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ACQ, Asthma Control Questionnaire
AQLQ, Asthma Quality of Life Questionnaire
BMI, Body mass index
FM, Fat mass
FFM, Fat-free mass
FM/FFM, Fat mass to fat-free mass ratio
FEV_1, Forced expiratory volume in the first second
FVC, Forced vital capacity
FEV_1/FVC, Forced expiratory volume in the first second to forced vital capacity ratio
GINA, Global Initiative for Asthma
HADS, Hospital Anxiety and Depression Scale
PADL, Physical Activity in Daily Life

ABSTRACT

Background: Fat mass to fat-free mass ratio (FM/FFM) assesses the combined effect of the balance between fat mass and fat-free mass. Aims: to evaluate the associations beetween FM/FFM and clinical outcomes in asthma and to compare clinical characteristics between individuals with higher and lower FM/FFM.
Methods: 128 participants with asthma underwent anthropometric, spirometry and bioelectrical impedance assessments. Physical activity in daily life (PADL) was assessed by the Actigraph for 7 days. Daily dose of inhaled medication, steps of pharmacological treatment, Asthma Control Questionnaire, Asthma Quality of Life Questionnaire and Hospital Anxiety and Depression Scale were also assessed. Participants were classified into two groups according to the 50th percentile of reference values for FM/FFM.
Results: Individuals with higher FM/FFM (n=75) used higher daily doses of inhaled corticosteroids, had worse lung function and fewer steps/day when compared to those with lower FM/FFM (n=53) ($P \leq 0.021$). Associations were found between absolute values of FM/FFM with lung function (FEV_1 and FVC [liters]): R^2=0.207 and 0.364;$P<0.0001$), and between the categories of lower or higher FM/FFM with steps of medication treatment (Cramer's V=0.218;P=0.016) and level of PADL (Cramer's V=0.236;P=0.009). The highest FM/FFM was a determining factor of physical inactivity (OR: 3.21;95%CI:1.17–8.78) and highest steps of pharmacological treatment (OR: 8.89;95%CI:1.23–64.08).
Conclusion: Higher FM/FFM is significantly associated with worse clinical characteristics in individuals with asthma, such as higher doses of inhaled corticosteroids, worse lung function and fewer steps/day. Moreover, higher FM/FFM is a determining factor of physical inactivity and the highest steps of pharmacological treatment for asthma.

Introduction

Asthma is a disease characterized by chronic inflammation of the airways that is defined by a history of respiratory symptoms that vary over time and in intensity, such as wheezing, dyspnea, chest tightness and coughing, along with variable expiratory airflow limitation.[1] Body composition is a factor that directly influences clinical outcomes in patients with asthma. There is a clinical phenotype of asthma called asthma with obesity,[1] in which obese individuals with asthma have more symptoms and exacerbations, worse disease control, greater consumption of medications for asthma and worse lung function.[2]

Most studies on asthma classify body composition using only the body mass index (BMI). Despite being a simple and widely used

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anthropometric variable, BMI has some limitations since it cannot distinguish the fat mass (FM) from the fat-free mass (FFM). Its calculation only takes into account the individual's height and weight (and not FM) and thus, in some cases, it may overestimate or underestimate adiposity.[3] Therefore, more specific measures may be required for a better understanding of body composition, such as FM and FFM, which can be obtained by bioelectrical impedance analysis.[4]

Fat mass to fat-free mass ratio (FM/FFM) is an integrated metabolic index for assessing body composition, which assesses the combined effect of the proportion between FM and FFM.[5,6] This relationship conceptualizes two contrasting characteristics for the maintenance of homeostasis: the metabolic load, defined as the magnitude of an insult in a system (corresponding to FM); and the metabolic capacity, which refers to the system's ability to neutralize the insult (corresponding to FFM).[5,6] In other words, FM/FFM indicates whether the amount of FM is adequate for the amount of FFM in an individual. In theory, higher ratio values indicate a less favourable balance between FM and FFM, and high FM/FFM has already been identified as an independent predictor of cardiac events and all-cause mortality in patients undergoing hemodialysis.[7] Additionally, those with high FM/FFM are more likely to have metabolic syndrome, prediabetes, diabetes mellitus and arterial hypertension,[8] and are more likely to develop metabolic syndrome and insulin resistance.[9]

Despite these clinical associations found so far with FM/FFM in other chronic diseases, this ratio has not been studied in individuals with asthma.The clinical impact of higher versus lower FM/FFM in these patients is unknown. Thus, the aims of this study were to verify the associations between FM/FFM and clinical outcomes in individuals with asthma, as well as to compare the clinical characteristics of these individuals between those with higher and lower FM/FFM values. Our hypothesis is that higher values of FM/FFM are associated with worse clinical outcomes in these individuals.

Methods

Participants and study design

This is a cross-sectional study performed at two research centers both located in Brazil: (1) Pitágoras-Unopar University (Londrina) (data collection from 2018 to 2020) and (2) University of Sao Paulo (Sao-Paulo) (data collection from 2016 to 2018). The participants were recruited from the pneumology outpatients services of the University Hospital of Londrina and the Clinics Hospital of the University of Sao Paulo Medical School. The study was approved by the Research Ethics Committee of both institutions (number 3060,314 and 2043,975, respectively). Inclusion criteria were: 18 years old or older, diagnosis of asthma according to the Global Initiative for Asthma (GINA),[1] pharmacological treatment for at least 6 months and clinical stability (i.e., without hospitalizations and emergency care for at least 30 days). Were excluded those who did not perform the body composition assessment. All participants signed a written informed consent. All the assessments (detailed description below) in each research center were performed by the same experienced investigators in charge of data collection based on standardized protocols. Preliminary results of this study have been previously reported in the form of abstract in the European Respiratory Society congress 2021.[10]

Assessments

General and anthropometric data

For the anthropometric evaluation, weight and height were measured with a scale and a stadiometer. The calculation of BMI was performed through the formula: weight(kg)/height^2(m).[3] In order to characterize the sample, self-reported data such as comorbidities and the daily dose of medication (inhaled corticosteroids and long-acting bronchodilator) were also collected. Participants were also classified according to the steps of pharmacological treatment for asthma (steps 1 to 5) following international asthma guideline.[1] Higher steps of pharmacological treatment indicate worse asthma severity.[1]

Lung function

Lung function assessment was performed using pre-bronchodilator spirometry performed via a simple spirometer (Spirometer MicroLab 3500, Care Fusion®, Ireland and Spirometer KoKo, nSpire Health, Inc.®, UK). The technique was performed according to international guidelines in both centers,[11] determining the forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC) and the FEV_1/FVC ratio. In addition to the absolute values (in liters), reference values for the Brazilian population were used as a frame for the calculation of FEV_1 and CVF in % of the predicted values.[12]

Body composition

Body composition was assessed using bioelectrical impedance analysis (tetrapolar at Pitágoras-Unopar University - Biodynamics 310TM, Biodynamics Corp, USA; and octopolar at University of São Paulo InBody720, Biospace, South Korea) according to the manufacturers' recommendations and according to the protocols described by Lukaski *et al*[13] and Gibson *et al*,[14] respectively. Participants were instructed to fasting for 8 hours and to empty their bladder at least 30 minutes before the test, as well as not to exercise, ingest coffee, tea, chocolate or alcoholic beverages for at least 12 hours before the test.[15] The test was performed without shoes or socks and metallic objects on the body were removed[15] (when not possible, the patient was not assessed). From the total values of FM and FFM obtained by bioelectrical impedance analysis, the ratio between them was calculated.[5,6] Bioelectrical impedance analysis has shown to be a valid and reliable tool that enables simple assessment of body composition in many clinical conditions.[15] The reproducibility of body composition measurements by bioelectrical impedance analysis in patients with chronic obstructive pulmonary disease was found to be excellent.[16,17]

Asthma control

Asthma control was assessed using the Asthma Control Questionnaire (ACQ). In this questionnaire, participants were asked to recall their symptoms during the previous week and to answer the first 6 questions (waking up at night, symptoms on waking, activity limitation, dyspnea, wheezing and use of short-term rescue medication). The seventh question concerns the FEV_1 in percentage of predicted pre-bronchodilator.[18] The items are equally weighted, with scores between 0 (fully controlled) and 6 (totally uncontrolled). There are two versions of this questionnaire: ACQ-7, in which the final score refers to the average score of the seven questions,[18] and ACQ-6, in which the final score concerns only the average of the first six questions and it does not take into account the last question about lung function.[19] This valid and reliable questionnaire is recommended by GINA.[1] A score $\leq$ 0.75 characterizes controlled asthma; between 0.76 and 1.49 partially controlled; and $\geq$ 1.50 uncontrolled.[18]

Quality of life

Quality of life was assessed by the Asthma Quality of Life Questionnaire (AQLQ), composed by 32 questions divided into 4 domains: activity limitations, symptoms, emotional function and exposure to environmental stimuli in the last two weeks.[20] The total score is the average of the 32 questions and varies between 1 (minimum score) and 7 (maximum score). The validation study shows the higher the score, the better the quality of life.[20]

Anxiety and depression

The levels of anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS), which is a scale composed by 14 questions, so that half of them refers to anxiety and the other half to depression. Each question has a score ranging from 0 to 3 points. The total score for each subscale can reach up to 21 points. The validation study shows the higher the score, the higher the levels of anxiety or depression.[21]

Physical activity in daily life (PADL)

The assessment of the level of PADL was performed using the validaded and largely used physical activity monitor *Actigraph* model wGT3X-BT.[22,23] The monitor was worn on the waist (by means of an elastic band) for the entire awake time during 7 consecutive days. Based on the average of valid days (i.e. ≥4 days with ≥8 hours of recording per day),[24] the main variables were the number of steps/day and the time spent/day in sedentary time, light activities, and moderate-to-vigorous activities, all in minutes and in percentage of the assessment time.[22,23] Individuals who performed ≥ 7000 steps/-day were classified as physically active and those who performed <7000 steps/day as physically inactive.[25,26]

Group classification

After the assessments, participants were classified into two groups according to higher or lower FM/FFM values. In the absence of specific reference values for the local population, reference values by Xiao et al. were used, specific for sex and age (from 18 to 90 years), which were developed from an international sample composed of 6342 white and non-Hispanic North-American individuals.[6] Participants were classified according to the 50th percentile from these reference values in two groups: 1) group with lower FM/FFM (≤50th percentile); and 2) group with higher FM/FFM (>50thpercentile).[6]

Statistical analysis

Normality in data distribution was evaluated using the Shapiro–Wilk test. In case of normal distribution, results were described as mean ± standard deviation; otherwise, as median [interquartile range 25–75%]. Categorical variables were described in absolute and relative frequency. The unpaired Student's *t*-test or the Mann-Whitney test were performed for comparisons of numeric variables between the groups and Chi-Square test for comparisons of categorical variables. Regarding correlations, Pearson or Spearman correlation coefficients were used according to normality in data distribution. Statistically significant correlations were classified as weak (<0.40), moderate (≥0.40 to <0.70) or strong (≥0.70).[27] Associations between BMI, absolute values of FM/FFM and clinical characteristics (numerical variables) were verified using Univariate Linear Regressions. Associations between categories of lower or higher FM/FFM with categorical variables were verified using the Chi-square and Cramer's V tests. Multinomial Logistic Regressions were performed to verify whether the FM/FFM was a determining factor for the variation of steps of pharmacological treatment and of the categories of PADL. The softwares used were SPSS 21.0 and GraphPad Prism 6.0. The level of statistical significance was $P < 0.05$.

Results

Two hundred and forty-five adults with asthma complied to inclusion criteria (77 recruited from the Pitágoras-UNOPAR University and 168 from the University of São Paulo), but 117 were excluded because they did not perform the body composition assessment. Thus, 128 adults with asthma were analyzed (61 from the Pitágoras-UNOPAR University and 67 from the University of São Paulo). From the total sample included in the study, 11 (9%) presented FM/FFM below or equal to the 5th percentile, 113 (88%) between the 5th and 95th percentile, and 4 (3%) above or equal to the 95th compared to the reference values. Fifty-three individuals were classified with lower FM/FFM and seventy-five with higher FM/FFM according to 50th percentile.

There was no difference between the two centers in the proportion of individuals classified in the groups (lower FM/FFM: 29 vs. 24; higher FM/FFM: 32 vs. 43, respectively; P=0.183). There was no difference between the two centers regarding sex, age, weight, height, BMI and lung function (P≥0.082 for all).

Table 1 shows the general characteristics of the individuals. There were no differences between the groups higher and lower FM/FFM in the proportion of men and women, age and height (P≥0.726 for all). The group with higher FM/FFM had higher weight, BMI, FM in kilograms and percentage, FFM in kilograms but lower FFM in percentage when compared to the group with lower FM/FFM (P≤0.001 for all).

Table 2 shows the comparisons between groups with lower or higher FM/FFM concerning their clinical characteristics. Those classified as having higher FM/FFM used higher daily doses of inhaled corticosteroids, had worse lung function (lower FEV_1 and FVC in liters and % predicted) and fewer steps/day when compared to those with lower FM/FFM (P≤0.021 for all).

Weak but significant linear correlations were found between FM/FFM with the number of comorbidities (r=0.206; P=0.020), daily dose of inhaled corticosteroids (r=0.295; P=0.001), FEV_1 in % predicted (r=-0.221; P=0.012), FVC in % predicted (r=-0.346; P<0.0001), ACQ7 (r=0.197; P=0.026), HADS anxiety (r=0.228; P=0.010), HADS depression (r=0.203; P=0.023) and steps/day (r=-0.203; P=0.026). The FM/FFM correlated moderately with FEV_1 in absolute values (r=-0.461; P<0.0001) and with FVC in absolute values (r=-0.597; P<0.0001). This ratio is strongly correlated with BMI (r=0.702; P<0.0001).

Associations of FM/FFM with FEV_1 in absolute values and with FVC in absolute values and % predicted were found (R^2 from 0.113 to 0.364; P<0.0001 for all) (Fig. 1), as well as with BMI (R^2=0.488; P<0.0001). BMI was also associated with FVC in absolute values and % predicted, however, with lower explanatory power (R^2 from 0.036 to 0.045; P<0.033 for all). There was no significant association between BMI and FEV_1 in absolute values.

Fig. 2 shows the associations between the categories of lower and higher FM/FFM with the categories of steps of pharmacological treatment for asthma and with level of PADL. Significant associations between higher FM/FFM with more severe steps of pharmacological

Table 1
Clinical and Demographic Characteristics of the Sample.

	Total sample (n=128)	Group with Lower FM/FFM (n=53)	Group with Higher FM/FFM (n=75)	*P*
Sex F/M, n (%)	97(76) / 31(24)	41(77) / 12(23)	56(75) / 19(25)	0.726
Age, years	45 [38 – 55]	46 [37 – 55]	45 [38 – 55]	0.917
Weight, kg	74 [63 – 83]	63 [59 – 71]	80 [74 – 91]	**<0.0001**
Height, m	1.60 [1.53 – 1.68]	1.61 [1.53 – 1.69]	1.60 [1.53 – 1.68]	0.784
BMI, kg/m^2	29.10 ± 5.40	24.90 ± 3.53	32.07 ± 4.45	**<0.0001**
Fat mass, kg	26 [19 – 31]	18 [13 – 21]	30 [26 – 34]	**<0.0001**
Fat mass, %	34 [29 – 38]	29 [21 – 34]	37 [33 – 41]	**<0.0001**
Fat-free mass, kg	48 [44 – 56]	45 [43 – 51]	50 [46 – 59]	**0.001**
Fat-free mass, %	66 [62 – 71]	71 [66 – 78]	62 [59 – 67]	**<0.0001**
FM/FFM	0.51 [0.40 – 0.62]	0.41 [0.27 – 0.50]	0.60 [0.49 – 0.69]	**<0.0001**

F: female; M: male; BMI: body mass index; FM/FFM: fat mass to fat-free mass ratio.

Table 2
Comparisons of the clinical characteristics between groups with lower and higher FM/FFM.

	Group withLower FM/FFM(n=53)	Group withHigher FM/FFM(n=75)	*P*
Comorbidities, number	3 [2 - 4]	3 [2 – 4]	0.829
PHARMACOLOGICAL TREATMENT			
Daily dose of inhaled corticosteroids, mcg	660 ± 430	842 ± 370	**0.021**
Daily dose of long-term BD, mcg	24 [12 – 24]	24 [21 – 25]	0.133
LUNG FUNCTION			
FEV_1, l	2.27 ± 0.74	1.91 ± 0.63	**0.004**
FEV_1, %predicted	71 ± 18	66 ± 17	**0.002**
FVC, l	3.20 ± 0.92	2.82 ± 0.77	**0.012**
FVC, %predicted	89 ± 15	79 ± 17	<**0.0001**
FEV_1/FVC, %	72 [64 – 78]	70 [61 – 75]	0.181
CLINICAL CONTROL			
ACQ-6, points	1.50 [0.67 – 2.16]	1.66 [0.91 – 2.33]	0.471
ACQ-7, points	1.71 [0.85 – 2.14]	1.86 [1.42 – 2.57]	0.084
PSYCHOSOCIAL DISTRESS			
AQLQ total, points	4.56 [3.60 – 5.35]	4.37 [3.48 – 5.20]	0.640
HADS anxiety, points	8 [5 – 11]	9 [6 – 12]	0.444
HADS depression, points	6 [3 – 9]	7 [4 – 10]	0.354
PHYSICAL ACTIVITY IN DAILY LIFE			
Steps/day, number	7818 [5226 – 10,437]	5825 [4863 – 8082]	**0.012**
Moderate to vigorous activities, min/day	24 [13 – 21]	19 [11 – 33]	0.132
Moderate to vigorous activities, %	3 [1 – 5]	2 [1 – 4]	0.182
Light activities, min/day	336 ± 98	320 ± 83	0.351
Light activities, %	38 ± 9	38 ± 9	0.970
Sedentary time, min/day	520 ± 97	502 ± 98	0.327
Sedentary time, %	59 ± 10	59 ± 10	0.770

FM/FFM: fat mass to fat-free mass ratio; BD: bronchodilator; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity; FEV_1/FVC: forced expiratory volume in the first second to forced vital capacity ratio; ACQ: *Asthma Control Questionnaire*; AQLQ: *Asthma Quality of Life Questionnaire*; HADS: *Hospital Anxiety and Depression Scale*.

treatment and physical inactivity profile were found (Cramer's V=0.218 and 0.236, respectively, P≤0.016 for both). Eighty percent of the individuals classified as having lower FM/FFM and 94% of the individuals classified as having higher FM/FFM were in stages 4 and 5 of the steps of pharmacological treatment for asthma (*P*=0.016) (Fig. 2A).

In the logistic regression models (tables 3 and 4), those with the higher FM/FFM were 3.21 times more likely to be physically inactive, as well as 8.89 times more likely to be classified in the highest steps of pharmalogical treatment for the disease (i.e. more severe, steps 4 and 5) than those with lower FM/FFM.

Discussion

This is the first study to use FM/FFM as a method of classifying body composition in individuals with asthma, as well as to verify the associations of this ratio with different clinical outcomes of the disease. The present study found that individuals with asthma who have higher FM/FFM use higher daily doses of inhaled corticosteroids, worse lung function and fewer steps/day when compared to those with lower FM/FFM. In addition, associations of this ratio were found with lung function, steps of pharmacological treatment for asthma and level of PADL in these individuals. Additionally, individuals with higher FM/FFM are more likely to be physically inactive and to be classified in stages 4 and 5 (i.e. more severe) of pharmacological treatment steps of the disease.

Body composition has been directly related to lung function in individuals with asthma. Jensen et al., found positive moderate correlations of total FFM with FEV_1 and FVC in male asthmatic children, but no correlations were found between FM and lung function in this population.[28] In contrast, Wang et al., found that the increase in the percentage of FM is associated with a reduction in FEV_1 and FVC also in boys with asthma.[29] Similarly, higher percentage of FM is associated with a reduction in FEV_1 and FVC in young adults.[30] Likewise, women with asthma presenting higher FM percentage are 1.75 times more likely to have limitations in lung function.[31] In addition to finding a moderate correlation between FM/FFM and lung function, our study confirms the impact of body composition on lung function in patients with asthma by showing that the use of the 50th percentile of the reference values for FM/FFM allows the discrimination of groups of patients with significant differences in lung function. This might have occured due to the increase in FM (which leads to higher values in FM/FFM), in which the increase of FM around the rib cage can lead to changes in the elastic properties of the chest wall, making these individuals to breathe with lower lung volumes.[32]

Lau *et al*., found that the percentage of FM is higher among female patients with airflow obstruction (including patients with asthma) using inhaled corticosteroids than in controls.[33] Individuals with asthma who have less skeletal muscle mass also use higher doses of inhaled corticosteroids.[34] In the present study, it was found that those with higher FM/FFM use higher daily doses of inhaled corticosteroids. A positive correlation between these variables was also found. One hypothesis for our findings is that the increased adiposity can lead to greater systemic inflammation, which can cause inflammation in asthma and, consequently, greater use of corticosteroids.[32]

The increase in FM/FFM can also occur due to a decrease in FFM.[5] It is known that patients with severe refractory asthma have a decrease in the FFM index[35] and that, the severity of asthma is related to the steps of pharmacological treatment for the disease, in which

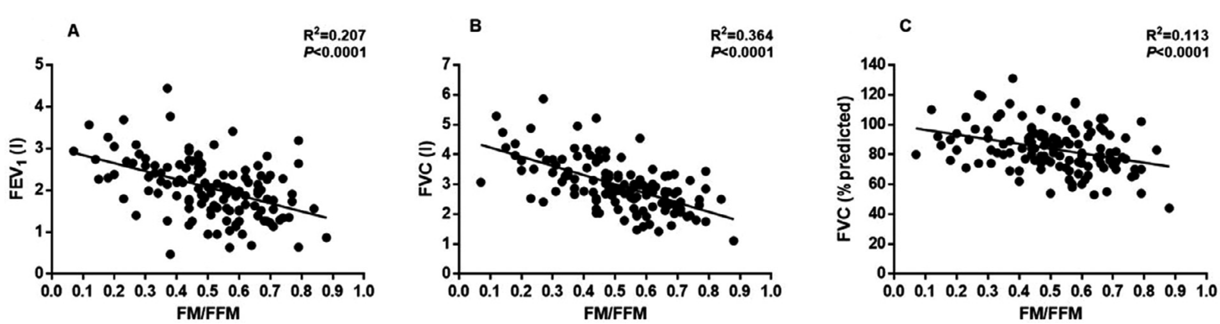

Fig. 1. Associations between the fat mass to fat-free mass ratio (FM/FFM) and forced expiratory volume in the first second (FEV_1) in liters (A), forced vital capacity (FVC) in liters (B) and in percentage of predicted (C).

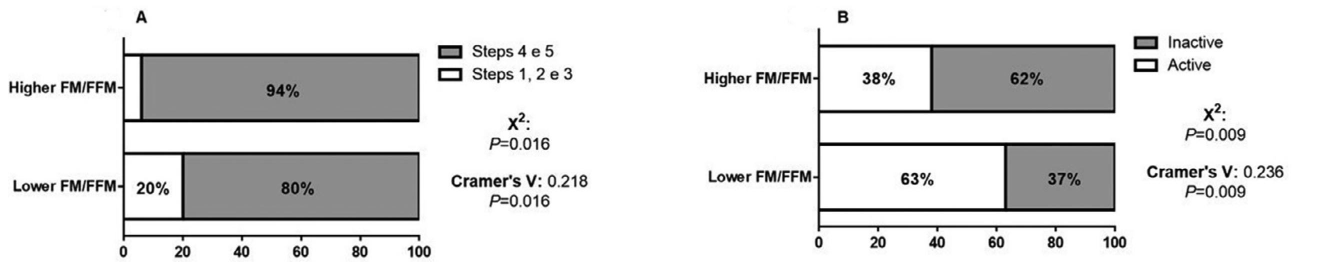

Fig. 2. Associations between the categories of lower and higher fat mass to fat-free mass ratio (FM/FFM) and categories of the steps of pharmacological treatment (A) and categories of physical activity in daily life (B).

individuals classified as having severe asthma are those in the steps 4 and 5 of pharmacological treatment.[1] Our study confirmed that individuals with severe asthma present worse body composition, since a higher FM/FFM was more pronounced in patients with worse disease severity.

Bruno *et al*., found a negative weak correlation between FM with total time of physical activity and a positive moderate correlation between FFM also with total time of physical activity in asthmatics with mild to moderate severity.[36] Correa-Rodríguez *et al*., found that FFM is also positively associated with total physical activity and moderate-to-vigorous activity in healthy young adults, but they did not find associations between FM and physical activity.[37] An association between body adiposity and the number of steps/day was also observed in healthy adults, so that those who perform ≥7500 steps per day have a lower occurrence of obesity classified by body fat (i.e. fat mass percentage ≥ 75th percentile in the sample).[38] The present study also found an association between body composition and PADL, in which those with higher FM/FFM performed fewer steps/day and were 3.21 times more likely to be physically inactive. Similarly, Abdo *et al*., found that a higher level of PADL is a predictor of lower fat mass and higher muscle mass in individuals with asthma.[34] This association is clinically relevant, because PADL is an important treatable trait in asthma, wherein higher levels of sedentary time are significantly associated with increased odds of exacerbation, hospitalization and with greater systemic corticosteroids bursts, while being more active is a protective factor for hospitalization.[39]

The results of this study can be translated into new implications for clinical practice. Healthcare professionals involved in the treatment of patients with asthma should be aware of the negative consequences of excess fat accumulation in relation to FFM in this population. In addition, our data suggest that screening for body composition abnormalities should be included in the routine initial assessment of patients with asthma. The interpretation of body composition variables should be done in light of reference values rather than relying solely on BMI and preventive strategies such as patient education should be considered to clarify the clinical relevance of the maintenance of adequate levels of FM, FFM and physical activity.

Future studies should investigate the frequency of low muscle mass and obesity in a larger sample of patients with asthma taking into account the relationship between the amount of muscle mass and body fat (or body weight) and considering the current available standardized definitions of sarcopenic-obesity.[40] In addition, studies should focus on the associations and functional consequences of these body composition abnormalities in this population. Longitudinal studies are suggested to verify whether FM/FFM can predict exacerbation, hospitalization and mortality in asthma. In addition, studies using multidisciplinary comprehensive pulmonary rehabilitation programs should be carried out in order to verify whether through exercise training, education, medication management and nutrition it is possible to reduce FM/FFM with respective positive clinical impact on the disease, such as the requirement of a lower daily dose of inhaled corticosteroids and an increase in levels of physical activity of daily life.

This study has some limitations: 1) cross-sectional design, in which it is not possible to infer causality and effect; 2) the reference values for FM/FFM used are from an international sample,[6] as specific reference values for the Brazilian population have not been developed; 3) the use of bioelectrical impedance analysis to assess body composition has some limitations, as it only estimates FM and FFM from the impedance (resistance and reactance), thus allowing the exact determination of FM and FFM only in individuals without significant hydroelectrolytic abnormalities[41]; 4) the use of different bioelectrical impedance equipments in the two centers (tetrapolar and octopolar); however, both devices present very strong correlations with the percentage of fat mass assessed by dual-energy x-ray absorptiometry (tetrapolar: r=0.91 and octopolar: r=0.94)[42] and participants from both centers were similarly distributed between the groups of higher and lower FM/FFM. Noteworthy, high quality multicentre studies have used the same tools of the present study to assess people with chronic pulmonary stable disease, this fact ease the comparison of our findings with previous and future studies.[34,39,43,44]Despite these limitations, this is the first study to classify the body composition of individuals with asthma from two different centers using FM/FFM and to verify their associations with clinical outcomes of the disease.

It can be concluded that FM/FFM is associated with clinical characteristics in individuals with asthma. Those with higher FM/FFM use higher daily doses of inhaled corticosteroids, have worse lung function and fewer steps/day when compared to those with lower FM/FFM. Additionally, there are associations between FM/FFM with lung function, steps of pharmacological treatment of the disease and level of physical activity in daily life, so that the higher FM/FFM value is a

Table 3
Determining factors of physical inactivity in individuals with asthma.

		β	*P*	*Odds ratio*	95% Confidence Interval Lower Limit	Upper Limit
Inactive (n=63)	Age, years	0.023	0.155	1.023	0.991	1.055
	Weight, kg	-0.002	0.924	0.998	0.968	1.030
	FEV_1, %predicted	0.014	0.216	1.014	0.992	1.037
	Higher FM/FFM	**1.168**	**0.023**	**3.215**	**1.176**	**8.787**
	Sex - Female	0.310	0.524	1.364	0.526	3.538

Reference category: Active.
FM/FFM: fat mass to fat-free mass ratio.

Table 4
Determining factors of the steps of pharmacological treatment for individuals with asthma.

		β	P	Odds ratio	95% Confidence Interval	
					Lower Limit	Upper Limit
Steps 4 e 5 (n=109)	Age. years	0.032	0.213	1.032	0.982	1.086
	Weight, kg	-0.038	0.160	0.962	0.912	1.015
	FEV_1, %predicted	-0.019	0.309	0.981	0.946	1.018
	Higher FM/FFM	**2.186**	**0.030**	**8.899**	**1.236**	**64.088**
	Sex - Female	0.774	0.265	2.168	0.555	8.461

Reference category: Steps 1, 2 and 3.
FEV_1: forced expiratory volume in the first second; FM/FFM: fat mass to fat-free mass ratio.
Sugiro colocar na legenda que o step 4 e 5 são mais graves

determining factor of physical inactivity and of the highest steps of pharmacological treatment for asthma.

Conflict of Interest

All authors have no conflict of interest to disclose.

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