc., San Diego, CA, USA).

RESULTS

Between 2020 and 2021, 128 patients ≥ 60 years of age with a diagnosis of moderate to severe asthma were assessed for eligibility and invited to participate in the study. A total of 32 patients were excluded for the following reasons: failure to provide written informed consent; being a current or former smoker with a smoking history > 10 pack-years; having severe pulmonary or extrapulmonary diseases; and having experienced an acute exacerbation in the past four weeks (Figure 1). Ninety-six patients were included in the analysis. The median age of participants was 67 (64-73) years. Most (78%) were women and non-White (91%) of low socioeconomic status.

Nineteen patients fulfilled the criteria for the frailty phenotype, with a 19.79% prevalence of frailty in our sample. HGS identified those at risk for frailty, with an AUC of 71.6% (61.5-80.4%; p < 0.002). An HGS cutoff of ≤ 19 kgf showed a sensitivity of 73.58% and a specificity of 67.53% (Figure 2). No significant adverse events occurred because of the HGS test or gait speed assessment.

We assessed the diagnostic properties of the index test at different cutoffs to define low muscle strength. Figure 3 illustrates positive predictive values (PPVs) and the respective LRs. For an HGS cutoff of ≤ 19 kgf, we obtained an LR+ of 2.27, with a PPV of approximately 40%, and an LR− of 0.39, with a PPV of approximately 6%.

We conducted a sensitivity analysis of the accuracy of the index test, adjusted by sex. Table 1 shows a distribution of sensitivity, specificity, LR+, and LR− for different HGS cutoffs for females and males. For females, the sensitivity of the index test was highest for a cutoff of ≤ 27 kgf (93.75%), with an LR− of 1.23, and the specificity of the test was highest for a cutoff of ≤ 12 kgf (86.44%). An HGS of ≤ 11 kgf showed an LR+ of 3.69, with a PPV of approximately 48%, and an HGS of ≤ 20 kgf showed an LR+ of 1.08, with a PPV of 21%. We obtained an LR− of 0.29, with a

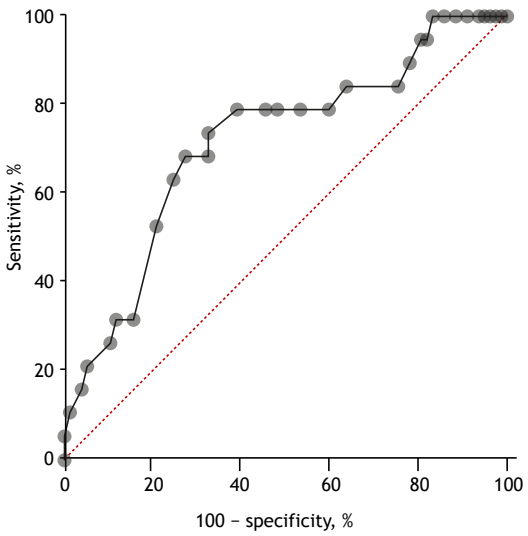

Figure 2. Diagnostic accuracy of the handgrip strength test, as determined by the AUC. A cutoff point of ≤ 19 kgf showed the best diagnostic accuracy, with a sensitivity of 73.58% and a specificity of 67.53%.

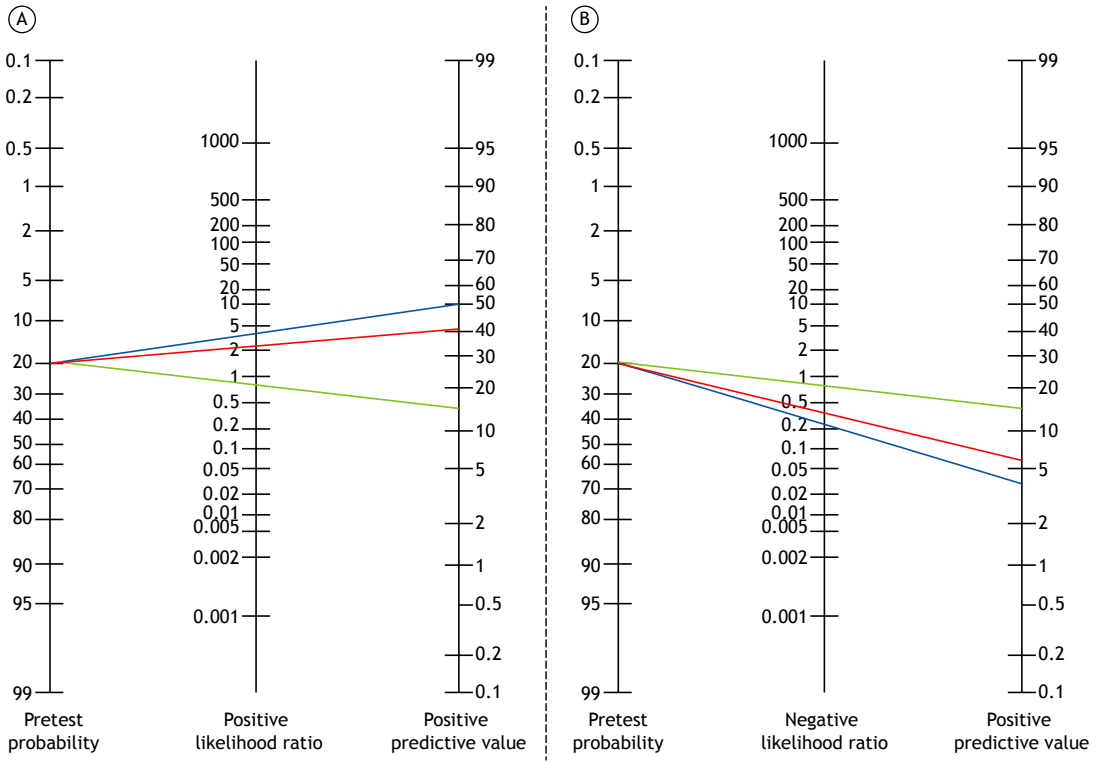

Figure 3. Fagan's nomogram showing the positive predictive values (PPVs) for several cutoffs and positive likelihood ratios (LR+), in A, and negative likelihood ratios (LR−), in B. In A, PPVs for a diagnosis of frailty based on handgrip strength (HGS) cutoffs of ≤ 11 kgf, ≤ 19 kgf, and ≤ 28 kgf (pretest probability of frailty, 19.79%). For an HGS cutoff of ≤ 19 kgf (red line), we obtained an LR+ of 2.27, with a PPV of approximately 40%; for an HGS cutoff of ≤ 11 kgf (green line), we obtained an LR+ of 4.05, with a PPV of 50%; and for an HGS cutoff of ≤ 28 kgf (blue line), we obtained an LR+ of 1.08, with a PPV of 16%. In B, LR− and PPVs for a diagnosis of frailty based on the same HGS cutoffs. For an HGS cutoff of ≤ 19 kgf (red line), we obtained an LR− of 0.39, with a PPV of approximately 6%; for an HGS cutoff of ≤ 11 kgf (green line), we obtained an LR− of 0.83, with a PPV of approximately 16%; and for an HGS cutoff of ≤ 28 kgf (blue line), we obtained an LR− of 0.27, with a PPV of approximately 4%.

Table 1. Diagnostic properties of the index test for frailty risk assessment in females and males.

Females					Males				
HGS cutoff, kgf	Sensitivity, %	Specificity, %	LR+	LR−	HGS cutoff, kgf	Sensitivity, %	Specificity, %	LR+	LR−
≤ 9	12.50	98.31	7.38	0.89	≤ 20	0.0	100	0.0	1.0
≤ 12	31.25	86.44	2.30	0.80	≤ 25	33.33	83.33	2.0	0.8
≤ 19	87.50	57.63	2.06	0.22	≤ 27	66.67	77.78	3.0	0.43
≤ 24	93.75	27.12	1.29	0.23	≤ 32	100	66.67	3.0	0.0

HGS: handgrip strength; LR+: positive likelihood ratio; and LH−: negative likelihood ratio.

PPV of 5%, for an HGS cutoff of ≤ 17 kgf. Regarding the diagnostic proprieties of the index test for males, an HGS of ≤ 27 kgf showed an LR+ of 3.00, with a PPV of 45%, and an LR− of 0.43, with a PPV of 5%.

Comparative analysis of asthma outcomes, comorbidities, and lung function by frailty status

Frail patients were significantly older (p = 0.04) than nonfrail patients (Table 2). Regarding comorbidities, most of the patients reported rhinitis (74%) and gastroesophageal reflux (60%); depression was less common, and dementia was rare.

Most of the patients reported high treatment adherence and correct inhaler technique. Adherence to up to 80% of the prescribed doses was self-reported by 83% and 79% of the patients in the nonfrail and frail groups, respectively. Approximately 90% of the patients in both groups demonstrated correct inhalation technique, without any critical errors. Regarding asthma control, most of the study participants were receiving treatment with medium-dose long-acting β_2 agonists and inhaled corticosteroids or high-dose inhaled corticosteroids, in accordance with the GINA recommendations for step 4 asthma treatment. There

was no significant difference in median 5-item Asthma Control Questionnaire scores between the groups, although 31% of the frail patients had uncontrolled disease, whereas 23% of the nonfrail patients had uncontrolled disease.

Lung function parameters did not differ significantly between the groups. Median FEV_1 values (in L and in % predicted, respectively) were 2.06 L (73%) in the nonfrail group and 1.89 L (72%) in the frail group. It should be noted that spirometry was not performed in 10 (10%) of the patients, because of biosafety issues during the COVID-19 pandemic. There were missing data for 7 (9%) of the patients in the nonfrail group and 3 (16%) of those in the frail group (Table 2).

We also analyzed the cumulative corticosteroid exposure in the previous year. We observed a higher frequency of use of corticosteroids in the frail group, although the difference was not significant. Notably, 68% of the patients in the frail group needed at least one oral corticosteroid course and 16% needed at least one parenteral corticosteroid course in the previous year. Both groups reported no hospital admissions for asthma in the previous year. There was no significant difference in muscle strength between the groups in relation to their cumulative corticosteroid exposure, with median HGS values of 23.00 (15-26) kgf and 21.00 (16-27) kgf in the frail and nonfrail groups, respectively (p = 0.869).

DISCUSSION

We investigated the diagnostic accuracy of the HGS test for assessing frailty risk in patients ≥ 60 years of age with moderate to severe asthma treated at a tertiary referral center in Brazil. Our findings suggest that HGS is a simple, reliable tool for clinicians to determine frailty risk in a point-of-care setting. There is minimal observer effect when assessing muscle strength with a hand dynamometer,[14] and any trained multidisciplinary team member can perform this procedure. Therefore, an easy-to-use, accurate diagnostic tool facilitates screening programs for frailty in elderly asthma patients.

In Brazil, the ongoing process of aging takes place in wide social inequality, often in precarious health and socioeconomic conditions.[25] Environments highly influence individual behavior and exposure to health risks. According to the WHO, an older person is someone over 60 years of age.[26] Indeed, life expectancy may vary in developed and developing countries because environments influence individual behavior, exposure to risks, and access to health services.[27]

HGS has historically been reliably used in the assessment of frailty.[13,14] We found a prevalence of frailty of approximately 20% in our sample. The predominance of moderate-to-severe asthma patients can partially explain this prevalence rate, which is higher than those reported in similar studies of older patients with asthma. In a study conducted in France, adult asthma patients were found to have a two-fold increased prevalence of frailty when compared with individuals without asthma (13% vs. 6%).[28] In a study conducted in Japan, the prevalence of frailty in outpatients with asthma was reported to be 14.5%.[6] Esophageal dysmotility and chronic aspiration are

Table 2. Baseline characteristics of the study population, stratified by the presence or absence of frailty.[a]

Variable	Group		p
	Nonfrail (n = 77)	Frail (n = 19)	
Age, years	67 [60-90]	69 [61-88]	0.04
Female sex	59 (76.6)	16 (84.2)	0.55
Non-White	71 (92.2)	17 (89.5)	0.65
Household income, number of times the Brazilian national minimum wage	1.9 [0.96-2.44]	1.0 [0.96-2.0]	0.20
BMI, kg/m^2	29.5 [26.5-33.1]	28.8 [23.7-33.7]	0.58
Spirometry[b]			
FEV_1, L	2.06 [1.7-2.5]	1.8 [1.3-2.2]	0.79
FEV_1, % predicted	72.6 [66.5-81.5]	80.5 [69.3-88.4]	0.17
FVC, L	1.3 [1.1-1.6]	1.3 [0.7-1.5]	0.22
FVC, % predicted	61.2 [47.3-69.2]	58.2 [45.4-80.7]	0.76
FEV_1/FVC	0.63 [0.51-0.83]	0.63 [0.47-0.84]	
ACQ-5 score	0.80 [0.2-1.6]	1.2 [0.2-1.6]	0.96
Oral corticosteroid tapers in the last year	34 (44.16)	13 (68.4)	0.07
Parenteral corticosteroid courses in the last year	7 (7.69)	3 (15.8)	0.37
Comorbidities			
Rhinitis	56 (72.7)	15 (78.9)	0.77
Gastroesophageal reflux	46 (59.7)	12 (73.2)	> 0.99
Depression	19 (24.6)	5 (26.3)	> 0.99
Dementia	1 (1.3)	0 (0)	0.36

ACQ-5: 5-item Asthma Control Questionnaire. [a]Data expressed as median [IQR] or n (%). [b]Spirometry data unavailable for 10 (10.41%) of the patients.

disorders that have been reported in older asthma patients.[29] This might explain the high prevalence of gastroesophageal reflux in our study population. In a recent study conducted in Japan, a positive association was found between lifetime cumulative corticosteroid exposure and a higher prevalence of muscle frailty and weakness.[30] In our study, no significant difference in muscle strength was found between the two groups of patients regarding their cumulative corticosteroid exposure. However, our study was not designed for this purpose and could have been underpowered to detect this relationship.

Mounting evidence indicates that frailty is a critical prognostic factor in patients with chronic respiratory disease.[31] Frailty assessment has been recommended in older adults.[32] Unfortunately, few studies have addressed the impact of frailty on asthma and vice-versa, particularly in patients with moderate to severe disease. Our findings corroborate that frailty is prevalent in this population. Interventions targeted to factors leading to the development of the frailty phenotype can contribute to improving clinical outcomes in elderly patients with asthma.

Several screening instruments have been validated to assess the risk of frailty. Choosing the most appropriate tool depends on the peculiarities of the health care system and the characteristics of the target population.[33] Despite well-established research protocols, there are several barriers to large-scale application in clinical practice.[9,34] HGS assessment is not time-consuming and is valuable as a single marker of frailty in elderly asthma patients. A more straightforward diagnostic tool such as the HGS test can help reduce patient discomfort and allow clinicians to close this gap in frailty screening programs.

In this study, HGS was found to be a reliable diagnostic tool for frailty risk assessment. Our results suggest that a cutoff of ≤ 19 kgf for females and a cutoff of ≤ 27 kgf for males constitute the optimal threshold for frailty in elderly asthma patients. As a screening method, HGS below 28 kgf showed a highly discriminative negative predictive value. Previous studies in the general geriatric population have reported accuracies ranging from 0.55 to 0.87.[35,36] The accuracy of the index test in asthma patients was slightly lower than the 0.91 reported in a study conducted in Canada and involving elderly individuals > 75 years of age receiving primary care.[13] Nonetheless, our findings suggest that this highly useful tool can contribute to population-based screening programs for frailty.

The frailty phenotype is a multifactorial condition related to a complex relationship of biological, environmental, and socioeconomic factors, which can differ across different populations. For example, in comparison with the participants of a study conducted in Europe,[37] our patients were more likely to be of non-White ethnicity and have lower socioeconomic status. Analyzing the social determinants of these disparities can contribute to a better understanding of the health-disease process in elderly asthma patients. Given the heterogeneous profile of disease severity, impaired peripheral muscle function, and socioeconomic characteristics in elderly patients with asthma worldwide, the HGS test requires validation on different populations.

This study has some limitations. First, 41 of the patients who met the eligibility criteria declined to participate. This might impact the external validity of our results; however, 75% of the eligible patients underwent frailty and HGS assessment. We conducted this study during the COVID-19 pandemic. Although it is possible that frail patients were most likely to decline to participate, the prevalence of frailty in our sample was higher than that reported in previous studies, including studies of elderly asthma patients.[6,28] Second, data from our sensitivity analysis should be interpreted with caution because of the reduced number of males in our sample. Several factors can contribute to a higher prevalence of asthma in elderly females, including postmenopausal hormonal changes, increased exposure to environmental triggers, and comorbidities. Hormonal changes during menopause can decrease estrogen levels, leading to airway inflammation and asthma symptoms.[38]

There is limited evidence on frailty treatment in older asthma patients. Current management strategies focus on symptom control and reducing exacerbations. However, a multidisciplinary approach addressing comorbidities and including nutritional intervention and exercise prescription might also improve frailty outcomes in patients with respiratory disease.[39,40] More research is needed to develop specific interventions for this population.

Understanding the frailty phenotype is a cornerstone in the management of asthma in the elderly. In our study, older adults with moderate to severe asthma had a higher prevalence of frailty than that reported in the general geriatric population in Brazil.[10] We demonstrated that HGS is an accurate diagnostic tool to assess the risk of frailty in patients with asthma. In a sex-stratified analysis, HGS cutoffs of ≤ 19 kgf in females and ≤ 27 kgf in males showed the best diagnostic accuracy for frailty risk assessment in older asthma patients. The development of a simple point-of-care diagnostic tool facilitates screening programs for frailty in older patients with chronic respiratory disease. Further investigation of HGS and other biomarkers of the frailty phenotype can bring promising results.

AUTHOR CONTRIBUTIONS

RGF, JB, and MP designed the study. RGF, VA, and MMFL collected the data. JB, AAC, and FH analyzed and interpreted the data and statistics. GPP and CVNS provided study material. RGF, JB, AAC, MP, and FH interpreted the results and wrote the manuscript. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

None declared.

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