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Inflammatory markers, sarcopenia and its diagnostic criteria among the elderly: a systematic review

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Abstract

Objective: To identify the relationship between inflammatory markers and sarcopenia, and the diagnostic criteria of the condition among the elderly. *Methods:* A systematic review was performed based on the consultation of the PubMed and LILACS databases. Eligible original articles were those involving individuals aged 60 years or more, which investigated sarcopenia [low muscle mass (MM) associated with poor muscle strength and/or reduced physical performance, according to the *European Working Group on Sarcopenia in Older People consensus* (EWGSOP)] or its diagnostic criteria, published in English or Portuguese, between 2010-2015. *Results:* Four articles were included in the review, the principle results of which were: the growth differentiation factor (GDF-15) exhibited a negative correlation with MM, handgrip strength and gait speed; the insulin-like growth factor-1 (IGF-1) correlated positively with MM; follistatin exhibited a weak correlation with physical performance; activin A and myostatin did not correlate with the diagnostic criteria; the highest tercile of extracellular heat shock protein 72 (eHsp72) was associated with lower median levels of MM, handgrip strength and gait speed; elderly persons with low MM had higher serum ferritin concentrations; women with low MM exhibited lower serum concentration levels of C-reactive protein (CRP). *Conclusion:* the six investigated inflammatory markers (GDF-15, IGF-1, follistatin, eHsp72, ferritin and CRP) were associated with the diagnostic criteria for sarcopenia, but not with sarcopenia itself. As research in this area is still developing, additional studies are required to broaden knowledge and eventually establish the role of these markers in the diagnosis and management of sarcopenia.

Keywords: Biomarkers. Elderly. Sarcopenia.

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INTRODUCTION

The aging process is triggered by physiological changes which occur distinctly among individuals and their organic systems. One of these changes is the change in body composition, where there is an increase in fat mass and visceral fat and an involuntary reduction of muscle mass[1]. According to the European Consensus on the definition and diagnosis of sarcopenia of the *European Working Group on Sarcopenia in Older People* (EWGSOP)[2], sarcopenia is a geriatric syndrome characterized by low muscle mass associated with low muscle strength and/or poor physical performance. This syndrome is associated with adverse outcomes such as functional disability (dependence)[2,3], low quality of life[3] and the risk of death[2].

The existence of these criteria makes it possible to diagnose three distinct stages of sarcopenia: pre-sarcopenia, when there is low muscle mass; sarcopenia, when there is low muscle mass associated with low muscle strength and/or low physical performance; and severe sarcopenia, when there is inadequacy in the three diagnostic criteria[2,4].

There are several mechanisms involved in the genesis and evolution of sarcopenia, including neuroendocrine factors (such as insulin-like growth factor 1 (IGF-1), insulin resistance), age-related factors (sexual hormones, apoptosis, mitochondrial dysfunction), inadequate nutrition/malabsorption, disuse (immobility, physical inactivity, zero severity) and neurodegenerative diseases (loss of motor neurons)[2,3]. Inflammation is another factor involved[1,3]. Studies have indicated the deleterious effects of inflammatory markers on muscle quantity, quality and functionality[5,6].

The inflammatory process results from changes in the anabolic and catabolic mediators. The decline in serum concentrations of anabolic hormones such as testosterone, growth hormone (GH), insulin and IGF-1 causes muscle catabolism. The reduction in GH and IGF-1 decreases the recruitment of satellite cells into the muscle tissue and protein synthesis. Consequently, there is increased production of inflammatory mediators such as pro-inflammatory cytokines, and inflammatory markers produced by hepatocytes that accelerate the process of muscle catabolism. In contrast, with the increased production of these inflammatory mediators, there is a reduction in anti-inflammatory mediators[4,7-9].

Despite knowledge of the role of inflammation in sarcopenia, studies on this topic and the relationship between inflammatory markers and the diagnostic criteria for sarcopenia among the elderly population are still incipient. Such research can contribute to a better understanding of the pathophysiology, diagnosis and management of sarcopenia.

Thus, the present article aims to identify, through a systematic review, the relationship between inflammatory markers and sarcopenia and its diagnostic criteria in the elderly.

METHODS

This systematic review was carried out in accordance with the recommendations proposed by the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA)[10], and it was registered in the *International Prospective Register of Systematic Reviews* (PROSPERO) under number CRD42015017926.

The eligibility criteria were original articles published in the period 2010-2015 in English or Portuguese, which addressed the relationship between inflammatory markers and sarcopenia and its diagnostic criteria in elderly persons with an age group of 60 years or older. Articles that did not evaluate the presence of sarcopenia (low muscle mass associated with low muscle strength and/or low physical performance) or its diagnostic criteria (muscle mass, strength and/or physical performance) as recommended by the European Consensus on the definition and diagnosis of sarcopenia of the EWGSOP[2] were excluded. Articles published from January to April 2010 were excluded because they were prior to the aforementioned Consensus[2]. Experimental studies with animals, *in vitro* studies, recommendations, guidelines, reviews, protocols, letters, editorials and case reports were also excluded.

The search strategies and sources were directed at articles included in the PubMed and Lilacs electronic databases, from January to February of 2016, with the last search carried out on 02/13/2016. For this process, the descriptors of the Medical Subject Headings (Mesh) and their correlates in Portuguese

of the Descriptors in Health Sciences (DeCS) were used: *sarcopenia*; *aged*; *older* and *elderly*; *biomarker* and *biomarkers* and *biologic marker* and *biologic markers*. The descriptors *inflammatory*; *inflammatory marker* and *inflammatory marker*s; *inflammatory biomarker* and *inflammatory biomarkers* and *inflammatory cytokines*, which were not included in the Mesh and the DeCS but were widely cited in articles, were also used. In order to widen the search the key words *biomarkers*: *serum marker* and *serum markers* described in the Mesh were inserted. The above descriptors and key words were used independently or combined with the aid of the conjunctions: AND and OR and the truncated term *sarcopeni**. The search sequence was: [(inflammatory OR biomarker OR biomarkers OR biologic marker OR biologic markers OR inflammatory marker OR inflammatory markers OR inflammatory biomarker OR inflammatory biomarkers OR serum marker OR serum markers OR inflammatory cytokines) AND (sarcopenia OR sarcopenias OR sarcopeni*) AND (aged OR older OR elderly)]. The filters used in the searches were: studies in humans published in the last six years.

The initial selection of articles was carried out by two independent reviewers who evaluated the suitability of the articles from the information provided in the title and abstract. Subsequently, the same reviewers evaluated the complete texts of the articles and made the final selection, according to the established criteria, on an independent basis. For registration, a standardized form was used, through which the authors independently extracted the following data: author(s); year of publication; study design; population (gender, place of recruitment, age/age range, sample size, country of study); objective; methods for measuring diagnostic criteria for sarcopenia; inflammatory markers evaluated; synthesis of main results regarding sarcopenia; conclusion of the study; studies with sarcopenia and/or studies involving the diagnostic criteria of sarcopenia. In cases of divergences in the selection of article(s), the third author also read the text and opted for the inclusion or exclusion of the same(s).

The quality and risks of bias of the articles included in the review were analyzed through the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE)[11] which evaluates the quality of observational studies through 22 criteria. The STROBE was translated into Portuguese and validated by Malta et al.[12]. For the scoring of the articles the methodology of Mendes et al.[13], where each of 22 criteria receives a score of 0 to 1, was used. After evaluating all the criteria, each article received a score of 0 to 22 from each reviewer and the final grade was obtained from the mean. The score was transformed into a percentage, with articles with a percentage superior to 50% considered of good quality.

RESULTS

Figure 1 shows the article selection flowchart in detail. As can be seen, 154 articles were initially identified, of which only four, all in English, were included in the systematic review.

Table 1 presents the absolute and relative scores of the quality of the four articles identified from the criteria established by STROBE for observational studies. All the articles achieved a percentage superior to 50%, being considered of good quality and thus were included in the present review.

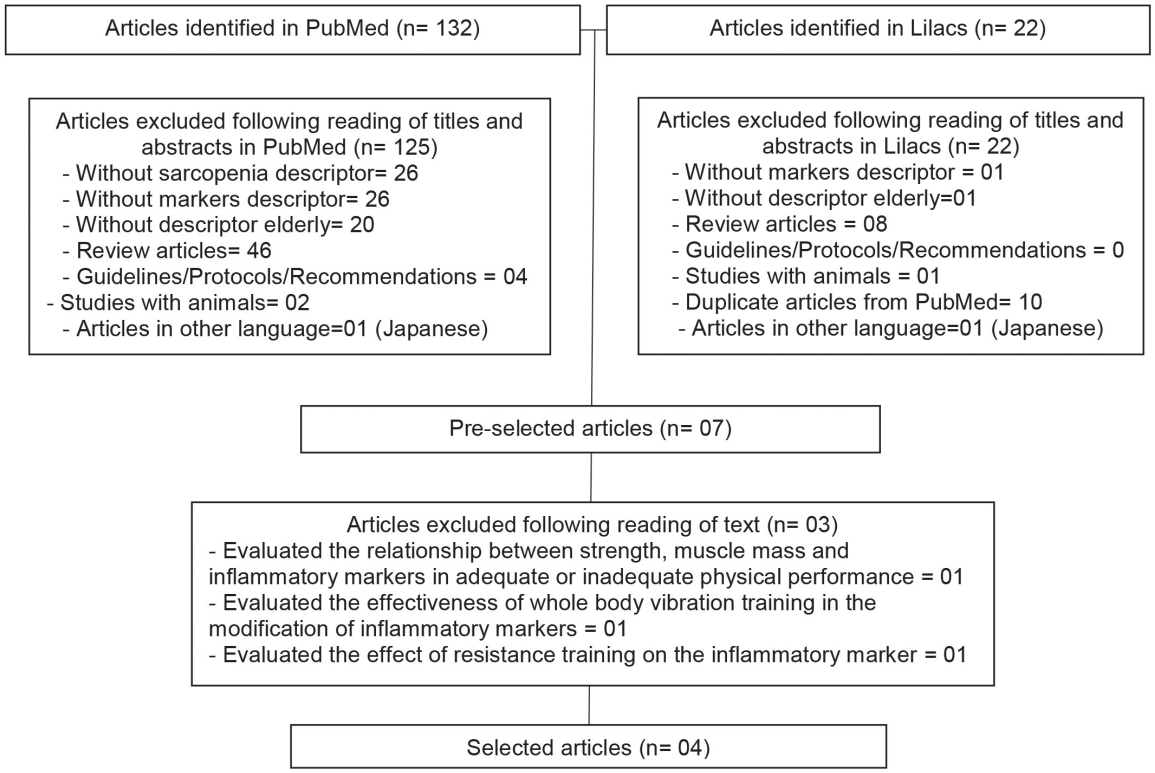

Figure 1. Flowchart of study selection. Santa Maria, Rio Grande do Sul, 2016.

Table 1: Score and quality percentage of included in accordance with STROBE. Santa Maria, Rio Grande do Sul, 2016.

Author(s)/year of publication	Quality of articles Score (%)
Hofmann et al., 2015[14]	18.5 (84.09)
Ogawa et al., 2012[15]	18.4 (83.63)
Chung et al., 2013[16]	19.1 (86.81)
Santos et al., 2014[17]	18.8 (85.45)

Regarding the outline of the included articles, all were observational studies, with one prospective[14] and three cross-sectional[15-17].

All the articles included described the relationship between inflammatory markers and the diagnostic criteria for sarcopenia. Hofmann et al.[14] and Ogawa et al.[15] evaluated this relationship with the three diagnostic criteria (muscle mass, muscular strength and physical performance) while Chung et al.[16] and Santos et al.[17] used the criterion of muscle mass. Only Hofmann et al.[14] evaluated this relationship with sarcopenia diagnosed according to the EWGSOP.

To evaluate muscle mass (MM), Hofmann et al.[14] and Ogawa et al.[15] used bioelectrical impedance analysis (BIA) as an instrument for assessing body composition, while Chung et al.[16] and Santos et al.[17] used Dual Energy X-ray (DEXA).

Muscle strength was assessed in two studies by the evaluation of hand grip strength (HGS) using dynamometry[14,15]. In addition to HGS, Hofmann et al.[14] verified muscle strength from isokinetic knee extension force using the Knee at 60º Isokinetic Peak Torque Test (PTE).

Physical performance was assessed by Hofmann et al.[14], using the Gait Speed Test (GS), the Six-Minute Walk Test and the Chair Stand Test. Ogawa et al.[15] used the GS test.

Eight inflammatory markers associated with sarcopenia and/or its diagnostic criteria were analyzed: growth differentiation factor (GDF-15); Insulin-like growth factor-1 (IGF-1); Follistatin; Activin A; and Myostatin, which make up the transforming growth factor beta (TGF-β) superfamily, in the study by Hofmann et al. Extracellular heat shock protein 72 (eHsp72) was analyzed by Ogawa et al[15]; Ferritin was evaluated in the study by Chung et al.[16] and C-reactive protein (CRP) was investigated by Santos et al.[17]. Ogawa et al.[15] also analyzed interleukin-6 (IL-6) combined with eHsp72 and its association with HGS.

In the study by Hofmann et al.[14], higher serum concentrations of GDF-15 and lower IGF-1 were found among elderly women regardless of whether they were classified as sarcopenic or non-sarcopenic. A significant correlation between GDF-15 and all the diagnostic criteria of sarcopenia, MM, muscle strength (HGS) and physical performance (Six-Minute Walk Test and GS) was also verified. IGF-1 and follistatin presented, respectively, a correlation only with the MM criteria and physical performance, evaluated by the Chair Stand Test. Activin A and myosin did not correlate with any of the diagnostic criteria for sarcopenia. No single or combined marker, meanwhile, reflected sarcopenia.

The study by Ogawa et al.[15] found that serum levels of eHsp72 were associated with all the diagnostic criteria for sarcopenia (low MM assessed by BIA, low muscle strength assessed by HGS, low physical performance assessed by GS), regardless of gender, age and incidence of pathologies, and a higher risk for low HGS when there were combined medium and high serum concentrations of IL-6 and eHsp72 adjusted for gender and age.

In the study by Chung et al.[16], elderly persons with low appendicular skeletal muscle mass (ASSM) had higher serum ferritin concentrations, although there was only a statistically significant difference among men. Santos et al.[17] found a correlation between CRP and fat free appendicular mass (FFAM) and higher serum concentrations of CRP in the elderly with low FFAM.

The characteristics of the articles, as well as the synthesis of the main results, are described in Chart 1.

Chart 1. Characterization of studies included in systematic review. Santa Maria, Rio Grande do Sul, 2016.

Autor(s)/ Year of publication/Study design	Population (gender, place of recruitment, age/age group, sample size, country) and objective	Methods for measuring diagnostic criteria for sarcopenia	Inflammatory markers evaluated	Synthesis of the main results regarding sarcopenia and conclusion of the study
Study with sarcopenia				
Hofmann et al.[14] Year: 2015 Design: Prospective study	Population: Young women living in the community - N= 17, Age= 22-28 years Elderly residents of long term care facilities - N= 81, Age= 65-92 years - Country= Austria Objective: Investigate whether serum concentrations of transforming growth factor beta (TGF-β) superfamily members such as GDF-15, myostatin, activin A or its follistatin antagonist, as well as IGF-1 differed between young and elderly women in different stages of dynapenia or with sarcopenia.	Muscle mass: - SMI was calculated through the MM/H^2 equation (kg/m^2) Method of measuring MM= BIA Cut-off point SMI= ≤6,75 kg/m^2 Muscle strength: - HGS= Evaluated by dynamometry Cut-off point HGS= considering best result. - PTE= evaluated knee extensor strength. Cut-off point PTE= ≤61.5 Nm Physical performance: - GS over ten-meter course=the time traveled at maximum speed over course of six meters was timed. Cut-off point= ≤1 m/s - Six Minute Walk Test= the maximum distance possible was travelled in six minutes. Cut-off point= distance in meters travelled in six minutes. - Chair stand test= sit and stand up from a chair as many times as possible in 30 seconds, Cut-off point= adequate when there was more than 50% control of the test. Women with low MM (SMI ≤6,75 kg/ m^2), combined with low muscle strength (PTE≤61.5 Nm) and/or low physical performance (GS) were considered sarcopenic.	- GDF-15 - IGF-1 - Follistatin - Activin A - Myostatin	GDF-15: the elderly had higher serum concentrations of GDF-15 (p<0.001) than the young women, regardless of the presence or absence of sarcopenia. GDF-15 exhibited a moderate negative correlation with MM (r= -0.320, p<0.01), a weak negative correlation with HGS (r= -0.290, p<0.01) and the 6-minute Walk Test 0.261, p<0.05) and a moderate positive correlation with *GS* (r=0.333, p<0.01) and age (r=0,388, p<0.01). IGF-1: The elderly had lower serum IGF-1 concentrations (p<0.001) than the young women, regardless of the presence or absence of sarcopenia. IGF-1 exhibited a moderate positive correlation with MM (r=0.365, p<0.01) and a moderate negative correlation with age (r= -0.359, p<0.01). In multiple linear regression analysis with the combination of markers, age and fat mass, IGF-1 was the only moderately predictive inflammatory marker for MM (+2.9%) Follistatin: follistatin presented a weak positive correlation with physical performance evaluated by the Chair Lift Test (r=0.220; p<0.05) among the elderly. No correlation was observed with age, MM, and physical performance. Activin A: there was no difference in serum concentration between elderly and young women, nor in terms of sarcopenia. No significant correlation was found with age and the diagnostic criteria for sarcopenia. Myostatin: There was no difference in serum concentration between elderly and young women, nor in terms of sarcopenia. No significant correlation was found with age and the diagnostic criteria for sarcopenia. Conclusion: the isolated or combined presence of inflammatory markers does not reflect sarcopenia in elderly women.

to be continued

Continued from Chart 1

Autor(s)/ Year of publication/Study design	Population (gender, place of recruitment, age/age group, sample size, country) and objective	Methods for measuring diagnostic criteria for sarcopenia	Inflammatory markers evaluated	Synthesis of the main results regarding sarcopenia and conclusion of the study
Studies involving the diagnostic criteria of sarcopenia				
Ogawa et al.[15] Year: 2012 Design: Cross-sectional study	Population: Elderly persons living in the community - N= 652 - N women= 382, N men= 270, Age= 65-96 years - Country= Japan Objective: evaluate serum concentrations of eHsp72 protein in elderly subjects and investigate their potential interaction with sarcopenia components (muscle strength, physical performance, and skeletal muscle mass).	Muscle mass: - Measurement method= BIA. Muscle strength: - Measurement method=dynamometry to identify HGS. Physical performance: - Measurement method=GS carried out on a flat course of 11 meters (the speed and number of steps were evaluated at the midpoint of 5 meters of the course).	- eHsp72	eHsp72: individuals with higher serum concentrations of eHsp72 (higher tercile) had significantly lower mean MM, HGS and GS levels than individuals with lower serum levels of eHsp72 ($p<0.01$). In the analysis of multiple logistic regression, adjusted for age, gender and incidence of pathologies, it was observed that the highest tercile of eHsp72 maintained a significant association with the lower terciles of MM (OR 2.72; CI 95%=1.21-6.16; $p<0.01$), HGS (OR 2.60; CI 95%=1.17-5.81; $p<0.01$) and low GS (OR 1.82; CI 95%=1.03-3.20; $p<0.01$). And there was a greater risk for low HGS when there were combined mean and high serum concentrations of IL-6 and eHsp72 adjusted for age and gender (OR 3.31; CI 95%=1.48-7.41). Conclusion: the presence of higher serum concentrations of eHsp72 was associated with changes in the diagnostic criteria for sarcopenia, which is a potential marker of sarcopenia.
Chung et al.[16] Year: 2013 Design: Cross-sectional study	Population: elderly persons in the community - N women= 1693, N men=1250, Age=60 years or older - Country= Korea Objective: to analyze the relationship of body composition with several factors for cardiometabolic risk in an elderly population participating in the Korea National Health and Nutrition Survey (KNHANES)	Muscle mass: - ASMM calculated through ASMM/W (kg) equation Method of measuring ASMM= DEXA Cut-off point= sarcopenia when % ASMM was 32.5% for men and 25.7% for women	- Ferritin	Ferritin: elderly persons with low ASMM had higher serum ferritin concentrations than the elderly with adequate ASMM, but with a statistically significant difference only among men ($p<0.001$). Conclusion: in relation to body composition, elderly persons with sarcopenic obesity presented greater resistance to insulin and the presence of more cardiometabolic risk factors than with obese or sarcopenic elderly persons.

to be continued

Continued from Chart 1

Autor(s)/ Year of publication/Study design	Population (gender, place of recruitment, age/age group, sample size, country) and objective	Methods for measuring diagnostic criteria for sarcopenia	Inflammatory markers evaluated	Synthesis of the main results regarding sarcopenia and conclusion of the study
Santos et al.[17] Year: 2014 Design: Cross-sectional study	Population: Post-menopausal women living in the community - N= 149, Age= mean of 67.17(±6.12) years - Country= Brasil Objective: To examine the association of sarcopenia and sarcopenic obesity with cardiometabolic risk factors in postmenopausal women.	Muscle mass: - FFAM= calculated by FFAM/H(m)^2 equation Measurement method of FFAM= DEXA Cut-off point: sarcopenia when low FFAM (<5.45 kg/m^2)	- CRP	CRP: Elderly patients with low FFAM had lower serum CRP concentrations when compared to the elderly with normal FFAM (p <0.05). There was also a positive and weak correlation between low FFAM and CRP (r=0.27, p<0.01). Conclusion: The criteria used to define sarcopenia were not associated with cardiometabolic risk.

BIA=bioelectrical impedance; DEXA=dual energy X-ray; EHsp72=extracellular heat shock protein; HGS=hand grip strength; GDF-15=growth differentiation factor; CI=Confidence Interval; IGF-1=insulin-like growth factor-1; SMI=skeletal mass index; FFAM/H(m)^2=fat free appendicular mass divided by height in meters squared; MM=muscle mass; MM/H (kg/m)^2=muscle mass divided by height squared in meters; Kg/m^2=kg per square meter; M/s=meters per second; FFAM=fat free appendicular mass; ASMM=appendicular skeletal muscle mass; ASSM/W (kg)=appendicular skeletal muscle mass divided by weight in kilograms; N=sample number; Nm=Newtons-meter; OR=Odds Ratio (chances); CRP=C-reactive protein; PTE=Knee at 60º Isokinetic Peak Torque Test; TGF-β=transforming growth factor beta; GS=gait speed.

DISCUSSION

The present article presents a systematic review of the relationship of inflammatory markers with sarcopenia and/or its components. Only four original articles that tackle this issue were identified, emphasizing the incipient nature of the theme. In this review, it was observed that only the study by Hofmann et al.[14] analyzed the association of inflammatory markers with sarcopenia (diagnosed according to the EWGSOP)[2]. The researchers included five markers in their analyzes: GDF-15[14], IGF-1[14], follistatin[14], activin A[14], and myostatin[14]. None of these markers were associated with sarcopenia. Ogawa et al.[15], Chung et al.[16], Santos et al.[17] and Hofmann et al.[14] investigated the association of inflammatory markers with the diagnostic criteria for sarcopenia, and identified eight inflammatory markers (eHsp72[15], ferritin[16], CRP[17], GDF-15[14], IGF-1[14], follistatin[14], activin A[14] and myostatin[14]). Of these, it was verified that six markers (eHsp72[15], ferritin[16], CRP[17], GDF-15[14], IGF-1[14] and follistatin[14]) exhibited an association with the diagnostic criteria for sarcopenia.

Regarding the quality of the articles, according to the STROBE criteria, the observational studies included presented percentages over 80%, which reflect their high quality, as the STROBE instrument assists in verifying the methodological transparency of a study[11].

The cytokine TGF-β and the components of its superfamily (activin A, myostatin, GDF-15 and follistatin), IGF-1 protein and the chemokine eHsp72, act in the immunologic system[18], in stress[19], in lymphoproliferative disorders [20] and especially in the inflammatory process[19,21,22]. They are considered markers of the inflammatory process of chronic non-communicable diseases such as heart disease[20], rheumatoid arthritis[18,22], systemic sclerosis[18] and osteoarthrosis[18].-

GDF-15 is poorly produced by the tissues, but its excessive production causes deleterious effects directly on muscle, which results in the reduction of muscle mass[23]. Bloch et al.[19] observed the association between higher serum concentrations of GDF-15 and the reduction of muscle mass in a study of elderly patients in intensive care. These results reinforce those obtained by Hofmann et al.[14] who found a negative correlation between GDF-15 and muscle mass, HGS and gait speed (p<0.01).

IGF-1 acts as a positive regulator of muscular growth[23]. However, the aging process triggers the decline of IGF-1[6]. Hofmann et al.[14] verified that elderly women, regardless of whether they were classified as sarcopenic or non-sarcopenic had lower serum IGF-1 concentrations (p<0.01) than young women. Follistatin, an antagonist of activin A and myostatin, as well as IGF-1, also acts as a positive regulator of muscle growth[23]. Activin A and myostatin, meanwhile, when excreted excessively, cause muscular atrophy and impairment, respectively, in muscle regeneration[23]. Hofmann et al.[24] when carrying out resistance training with 41 elderly women evaluated at the beginning and at the third and the sixth month of training, observed that higher serum follistatin concentrations were associated with longer training times (p=0.008), but found no changes in the serum concentrations of activin A and myostatin. These results are similar to those found by Hofmann et al.[14].

At high concentrations EHsp72 reflects the level of cellular stress that contributes to a decrease in muscle mass[21]. Ogawa et al.[15] observed the association between increased eHsp72 and low muscle mass. Similarly, Perreault et al.[21], in a study with 26 elderly subjects undergoing 16 weeks of physical training, found that the reduction of serum concentrations of eHsp72 increased the amount of muscle mass (p=0.03), due to the decrease of the inflammatory process.

The association between the higher serum concentrations of the inflammatory markers GDF-15 and eHsp72 and low HGS, investigated by Hofmann et al.[14] and Ogawa et al.[15], respectively, corroborate with the results of Baylis et al.[25], which found an association between greater Inflammatory load and low HGS (p=0.001). Ogawa et al.[15] reported a higher risk for low HGS among elderly persons (OR 3.31, CI 95% = 1.48-7.41) with combined medium and high serum concentrations of eHsp72 and IL-6. IL-6 is considered one of the most important inflammatory mediators in the aging process and is positively

correlated with a reduction of lean mass[26], functional decline[26] and mortality[26]. A study by Puzianowska-Kuźnicka et al.[27] with 3,496 elderly persons, found that serum IL-6 concentrations increase with age and are associated with poorer physical performance and greater cognitive deficit (p<0.001).

Ferritin, considered an acute phase protein, is involved in the systemic inflammatory process[28] and oxidative stress[29]. Similar to Chung et al.[16], who observed higher serum ferritin concentrations among sarcopenic elderly persons, Kim et al.[30], when evaluating the association between serum ferritin and sarcopenia in 952 men and 1380 elderly women (60 years and older), also identified the presence of higher serum ferritin concentrations among sarcopenic women (p<0.001).

Higher serum concentrations of CRP are associated with disability and mortality, an increased risk of low muscle strength, and are correlated with lower muscle mass in older individuals[31-33]. Legrand et al.[34], in a study with 567 elderly persons, found that high CRP values were associated with a low score in the Short Physical Performance Battery (SPPB) that evaluates physical performance.

It should be noted that elderly individuals with preserved muscle mass may present alterations in inflammatory markers. This is because *inflammaging* (the chronic and low-grade systemic inflammation common in aging) is due to changes in the immune system, inflammatory mediators, changes in body composition (increase in adipose tissue), and acute and chronic diseases that independently increase the inflammatory markers[35].

Finally, the use of different methods and cut-off points to diagnose and measure the diagnostic criteria for sarcopenia can be considered limiting factors of this systematic review, which may overestimate or underestimate the prevalence of the same. Another limiting factor was the populational heterogeneity of the studies, with populations composed of men and women in different countries, which made it impossible to ascertain the inflammatory profile of a specific population.

CONCLUSION

Four articles were included in this systematic review. Only one evaluated sarcopenia diagnosed in accordance with the EWGSOP Consensus.

None of the five inflammatory markers studied (GDF-15, IGF-1, follistatin, activin A and myostatin) were found to be associated with sarcopenia.

Of the eight inflammatory markers studied (GDF-15, IGF-1, follistatin, activin A, myostatin, eHsp72, ferritin and CRP), only two (activin A and myostatin) were not associated with the diagnostic criteria for sarcopenia.

In this context, the scarcity of studies on the relationship between inflammatory markers and sarcopenia and its diagnostic criteria points out the need for further research on the subject, in order to contribute to a deeper understanding of the pathophysiological mechanisms of sarcopenia, as well as the establishment of inflammatory markers in the diagnosis, intervention and accompanying of this condition.

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