Examining the Prevalence of Sarcopenic Obesity and its Association with Frailty in Community-Dwelling Middle Aged and Older Females

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Abstract

Sarcopenic obesity is the co-existence of low muscle mass and excess fat mass and can place frail individuals at increased risk of disability, chronic diseases, and mortality. Due to a lack of standardized criteria, the prevalence of sarcopenic obesity varies across definitions. The purpose of this cross-sectional study is to determine the prevalence of sarcopenic obesity using different published diagnostic criteria and its association with frailty in a population of Manitoba females, aged 55 years and older. Further, the prevalence of sarcopenic obesity and its association with frailty with the addition of handgrip strength (HGS) stratified by Body Mass Index (BMI) to sarcopenic obesity diagnostic criteria was examined to determine if the inclusion of HGS as part of existing diagnostic criteria strengthens the association between sarcopenic obesity and frailty. Finally, the relationship between BMI, waist circumference (WC) and frailty were explored to determine if a U-shaped relationship was observed in the study cohort. The relationship between Percentage Body Fat (%BF), WC, and frailty was also explored to determine if %BF exhibits a similar relationship with frailty compared to BMI. Diagnostic criteria were selected for analysis if body composition was measured using Bioelectric impedance analysis (BIA) and sex-specific (female) cut-off values were included. 20 diagnostic criteria were considered for analysis. The association between frailty and sarcopenic obesity was determined using a Spearman's correlation. An unpaired t-test was performed in any models that were correlated in order to compare the frailty index scores between sarcopenic obesity levels. The prevalence of sarcopenic obesity ranged from 0% - 39%. Sarcopenic obesity was only significantly associated with frailty when using weight-adjusted or unadjusted diagnostic criteria, whereas there was no difference in frailty index scores in height-adjusted definitions. The addition of HGS lowered the prevalence of sarcopenic obesity in this cohort, ranging from 0%-5% and did not change the association with frailty in any criteria that did not already demonstrate an association. Lastly, a U-shaped relationship was not observed in this cohort, however, frailty index scores were higher in those within the top two BMI (30.1-35 kg/m^2 and $>35kg/m^2$) and top two %BF (37-41.7% and >41.8%) categories in the high WC group. This research expands the understanding of current sarcopenic obesity published diagnostic criteria and their association with frailty. The research revealed that weight-adjusted sarcopenic obesity criteria detect differences in frailty. Further, this thesis demonstrated that the inclusion of HGS in criteria did not improve the association between sarcopenic obesity and frailty. Finally, the cohort did not

have a U-shaped relationship between frailty and BMI, or frailty and %BF in either low or high WC groups.

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Chapter 1: Literature Review

1.1 Aging Population

By 2025, it is projected that people over the age of 55 will account for over a third of the Canadian population (Statistics Canada, 2020). With this aging population and prolonged life expectancy, the prevalence of chronic diseases and age-related health deficits will increase. Currently, people 55 years and older make up make up 30% of the total Canadian population, yet half of the healthcare costs are used towards caring for this population (Chen et al, 2018). This places pressure of the Canadian healthcare system to provide the services these individuals need. However, not everyone of the same chronological age has the same health status (Howlett et al., 2014). This is due to individual variations of biological aging and the factors that place people at higher risk of chronic disease and adverse health outcomes.

1.2 Theories of Aging

There are many theories that have been proposed to explain the process of aging; however, contemporary biological theories of aging in humans have two main categories: 1) programmed theory; and 2) damage theory. The programmed theory states that aging follows a biological timeline that is regulated by changes in gene expression that influence the body systems for maintenance, growth, repair and immune responses (Jin et al, 2010). This theory implies that over time our bodies are naturally programmed to decline, in which our immune systems, endocrine systems and DNA are all pre-set to cause aging. Whereas the damage theory emphasizes environmental harm to living organisms that cause collective destruction at various levels as the cause of aging (Li et al., 2017).

1.3 Defining Frailty

Frailty has been proposed as a way to measure the accumulation of damage over time. While there is currently no operational definition for frailty, there is a general consensus that frailty is a state of increased physiological vulnerability resulting from reduced reserve and loss of physiological function across multiple systems, resulting in the reduced ability to cope with

normal or minor stressors (Clegg, 2014). Frailty has also been described as deficits to physiological systems and the inability to maintain homeostasis when challenged by stressors (Bray et al., 2016). Although frailty is observed across the life span, older individuals have the highest prevalence of frailty (Kehler et al., 2017a). As chronological age increases, we become less resilient and eventually are unable to maintain proper functional capacity, resulting in physical frailty.

1.4 Frailty Assessments

Frailty status predicts incidence of falls, worsening mobility, and activity of daily living (ADL) function, hospitalization, and death (Clegg, 2014). Therefore, being able to accurately measure frailty is important for clinical practice. The general principle of frailty assessments is to account for how smaller sub-cellular deficits scale to become clinically evident. Many investigators have proposed tools to evaluate frailty across various systems and have included a range of variables that can be measured (Clegg et al., 2013; Fried et al., 2001; Howlett et al., 2014; Searle et al., 2008). Different assessment tools are employed depending on the context, ease of administration and purpose for the assessment (Buta, et al., 2017; Oviedo-Briones et al., 2020). Buta, et al. (2017), identified 67 frailty instruments used across various clinical and research settings and found that the most frequently cited instruments are the Fried Frailty Phenotype (FP) and the Rockwood Frailty Index (FI).

Fried et al., (2001) defines frailty as a distinct clinical syndrome and uses the "cycle of frailty" to explain multifaceted loss of physiologic reserve. Since physiologic reserve cannot be measured, the phenotypic criteria serve as surrogates to observe the reduction in adaptive capacity. The FP uses five criteria including: exhaustion, weight loss, diminished activity, slow walking speed and weak grip strength. Fried et al, (2001) assessed exhaustion with the Center for Epidemiologic Studies – Depression Scale. Unintentional weight loss was assessed with the use of a questionnaire asking "In the last year, have you lost more than 10 pounds unintentionally (i.e., not due to dieting or exercise)?" If yes, then the participant was given a point for this criterion. Physical activity levels were assessed with the Minnesota Leisure Time Activity questionnaire. The FP criteria also stratified by age with sex-specific cut-offs and those below three or more standardized cut points are deemed to be frail (Fried et al., 2001). Thus, an

individual is deemed pre-frail if they present with one to two out of five and robust if they present with none of the above mentioned criteria (i.e. 0 = robust; 1-2 = pre-frail; ≥ 3 = frail). (Fried et al., 2001). The FP is most commonly used to assess risk for adverse health outcomes such as death, institutionalization, and falls (Buta,et al., 2017).

The FI was developed by Rockwood, et al. (2011), to measure frailty as the proportion of age-related health deficits by counting the number of deficits accumulated, including diseases, physical and cognitive impairments, psychosocial risk factors, and common geriatric syndromes. If an individual accumulates a pre-determined number of deficits from an index, they are deemed to be frail (Searle et al., 2008). An individual can accumulate many deficits before they present with physical signs of frailty. A FI can be created with pre-existing health data; however, there is a standard procedure to follow when selecting deficits to include. For variables to be included in an FI as deficits, they must satisfy five criteria: 1) the variables must be deficits associated with health status. Greying hair and wrinkling skin are age-related and cannot be included. 2) The prevalence of a variable must generally increase with age. 3) The chosen deficits must not saturate too early. For example, changes in eye site are nearly universal by age 55. 4) Overall, selected deficits must make up a frailty index that covers a range of body systems. 5) If a single frailty index is to be used serially on the same people, the deficits used on the index need to remain the same for each assessment (Searle et al., 2008). A FI typically contains about 30 or more deficits, and a greater number of included deficits is associated with a more accurate frailty score (Searle et al., 2008).

1.5 Sarcopenia and Frailty

Maintaining the health of the musculoskeletal system plays an important role in maintaining functional independence, reducing the risk of falling, and overall wellbeing (Clegg et al., 2013). It has been noted that loss of muscle strength and power is just as detrimental to an individual's health status as changes to muscle mass. Fried et al., (2001) includes weakness within the "cycle of frailty" model and relates the five criteria to loss of muscle mass and factors related to the development of poor muscle mass. In individuals younger than 50, muscle catabolism and anabolism are balanced so one does not supersede the other. This is regulated by the brain, endocrine and immune systems and is influenced by nutrition and physical activity levels.

Failing neural and endocrine systems and disease will hamper homeostatic balance and contribute to muscle loss. Inflammatory cytokines including IL-6, and TNFα are responsible for the breakdown of muscle tissue into amino acids to be used for energy (Chen et al., 2014). This process can become destructive when there is an overactive inflammatory response leading to loss of muscle mass and strength, causing a decline in functional ability such as low gait speed and grip strength (Clegg, 2014; Evans et al., 2021). Aging greatly influences the balance between muscle catabolism and anabolism. With age the balance is disturbed causing a shift towards increasing catabolism and subsequently to a loss of muscle mass. The Baltimore Longitudinal Study of Aging (BLSA) investigated age-associated skeletal muscle changes in the upper extremities. It reported that there was only a modest (10%) decrease in muscle size between 24 and 50 years old; whereas, muscle mass, strength and power all declined significantly beginning at age 50 in both women and men (Metter et al., 1997). In fact, people between the ages of 50 and 80 years can experience an annual 1% -2% decrease in muscle cross sectional area after their fifth decade (Buch et al., 2016; Cruz-Jentoft et al., 2019; Metter et al., 1997). This gradual age-related decline in muscle mass may eventually lead to sarcopenia.

Sarcopenia is a progressive skeletal muscle disorder associated with increased likelihood of adverse outcomes, such as falls, fractures, physical disability and mortality (Cruz-Jentoft et al., 2019). In the most recent European Working Group on Sarcopenia in Older People (EWGSOP) consensus statement, sarcopenia is now considered a muscle disease, with both low muscle strength (function) and low muscle mass (quantity) as the principal determinants (Cruz-Jentoft et al., 2019). Progressive losses of skeletal muscle mass, strength and power are closely associated with aging and are considered a key components of frailty (Clegg, 2014; Fried et al., 2001). Over time, the human body is unable to maintain muscle mass and disease can accelerate the progress of muscle loss. This can lead to a reduced aerobic capacity (decreased VO_{2max}), resting metabolic rate, and muscle strength and power (Fried et al., 2001). All these factors contribute to an overall decline in total energy expenditure and further reductions in muscle mass (Fried et al., 2001). It should be noted that there is a differentiation between normal age-related loss in muscle mass and strength and unhealthy reductions that impair physical capacity (Buch et al., 2016). Although loss of muscle mass is an universal problem as people age, negative consequences such as increased health care costs, physical impairment, disability, falls, fractures and frailty are more prevalent when a concerningly low amount of muscle loss is reached (Purcell et al., 2021).

Therefore, being able to measure muscle strength and mass is essential to identify those who would most benefit from intervention.

1.5.1 Measuring Sarcopenia

Diagnostic methods for measuring sarcopenia in clinical practice include approaches such as dual energy x-ray absorptiometry (DEXA) scan, Bioelectrical Impedance Analysis (BIA), handgrip strength (HGS), gait speed and functional fitness tests. The DEXA scan is considered a gold standard method to measure body composition. For example, de Campos et al., (2020) used DEXA data to diagnosis sarcopenia using relative muscle mass in older adults. Participants were classified as sarcopenic when the appendicular skeletal muscle mass index (ASMMI) was<7.26 kg/m^2 for men, and <5.45 kg/m^2 for women (de Campos et al., 2020). Muscle mass is correlated with body size; therefore, individuals with a larger body size typically have larger muscle mass. Thus, quantifying muscle mass must be adjusted for body size in different ways. This is usually done by dividing muscle mass by height squared, weight or body mass index. There is an ongoing debate about the preferred relative adjustment methods and whether the same method can be applied across a variety of populations (Cruz-Jentoft et al., 2019).

BIA is another method that measures whole and segmental body composition, thorough estimating body composition based on whole-body electrical conductivity and demonstrated excellent agreements in middle aged females for measurement of lean mass (kg) (intraclass correlation (ICC) $\geq$0.96 p<0.001), fat mass (ICC $\geq$ 0.93 p<0.001) and body fat percentage (ICC $\geq$ 0.88 p<0.001) compared to DEXA (Ling et al., 2011). BIA has advantages in terms of its simplicity, thus making it an attractive tool to measure body composition especially in older adults and less mobile subjects. It is also relatively inexpensive compared to the other techniques and does not expose subjects to radiation (Ling et al., 2011). Since estimates of muscle mass differ with different instrument brands, variables such as age, ethnicity and other related discrepancies between patients should be considered (Cruz-Jentoft et al., 2019). Additionally, BIA measurements can be influenced by hydration status and are marginally affected by metallic implants. Therefore proper pre-assessment instructions need to be followed and consider needs to be taken when assessing individuals with joint replacements and/or pacemakers (Ling et al., 2011). For affordability and portability, BIA determinations of muscle mass may be preferable to

DEXA; however, more information is needed to validate BIA for specific populations (Cruz-Jentoft et al., 2019).

DEXA and BIA only assess body composition, and it has been demonstrated that muscle strength, along with muscle mass, is also impacted by aging (Cruz-Jentoft et al., 2019; Evans et al., 2021; Roh & Choi, 2020). Muscle strength declines with age due to a reduction in muscle fibre size and number, particularly type II fibres, and reduced synthesis of muscle protein (Evans et al., 2021). In 2018, the revised EWGSOP updated the definition of sarcopenia aimed to improve the early detection and treatment of sarcopenia and its risk in clinical practice. EWGSOP adopted low muscle strength as another principal determinant of sarcopenia. The EWGSOP used grip strength to define low muscle strength, and suggested measures of physical performance, such as gait speed and/or Timed Up and Go test, can be used to assess the physical presentations of sarcopenia (Roh & Choi, 2020). R. Rikli, (1999), developed a function fitness test for older adults which six items and one alternative that are designed to assess physical function. These items include lower and upper body strength, lower and upper body flexibility, aerobic endurance, and agility/dynamic balance. Body mass index was also assessed as an estimation of fat mass. Upper and lower body strength assessments include an arm curl and 30-second chair stand test, respectively.

Measuring grip strength is simple and inexpensive. Low grip strength is a powerful predictor of poor patient outcomes such as longer hospital stays, increased functional limitations, poor health-related quality of life and death (Cruz-Jentoft et al., 2019; Syddall et al., 2003). Accurate measurement of grip strength requires a calibrated handheld dynamometer under well-defined test conditions with interpretive data from appropriate reference populations. Grip strength serves as a reliable surrogate for upper body strength. Due to ease of use, grip strength is advised for routine use in hospital practice, clinical research settings, and in community health (Cruz-Jentoft et al., 2019). A dynamometer is validated and widely used tool for measuring grip strength, and there are different brands that have been used throughout research and healthcare settings. Purcell et al., (2021) defined low HGS as < 16 kg in females and < 27 kg in males, based upon the highest measure from the dominant hand, in a sample of 11,655 $\geq$ 65 years old from the Canadian Longitudinal Study of Aging (CLSA). These cut-offs were based on the updated recommendations by the EWGSOP (Cruz-Jentoft et al., 2019). Fried et al., (2001)

created grip strength criteria to screen for low upper body muscle strength, termed 'weakness' that was adjusted for by sex and body mass index. These cut-offs can be found in Table 1. The 30-second chair stand test can be used as a measure of lower body strength (Cruz-Jentoft et al., 2019; R. Rikli, 1999) by counting how many times a patient can rise and sit from a chair over a 30-second interval. Since the chair stand test requires both strength and endurance, this test is a qualified but convenient measure of strength (Cruz-Jentoft et al., 2019; Syddall et al., 2003).

1.6 Body Mass Index (BMI)

Body mass index (BMI), is a measure of weight adjusted for height, calculated as weight in kilograms divided by the square of height in meters (kg/m^2). BMI is a simple, inexpensive, and non-invasive estimation of body fat and with access to the proper equipment, it can be routinely measured and calculated with reasonable accuracy (Centers of Disease Control (CDC), 2011). The World Health Organization (WHO) uses BMI cut-offs to define underweight ($\leq$ 18.5 kg/m^2), normal weight (18.5 – 24.9 kg/m^2), overweight (25– 29.9 kg/m^2) and obese ($\geq$30 kg/m^2) (CDC, 2011; Roh & Choi, 2020). Currently, 28.0% of Canadians over the age of 55 have a BMI in the obese category and another 40.3% have a BMI in the overweight category (Purcell et al., 2021).

1.6.1 BMI and Frailty

Research has identified a U-shaped, see Figure 1, relationship between BMI and frailty, indicating that overweight (25– 29.9 kg/m^2) and underweight ($\leq$ 18.5 kg/m^2) individuals are more likely to be frail compared to their normal weight peers (Buch et al., 2016; Hanlon et al., 2018; Hubbard et al., 2010). That data suggests that BMI is associated with risk of frailty and mortality, yet a higher BMI seems to have a protective quality against drastic declines in health status (Lee et al., 2014). The obesity paradox describes the protective effects an overweight or obese individual may have against frailty and mortality (Lee et al., 2014). A possible explanation is that individuals who are overweight may have a higher reserve capacity than those who are normal and underweight. This allows overweight people to attenuate loss of body mass and improve their chances of recovery. The Health and Retirement Study (HRS), a prospective multistage cohort study in the United States examined the relationship between frailty and body weight in a sample of men and women aged 51 – 61 years old (Bowen, 2012). Bowen, (2012)

found that those who were overweight (25– 29.9 kg/m^2) or obese (≥30 kg/m^2) and either pre-frail or frail had a 27% ($p \leq 0.05$) reduced instrumental activities of daily living (IADL) disability rate, compared to underweight (≤ 18.5 kg/m^2) pre-frail individuals, which were associated with a 51% ($p \leq .001$) increase in IADL disabilities. This protective quality could be due to excess adipose tissue that prevents the rapid loss of weight, which is often characteristic associated with frailty. In addition, frail older adults with excess body weight have higher bone mineral density than their underweight peers, reducing their risk for osteoporosis, injurious falls, hip fracture and reduces thing risk for disability (Bowen, 2012). Although there may be this protective quality of higher body mass, there are drawbacks to having increased adiposity.

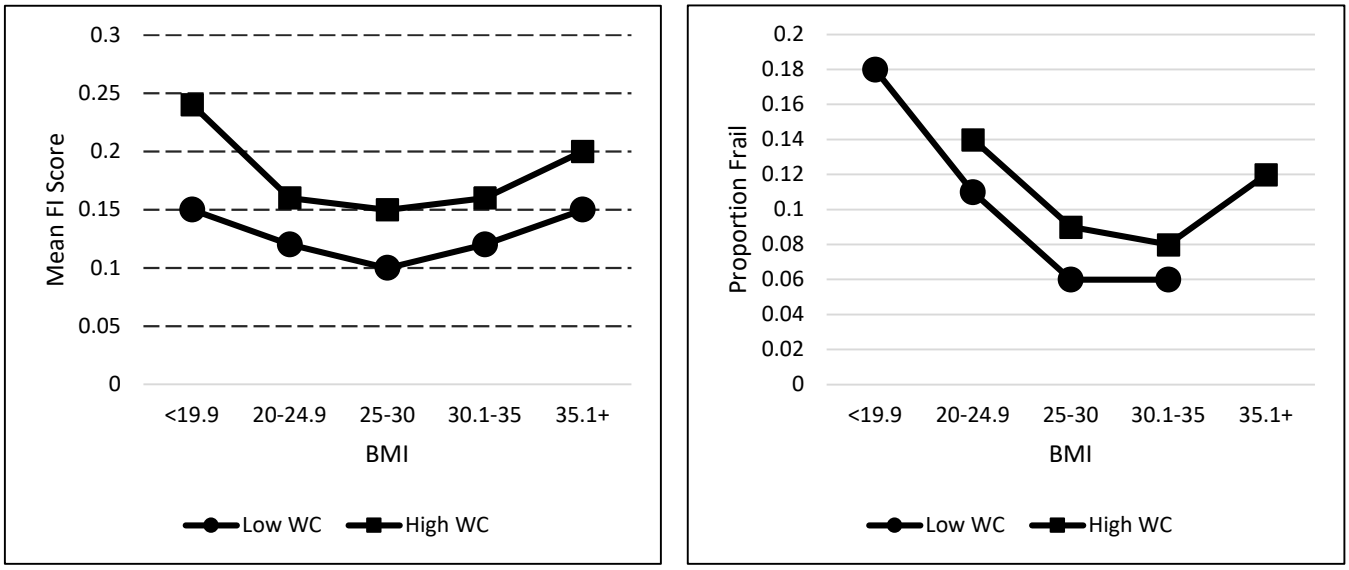

Figure 1: Adapted from left to right, mean frailty index (FI) score and Fried frailty score in the English Longitudinal Study of Aging Wave 2 by BMI and Waist Circumference from Hubbard (2009).

1.6.2 BMI and body fat percentage

Since weight and height cannot differentiate between fat and lean body mass, BMI is a surrogate measure of body fat (CDC, 2011). It has been demonstrated that percent body fat (%BF) varies between subjects with the same BMI. Romero-Corral et al., (2008) found that subjects with a BMI of 25 kg/m^2 had %BF distributions of 13.8 to 35.3% and 26.4 to 42.8% in

male and female participants, respectively. Traditional BMI cut-offs alone may not be appropriate in geriatric populations (Purcell et al., 2021), due to age-related loss of height caused by vertebral body compression and altered femoral neck angle (Evans et al., 2021) and increased tendency toward central adiposity. These factors alter the relationship between weight and BMI, therefore %BF has also been used by investigators to define overweight and obesity thresholds, with median %BF being used in studies with subjects over the age of 55 years old (Baumgartner, 2000; de Campos et al., 2020).

1.7 Sarcopenic Obesity

Although an overweight or obese individual may have a protective quality against drastic declines in health status, they are still more likely to be frail compared to normal weight populations. This may be due to excess adiposity potentially masking the loss of muscle mass while total weight appears to remain relatively stable (Barazzoni et al., 2018; Tomlinson et al., 2016). The shift is body composition leading to increased fat mass combined with a reduction in muscle mass as been referred to as sarcopenic obesity, see Figure 2 (Baumgartner, 2000). There is currently no widely accepted definition for sarcopenic obesity, although the term describes the coexistence of both obesity characterized as excess body fat mass and sarcopenia characterized low muscle mass. Baumgartner, (2000) was the first to utilize the term sarcopenic obesity and described it as a silent, progressive condition, closely associated with aging.

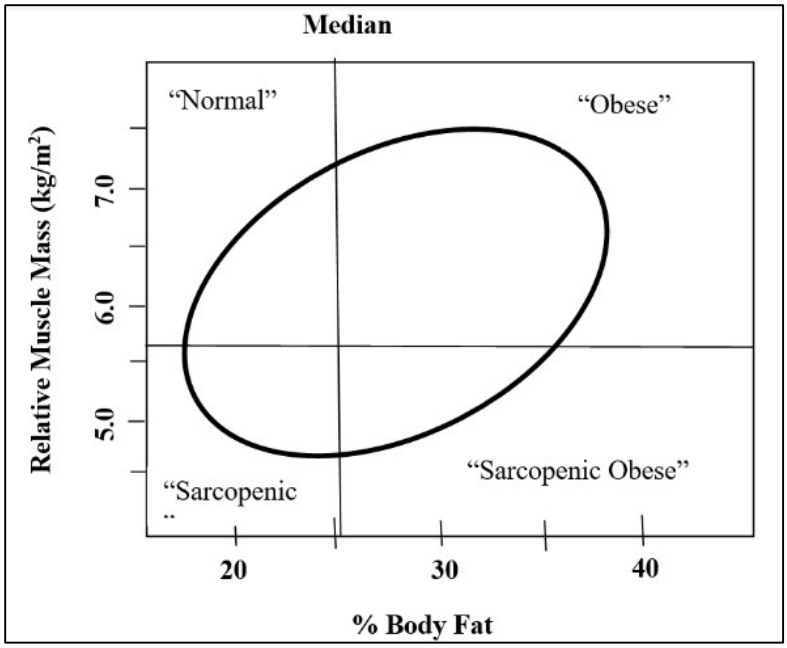

Figure 2: Adapted from Theoretical relationship between Relative Skeletal Muscle Mass Index and %Fat, illustrating the approach used to categorize subjects as "Normal," "Obese," "Sarcopenic," and "Sarcopenic-Obese from Baumgartner (2000).

Definitions of sarcopenic obesity have varied throughout the literature for the past two decades, causing difficulties in making an accurate diagnosis, performing epidemiologic studies, and developing treatment strategies (Purcell et al., 2021; Roh & Choi, 2020). Purcell et al., (2021) investigated the prevalence of sarcopenic obesity using different published definitions in older Canadian adults. In their research, Purcell et al., (2021) applied a total of 29 different diagnostic criteria, resulting in sarcopenic obesity prevalence ranging from 0%-85% (Purcell et al., 2021). What has been consistent within the literature is that sarcopenic obesity has a 10%-30% higher prevalence in people over the age of 55 years compared to individuals between the ages of 18-55 years old, since both risk and prevalence increase with age (Baumgartner, 2000; Cruz-Jentoft et al., 2019; Purcell et al., 2021).

The prevalence of sarcopenic obesity varies depending upon what definition is used and ethnicity of the population. The US National Health and Nutrition Examination Survey (NHANES) examined 4,984 people aged 60 years and older and reported a prevalence of 12.6% in males and 33.5% in females The prevalence of sarcopenic obesity increased with age,

reaching up to 48.0% and 27.5% in females and males respectively, in those 80 years and older (Purcell et al., 2021). In a Brazilian study of 270 non-institutionalised older people, mean age 77.5 years, the prevalence of sarcopenic obesity was 29.3% but contrary to the NHANES study, the prevalence was higher among men at 65.3% than among women at 34.6% (de Campos et al., 2020; Evans et al., 2021; Purcell et al., 2021). This could be due to the difference in the evaluation methods, criteria, or ethnic differences of the participants. Data from the Korean NHANES reported a prevalence of 7.8% for men and 9.6% for women among 1,583 older people, with a mean age of 72.8 years (Evans et al., 2021; Purcell et al., 2021). Recently 119,494 participants, aged 18-90 years were included in the Dutch Lifelines cohort study which showed an overall prevalence of 0.9% for men and 1.4% for women (Purcell et al., 2021). Age was a significant determinant of sarcopenic obesity with a prevalence of 0.4% for those aged 20-29.9 years, 2.6% in those aged 60-69.9 years, 4.2% in those aged 70-79.9 years and 12.2% in those aged 80-89.9 years. Females had a higher prevalence than men in all age groups especially in those aged 80-89 at 16.7% compared to 6.3% in males (Evans et al., 2021; Purcell et al., 2021).

The prevalence also varies greatly depending upon the threshold's investigators use. Baumgartner was also the first to define low muscle mass index as less than two standard deviations below a sex-specific reference for a young, healthy population and a median body fat percentage (Baumgartner, 2000; Stenholm et al., 2008). In a study analysing the prevalence of sarcopenic obesity in non-institutionalized older adults in Brazil, de Campos et al., (2020), defined body composition thresholds to diagnose sarcopenic obesity. A DEXA scan was used for the evaluation of body composition, which is a gold standard method since it provides the greatest precision and validity. For women, the diagnosis of sarcopenic obesity was defined as a body fat percentage $\geq$ 38% and appendicular skeletal muscle mass index of < 5.45 kg/m^2. For men, a fat percentage $\geq$ 27% and appendicular skeletal muscle mass index <7.26 kg/m^2 was defined as sarcopenic obesity. This study evaluated 270, predominantly female, older adults, with a mean age of 77.5 years. The prevalence of sarcopenic obesity of the entire study population was 29.3%, with the prevalence in men being 65.3% and among women was 34.6%. Among the individuals with sarcopenic obesity, more than a third had low gait speed and reduced hand-grip strength (de Campos et al., 2020). Other studies have also observed significantly lower grip strength in individuals who are sarcopenic and obese compared to those who are obese (Baumgartner, 2000). The cycle of reduced functional capacity caused by slower

gait leads to a reduction in overall energy expenditure, reduced muscle mass and strength, increased fat mass, and reduced aerobic capacity which all further contribute to increased walking time in older adults (Fried et al., 2001).

Sarcopenic obesity has been associated with poor quality of life and all-cause mortality. In a meta-analysis of prospective cohort studies, sarcopenic obesity defined by mid-arm muscle circumference and muscle strength criteria, significantly increased the risk of mortality at 1.46 hazard ratio (HR; 95% confidence interval (CI) 1.23–1.73) and 1.23 HR (95% CI,1.09–1.38), respectively (Tian & Xu, 2016).This negatively affects individuals and the healthcare system since sarcopenic obesity is associated with an increased likelihood of developing insulin resistance, and cardiovascular disease (CVD) compared to patients who are only sarcopenic or obese (Buch et al., 2016). In the Cardiovascular Health Study (CHS), 3,366 community-dwelling men and women aged 65 and older were followed for eight years. Sarcopenic obesity, defined according to muscle strength, was modestly and independently associated with increased CVD risk at 1.23 hazard ratio (HR) (95% CI 0.99–1.54), and congestive heart failure at 1.42 HR (95% CI 1.05–1.91) (Buch et al., 2016). One explanation is that obesity exacerbates sarcopenia, increases the infiltration of fat into muscle, lowers physical function and increases risk of cardiovascular disease and mortality (Cruz-Jentoft et al., 2019). When examining the relationships between body composition, physical function, and quality of life in community-dwelling older adults, obese individuals older than 65 years of age were matched for age and sex with nonobese frail and non-frail nonobese subjects. Although the obese subjects had the largest amount of lean tissue, when it was expressed as a percentage of body weight, the percentage of lean tissue mass was the lowest in the obese older adult group compared to the other groups (Jarosz & Bellar, 2009). This is reflected in the fact that sarcopenic obese individuals are two to three times more likely to report the development of instrumental ADL disability than those who were obese and not sarcopenic, sarcopenic and not obese, or of normal body composition(Jarosz & Bellar, 2009). Instrumental ADLs (IADL) include activities such as using the telephone, getting groceries, and making meals and other activities that are key for independent living (Jarosz & Bellar, 2009). In contrast to this Hirani et al., (2017) found no association between sarcopenic obesity and IADL disability after five year follow up in a male only sample. This is due to different definitions and measurement criteria used.

Currently sarcopenic obesity is measured by criteria characterizing sarcopenia and obesity separately. DEXA, CT and MRI have all been used to qualify body composition and are reliable ways to obtain a diagnosis (Baumgartner, 2000; de Campos et al., 2020). However, these imaging technologies and equipment are not portable or as easily accessible, which is important in large epidemiological studies. Therefore, more research is needed to define sarcopenic obesity using other technologies that are safe, inexpensive and widely available including anthropometry (such as skinfolds or waist circumference), BIA and ultrasound (D. C. Lee et al., 2016).

1.7.1 Sarcopenic obesity and frailty

Only within the last two decades has the impact of sarcopenic obesity on frailty been highlighted. Hirani et al., (2017) examined the longitudinal association between sarcopenic obesity and frailty in males which examined baseline measures, two and five year follow ups. They found that both sarcopenic obesity and appendicular lean mass (ALM): BMI - fat percentage interaction were both associated with increased risk of frailty (2.00 OR 95% CI 1.42-2.82) after full adjustment of confounders and covariates of clinical significance. There have not been any other longitudinal studies showing the temporal relationship between continuous measures of body compositions and/or sarcopenic obesity and frailty (Hirani et al., 2017). Buch et al., (2016) examined the synergistic effects of sarcopenia and obesity on frail individuals and the development of metabolic syndrome. After adjusting for age, sex, smoking status, alcohol consumption and physical activity level, the prevalence of the metabolic syndrome was still higher in the sarcopenic obese group (odds ratio (OR)=8.28; (95% CI 4.45–15.4), compared to the obese only (OR=5.51 (95% CI 2.81– 10.8) or sarcopenic only groups (OR=2.64 (95% CI 1.08–6.44). Older frail adults with sarcopenic obesity also experience considerable weakness from a decrease in muscle mass and strength along with the need to move a greater body weight. This shift in body composition contributes to the low physical activity (Clegg et al., 2013) observed in older frail individuals. Further understanding about the association of sarcopenic obesity and frailty, knowledge about the prevalence of sarcopenic obesity in various clinical settings and patient subgroups, its clinical impacts in patient risk stratification, and effective prevention and treatment strategies are critical to address. Although it is clear that sarcopenic obesity is an issue for frail individuals, it can go under-reported. This may be due to the fact that

no guidelines or established cut-offs that are generalizable to all populations exist to guide the detection of sarcopenic obesity and that no consensus definition for sarcopenic obesity exists.

Chapter 2: Statement of Problem and Methods

2.0 Statement of Problem

Both obesity and sarcopenia have independent associations with functional status, disability, and falls (Baumgartner, 2000). Sarcopenic obesity also has the greatest impact on overall health (Baumgartner, 2000). Therefore, the proper identification of those who develop sarcopenic obesity will help guide practitioners to direct resources to those who would most benefit from intervention to preserve muscle mass while ensuring healthy weight management. Further, the co-existence of sarcopenic obesity and frailty places individuals at greater risk of disability and chronic conditions since they are more vulnerable to declines in health status. Due to varying diagnostic criteria for sarcopenic obesity utilized throughout the literature, a streamlined way to clinically assess sarcopenic obesity has not emerged. Population specific screening is important to develop criteria for all subgroups; therefore, evaluating the prevalence of sarcopenic obesity in a sample of Manitoba females by using current published diagnostic criteria with tools that are simple and cost effective may improve frailty risk screening. Furthermore, preserving physical function is critical for those who are most at risk of becoming frail. Sarcopenic obese individuals have increased body fat, which can mask muscle composition changes (e.g., sarcopenia). Thus, individuals with sarcopenic obesity may not be recognized as frail unless muscle strength or functional performance is tested. The EWGSOP published the most recent consensus on sarcopenia screening in 2019. Based upon evidence from previous investigations, the EWGSOP recommended that HGS be used as a function performance measure for sarcopenia along with compositional criteria. However, only some of the diagnostic criteria for sarcopenic obesity published prior to 2019 include HGS with compositional outcomes as a metric. Therefore, it is not well understood if HGS is an appropriate addition to all diagnostic criteria for sarcopenic obesity. Additionally, it is worth noting that the EWGSOP only recommended a single HGS cut-off (≤16kg for females). This recommendation does not align with current understanding that an increase in body size equates to an increase in absolute strength. Measures of HGS stratified by BMI have been put forth by Fried et al., (2001). Therefore, the addition of a stratified HGS functional measure along with the compositional criteria may be useful when screening for sarcopenic obesity and identify those who are most frail.

2.1 Objectives:

The five objectives of this thesis are to:

1) determine the prevalence of sarcopenic obesity using different published diagnostic criteria in a population of Manitoba females, 55 years of age and older.

2) determine if frailty index scores differ between those who are sarcopenic obese and those who are not for each diagnostic criterion.

3) determine if there is an association between sarcopenic obesity and frailty using the diagnostic criteria examined.

4) determine if the U-shaped relationship between frailty and BMI is observed in the cohort and use %BF as another measure of adiposity.

5) determine the prevalence of sarcopenic obesity using different compositional criteria with the addition of handgrip strength stratified by body mass index.

2.2 Hypotheses:

1) Those with sarcopenic obesity will be more frail compared to those who are not.

2) There will be a correlation between sarcopenic obesity and frailty.

3) The addition of handgrip strength as a criterion for sarcopenic obesity will strengthen the association with frailty.

2.3 Methods

2.3.1 Research Design

The present study will utilize a secondary, cross-sectional analysis of baseline data from the Women's Advanced Risk-Assessment in Manitoba (WARM) Hearts research study, which is a prospective, observational study that will recruit about 1000 women to test a novel prognostic tool for identifying women at risk of cardiovascular disease (ClinicalTrials.gov Identifier: NCT03938155). This cross-sectional study will analyze the first 430 subjects that completed data

collection. This study protocol was reviewed by both the University of Manitoba Health Research Ethics Board and the St. Boniface Hospital Research Review Committee. A detailed protocol paper describing the WARM Hearts cohort is being prepared for publication. This study will follow Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines designed for cohort, case-control and cross-sectional studies (von Elm et al., 2014) and the Sex and Gender Equity in Research (SAGER) reporting guidelines (Heidari et al., 2016). A checklist for each of these guidelines can be found in Appendix A and Appendix B, respectively.

2.3.2 Participants

Study recruitment was done through convenient sampling methods including newspaper advertisements, media advertising and radio interviews. Those who were interested in participating in the cohort study were instructed to contact the research team by telephone or email and eligibility screening was done during this contact. The inclusion criteria were:

1. Women aged 55 years and older; and,
2. Resident of Manitoba and must have a Manitoba Personal Health Information Number (PHIN).

Exclusion criteria:

1. Previous hospitalization or diagnosis of ischemic heart disease, acute myocardial infarction, stroke, percutaneous coronary intervention, coronary artery bypass surgery, congestive heart failure, or peripheral artery disease; and,
2. Previous participation in "The Assessment of Large and Small Artery Elasticity for the Early Detection of Cardiovascular Disease (NCT02863211)" research study

If eligible, participants were scheduled for two appointments at the (1) Active Living Centre, University of Manitoba, Winnipeg and their second appointment at the (2) Albrechtsen St. Boniface General Hospital Research Centre, Winnipeg, Manitoba. Data collection was performed at both appointments which were approximately 8-14 days apart and take-home

questionnaires were provided at the first appointments and completed forms were returned at the second appointment.

2.3.3 Study procedure

Participants were given pre-appointment instructions prior to the first appointment including no food, smoking or caffeine for 2 hours and no alcohol or strenuous exercise within 6 hours of the appointment. Prior to the second appointment participants were also given fasting instructions including no food, alcohol, or caffeine for 8 hours prior to the appointment. These instructions minimized the influence that caffeine, nicotine, alcohol consumption and exercise may have on study outcomes.

2.3.4 Anthropometry and body composition

Height was measured with a portable Seca stadiometer to the nearest 0.5cm without shoes. In accordance with the Canadian Society for Exercise Physiology (CSEP) guidelines waist circumference (WC) was measured at the arc of the superior iliac crest to the nearest 0.5cm on the skin, if possible (Canadian Society for Exercise Physiology (CSEP), 2020). Body composition (muscle mass (kg), segmental lean analysis (kg), and %BF) and weight were assessed by the InBody 270 which uses bioelectrical impedance analysis (Ling et al., 2011). Participants were asked to remove shoes, socks and clean their hands and feet before stepping onto the InBody platform. Arms and legs were slightly spread so that they were not in contact with other parts of the body.

2.3.5 Handgrip strength

Handgrip strength was used as a proxy measure of muscle strength and was assessed using a JAMAR ®handheld dynamometer (Clegg et al., 2013). Handgrip strength is a simple measure that is widely used in clinical practice and research and strongly correlates with whole-body muscle strength (Cruz-Jentoft et al., 2010). Participants sat in a chair with their elbows flexed at a 90º angle and were instructed to hold and squeeze a handheld dynamometer as hard as

possible. This procedure was performed in both hands twice and measured to the nearest 2 kg of force for each hand, with the highest value being considered for analysis. Previous research has discovered the 'strength to size ratio' indicating that as people increase their weight, their absolute muscle strength also increases (Moreira et al., 2016; Purcell et al., 2021), therefore, handgrip strength was stratified by BMI, based of the cut offs by Fried et al., (2001) in this cohort study (Table 1).

Table 1: Fried handgrip strength cut-offs stratified by BMI for females

BMI (kg/m^2)	**Grip strength (kg)**
≤ 23	≤ 17
23.1-26	≤17.3
26.1-29	≤ 18
> 29	≤21

Adapted from Criteria used to define frailty from Fried et al. (2001).

2.3.6 Sarcopenic obesity diagnostic criteria

Twenty-six (26) published diagnostic criteria were identified, based upon the critical appraisal by Donini et al., (2020), that measure body composition using BIA. Six were excluded due to lack of sex-specific criteria and the inclusion of measurements not collected as a part of WARM Hearts. The remaining 20 published diagnostic criteria were considered for this analysis. Criteria were included if body composition was assessed using BIA and if the study included female subjects with female specific criteria. Prevalence of sarcopenic obesity was first determined for each diagnostic criterion. Any criteria with 0% prevalence in this cohort was excluded from further analysis.

2.3.7 Frailty status

The FI approach uses a proportion of health deficits out of the total number of health variables considered to calculate frailty as a continuous variable (Appendix C). This study used a modified version of the 42 item WARM Hearts FI (Rose et al., 2021). The FI for this project will

exclude handgrip strength, WC, fat mass (FM) and/or fat free mass (FFM) from the original FI, if any of these variables are used in the diagnostic criteria. For criteria that does not include any of the mentioned variables, those variables will be considered in the FI score calculation. The FI was created according to guidelines described by Searle et al., (2008). Briefly, the guidelines include: (1) deficits must have an association with health status; (2) deficit prevalence should increase with chronological age; (3) health deficits should not saturate too early; (4) deficits should cover a broad range of physiological systems; (5) frailty indices should be kept the same if planned to be used on the same cohort at multiple time points.Variables for the FI were collected at both the first and second appointments and through the take-home questionnaires.

2.3.8 Statistical Analysis

Statistical analyses were performed using SPSS software, Version 26.0 (IBM Corporation, Armonk, NY, USA). Descriptive statistic presented as mean ± standard deviation for continuous variables and as number (n) and percent of the population (%) for categorical variables. Prevalence of sarcopenic obesity is reported as the proportion of the population that meet the cut-offs thresholds. Prevalence is reported for each published diagnostic criteria, with sarcopenic obesity being a binary outcome (yes or no). An unpaired t-test examined the mean FI scores between those who are classified as sarcopenic obese and those who are not (reference) for each diagnostic criteria. Spearman's correlation was used to examine the association between frailty, measured by the FI as a continuous variable, and sarcopenic obesity. The same analyses were preformed with the addition of handgrip strength. One-way ANOVA analysis was used to examine the differences between mean FI scores by BMI and for FI scores by WC. While both a one-way and a two-way ANOVA was used to examine the differences between FI scores and %BF as well as FI scores and WC. Tukey post-hoc accounted for multiple comparisons. An unpaired t-test was used to determine if frailty index scores differ between those who are classified as sarcopenic obese and those who are not in any models that demonstrate a correlation and Bonferroni correction will be used to account for multiple comparisons. A p value of ≤ 0.05 will be deemed statistically significant. Correlation categories will be as follows; 0 indicates no correlation; > 0 - 0.1 indicates a poor correlation; 0.1 - 0.3 indicates a fair correlation; 0.3 - 0.6

indicates a moderate correlation; 0.6 - 0.8 indicates a strong correlation and > 0.8 indicates a very strong correlation (Akoglu, 2018).

Chapter 3: Results

3.0 Cohort Characteristics

Four-hundred and thirty (430) females had complete data and were included in this thesis cohort. The mean age of the cohort was 65 ± 6 years, 430 (100%) had an assigned sex at birth as female and 429 (99.8%) self-identified as women and one self-identified as non-binary. All 430 participants were included in the analyses. 415 (96.5%) self-identified as Caucasian. Due to the low number of participants that self-reported as other than Caucasian, different ethnicities are not being reported in this thesis. Body composition and anthropometric measures in this cohort consisted of a mean BMI of 26 ± 5.0 kg/m^2; mean height was 163.5 ± 5.5 cm; mean weight was 70.5 ± 13.7 kg, and mean WC was 91.5 ± 12 cm. Mean fat mass was 25.4 ± 9.7 kg; mean body fat percentage was 35.0 ± 7.5 % and mean skeletal muscle mass was 24.5 ± 3.5 kg. The mean resting systolic and diastolic blood pressure of the cohort was 124 ± 15 mmHg and 74 ± 9 mmHg, respectively. The mean resting heart rate was 68 ± 10 bpm. Mean HDL cholesterol was 1.73 ± 0.46 mmol/L; the mean LDL cholesterol level was 3.45 ± 0.90 mmol/L, and total cholesterol was 5.29 ± 0.95 mmol/L. Mean fasting glucose was 5.81 ± 0.64 mmol/L and mean triglycerides was 1.12 ± 0.53 mmol/L. For this cohort, the mean Framingham Risk Score (FRS) 10-year risk was 6.94 ± 4.19, with 63 (15%) participants having an elevated CVD risk (FRS ≥ 10%). The mean FI score was 0.13 ± 0.07, with 160 categorized as robust, 245 as pre-frail and 25 as frail. Participants who lived alone accounted for 21.3% of the cohort and participants who had completed post-secondary education composed 78.6% of the cohort. Ex or current smokers composed of 45.2% of the cohort. Cohort characteristics for the overall cohort are included in Table 2.

Table 2: Cohort Characteristics

Characteristic	**Total Cohort n= 430**
Age (years)	65 ± 6
Assigned Sex at Birth, female (%)	430 (100%)
Gender Identity, n=woman (%)	429 (99.8%) *

Race, n=Caucasian (%)	415 (96.5%)
Height (cm)	163.5 ± 5.5
Weight (kg)	70.5 ± 13.7
Waist Circumference (cm)	91.5 ± 12
BMI (kg/m^2)	26 ± 5
Fat Mass (kg)	25.4 ± 9.7
Body Fat Percentage (%)	35.0 ± 7.5
Skeletal Muscle Mass (kg)	24.5 ± 3.5
Systolic Blood Pressure (mmHg)	124 ± 15
Diastolic Blood Pressure (mmHg)	74 ± 9
Resting Heart Rate (bpm)	68 ± 10
HDL cholesterol (mmol/L)	1.73 ± 0.46
LDL cholesterol (mmol/L)	3.45 ± 0.90
Total cholesterol (mmol/L)	5.29 ± 0.95
Triglycerides (mmol/L)	1.12 ± 0.53
Fasting Glucose (mmol/L)	5.81 ± 0.64
WH Frailty Index Score	0.13 ± 0.07
FRS 10 year risk (%)	6.94 ± 4.19
Living Alone, n (%)	90 (21.3%)
Ex/Current Tobacco Use, n (%)	184 (45.2%)
Post-secondary Education, n (%)	337 (78.6%)

Continuous variables expressed as Mean ± standard deviation; categorical variables expressed as n (%). ***BMI****, Body Mass Index;* ***FRS****, Framingham Risk Score;* ***HDL****, High-Density Lipoprotein;* ***LDL****, Low-Density Lipoprotein;* ***WH****, WARM Hearts. *One participant identified as*

non-binary. Due to the low number of participants that self-reported as other than Caucasian, different ethnicities are not being reported in this thesis.

3.1 Prevalence of Sarcopenic Obesity

To determine the prevalence of sarcopenic obesity, twenty published diagnostic criteria were identified. Criteria were considered if body composition measures were taken using bioelectric impedance analysis and had sex-specific (female) criteria. A list of the published diagnostic criteria is reported in Table 3. The prevalence of sarcopenic obesity ranged from 0% based on the criteria from Bahat et al., (2021), Balachandran et al. (2014), De Rosa et al. (2015), Muscariello et al. (2016), Siervo et al. (2012), and Srikanthan et al. (2010) up to 39% based upon the criteria reported by Chen et al. (2017).

Table 3: Prevalence of sarcopenic obesity with different diagnostic criteria

Authors	Sarcopenia criteria	Obesity criteria	Functional criteria	Prevalence in the WARM Hearts Cohort (%)
Aibar-Almazan et al. (2018)	hASMI $\leq$ 6.42 kg/m^2	%BF $\geq$ 35%	HGS $\leq$ 20kg	5%
Baek et al. (2013)	hASMI below the 50th percentile ($\leq$ 6.56 kg/m^2)	BMI $\geq$ 25 kg/m^2	-	16%
Bahat et al. (2021)	hSMI $\leq$ 7.4 kg/m^2	BMI $\geq$ 30 kg/m^2	HGS $\leq$ 22kg	0%
Balachandran et al. (2014)	hASMI $\leq$ 6.76 kg/m^2	BMI $\geq$ 30 kg/m^2	HGS $\leq$ 20kg	0%
Batsis et al. (2014)	hSMI $\leq$ 6.75 kg/m^2	%BF $\geq$ 38%	-	0.23%
Biolo et al. (2015)	FM/FFM Ratio $\leq$ 0.4	BMI $\geq$ 25 kg/m^2	-	0.5%
Chen et al. (2017)	wASMI $\leq$ 25.6%	BMI $\geq$ 25 kg/m^2 and WC $\geq$ 88 cm	-	39%
Davison et al. (2002)	SMI $\leq$ 6.52 kg/m^2	%BF in the highest two quintiles ($\geq$ 36.7%)	-	0.23%

De Rosa et al. (hSMI) (2015)	a: 5.76 to 6.75 kg/m^2 b: ≤ 5.75 kg/m^2	a: BMI ≥ 30 kg/m^2 b: BMI ≥ 30 kg/m^2	-	a: 0% b: 0%
De Rosa et al. (wSMP) (2015)	a: 22.2% to 27.6% b: ≤ 22.1%	a: BMI ≥ 30 kg/m^2 b: BMI ≥ 30 kg/m^2	-	a: 2.6% b: 0%
Ishii et al. (2016)	hASMI ≤ 5.8 kg/m^2	%BF in the highest quintile (≥ 41.6%)	HGS ≤ 20kg	0.5%
Joppa et al. (2016)	FFMI < 10th percentile of the reference value	FMI 90th percentile of the reference values	-	2.3%
Kemmler et al. (2016)	hASMI in the lowest quintile of the sample	BMI ≥ 30 kg/m^2 and ≥ 35% BF	HGS ≤ 20kg	0%
Lee et al. (2016)	wSMI≤ 32.2	%BF within two highest quintiles (≥ 36.7%)	HGS ≤ 18kg	22%
Lu et al. (2013)	wSMI two or more standard deviations below mean (≤ 27.1)	BMI ≥ 25 kg/m^2	-	1.6%
Moreira et al. (2016)	hSMI ≤ 20th percentile of the sample (≤ 5.99 kg/m^2)	WC ≥ 88cm	-	7%
Munoz-Arribas et al. (2013)	SM ≤ two lowest quintiles of the sample (≤ 11.5 kg)	%BF in the two highest quintiles (≥ 36.7%)	-	16%
Muscariello et al. (2016)	hSMI two standard deviations below the mean of young reference group	1) BMI ≥ 30.0 kg/m^2, 2) WC ≥ 88.0 cm, 3) FM% ≥ 35.0%, and 4) FMI ≥ 9.5 kg/m^2	-	0%
Pedrero-Chamiz et al. (2015)	hRMM within the lower two quintiles (≤ 8.74 kg/m^2)	%BF within the two highest quintiles (≤ 36.7%)	-	12%
Siervo et al. (2012)	hSMI two standard deviations below the mean of young reference group (≤ 6.76 kg/m^2)	1) BMI ≥ 30.0 kg/m^2, 2) WC ≥ 88.0 cm, 3) FM% ≥ 35.0%, and 4) FMI ≥ 9.5 kg/m^2	-	0%
Srikanthan et al. (2010)	hSMI ≤ 22%	BMI ≥ 30 kg/m^2	-	0%

Prevalence expressed as precent (%). ***BMI****, Body Mass Index;* ***ASM****, Appendicular Skeletal Mass;* ***ASMI****, Appendicular Skeletal Mass Index;* ***%BF****, Percentage Body Fat;* ***WC****, Waist Circumference;* ***FM****, Fat Mass;* ***FFM****, Fat Free Mass;* ***SM****, Skeletal Mass;* ***SMI****, Skeletal Mass*

Index; ***RMM****, Relative Muscle Mass;* ***SMP****, Skeletal Mass Percentage;* ***h****, height-adjusted;* ***w****, weight-adjusted;* ***kg****, kilograms;* ***m****, meters.*

3.2 Difference in frailty index scores

Unpaired t-tests were performed for each diagnostic criteria to determine if the frailty index scores differed between those categorized as sarcopenic obese and the reference group who were not categorized as sarcopenic obese for each published diagnostic criteria. Table 4 summarizes the group comparison data and reports the t-statistic; whereas Appendix D presents bar graphs of the grouped data for each diagnostic criteria. Statistically significant differences were found between the sarcopenic obese group and the reference group for five diagnostic criteria, namely the criteria published by Chen et al. (2017), De Rosa et al., (2015), Lee et al., (2016), Lu et al., (2013), Muñoz-Arribas et al., (2013). The FI scores were not different for any of the remaining nine published diagnostic criteria for sarcopenic obesity verse reference groups.

Table 4: Difference in frailty index scores

Authors	Reference (not sarcopenic obese)	Sarcopenic obese	t(df)	p-value
Aibar-Almazan et al.	0.13 ± 0.06 (n=407)	0.15 ± 0.07 (n=23)	$t(429)=1.50$	0.12
Baek et al.	0.13 ± 0.07 (n=363)	0.13 ± 0.05 (n=67)	$t(429)=0.12$	0.90
Batsis et al.	0.13 ± 0.06 (n=429)	0.10 ± 0.00 (n=1)	$t(429)=0.47$	0.63
Biolo et al.	0.13 ± 0.06 (n=428)	0.09 ± 0.01 (n=2)	$t(429)=0.77$	0.44
Chen et al.	0.11 ± 0.05 (n=261)	0.16 ± 0.07 (n=169)	$t(429)=6.62$	<0.001 *
Davison et al.	0.12 ± 0.06 (n=429)	0.10 ± 0.00 (n=1)	$t(429)=0.47$	0.63
De Rosa et al. (wSMP)	0.13 ± 0.06(n=419)	0.22 ± 0.069 (n=11)	$t(429)=4.29$	<0.001 *
Ishii et al.	0.13 ± 0.06 (n=425)	0.13 ± 0.02 (n=5)	$t(429)=0.15$	0.88
Joppa et al.	0.13 ± 0.06 (n=420)	0.15 ± 0.06 (n=10)	$t(429)=1.03$	0.30
Lee et al.	0.13 ± 0.06 (n=393)	0.17 ± 0.07 (n=37)	$t(429)=2.60$	0.009 *
Lu et al.	0.13 ± 0.06 (n=423)	0.26 ± 0.06 (n=7)	$t(429)=5.06$	<0.001 *
Moreira et al.	0.13 ± 0.07 (n=399)	0.14 ± 0.04 (n=31)	$t(429)=0.79$	0.42
Munoz-Arribas et al.	0.12 ± 0.07 (n=363)	0.15 ± 0.05 (n=67)	$t(429)=2.07$	0.03 *
Pedrero-Chamizo et al.	0.13 ± 0.07 (n=379)	0.11 ± 0.05 (n=51)	$t(429)=0.973$	0.33

Frailty index scores as continuous variables expressed as Mean ± standard deviation (n=sample size) compared using unpaired t-test; ***t****, t-statistic;* ***df****, degrees of freedom; * denotes statistical significance.*

3.3 Association between sarcopenic obesity and frailty

Spearman's correlation was performed for each diagnostic criteria to determine if there is an association between sarcopenic obesity and frailty. Correlation coefficients ranged from poor (>0 – 0.1) to fair (0.1 – 0.3), Table 5 summaries these findings. Statically significant correlations were observed for five of the published diagnostic criteria, specifically the criteria published by Chen et al. (2017), De Rosa et al., (2015), Lee et al., (2016), Lu et al., (2013), and Muñoz-Arribas et al., (2013). These are the same criteria that had statistically significant differences between FI scores. No correlations were identified for the other nine published criteria. Scatter plots of this data for each criteria is reported in Appendix E.

Table 5: The association between frailty and different sarcopenic obesity diagnostic criteria

Authors	Sarcopenia criteria	Obesity criteria	Functional criteria	Correlation coefficient	p-value
Aibar-Almazan et al.	hASMI $\leq$ 6.42 kg/m^2	%BF $\geq$ 35%	HGS $\leq$ 20kg	0.07	0.10
Baek et al.	hASMI below the 50th percentile ($\leq$ 6.56 kg/m^2)	BMI $\geq$ 25 kg/m^2	-	0.03	0.45
Batsis et al.	hSMI $\leq$ 6.75 kg/m^2	%BF $\geq$ 38%	-	0.04	0.39
Biolo et al.	FM/FFM Ratio $\leq$ 0.4	BMI $\geq$ 25 kg/m^2	-	0.04	0.33
Chen et al.	wASMI $\leq$ 25.6%	BMI $\geq$ 25 kg/m^2 and WC $\geq$ 88 cm	-	0.29	<0.001 *
Davison et al.	hSMI $\leq$ 6.52 kg/m^2	%BF in the highest two quintiles ($\geq$ 36.7%)	-	0.02	0.57
De Rosa et al. (wSMP)	wSMP $\leq$ 27.6%	BMI $\geq$ 30 kg/m^2	-	0.19	<0.001 *
Ishii S et al.	hASMI $\leq$ 5.8 kg/m^2	%BF in the highest quintile ($\geq$ 41.6%)	HGS $\leq$ 20kg	0.01	0.85
Joppa et al.	FFMI < 10th percentile of the reference value	FMI 90th percentile of the reference values	-	0.05	0.24
Lee et al.	wSMI $\leq$ 32.2	%BF within two highest quintiles ($\geq$ 36.7%)	HGS $\leq$ 18kg	0.12	0.009 *
Lu et al.	wSMI two or more standard deviations below mean ($\leq$ 27.1)	BMI $\geq$ 25 kg/m^2	-	0.18	<0.001 *
Moreira et al.	hSMI $\leq$ 20th percentile of the	WC $\geq$ 88cm	-	0.06	0.16

	sample (≤ 5.99 kg/m^2)				
Munoz-Arribas et al.	SM ≤ two lowest quintiles of the sample (≤ 11.5 kg)	%BF in the two highest quintiles (≥ 36.7%)	-	0.13	0.005 *
Pedrero-Chamizo et al.	hRMM within the lower two quintiles (≤ 8.74 kg/m^2)	%BF within the two highest quintiles (≥ 36.7%)	-	0.08	0.06

***BMI**, Body Mass Index; **ASM**, Appendicular Skeletal Mass; **ASMI**, Appendicular Skeletal Mass Index; **%BF**, Percentage Body Fat; **WC**, Waist Circumference; **FM**, Fat Mass; **FFM**, Fat Free Mass; **SM**, Skeletal Mass; **SMI**, Skeletal Mass Index; **RMM**, Relative Muscle Mass; **SMP**, Skeletal Mass Percentage; **h**, height-adjusted; **w**, weight-adjusted; **kg**, kilograms; **m**, meters; * denotes statistical significance.*

3.4 BMI and frailty

One-way ANOVA analysis was performed to examine the differences between FI scores across five BMI categories, <19.9 kg/m^2, 20-24.9 kg/m^2, 25-30 kg/m^2, 30.1-35 kg/m^2, and >35.1 kg/m^2 for the full cohort. A Tukey's post-hoc was used to identify differences between specific means when the ANOVA was significant. Statistically significant differences in FI scores were identified (p=<0.001) between the highest quintile (>35.1 kg/m^2) and the lower four quintiles (Table 6), as well as the second highest quintile (30.1-35 kg/m^2) and the bottom three quintiles.

Participants were then separated into two WC groups, either low WC (<88cm) or high WC (>88cm) and categorized into the same five BMI categories. Two BMI categories in the low WC level, 30.1-35 kg/m^2 and >35.1 kg/m^2 and one BMI category in the high WC level, <19.9 kg/m^2 , did not contain any subjects (n=0), and were excluded. Given this unequal distribution of participants within the various levels of BMI, an analysis approach was developed to examine the low WC group data independently from the high WC group. To do this, a one-way ANOVA was used to examine the differences between FI scores in only the low WC group across the three levels of BMI categories (<19.9 kg/m^2, 20-24.9 kg/m^2, and 25-30 kg/m^2). This approach was needed because there were no participants (n=0) categorized into the 30.1-35 kg/m^2 or >35.1 kg/m^2 groups. No statistically significant differences were identified between BMI categories in the low WC group. A similar approach was then utilized to examine difference in FI scores in only the high WC group across four BMI categories (20-24.9 kg/m^2, 25-30 kg/m^2, 30.1-35 kg/m^2, and >35.1 kg/m^2). This approach was needed because the <19.9 kg/m^2 category did not

contain any subjects (n=0). Significant differences were identified (p=<0.001) between FI scores, where the highest quintile (>35.1 kg/m^2) differed from three quintiles (20-24.9 kg/m^2, 25-30 kg/m^2, 30.1-35 kg/m^2). As well as the second highest quintile (30.1-35 kg/m^2) from two quintiles (20-24.9 kg/m^2, 25-30 kg/m^2). ANOVA results for BMI and WC are reported in Table 6.

Table 6: One-way ANOVA Results for FI scores by BMI and WC

	Body mass index (kg/m^2)					
	<19.9	20-24.9	25-30	30.1-35	>35.1	P-Value
One- way ANOVA for all participants despite their WC across 5 BMI categories	0.10 ± 0.06 (n=19)	0.11 ± 0.05 (n=178)	0.13± 0.05 (n=151)	0.17 ± 0.07 [a,b,c] (n=57)	0.22 ± 0.08 [a,b,c,d] (n=25)	<0.001 *
One-way ANOVA Low WC across 3 BMI categories	0.10 ± 0.06 (n=19)	0.11 ± 0.06 (n=124)	0.12 ± 0.03 (n=26)	n=0	n=0	0.864
One-way ANOVA High WC across 4 BMI categories	n=0	0.13 ± 0.04 (n=54)	0.14 ± 0.06 (n=125)	0.17 ± 0.07 [b,c] (n=57)	0.22 ± 0.08 [b,c,d] (n=25)	<0.001 *

*Continuous variables expressed as Mean ± standard deviation (n=sample size) compared using one-way ANOVA; * denotes statistical significance, Low WC =<88cm; High WC = >88cm; [a] = different from <19.9 kg/m^2; [b] = different from 20-24.9 kg/m^2; [c] = different from 25-30 kg/m^2; [d]=different from 30.1-35 kg/m^2.*

3.5 %BF and frailty

Quintiles were created to separate subjects by %BF (<28.7%, 28.8-33.4%, 33.5-36.9%, 37-41.7%, and >41.8%). In order to be consistent with the previous approach described in section 3.4, one-way ANOVA analysis was performed to examine the differences between %BF quintiles and Tukey's post-hoc examined the multiple comparisons of specific groups. Statistically significant differences were identified between the highest quintile (>41.8%) and the

bottom four quintiles. As well as the second highest quintile (37-41.7%) and the bottom three quintiles.

Participants were then separated into two WC groups, either low WC (88cm) or high WC (>88cm) and categorized into the same five BMI categories. This was done to compare the results to the English Longitudinal Study on Aging, which separated and compared low and high WC groups. Separating by WC also accounts for central adiposity, since BMI alone does not provide insight into the distribution of body mass and composition. There was interest about if a U-shaped relationship would be observed in both WC groups, just one of the WC groups, or neither. A one-way ANOVA analysis was performed to examine the differences between FI scores for the low WC group across the same five %BF. No statistically significant differences were identified between %BF categories in the low WC group. A one-way ANOVA analysis was then performed to examine the differences between FI scores for the high WC group across the same five %BF categories. Significant differences were identified between FI scores by %BF for the high WC group. With differences between the highest quintile (>41.8%) and the bottom four quintiles. As well as the second highest quintile (37-41.7%) and the bottom quintile (<28.7%) and middle quintile (33.5-36.9%). ANOVA results for %BF and WC are reported in Table 7. Bar and line graphs for these results can be found in Appendix F.

Table 7: One-way ANOVA Results for FI scores by %BF and WC

	Percentage Body Fat (%)					
	<28.7	28.8-33.4	33.5-36.9	37-41.7	>41.8	P-Value
One-way ANOVA across 5 %BF quintiles and two WC levels	0.10 ± 0.05 (n=87)	0.12 ± 0.06 (n=87)	0.12 ± 0.05 (n=86)	0.14 ± 0.06 [a,c] (n=89)	0.19 ± 0.08 [a,b,c,d] (n=81)	<0.001*
One-way ANOVA Low WC and %BF	0.10 ± 0.05 (n=73)	0.11 ± 0.05 (n=45)	0.11 ± 0.05 (n=32)	0.12 ± 0.08 (n=17)	0.11 ± 0.01 (n=2)	0.53
One-way ANOVA High WC and %BF	0.10 ± 0.05 (n=14)	0.12 ± 0.04 (n=42)	0.12 ± 0.05 (n=54)	0.15 ± 0.05 (n=72)	0.19 ± 0.08 [a,b,c,d] (n=79)	<0.001*

*Continuous variables expressed as Mean ± standard deviation (n=sample size) compared using one-way ANOVA; * denotes statistical significance, Low WC =<88cm; High WC = >88cm; [a] = different from <28.7%; [b] = different from 28.8-33.4%; [c] = different from 33.5-36.9%; [d]=different from 37-41.7%.*

Separating by %BF quintiles created balanced groups and after dividing the participants into WC levels (low and high), no group had zero (n=0) participants. Therefore, a two-way ANOVA (2x5) analysis was also performed to examine the differences between FI scores as well as to examine the interaction between WC and %BF. Two-way ANOVA results can be found in Table 8. Main effects were detected in %BF (p=0.04), where differences between groups were detected between >41.8% and <28.7%, 28.8-33.4%, 33.5-36.9% and 37-41.6% (p=<0.0001). Additional between group differences were detected between the 37-41.6% group and the <28.7%, 28.8-33.4%, and 33.5-36.9% categories (p=<0.0001). A main effect of WC (p=0.02) was identified, indicating that those with a high WC had higher FI scores (0.15 ± 0.07) compared to those with a low WC (0.11 ± 0.05) (p=<0.0001). No interaction effects were identified by the two-way ANOVA between low and high WC groups and %BF categories. Bar and line graphs for these results can be found in Appendix G.

Table 8: Two-way ANOVA results for FI scores by %BF and WC

	Waist Circumference Categories	
%BF Categories	**Low WC (<88 cm)**	**High WC (>88 cm)**
Participants <28.7%	0.10±0.05 (n=73)	0.10±0.05 (n=14)
Participants between 28.8-33.4%	0.11±0.05 (n=45)	0.12±0.04 (n=42)
Participants between 33.5-36.9%	0.10±0.05 (n=32)	0.11±0.05 (n=54)
Participants between 37-41.7%	0.12±0.07 (n=17)	0.14±0.05 (n=74)
Participants >41.8%	0.10±0.09 (n=2)	0.19±0.08 (n=77)

Continuous variables expressed as Mean ± standard deviation (n=sample size) compared using two-way ANOVA; A main effect of %BF (p=0.04) was detected, where >41.8% was greater than all other categories (p=<0.0001) and the 37-41.6% group was greater than the <28.7%, 28.8-33.4%, and 33.5-36.9% categories (p=<0.0001). A main effect of WC (p=0.02) was detected where FI scores for the high WC are greater than low WC (p=<0.0001).

3.6 Summary

Table 9 provides an overview of the data thus far and includes additional comments about each diagnostic criterion. Out of twenty diagnostic criteria, thirteen used SM, and seven used ASM. ASM is the sum of the muscle mass of the four limbs, while SM is total body muscle mass. Baumgartner, (2000), first proposed the term sarcopenia obesity along with diagnostic criteria that included a height-adjust ASM and %BF. Fifteen adjusted muscle mass by height, four by weight and one was unadjusted. Ten used %BF, eleven used BMI, four used WC and two used FMI. Six had HGS as a functional measure to diagnosis sarcopenia. It appears only the diagnostic criteria that use a weight-adjusted or unadjusted sarcopenia criteria were statistically significant when examining the differences in FI scores between those who are sarcopenic obese and those who are not (reference group) and the association of sarcopenic obesity with frailty. However, there are varying obesity measures amongst the weight-adjusted criteria. Other criteria that included height-adjusted muscle mass indices, with varying obesity measures and cut-offs, were not statistically significant. The only statistically significant criteria to include HGS as a functional measure, as recommended by the EWGOSP was by Lee, et al. (2016), which had a weight-adjusted SMI.

Table 9: Summary

Author	Sarcopenia Criteria	Obesity Criteria	Functional Criteria	Aim 1 (Prevalence)	Aim 2-t(df) (p-value)	Aim 3 - correlation coefficient (p-value)	Comments
Aibar-Almazan et al.	hASMI $\leq$ 6.42 kg/m^2	%BF $\geq$ 35%	HGS $\leq$ 20 kg	5%	*t*(429)=1.50 (0.12)	0.07(0.10)	Height-adjusted sarcopenia criteria, weight-adjusted obesity criteria and meets EWG guidelines
Baek et al.	hASMI below the 50th percentile ($\leq$ 6.56 kg/m^2)	BMI $\geq$ 25 kg/m^2	-	16%	*t*(429)=0.11 (0.90)	0.03(0.35)	Height-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines
Bahat et al.	hSMI $\leq$ 7.4 kg/m^2	BMI $\geq$ 30 kg/m^2	HGS $\leq$ 22 kg	0%	-	-	Height-adjusted sarcopenia criteria, height-adjusted obesity criteria and does meets EWG guidelines
Balachandran et al.	hASMI $\leq$ 6.76 kg/m^2	BMI $\geq$ 30 kg/m^2	HGS $\leq$ 20 kg	0%	-	-	Height-adjusted sarcopenia criteria, height-adjusted obesity criteria and does meets EWG guidelines
Batsis et al.	hSMI $\leq$ 6.75 kg/m^2	%BF $\geq$ 38%	-	0.23%	*t*(429)=0.47 (0.63)	0.04(0.39)	Height-adjusted sarcopenia criteria, weight-adjusted obesity criteria and does not meet EWG guidelines
Biolo et al.	FM/FFM Ratio $\leq$ 0.4	BMI $\geq$ 25 kg/m^2	-	0.5%	*t*(429)=0.77 (0.44)	0.04(0.33)	Fat free mass-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines
Chen et al.	wASMI $\leq$ 25.6%	BMI $\geq$ 25 kg/m^2 and WC $\geq$ 88 cm	-	39%	*t*(429)=6.62(<0.001 *)	0.29(<0.001 *)	Weight-adjusted sarcopenia criteria, height-adjusted obesity criteria with central adiposity measure and does not meet EWG guidelines
Davison et al.	hSMI $\leq$ 6.52 kg/m^2	%BF in the highest two quintiles ($\geq$ 36.7%)	-	0.23%	*t*(429)=0.47 (0.63)	0.02(0.57)	Height-adjusted sarcopenia criteria, weight-adjusted obesity criteria and does not meet EWG guidelines
De Rosa et al. (hSMI)	hSMI a: 5.76 to 6.75 kg/m^2 b: $\leq$ 5.75 kg/m^2	BMI $\geq$ 30 kg/m^2	-	0%	-	-	Height-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines
De Rosa et al. (wSMP)	w SMP: 22.2% to 27.6%	BMI $\geq$ 30 kg/m^2	-	2.6%	*t*(429)=4.29(<0.001 *)	0.19(<0.001 *)	Weight-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines

Ishii et al.	hASMI ≤ 5.8 kg/m^2	%BF in the highest quintile (≥ 41.6%)	HGS ≤ 20 kg	0.5%	*t*(429)=0.14(0.88)	0.01(0.85)	Height-adjusted sarcopenia criteria, weight-adjusted obesity criteria and meets EWG guidelines
Joppa et al.	hFFMI < 10th percentile of the reference value	hFMI 90th percentile of the reference values	-	2.3%	*t*(429)=1.03(0.30)	0.05(0.244)	Height-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines
Kemmler et al.	hASMI in the lowest quintile of the sample	BMI ≥ 30 kg/m^2 and ≥ 35% BF	HGS ≤ 20 kg	0%	-	-	Height-adjusted sarcopenia criteria, weight and height-adjusted obesity criteria (subject must fulfill both) and meets EWG guidelines
Lee et al.	w SMI ≤ 32.2	%BF within two highest quintiles (≥ 36.7%)	HGS ≤18 kg	4%	*t*(429)=2.60(0.009 *)	0.12(0.009 *)	Weight-adjusted sarcopenia criteria, weight-adjusted obesity criteria and meets EWG guidelines
Lu et al.	w SMI two or more standard deviations below mean (≤ 27.1)	BMI ≥ 25 kg/m^2	-	1.6%	*t*(429)=5.06(<0.001 *)	0.18(<0.001 *)	Weight-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines
Moreira et al.	hSMI ≤ 20th percentile of the sample (≤ 5.99 kg/m^2)	WC ≥ 88cm	-	7%	*t*(429)=0.79(0.426)	0.06(0.168)	Height-adjusted sarcopenia criteria, central adiposity measured obesity criteria and does not meet EWG guidelines
Munoz-Arribas et al	SM ≤ two lowest quintiles of the sample (≤ 11.5 kg)	%BF in the two highest quintiles (≥ 36.7%)	-	15%	*t*(429)=2.07(0.03 *)	0.13(0.005 *)	Sample-adjusted sarcopenia criteria, weight-adjusted obesity criteria and does not meet EWG guidelines
Muscariello et al.	hSMI two standard deviations below the mean of young reference group	1) BMI ≥ 30.0 kg/m^2, 2) WC ≥ 88.0 cm, 3) FM% ≥ 35.0%, and 4) FMI ≥ 9.5 kg/m^2	-	0%	-	-	Height-adjusted sarcopenia criteria, weight, height, and central adiposity-adjusted obesity criteria (subject had to fulfill all 4) and does not meet EWG guidelines
Pedrero-Chamizo et al.	hRMM within the lower two quintiles (≤ 8.74 kg/m^2)	%BF within the two highest quintiles (≤ 36.7%)	-	12%	*t*(429)=0.97(0.331)	0.08(0.06)	Height-adjusted sarcopenia criteria, weight-adjusted obesity criteria and does not meet EWG guidelines

Siervo et al.	hSMI two standard deviations below the mean of young reference group ($\leq$ 6.76 kg/m^2)	1) BMI $\geq$ 30.0 kg/m^2, 2) WC $\geq$ 88.0 cm, 3) FM% $\geq$ 35.0%, and 4) FMI $\geq$ 9.5 kg/m^2	-	0%	-	-	Height-adjusted sarcopenia criteria, weight, height, and central adiposity-adjusted obesity criteria (subject had to fulfill all 4) and does not meet EWG guidelines
Srikanthan et al.	hSMI $\leq$ 22%	BMI $\geq$ 30 kg/m^2	-	0%	-	-	Height-adjusted sarcopenia criteria, height-adjusted obesity criteria and does not meet EWG guidelines

***BMI**, Body Mass Index; **ASM**, Appendicular Skeletal Mass; **ASMI**, Appendicular Skeletal Mass Index; **%BF**, Percentage Body Fat; **WC**, Waist Circumference; **FM**, Fat Mass; **FFM**, Fat Free Mass; **SM**, Skeletal Mass; **SMI**, Skeletal Mass Index; **RMM**, Relative Muscle Mass; **SMP**, Skeletal Mass Percentage; **EWG**, European Working Group; **h**, height-adjusted; **w**, weight-adjusted; **kg**, kilograms; **m**, meters; * denotes statistical significance.*

3.7 Prevalence of sarcopenic obesity with BMI stratified handgrip strength

Compositional measures from each diagnostic criteria were used to generate new criteria that included BMI stratified HGS. Any criteria which had HGS cut-offs as a functional criterion, was replaced with the BMI stratified HGS. Six of the twenty original criteria had a single HGS cut-off as a functional criterion; whereas, none of the twenty original criteria had stratified HGS cut-offs. Replacing the original HGS from the six criteria with the stratified HGS cut-offs accounts for the size of the participants and allows for comparison to other criteria that did not have HGS as part of their original diagnostics. A list of the published diagnostic criteria with stratified HGS can be found in Table 10. Subjects were separated by BMI categories and assigned the corresponding HGS cut-off, see Table 1.

To determine the prevalence of sarcopenic obesity with the addition of handgrip strength, the same process identified in section 3.1 was followed. The prevalence of sarcopenic obesity ranged from 0% based on the criteria from Bahat et al. (2021), Balachandran et al. (2014), De Rosa et al. (2015), Muscariello et al. (2016), Siervo et al. (2012), and Srikanthan et al. (2010) up to 5% based upon the Lee et al., (2016) criteria.

Table 10: Prevalence of sarcopenic obesity with the addition of HGS to composition criteria

Authors	Original prevalence	Sarcopenia criteria	Obesity criteria	HGS Functional criteria BMI (kg/m^2)	Prevalence In WARM Hearts Cohort with BMI Stratified Handgrip (%)
Aibar-Almazan et al. (2018)	5%	hASMI $\leq$ 6.42 kg/m^2	%BF $\geq$ 35%	HGS $\leq$ 20kg (removed) HGS: $\leq$ 23kg/m^2 = $\leq$ 17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$ 18kg > 29kg/m^2 = $\leq$21kg	4%
Baek et al. (2013)	16%	hASMI below the 50th percentile ($\leq$ 6.56 kg/m^2)	BMI $\geq$ 25 kg/m^2	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	3%
Bahat et al. (2021)	0%	hSMI $\leq$ 7.4 kg/m^2	BMI $\geq$ 30 kg/m^2	HGS $\leq$ 20kg (removed) HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0%
Balachandran et al. (2014)	0%	hASMI $\leq$ 6.76 kg/m^2	BMI $\geq$ 30 kg/m^2	HGS $\leq$ 20kg (removed) HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0%
Batsis et al. (2014)	0.23%	hSMI $\leq$ 6.75 kg/m^2	%BF $\geq$ 38%	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0%

Biolo et al. (2015)	0.5%	FM/FFM Ratio $\leq$ 0.4	BMI $\geq$ 25 kg/m^2	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0%
Chen et al. (2017)	39%	w ASMI $\leq$ 25.6%	BMI $\geq$ 25 kg/m^2 and WC $\geq$ 88 cm	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	7%
Davison et al. (2002)	0.23%	hSMI $\leq$ 6.52 kg/m^2	%BF in the highest two quintiles ($\geq$ 36.7%)	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0%
De Rosa et al. (hSMI) (2015)	a:0% b:0%	a: 5.76 to 6.75 kg/m^2 b: $\leq$ 5.75 kg/m^2	a: BMI $\geq$ 30 kg/m^2 b: BMI $\geq$ 30 kg/m^2	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	a:0% b:0%
De Rosa et al. (wSMP) (2015)	a:2.6% b: 0%	a: 22.2% to 27.6% b: $\leq$ 22.1%	a: BMI $\geq$ 30 kg/m^2 b: BMI $\geq$ 30 kg/m^2	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	a:0.7% b:0%
Ishii et al. (2016)	2.6%	hASMI $\leq$ 5.8 kg/m^2	%BF in the highest quintile ($\geq$ 41.6%)	HGS $\leq$ 20kg (removed) HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.4%
Joppa et al. (2016)	0.5%	FFMI < 10th percentile of the reference value	FMI 90th percentile of the reference values	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg	0.4%

				26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	
Kemmler et al. (2016)	2.3%	hASMI in the lowest quintile of the sample	BMI ≥ 30 kg/m^2 and ≥ 35% BF	HGS ≤ 20kg (removed) HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0%
Lee et al. (2016)	0%	w SMI ≤ 32.2	%BF within two highest quintiles (≥ 36.7%)	HGS ≤ 18kg (removed) HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	5%
Lu et al. (2013)	4%	w SMI two or more standard deviations below mean (≤ 27.1)	BMI ≥ 25 kg/m^2	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0%
Moreira et al. (2016)	1.6%	hSMI ≤ 20th percentile of the sample (≤ 5.99 kg/m^2)	WC ≥ 88cm	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	1.4%
Munoz-Arribas et al. (2013)	7%	SM ≤ two lowest quintiles of the sample (≤ 11.5 kg)	%BF in the two highest quintiles (≥ 36.7%)	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	3%
Muscariello et al. (2016)	15%	hSMI two standard deviations below the mean of young reference group	1) BMI ≥ 30.0 kg/m^2, 2) WC ≥ 88.0 cm, 3) FM% ≥ 35.0%, and 4) FMI ≥ 9.5 kg/m^2	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0%

Pedrero-Chamiz et al. (2015)	0%	hRMM within the lower two quintiles (≤ 8.74 kg/m^2)	%BF within the two highest quintiles (≤ 36.7%)	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	3%
Siervo et al. (2012)	12%	hSMI two standard deviations below the mean of young reference group (≤ 6.76 kg/m^2)	1) BMI ≥ 30.0 kg/m^2, 2) WC ≥ 88.0 cm, 3) FM% ≥ 35.0%, and 4) FMI ≥ 9.5 kg/m^2	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0%
Srikanthan et al. (2010)	0%	hSMI ≤ 22%	BMI ≥ 30 kg/m^2	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0%

Prevalence expressed as precent (%). ***BMI****, Body Mass Index;* ***ASM****, Appendicular Skeletal Mass;* ***ASMI****, Appendicular Skeletal Mass Index;* ***%BF****, Percentage Body Fat;* ***WC****, Waist Circumference;* ***FM****, Fat Mass;* ***FFM****, Fat Free Mass;* ***SM****, Skeletal Mass;* ***SMI****, Skeletal Mass Index;* ***RMM****, Relative Muscle Mass;* ***SMP****, Skeletal Mass Percentage;* ***removed****, original functional criteria removed;* ***h****, height-adjusted;* ***w****, weight-adjusted;* ***kg****, kilograms;* ***m****, meter.*

3.8 Difference in frailty index scores with stratified HGS

Unpaired t-tests were performed for each diagnostic criteria with the inclusion of BMI stratified HGS to determine if the frailty index scores differed between those categorized as sarcopenic obese and the reference group who were not categorized as sarcopenic obese for each published diagnostic criteria. Any criteria with a prevalence of 0% was not considered for this part o the analysis. Table 11 summarizes the group comparison data and reports the t-statistic; whereas Appendix D presents bar graphs of the grouped data for each diagnostic criteria. Statistically significant differences were found between the sarcopenic obese group and the reference group for four different diagnostic criteria, specifically the criteria published by Chen et al. (2017), De Rosa et al., (2015), Lee et al., (2016), Muñoz-Arribas et al., (2013). This is similar to the previous analysis in section 3.2 examining the original diagnostic criteria, with the exception of the criteria by Lu et al., (2013), since the criteria that included the BMI stratified HGS had a prevalence of 0%. The FI scores were not different for any of the remaining six diagnostic criteria for sarcopenic obesity verse reference groups.

Table 11: Differences in frailty index scores with the inclusion of HGS

Authors	Reference (not sarcopenic obese)	Sarcopenic obese	t(df)	p-value
Aibar-Almazan et al.	0.13 ± 0.06 (n=413)	0.16 ± 0.08 (n=17)	$t(429)=1.49$	0.14
Baek et al.	0.13 ± 0.07 (n=417)	0.15 ± 0.07 (n=13)	$t(429)=0.89$	0.37
Chen et al.	0.12 ± 0.06 (n=400)	0.17 ± 0.08 (n=30)	$t(429)=2.82$	0.005 *
De Rosa et al. (SMP)	0.10 ± 0.06 (n=426)	0.22 ± 0.06 (n=4)	$t(429)=2.31$	0.02 *
Ishii et al.	0.13 ± 0.07 (n=428)	0.13 ± 0.01 (n=2)	$t(429)=0.05$	0.95
Joppa et al.	0.13 ± 0.06 (n=428)	0.12 ± 0.01 (n=2)	$t(429)=0.25$	0.79
Lee et al.	0.12 ± 0.06 (n=409)	0.19 ± 0.08 (n=21)	$t(429)=4.36$	<0.001 *
Moreira et al.	0.13 ± 0.07 (n=424)	0.11 ± 0.04 (n=6)	$t(429)=0.48$	0.63
Munoz-Arribas et al.	0.13 ± 0.06 (n=417)	0.17 ± 0.07 (n=13)	$t(429)=2.59$	0.010 *
Pedrero-Chamizo et al.	0.13 ± 0.06 (n=417)	0.15 ± 0.06 (n=13)	$t(429)=1.11$	0.26

Frailty index scores as continuous variables expressed as Mean ± standard deviation (n=sample size) compared using unpaired t-test; ***t****, t-statistic;* ***df****, degrees of freedom;* ***** *denotes statistical significance.*

3.9 Association between sarcopenic obesity and frailty with HGS

Spearman's correlation was performed for each diagnostic criteria with the inclusion of BMI stratified HGS to determine if there is an association between sarcopenic obesity and frailty. Any criteria with a prevalence of 0% was not considered for this part of the analysis. Table 10 summarizes the diagnostic criteria by author and the correlation coefficients. Correlation coefficients ranged from poor (>0 – 0.1) to fair (0.1 – 0.3). Statistically significant correlations were observed for four of the diagnostic criteria, namely the criteria published by Chen et al. (2017), De Rosa et al., (2015), Lee et al., (2016), and Muñoz-Arribas et al., (2013). These are the same criteria that had significant differences between FI scores in section 3.8 and similar to the analysis that did not include stratified HGS in section 3.3, with the exception of the criteria by Lu et al., (2013). No significant correlations were identified for the other six published criteria.

Table 12: Correlation between sarcopenic obesity and frailty with the inclusion of HGS

Authors	Sarcopenia criteria	Obesity criteria	Functional criteria	Correlation coefficient	p-value
Aibar-Almazan et al.	hASMI $\leq$ 6.42 kg/m^2	%BF $\geq$ 35%	HGS $\leq$ 20kg (removed) HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.04	0.33
Baek et al.	hASMI below the 50th percentile ($\leq$ 6.56 kg/m^2)	BMI $\geq$ 25 kg/m^2	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.03	0.45
Chen et al.	w ASMI $\leq$ 25.6%	BMI $\geq$ 25 kg/m^2 and WC $\geq$ 88 cm	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.11	0.02 *
De Rosa et al. (SMP)	wSMP $\leq$ 27.6%	BMI $\geq$ 30 kg/m^2	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.10	0.02 *
Ishii S et al.	hASMI $\leq$ 5.8 kg/m^2	%BF in the highest quintile ($\geq$ 41.6%)	HGS $\leq$ 20kg (removed) HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.02	0.68
Joppa et al.	FFMI < 10th percentile of the reference value	FMI 90th percentile of the reference values	HGS: $\leq$ 23kg/m^2 = $\leq$17kg 23.1-26kg/m^2 = $\leq$17.3kg 26.1-29kg/m^2 = $\leq$18kg > 29kg/m^2 = $\leq$21kg	0.005	0.91

Lee et al.	w SMI ≤ 32.2	%BF within two highest quintiles (≥ 36.7%)	HGS ≤ 18kg (removed) HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0.17	<0.001 *
Moreira et al.	hSMI ≤ 20th percentile of the sample (≤ 5.99 kg/m^2)	WC ≥ 88cm	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0.02	0.68
Munoz-Arribas et al.	SM ≤ two lowest quintiles of the sample (≤ 11.5 kg)	%BF in the two highest quintiles (≥ 36.7%)	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0.11	0.01 *
Pedrero-Chamizo et al.	hRMM within the lower two quintiles (≤ 8.74 kg/m^2)	%BF within the two highest quintiles (≥ 36.7%)	HGS: ≤ 23kg/m^2 = ≤17kg 23.1-26kg/m^2 = ≤17.3kg 26.1-29kg/m^2 = ≤18kg > 29kg/m^2 = ≤21kg	0.06	0.19

***BMI**, Body Mass Index; **ASM**, Appendicular Skeletal Mass; **ASMI**, Appendicular Skeletal Mass Index; **%BF**, Percentage Body Fat; **WC**, Waist Circumference; **FM**, Fat Mass; **FFM**, Fat Free Mass; **SM**, Skeletal Mass; **SMI**, Skeletal Mass Index; **RMM**, Relative Muscle Mass; **SMP**, Skeletal Mass Percentage; **removed**, original functional criteria removed; **h**, height-adjusted; **w**, weight-adjusted; **kg**, kilograms; **m**, meters; * denotes statistical significance.*

3.10 Weight-adjusted models

Based upon the findings in Table 9, further investigation is warranted to examine how sarcopenia adjusted by weight is associated with frailty depending upon what obesity criteria it is paired with. Therefore, the weight-adjusted sarcopenia criteria by Chen, et al. (2017), (ASMI ≤25.6%), was paired with different obesity measures. Table 12 shows the differences in FI scores between those who are sarcopenic obese and those who are not. Obesity criteria were taken from each published diagnostic criteria, see Table 9. Prevalence of sarcopenic obesity was higher, with a range of 18% - 45% and all were statistically significant, and t-statistics were larger than those presented in Tables 4 and 10.

Table 13: Difference in FI scores between based upon Chen, et al. (2017) and different obesity criteria

Weight-Adjusted ASMI ≤ 25.6% (Chen et al.)				
Obesity Criteria	**Reference**	**Sarcopenic Obese**	***t*(df)**	**p-value**
BMI ≥25 kg/m^2	0.11 ± 0.05 (n=250)	0.16 ± 0.07(n=180)	*t*(429)= 6.06	<0.001*
BMI ≥25 kg/m^2 & WC ≥88 cm	0.11 ± 0.05 (n=264)	0.16 ± 0.07 (n=166)	*t*(429)= 6.80	<0.001*
BMI ≥30 kg/m^2	0.12 ± 0.06 (n=351)	0.18 ± 0.08 (n=79)	*t*(429)= 8.10	<0.001*
BMI ≥30 kg/m^2 & WC ≥88 cm	0.12 ± 0.06 (n=351)	0.18 ± 0.08 (n=79)	*t*(429)= 8.13	<0.001*
BMI ≥30 kg/m^2+%BF ≥35%	0.12 ± 0.06 (n=351)	0.18 ± 0.08 (n=79)	*t*(429)= 8.10	<0.001*
WC ≥88 cm	0.12 ± 0.06 (n=251)	0.16 ± 0.07 (n=179)	*t*(429)= 6.22	<0.001*
%BF ≥35%	0.11 ± 0.05 (n=233)	0.15 ± 0.07 (n=197)	*t*(429)= 5.64	<0.001*
%BF ≥38%	0.11 ± 0.05 (n=286)	0.17 ± 0.07 (n=144)	*t*(429)= 7.52	<0.001*
%BF ≥36.7%	0.11 ± 0.05 (n=262)	0.16 ± 0.07 (n=168)	*t*(429)= 7.80	<0.001*
%BF ≥41.6%	0.11 ± 0.05 (n=345)	0.18 ± 0.08 (n=85)	*t*(429)= 9.35	<0.001*
BMI ≥30 kg/m^2, WC ≥88 cm, %BF >35 & FMI >9.5 kg/m^2	0.12 ± 0.05 (n=351)	0.18 ± 0.08 (n=79)	*t*(429)= 8.10	<0.001*

Frailty index scores as continuous variables expressed as Mean ± standard deviation (n=sample size) compared using unpaired t-test; ***t****, t-statistic;* ***df****, degrees of freedom; * denotes statistical significance.*

To compare to the previous analyses in Tables 5 and 11, Spearmen's correlation was run for each obesity criteria paired with the weight-adjustd sarcopenia criteria. All were statistically significant, and all criteria ranged from a fair (0.1 - 0.3) to moderate (0.3 - 0.6) correlation. These criteria yielded higher correlation coefficients compared to the analyses in Tables 5 and 11, which ranged from poor (>0 - 0.1) to fair (0.1 – 0.3).

Table 14: Association between frailty and sarcopenia obesity based upon Chen, et al. (2017) and different obesity criteria

Weight-Adjusted ASMI ≤ 25.6% (Chen et al.)		
Obesity Criteria	**Correlation coefficient**	**p-value**
BMI ≥25 kg/m^2	0.27	<0.001*
BMI ≥25 kg/m^2 & WC ≥88 cm	0.31	<0.001*
BMI ≥30 kg/m^2	0.33	<0.001*
BMI ≥30 kg/m^2 & WC ≥88 cm	0.33	<0.001*
BMI ≥30 kg/m^2+%BF ≥35%	0.33	<0.001*
WC ≥88 cm	0.28	<0.001*
%BF ≥35%	0.25	<0.001*
%BF ≥38%	0.33	<0.001*
%BF ≥36.7%	0.35	<0.001*
%BF ≥41.6%	0.38	<0.001*
BMI ≥30 kg/m^2, WC ≥88 cm, %BF >35 & FMI >9.5 kg/m^2	0.33	<0.001*

***BMI**, Body Mass Index; **ASM**, Appendicular Skeletal Mass; **ASMI**, Appendicular Skeletal Mass Index; **%BF**, Percentage Body Fat; **WC**, Waist Circumference; **FM**, Fat Mass; **FMI**, Fat Mass Index; **kg**, kilograms; **m**, meters; * denotes statistical significance.*

Chapter 4: Discussion

4.1 Primary objectives

A variety of diagnostic criteria have been used to define sarcopenic obesity, since there is no standardized metrics (Donini et al., 2020; Hirani et al., 2017; Purcell et al., 2021). This creates a lack of understanding about what diagnostic criteria is most appropriate when screening for frailty. Identifying the most appropriate diagnostic criteria of sarcopenic obesity for a given population may improve screening methods, awareness, and prevention of functional health decline. The objectives of the present study were to: (1) determine the prevalence of sarcopenic obesity using different published diagnostic criteria in a sample of Manitoba females, 55 years of age and older, (2) determine if frailty index scores differ between those who are sarcopenic obese and those who are not for each diagnostic criterion, (3) determine if there is an association between sarcopenic obesity and frailty using the diagnostic criteria examined, (4) determine if the U-shaped relationship between frailty and BMI is observed in the cohort and use %BF as another measure of adiposity, and (5) determine the prevalence of sarcopenic obesity using different compositional criteria with the addition of handgrip strength stratified by body mass index. It was hypothesized that those who are sarcopenic obese will be more frail compared to those who are not, that there will be a correlation between sarcopenic obesity and frailty and lastly, the addition of handgrip strength as a criterion for sarcopenic obesity will strengthen the association with frailty.

Results from the first objective revealed considerable heterogeneity between diagnostic criteria that resulted in a range of prevalence of sarcopenic obesity in this study cohort, form 0%-39%. The large range of prevalence was expected since the Canadian Longitudinal Study on Aging (CLSA) reported a range in prevalence of 0%-80% in females. However, the range in prevalence of sarcopenic obesity was lower in the present study cohort compared to the CLSA. The CLSA included men and women over the age of 65, with a mean age 73.1 ± 5.7 years old; whereas, the present study cohort was 65 ± 6 years old. The present study expands on the findings of the CLSA by including participants between the ages of 55 and 65 years old.

Age plays a crucial role in changes to body composition. When examining middle-aged to older adults, it must be considered whether the cut-off values to define sarcopenic obesity are based upon a young (reference population) or a contemporary (similar) group. This can explain,

in part, the variation of prevalence in the present study population (Donini et al., 2020). For example, Baek et al, (2013), Ishii et al, (2016), and Lee et al, (2016), all used cut-off values derived from young populations and characterized low muscle mass as two or one standard deviations below the mean of the young reference group. Whereas Kemmler et al. divided their study sample into five qual groups (quintiles). Two comparable diagnostic criteria by Muscariello et al., (2016) and Siervo et al., (2012) had a 0% prevalence in this cohort. Both used a young reference group to create their sarcopenia cut-off and had four obesity criteria (1) BMI $\geq$ 30.0 kg/m^2, 2) WC $\geq$ 88.0 cm, 3) FM% $\geq$ 35.0%, and 4) FMI $\geq$ 9.5 kg/m^2). Compared to diagnostic criteria by Pedrero-Chamizo et al., (2015) and Muñoz-Arribas et al., (2013) had prevalence of 12% and 15%, respectively and used quintiles by selecting the top two quintiles of %BF and the lowest quintile of hASMI as cut-offs. This demonstrates how large variations caused by small differences in cut-offs highlights the importance of selecting criteria that are appropriate for specific individuals or populations with reasonable specificity and sensitivity.

Body composition is affected by ethnicity and sex (Alonso et al., 2017; Heyms et al., 2016; Park et al., 2020), therefore, the sex and ethnicities of the sample population need to be taken in account when selecting or creating sarcopenic obesity diagnostic criteria (Chen et al., 2020; Purcell et al., 2021). For instance, males have higher muscle mass than females, both in absolute and relative mass, and the difference appears to be greater in the upper compared to the lower body (Batsis et al., 2013; Lambris, 2017). Purcell et al. (2021), found body composition and anthropometric differences between males and females, age $\geq$ 65 years old. Male participants were taller (males: 174 cm $\pm$ 6.8; females: 159.9 cm $\pm$ 6.3; $p < 0.001$), weighed more (males: 85 kg $\pm$ 14.4; females: 73.9 kg $\pm$ 14.9; $p < 0.001$) and had higher amounts of ASM (males: 26 kg $\pm$ 3.9; females: 17.4 $\pm$ 3; $p < 0.001$) than female participants. Whereas female participants had a higher fat mass (males: 25.6 kg $\pm$ 8.2; females: 29.8 kg $\pm$ 9.6; $p < 0.001$), %BF (males: 29.6% $\pm$ 5.3; females: 40.7% $\pm$ 5.9; $p < 0.001$) and FMI (males: 8.5 kg/m2 $\pm$ 2.6; females: 11.7 kg/m^2 $\pm$ 3.8; $p < 0.001$) compared to male participants. Accumulation of adipose tissue tends to happen around the hips and thighs for females (pear shape), whereas males generally deposit adipose tissue around the trunk and abdomen (apple shape) (Lambris, 2017). Generally, muscle mass is highest in African Americans, followed by Caucasian, Hispanic, and Asian peoples, while %BF is highest among Asian subjects (Wang et al., 1994; Silva et al., 2010, Purcell et al., 2021).

However, it was not possible to examine sex and ethnicity differences in the present study due to the purposeful recruitment of an all-female cohort and the low number of participants who do not self-identify as Caucasian. However, this would inevitably lead to difficulties when comparing data collected from different populations and settings. For example, the diagnostic criteria used by Chen et al., (2017) was created for a randomized control trial of subjects in Taiwan. The utilization of cut-offs from that Taiwan cohort in the present study which recruited a cohort that was predominately Caucasian participants, likely resulted in a higher prevalence (39%) of sarcopenic obesity. In contrast, the cross-sectional analysis by Kemmler et al. (2016), examined the prevalence of sarcopenic obesity in a population of participants from Germany using a height-adjusted ASM < 5.99 kg/m^2 and BMI > 30 kg/m^2 and %BF > 35%. The resulting prevalence in their finding (2.5%) was comparable to the prevalence in the present study cohort (2.3%). The predominate ethnicity from the German cohort (100% Caucasian) was similar to the WARM Hearts cohorts (96.5% Caucasian). Indicating that if diagnostic criteria are being selected based on other published criteria, the predominate ethnicity of the study population which the criteria originated from needs to be compared to the population under observation that it is being applied to.

4.2 Sarcopenic obesity and its association with frailty

There is inconsistency throughout the literature about if those who are sarcopenic obese are indeed at increased risk of adverse health outcomes or worsening disease condition compared to those who are sarcopenic or obese alone. It is, however, understood that frailer individuals are at an increased risk of decline in health status and chronic diseases (Afilalo et al., 2009). It has been noted that obesity is a driving factor of CVD and other metabolic syndromes independent of sarcopenia. Therefore, the second objective compared FI scores between those who were categorized as sarcopenic obese and those who were not (reference group), for each diagnostic criteria. In the original analysis, significant differences in FI scores only presented in criteria that included a weight-adjusted or unadjusted sarcopenia measure, while no significant differences were found in any of the height-adjusted models. Therefore, those who were characterized as sarcopenic obese in the weight-adjusted or unadjusted diagnostic criteria were frailer compared to participants who were not.

When examining the association between sarcopenic obesity and frailty the same weight-adjusted and unadjusted diagnostic criteria that had statistically significant differences in FI scores had significant associations with frailty. These results suggest that sarcopenia defined by a weight-adjusted or unadjusted muscle mass may be able to better detect those who are frail. Adjustment methods specific to the morbidities of interest should be selected to improve sensitivity. Baumgartner et al, (2000) defined sarcopenia as height-adjusted appendicular skeletal mass (ASM/m^2), and this criterion has been used extensively to estimate muscle mass in older adults. However, it has been found that height-adjusted ASM may primarily identify participants with low BMI (<19.9 kg/m^2) as sarcopenic and underestimate sarcopenia in overweight to obese (30.1-35 kg/m^2, >35.1 kg/m^2) participants (Kim et al., 2017). Furthermore, Furushima et al., (2017) found that cardiometabolic disease risk factors were associated with weight-adjusted ASM ($p<0.05$) compared to height-adjusted ASM, which were not significant. Conversely, height-adjusted ASM had an association ($p<0.05$) with risk factors for osteoporosis and that weight-adjusted ASM did not. Tian & Xu, (2016), found no associations with all-cause mortality were only found using SMM adjusted by BMI. This thesis contributes a proposed weight-adjustment method of muscle mass to detect frailty in sarcopenic obese females.

Based on the observed weight-adjusted diagnostic criteria results, another analysis was performed to examine the difference in FI scores and the association between frailty and sarcopenic obesity. Specifically, diagnostic criteria were created by using a weight-adjusted sarcopenia measure by Chen et al. (2017), and different obesity criteria, see Table 12. All revised weight-adjusted criteria were statistically significant and correlation coefficients were larger compared to the coefficients from the original criteria and the criteria with the addition of HGS. It should be noted that the sarcopenia criteria by Chen et al. (2017), is one of many weight-adjusted muscle mass models. This example approach demonstrates that a weight-adjusted model may better detect participants with higher levels of frailty. Although it is known that one's height reduces with age, weight can change drastically over a smaller amount of time. Unexpected weight loss is also a marker of frailty status in the Fried phenotype model of frailty (Fried et al., 2001). Therefore, weight can capture compositional changes over time in a much more sensitive way compared to height, making weight an appropriate adjustment method for detecting frailty in sarcopenic obese individuals.

The EWGSOP makes no recommendations about how to adjust SMM or ASM for body size. They do, however provide cut-off values that include a non-adjusted ASM of <20 kg and <15 kg for men and women, respectively and a height-adjust appendicular skeletal mass index (ASM/m^2) of <7 kg/m^2 for men and <5.5 kg/m^2 for women (Cruz-Jentoft et al., 2019). Adjustment methods are critical to consider when examining the association of muscle mass and/or sarcopenic obesity with chronic diseases or predicting adverse health outcomes. For example, Peppa et al., (2014) used five height-adjusted sarcopenia models and BMI as an obesity criteria to characterize postmenopausal females for sarcopenic obesity to examine the association between lean body mass, obesity and cardiometabolic disease. They found the higher amounts of lean body mass were unfavorably associated with cardiometabolic risk factors. These findings are in direct contrast with large epidemiological studies (Buch et al., 2016), and these results may have been yielded due the selected adjustment methods.

4.3 Sarcopenic obesity, frailty and HGS

The EWGOSP recommends a physical performance measure as part of the diagnosis of sarcopenia. HGS cut-offs recommended by the EWGOSP are ≤27 kg for men and ≤16 kg for women. The Asian Working Group for Sarcopenia (AWGS) consensus in 2019 suggested that physical performance measures such as HGS, chair stand and Short Physical Performance Battery could diagnose sarcopenia alone in community-dwelling Asian adults (Chen et al., 2020). Some sarcopenic obesity criteria use HGS in addition to a skeletal muscle mass measures as a part of the requirement to diagnose sarcopenia. HGS cut-offs vary, ranging from 16-22 kgs. However, there has been no recommendation to account for body size when including HGS. To account for the differences in body size Fried et al, (2001) used a BMI stratified HGS, to assign different cut-offs based on BMI, see Table 1.

The fifth objective in the present study aimed to determine the prevalence of sarcopenic obesity and its association with frailty with the addition of BMI stratified HGS to each diagnostic criterion. The prevalence of sarcopenic obesity decreased for each diagnostic criteria after the addition of the stratified HGS measure. This is consistent with the literature since additional diagnostic criteria creates more exclusive parameters and screens people out who do not meet all the criteria. Prevalence of sarcopenic obesity was also reduced when BMI stratified HGS

replaced a single cut-off for criteria that originally included HGS as a physical performance measure.

The differences in FI scores between those who were sarcopenic obese and those who were not, based on the new stratified HGS were examined. Diagnostic criteria that used weight-adjusted or unadjusted sarcopenia measures, produced statistically significant differences. While height-adjusted diagnostic criteria were not significant. This is consistent with the previous analysis of the original diagnostic criteria. Even with the addition of HGS as a functional criterion, if the methods of adjustment for compositional (muscle and fat mass) criteria vary, then certain physical performance measure may not provide additional sensitivity. Although the present study demonstrated that the addition of HGS to existing criteria did not change the association with frailty for definitions that did not already demonstrate a correlation, Purcell et al, (2021), found that most sarcopenic obesity diagnostic criteria were frequently associated with low HGS regardless of the adjustment method. Given the importance of HGS in predicting adverse health outcomes and the ease of use in clinical and research settings, it could be used as a risk stratification tool for individuals with already low muscle mass or as a screening methods for community-dwelling adults (L. Chen et al., 2020; Cruz-Jentoft et al., 2019).

Though it was not assessed in the present study, Bouzon et al., (2017) recommended the standardization of frailty phenotype measures according to the characteristics of the population. Due to phenotypic diversity, there is large variations in the prevalence of frailty among different populations (Bouzon et al., 2017). This results in misclassification of participants and therefore, improper assessment of risk stratification. Following the same principles as Fried et al. (2001), creating a standardized sarcopenic obesity measure involves using the lowest quintile of the cohort being assessed to develop criteria cut-offs. This approach was not implemented in the present study but will be done when the full n=1000-person cohort is recruited into the WARM Hearts trial. Compared to the original Fried frailty phenotype criteria, it has been demonstrated that a standardized phenotype approach consistently identified prefrail participants as an intermediate risk group between robust and frail groups and predicted death and hospitalization at shorter times ($p \leq 0.05$) (Alonso et al., 2017). Based on the present study, it appears that standardization of muscle mass by weight-adjusted models would be the most appropriate when screening for sarcopenic obesity in frail individuals.

4.4 BMI, %BF and frailty

Hubbard et al., (2010) observed a U-shaped relationship between frailty and BMI in a population of 3000 community-dwelling men and women aged 50 years and older in England. Indicating that overweight (25– 29.9 kg/m^2) and underweight ($\leq$ 18.5 kg/m^2) individuals are more likely to be frail compared to their normal weight peers. The fourth objective was to determine if this same U-shaped relationship would be observed in this study cohort, which it was not. However, FI scores were significantly higher when BMI was between 30.1-35 kg/m^2 and >35.1 kg/m^2 (0.17 ± 0.07 and 0.22 ± 0.08; $p<0.001$) compared to the lower three categories ($\leq$ 19.9 kg/m^2, 20-24.9 kg/m^2 and, 25– 29.9 kg/m^2). This is consistent with Hubbard's findings that overweight individuals were frailer compared to the normal weight peers. After separating participants by WC and BMI, a U-shaped relationship was still not observed in the WARM Hearts cohort. This is likely attributed to the fact that two groups in the low WC category (30.1-35 kg/m^2 and >35.1 kg/m^2) and one group in the high WC category (<19.9 kg/m^2) contained an n=0. The sample size of the present study (n = 430) may explain the lack of participants in the three BMI (i.e.; $\leq$ 19.9 kg/m^2, 20-24.9 kg/m^2 and, 25– 29.9 kg/m^2) groups. Therefore, a U-shaped relationship may be detected in the future with the complete (n=1000) WARM Hearts cohort once the study has recruited the entire sample.

It is suggested that BMI may not be an accurate measure of adiposity. Some investigators have criticized BMI, noting that it does not consider age, muscle mass, bone density, overall distribution of fat mass, and racial and sex differences. %BF is another measure of adiposity, using this measure another aim was to determine if the U-shaped relationship exists. A U-shaped relationship was not observed in this cohort between %BF and frailty. Two-way ANOVA analysis revealed no statistically significant differences for %BF and WC interaction. Once participants were separated into WC groups (high and low) and %BF categories, no significant differences were found between %BF categories in the low WC group. There were significant main effects identified between %BF categories in the high WC group. Namely the highest two BMI categories (37-41.6% and 41.7%+) and the lower three (≤28.7%, 28.8-33.4%, and 33.5-36.9%). Therefore, the U-shaped relationship only partially appears in the high WC group when %BF is high. Although no statistically significant differences and no interaction effects were identified between low and high WC groups and %BF categories, there were also no differences

found within the low WC group between any of the %BF categories. This suggests that a rise in %BF may not result in higher FI score for those with a low WC (<88 cm). Historically it has been understood that having a higher fat mass can have a protective quality against decline in health status (the obesity paradox) (Bowen, 2012). Pre-frail or frail individual who were also overweight had a 27% ($p \leq 0.05$) reduced IADL disability rate, compared to underweight pre-frail individuals, which were associated with a 51% ($p \leq .001$) increase in IADL disabilities. Further, in hospital mortality decreased with an increase in body mass, with overweight patients having lower mortality risk compared to normal weight patients (OR 1.34 (95% CI 1.15-1.58, p = .0003). However, this has been typically examined using BMI as the proxy measure for adiposity. This data suggests that a possible U-shaped relationship may exist between frailty, %BF in people of high WC, but not low WC. It is possible that a U-shaped relationship may be detected with the complete (n=1000) WARM Hearts cohort once the study has recruited the entire sample. Future studies should examine this possible relationship between %BF and frailty.

4.5 Strengths and limitations

A key strength within the present study is the assessment of multiple diagnostic criteria of sarcopenic obesity and this is the first study to examine the prevalence of sarcopenic obesity and its relationship with frailty in an all-female cohort from the ages of 55 and older. A second strength is the ease and simplicity of BIA analysis. BIA machines are portable and do not take long to assess body composition, making BIA ideal for large cohort studies. BIA is a valid measure of body composition and the EWGOSP recommends BIA as an acceptable assessment for body composition analysis (Cruz-Jentoft et al., 2019). However, there are some limitations to consider. It is acknowledged that BIA generally underestimates %BF by about 4% (p=<0.005) and overestimates muscle mass by 3-4 kg (p=<0.005) compared to DEXA (Brief et al., 2019). This discrepancy may be caused by the influence of hydration status, as higher levels of hydration can cause an artificial increase in fat free mass measured by BIA. Thus, this precision difference between BIA and DEXA should be considered when interpreting body composition data from studies that utilize the two different assessment techniques. This is directly relevant when comparing the current study to other investigations that examined body composition by DEXA.

Due to the use on convenience sampling methods for participant recruitment, there is a potential for sample bias; therefore, the participants may not be representative of the overall population of females in Manitoba. It is likely that the participants of the WARM Hearts trial are health consumers, which limits the external validity of the cohort study. Additionally, the convenience sample recruitment strategy likely reduced the prevalence of severe frailty in this cohort. The prevalence of frail participants was 5% in this study cohort, which is lower compared the 11.6% and 20.2% for those over the age of age of 55 and 65, respectively, reported by Kehler et al., (2017). Indicating that those who are in worse health likely may not have participated in this study. The convenience sampling methods also resulted in recruiting a cohort that was predominately comprised of Caucasian females, which limits the generalisability of these findings as Caucasians make up only 72% of the Canadian population (Statistics Canada, 2020). Convenience sampling is an effective way to recruit participants for the large target sample (n=1000) the WARM Hearts study is intending to recruit, as it is cost effective. Resources were not available to implement a random sampling approach, to recruitment a sample that is perfectly representative of the female population in Manitoba. Rather, television and radio advertisements were utilised to prompt interest in participation. This advertisement strategy may reach a large proportion of Manitoba citizens; however, it is possible that the specific television and radio channels where the research recruitment communication was disseminated may not be accessible to all Manitobans. This may have resulted the recruitment of more urban-dwelling participants compared to rural or remote populations.

This research is a secondary analysis of data. Due to the cross-sectional design, the identified associations between sarcopenic obesity and frailty cannot be interpreted as causal. It is also acknowledged that the sample size analyzed in this thesis was n=430, which occurred because the COVID-19 pandemic paused the WARM Hearts trial recruitment for 12 months during my graduate program and this n=430 was the data that was available at the time. Lastly, this thesis was not intended to determine if one diagnostic criterion was better than others. Comparing multiple criteria was done due to the lack of a standardized diagnostic criteria for sarcopenic obesity and the relatively small sample size (n=430).

4.6 Future research directions

Future research to address the association between sarcopenic obesity and frailty should use the full WARM Hearts cohort (n=1000). Comparisons between different body-size adjustment methods (weight, height, BMI) when determining muscle mass should be investigated to determine the most appropriate methods for different populations. How well the addition of physical performance measures to sarcopenic obesity diagnostic criteria improve the predictive quality to screen for frailty and if measures should be stratified by body size, age or sex is necessary for specific and sensitive tools. Lastly, continued research about the mass and distribution of muscle and fat and its association with frailty is important to target those most at risk of adverse health outcomes and creation of appropriate interventions.

4.7 Conclusion

Population aging is a global phenomenon and frailty is a way to measure the accumulation of deficits that occurs with the early onset of biological aging (Jin, 2010). Frailty status can be used to predict adverse health outcomes (Clegg et al., 2013; Fried et al., 2001; Searle et al., 2008). Sarcopenia is the age-related loss of muscle mass and is a key component of frailty (Clegg et al., 2013). Obesity is prevalent of older adults and can mask sarcopenia. The co-existence of both is termed sarcopenic obesity. There is a not a standardized way to measure sarcopenic obesity leading to variation in prevalence and conflicting results about its association with chronic conditions. In the EWGOSP most recent consensus (Cruz-Jentoft et al., 2019), experts agreed that low muscle strength can be used as a metric to diagnosis sarcopenia and has been used in some of the sarcopenic obesity diagnostic criteria. The prevalence of sarcopenic obesity ranged from 0%-39%. Individuals who were sarcopenic obese were more frail than the reference group when the criteria used to define sarcopenic obesity included muscle mass as either unadjusted or adjusted by weight; however, no differences in frailty status were detected between groups when the sarcopenic obesity criteria were adjusted by height. Similarly, associations between sarcopenic obesity and frailty were only significant in weight-adjusted diagnostic criteria. The addition of HGS reduced the prevalence of sarcopenic obesity, where the prevalence ranged from 0%-5% when added to current published definitions and did not strength the association between frailty and sarcopenic obesity for any of the diagnostic criteria. These

results highlight the importance of selecting an appropriate diagnostic criterion for sarcopenic obesity, reinforces the need to develop population-specific sarcopenic obesity criteria, and informs the selection of adjustment methods for sarcopenic obesity in middle aged-older females who are community-dwelling. More specifically, it appears that weight-adjusted criteria to identify people with sarcopenic obesity, compared to a reference group, can distinguish differences in frailty status. Finally, a U-shaped relationship was not observed in this cohort; however, frailty index scores were higher in those with BMI scores of 30.1-35 kg/m^2 and >35kg/m^2 as well as %BF categorized into bins of 37-41.7% and >41.8% in a sample of women with high WC. Future research should examine the association between frailty and sarcopenic obesity with the full WARM Hearts cohort (n=1000).

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Appendix A: STROBE guidelines

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	i
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	ii
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-15
Objectives	3	State specific objectives, including any prespecified hypotheses	16
Methods			
Study design	4	Present key elements of study design early in the paper	16
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	16
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	17
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	15-20
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	15-20
Bias	9	Describe any efforts to address potential sources of bias	--
Study size	10	Explain how the study size was arrived at	21

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	15-20
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	20
		(*b*) Describe any methods used to examine subgroups and interactions	--
		(*c*) Explain how missing data were addressed	--
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	--
		(*e*) Describe any sensitivity analyses	--
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	21
		(b) Give reasons for non-participation at each stage	--
		(c) Consider use of a flow diagram	--
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	21-11
		(b) Indicate number of participants with missing data for each variable of interest	--
Outcome data	15*	Report numbers of outcome events or summary measures	--
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	23-43
		(*b*) Report category boundaries when continuous variables were categorized	27-30

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	--
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	44-45
Discussion			
Key results	18	Summarise key results with reference to study objectives	46-53
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	53-54
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	53-54
Generalisability	21	Discuss the generalisability (external validity) of the study results	53-54
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	--

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Appendix B: SAGER guidelines

General principles	
• Authors should use the terms *sex* and *gender* carefully in order to avoid confusing both terms.	
• Where the subjects of research comprise organisms capable of differentiation by sex, the research should be designed and conducted in a way that can reveal sex-related differences in the results, even if these were not initially expected.	
• Where subjects can also be differentiated by gender (shaped by social and cultural circumstances), the research should be conducted similarly at this additional level of distinction.	
Recommendations per section of the article	
Title and abstract	If only one sex is included in the study, or if the results of the study are to be applied to only one sex or gender, the title and the abstract should specify the sex of animals or any cells, tissues and other material derived from these and the sex and gender of human participants.
Introduction	Authors should report, where relevant, whether sex and/or gender differences may be expected.
Methods	Authors should report how sex and gender were taken into account in the design of the study, whether they ensured adequate representation of males and females, and justify the reasons for any exclusion of males or females.
Results	Where appropriate, data should be routinely presented disaggregated by sex and gender. Sex- and gender-based analyses should be reported regardless of positive or negative outcome. In clinical trials, data on withdrawals and dropouts should also be reported disaggregated by sex.
Discussion	The potential implications of sex and gender on the study results and analyses should be discussed. If a sex and gender analysis was not conducted, the rationale should be given. Authors should further discuss the implications of the lack of such analysis on the interpretation of the results.

Appendix C: WH-Frailty Index

#	Domain	Tools	Variable	Cut Offs	Reference
1*	Physical	Hand Dynamometer	Grip Strength	[BMI ≤ 23, 1=≤ 17 kg, 0=>17 kg], [BMI 23.1-26, 1=≤ 17.3 kg, 0=>17.3 kg], [BMI 26.1-29, 1=≤ 18 kg, 0=>18 kg], BMI >29, 1=≤21 kg, 0=>21 kg]	Fried (2001)
2	Physical	Seniors Fitness Test	Chair Stand	[Age 50-64: 1=12], [Age 65-69: 1=11], [Age 70-74: 1=10], [Age 75-79: 1=10], [Age 80-84: 1=9], [Age 85-89: 1=8], [Age 90-94: 1=< 4, 0=> 4]	Rikli & Jones (2002)
3	Physical	5M Gait Speed Test	Gait Speed	[Height < 159 cm - 1=< 0.76 m/s, 0=>0.76 m/s], [Height >159 cm - 1=< 0.65 m/s, 0=>0.65 m/s]	Fried (2001)
4	Physical	Paffenbarger PA Questionnaire	Self Report PA	1= < 270 kcal/week, 0= > 270 kcal/week	Fried (2001)
5	Physical	Seniors Fitness Test	Arm Curls	[Age 50-64: 1=13], [Age 65-69: 1=12], [Age 70-74: 1=12], [Age 75-79: 1=11], [Age 80-84: 1=10], [Age 85-89: 1=10], [Age 90-94: 1=8]	Rikli & Jones (2002)
6	Physical	Seniors Fitness Test	Back Scratch	[Age 50-64: 1=<-3, 0=>-3], [Age 65-69: 1=<-3.5, 0=>-3.5], [Age 70-74: 1=<-4.0, 0=>-4.0], [Age 75-79: 1=<-5, 0=>-5], [Age 80-84: 1=<-5.5, 0=>-5.5], [Age 85-89: 1=<-7, 0=>-7], [Age 90-94: 1=<-8, 0=>-8]	Rikli & Jones (2002)
7	Physical	Seniors Fitness Test	Sit and Reach	[Age 50-64: 1=<-0.5, 0=>-0.5], [Age 65-69: 1=<-0.5, 0=>-0.5], [Age 70-74: 1=<-1, 0=>-1], [Age 75-79: 1=<-1.5, 0=>-1.5], [Age 80-84: 1=<-2, 0=>-2], [Age 85-89: 1=<-2.5, 0=>-2.5], [Age 90-94: 1=<-4.5, 0=>-4.5]	Rikli & Jones (2002)
8	Physical	Seniors Fitness Test	8ft up and go	[Age 50-64: 1=>6.0, 0=6.4, 0=7.1, 0=7.4, 0=8.7, 0=9.6, 0=11.5, 0=<11.5]	Rikli & Jones (2002)
9	Physical	Seniors Fitness Test	6 Min Walk	[Age 50-64: 1=498.35], [Age 65-69: 1=457.20], [Age 70-74: 1=438.91], [Age 75-79: 1=397.76],	Rikli & Jones (2002)

				[Age 80-84: 1=352.04], [Age 85-89: 1=310.90], [Age 90-94: 1=251.46	
10*	Weight	Tape Measure	Waist Circumference	1=>88 cm, 0=< 88 cm	Kehler (2020)
11*	Body Comp	InBody	Fat Mass (kg)	1=36.1, 0=18.2-36.099	Kehler (2020)
12*	Body Comp	InBody	Fat-Free Mass (kg)		Kehler (2020)
13	Mood/Depression	PHQ-9	PHQ-9 Score	1=20-27 (severe), 0.80=15-19 (moderately severe), 0.60=10-14 (moderate), 0.40=5-9 (mild), 0.20=1-4 (minimal), 0=0 (none	Kroenke (2001)
14	Mood/Depression	"Medical Conditions"	Clinical Diagnosis of Depression/Anxiety	1=yes, 0=no	
15	Cognition	MoCA	MoCA Score	1= < 25, 0= > 26	Nasreddine (2006)
16	Nutrition	Self Report Questionnaire	Unintentional Weight Loss	1=yes, 0=no	Fried (2001)
17	Nutrition	Self Report Questionnaire	Decline in Food Intake	1=yes, 0=no	Reber (2019)
18	Nutrition/ QOL	SCREEN II	Is biting or chewing food difficult for you	1=Often or always, .6666=Sometimes, .3333=Rarely, 0=Never	
19	Nutrition/ QOL	SCREEN II	Do you have any problems getting your groceries?	1=Always, .6666=Often, .3333=Sometimes, 0=Never or Rarely	
20	Exhaustion	CES-D	Feel everything was an effort	1=Most (3), .6666=Moderate (2), .3333=Sometimes (1), 0=Rarely (0)	Fried (2001)

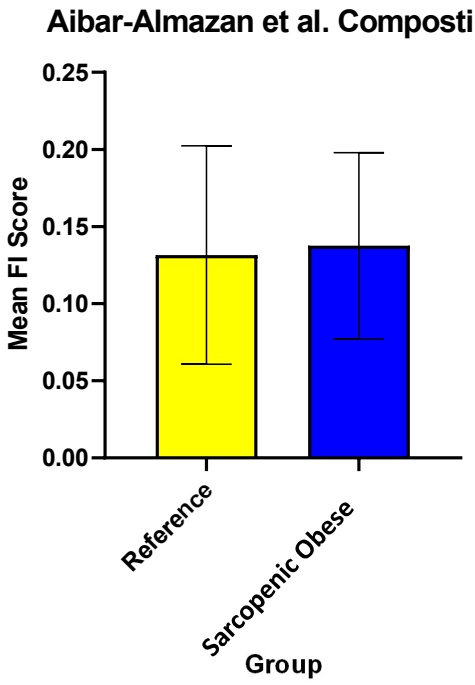
21	Exhaustion	CES-D	Could not "get going"	1=Most (3), .6666=Moderate (2), .3333=Sometimes (1), 0=Rarely (0)	Fried (2001)
22	Quality of Life	EQ-5D-5L	Mobility	1=Extreme, 0.75=Severe, 0.50=Moderate, 0.25=Slight, 0=None	Janssen (2008)
23	Quality of Life	EQ-5D-5L	Self Care	1=Extreme, 0.75=Severe, 0.50=Moderate, 0.25=Slight, 0=None	Janssen (2008)
24	Quality of Life	EQ-5D-5L	Usual Activites	1=Extreme, 0.75=Severe, 0.50=Moderate, 0.25=Slight, 0=None	Janssen (2008)
25	Quality of Life	EQ-5D-5L	Pain/Discomfort	1=Extreme, 0.75=Severe, 0.50=Moderate, 0.25=Slight, 0=None	Janssen (2008)
26	Quality of Life	EQ VAS	Rate Health Today	1-(EQ-VAS score/100)	Janssen (2008)
27	Comorbidities	“Medical History”	Diabetes	1=yes, 0=no	Kehler (2017)
28	Comorbidities	“Medical History”	Arthritis	1=yes, 0=no	Kehler (2017)
29	Comorbidities	“Medical History”	Sleep Apnea	1=yes, 0=no	Kehler (2017) Kehler (2020)
30	Comorbidities	“Medical History”	Cancer	1=yes, 0=no	Kehler (2017)
31	Comorbidities	“Medical History”	IBD	1=yes, 0=no	Kehler (2020)
32	Comorbidities	“Medical History”	Asthma	1=yes, 0=no	Kehler (2020)
33	Lab Values	Blood Pressure	Resting Systolic BP	1 = <90 or >140 mmHg, 0= 90-140 mmHg	Kehler (2020)
34	Lab Values	Blood Pressure	Pulse Pressure	1 = <30 or >60 mmHg, 0= 30-60 mmHg	Kehler (2020)
35	Lab Values	Heart Rate Monitor	Resting Heart Rate	1 = <60 or >99 bpm, 0= 60-99 bpm	Kehler (2017)

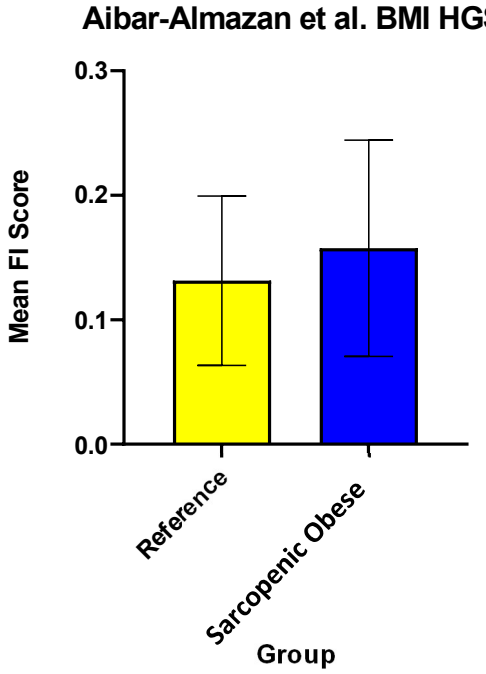
					Kehler (2020)
36	Lab Values	Blood Draw	Fasting Glucose	1 = <3.9 or >6.1mmol/L, 0= 3.9-6.3 mmol/L	Kehler (2017) Kehler (2020)
37	Lab Values	Blood Draw	Total Cholesterol	1 = >6.2mmol/L, 0= ≤6.2mmol/L	Kehler (2020)
38	Lab Values	Blood Draw	Triglycerides	1 = ≥6.67mmol/L, 0= < 6.67mmol/L	Kehler (2020)
39	Lab Values	Blood Draw	HDL Cholesterol	1 = < 1.03mmol/L, 0= > 1.03mmol/L	Kehler (2020)
40	Lab Values	Blood Draw	LDL Cholesterol	1 = <0.98 or >3.36 mmol/L, 0= 0.98-3.36 mmol/L	Kehler (2020)
41	Sleep Quality	PSQI	PSQI	1=5-21, 0=0-4	Tsai (2005)
42	Medications	# of Medications	# of Medications	1=>5, 0=0-4	

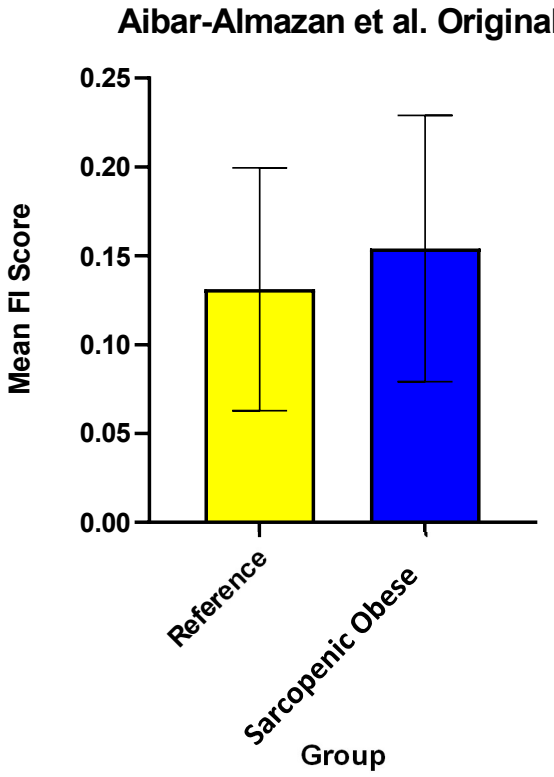
* Excluded

Appendix D: Comparison of FI scores between sarcopenic obesity diagnostic criteria and BMI stratified HGS

1







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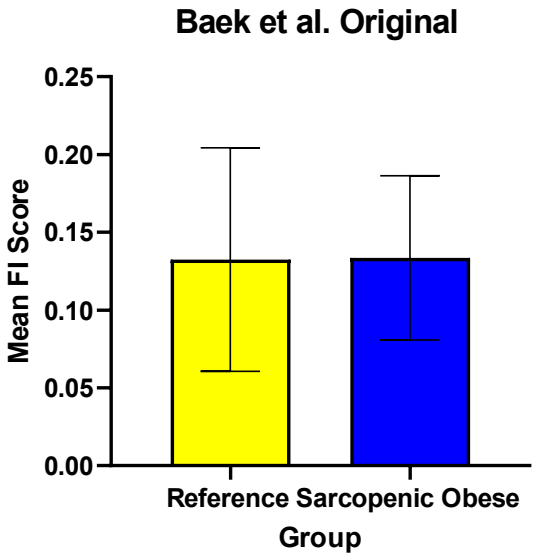
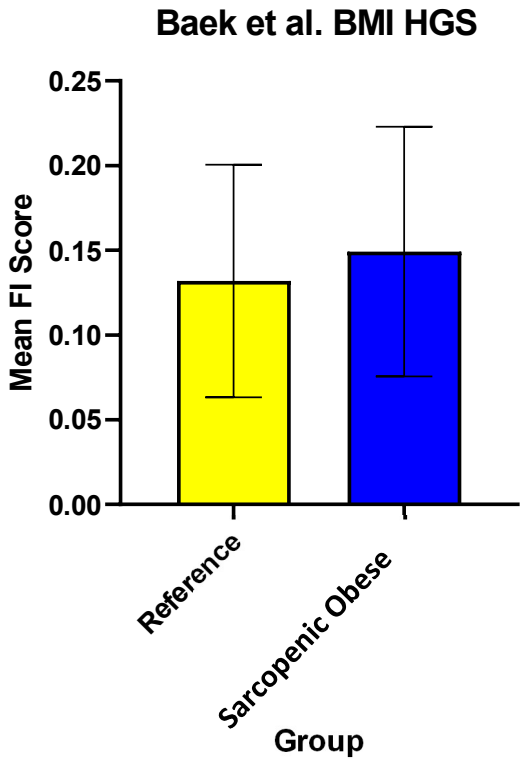
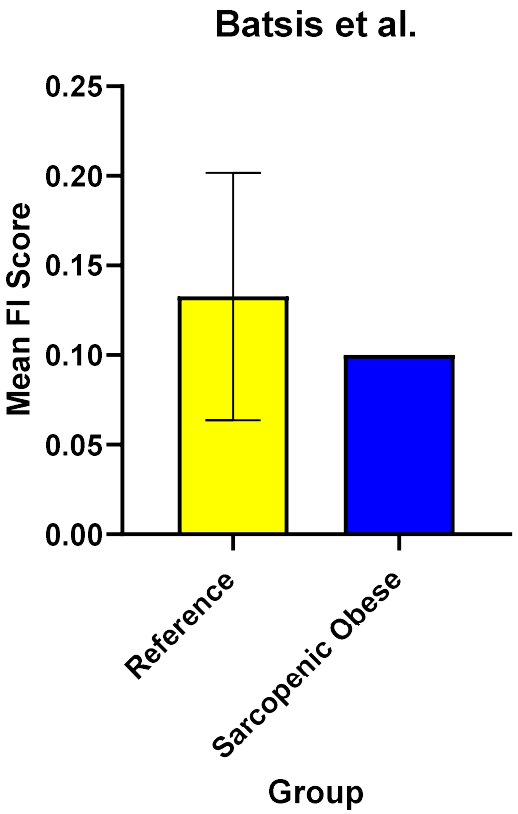
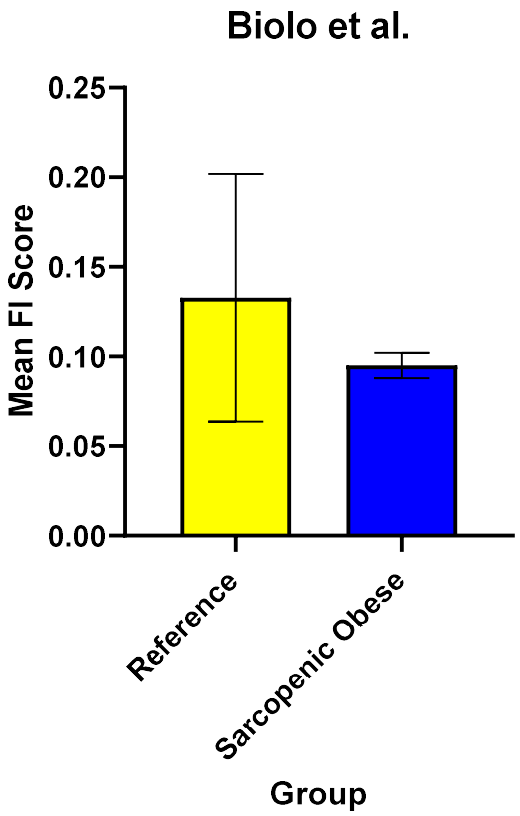

Baek et al. Original
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference Sarcopenic Obese
Group


Baek et al. BMI HGS
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

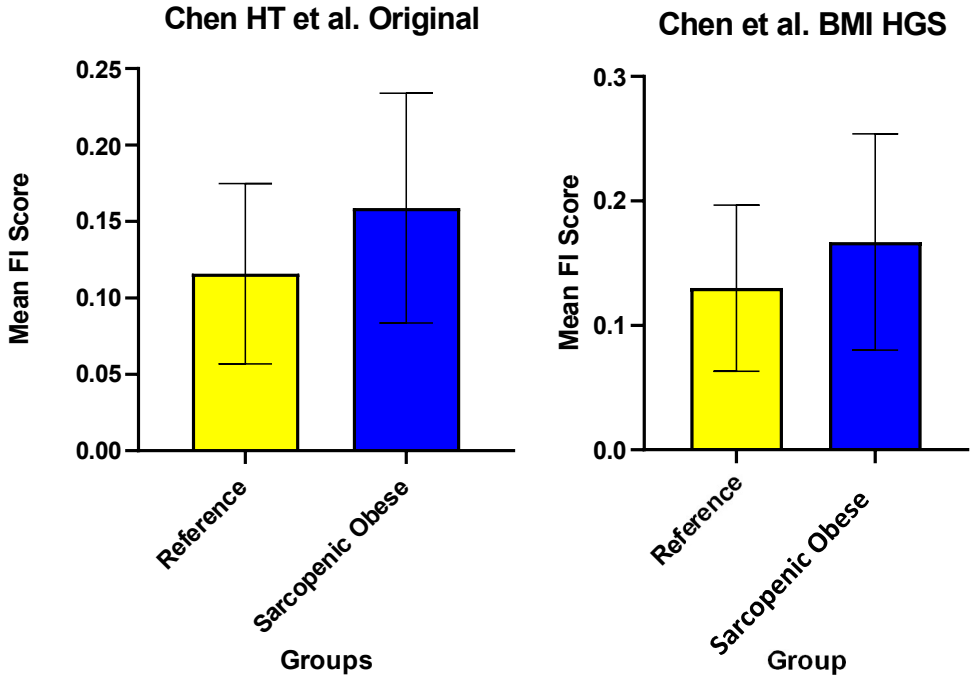
3


Batsis et al.
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

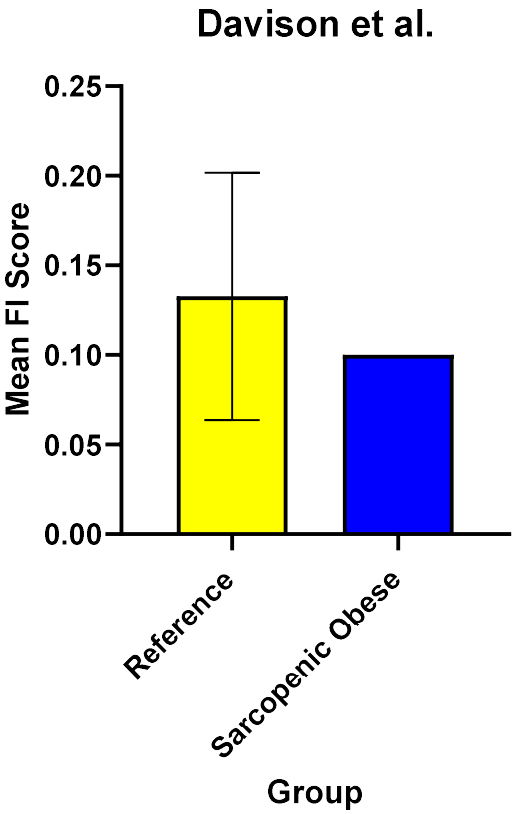
4


Biolo et al.
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

5

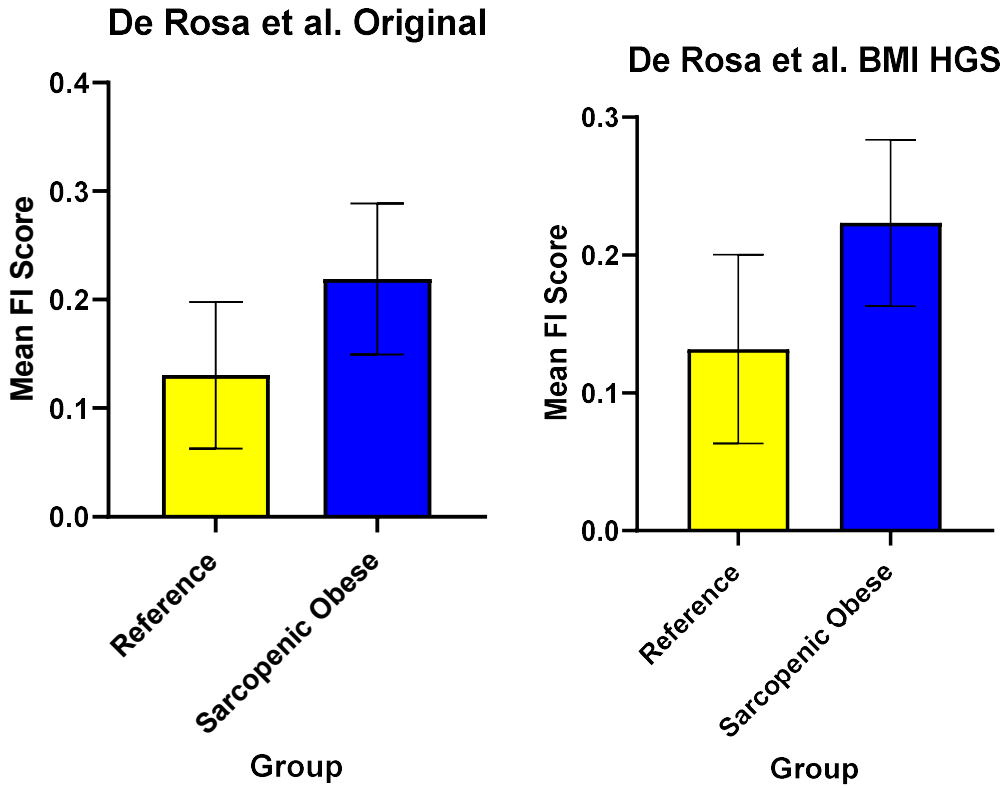

Chen HT et al. Original
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Groups
Chen et al. BMI HGS
Mean FI Score
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group

6

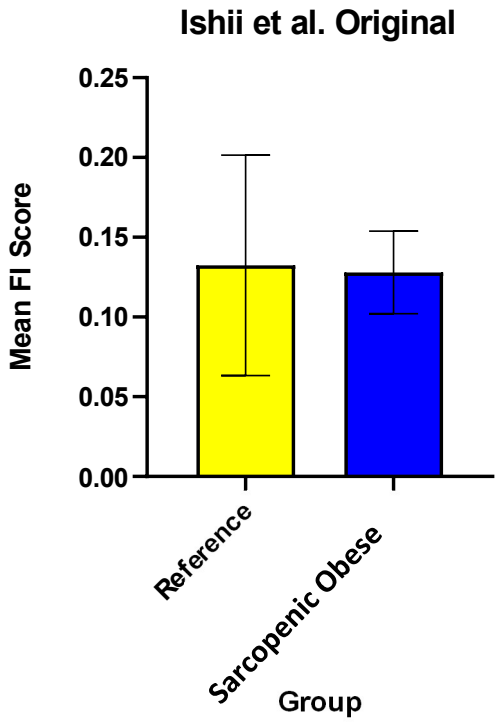

Davison et al.
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

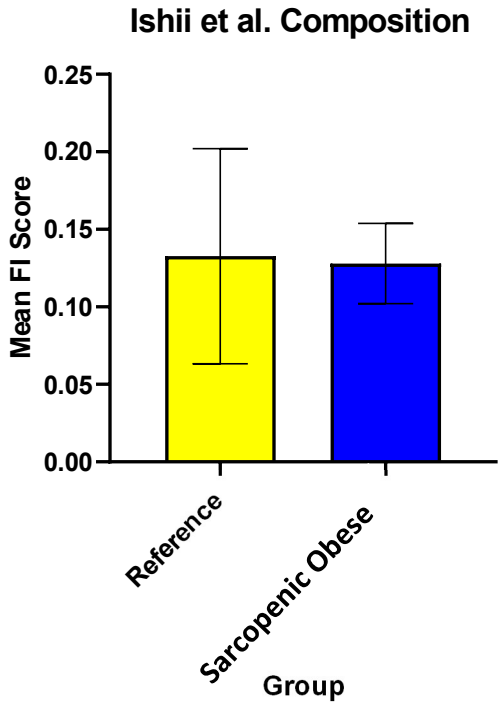
n=1

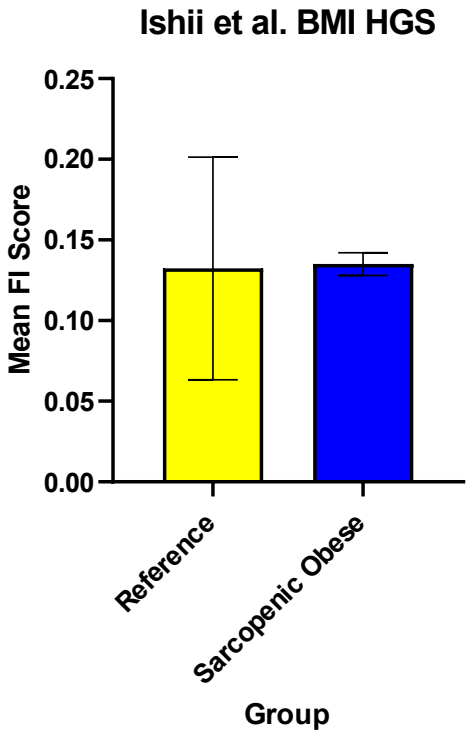
7


De Rosa et al. Original
Mean FI Score
0.4
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group
De Rosa et al. BMI HGS
Mean FI Score
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group

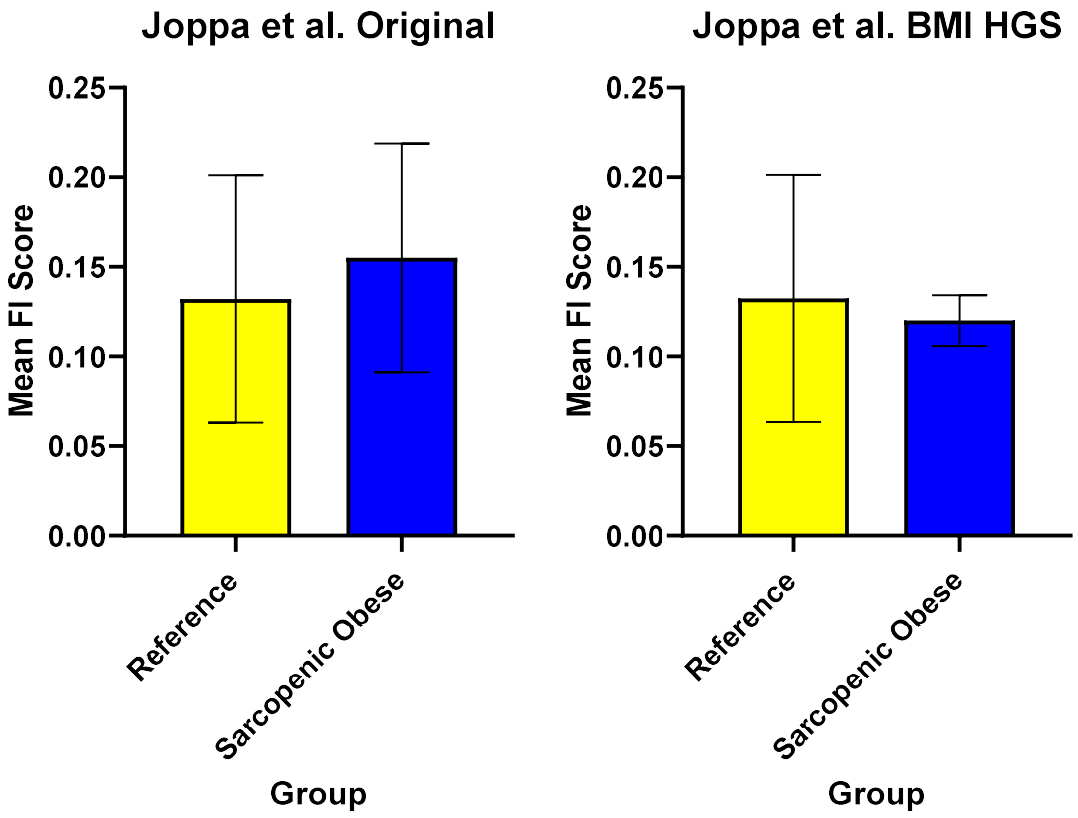
8

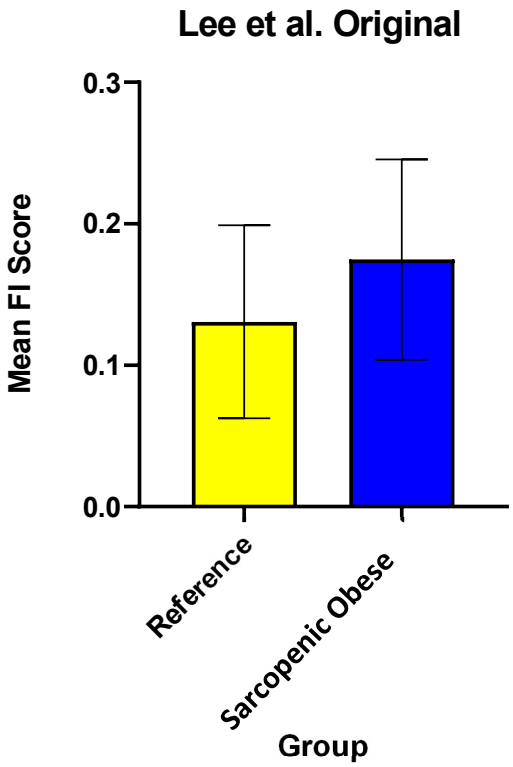

Ishii et al. Original
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

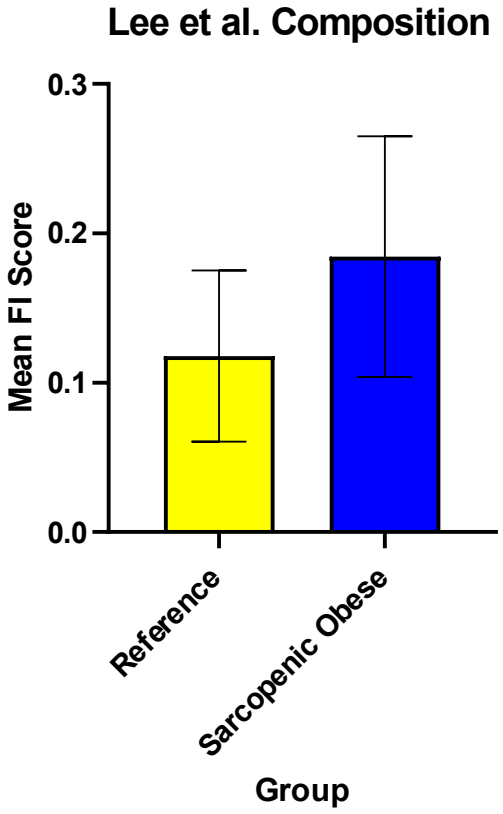

Ishii et al. Composition
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

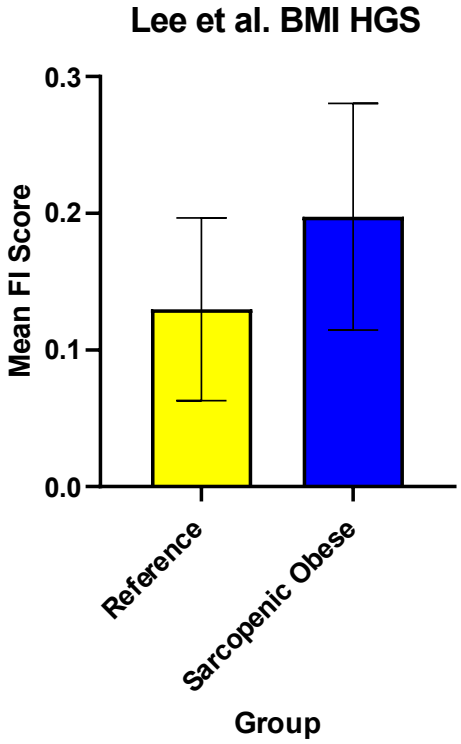

Ishii et al. BMI HGS
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

9

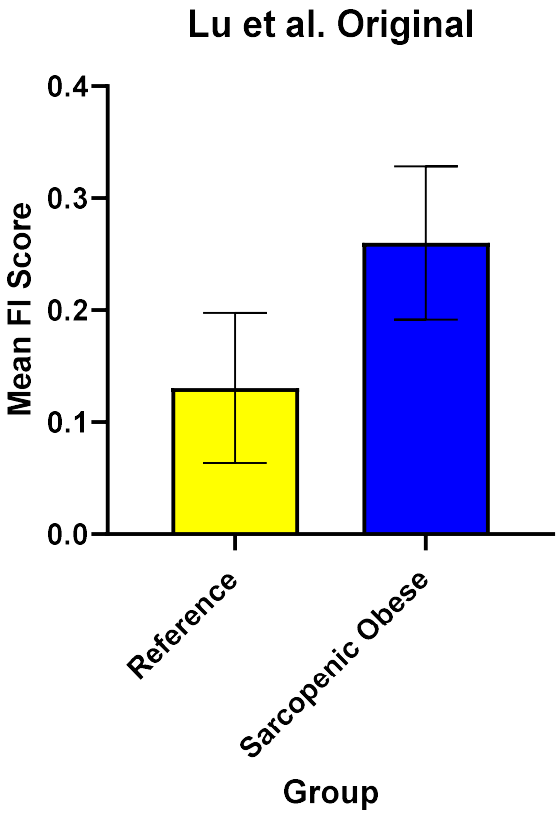

Joppa et al. Original
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group
Joppa et al. BMI HGS
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group


Lee et al. Original
Mean FI Score
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group

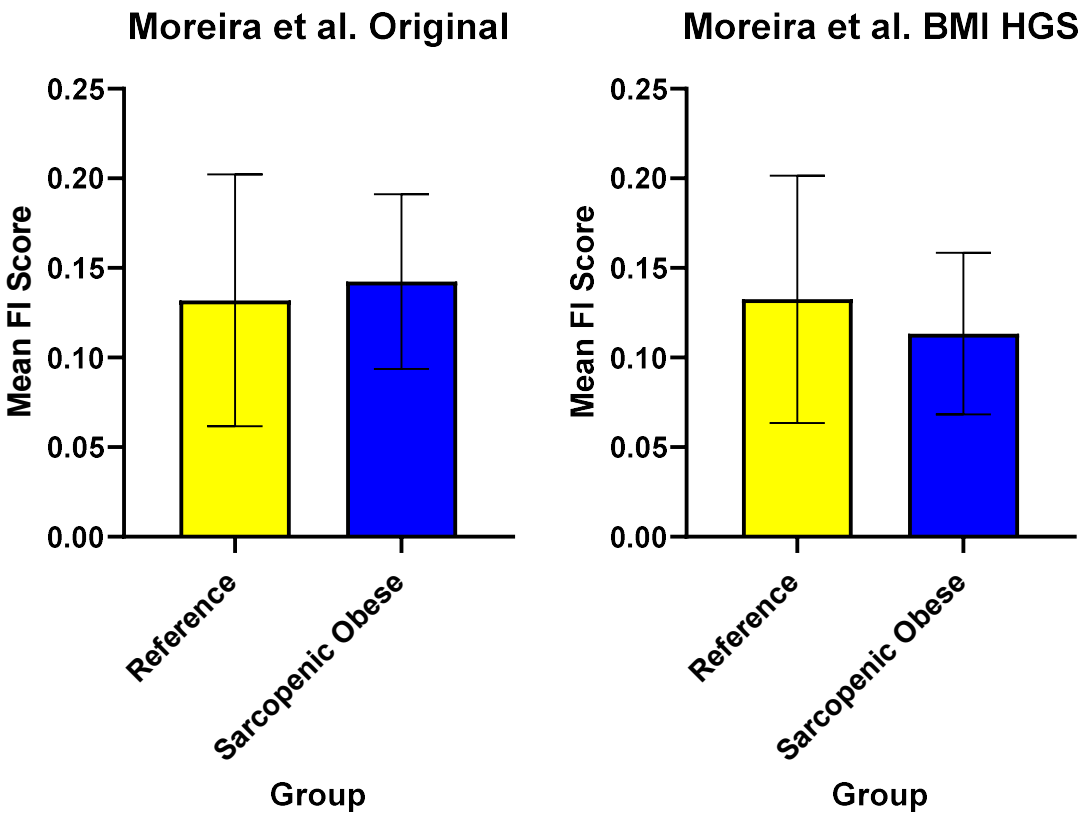

Lee et al. Composition
Mean FI Score
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group


Lee et al. BMI HGS
Mean FI Score
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group

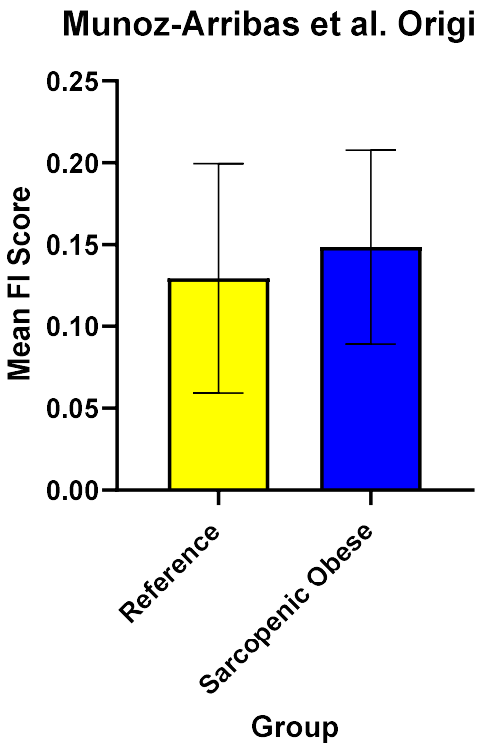
11

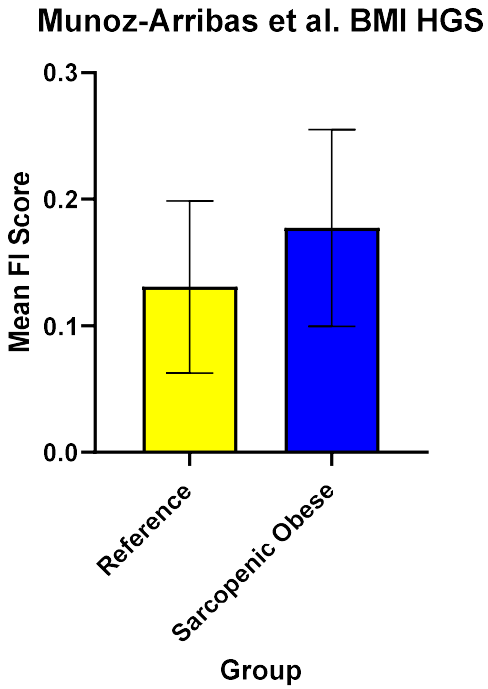

Lu et al. Original
Mean FI Score
0.4
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group

12

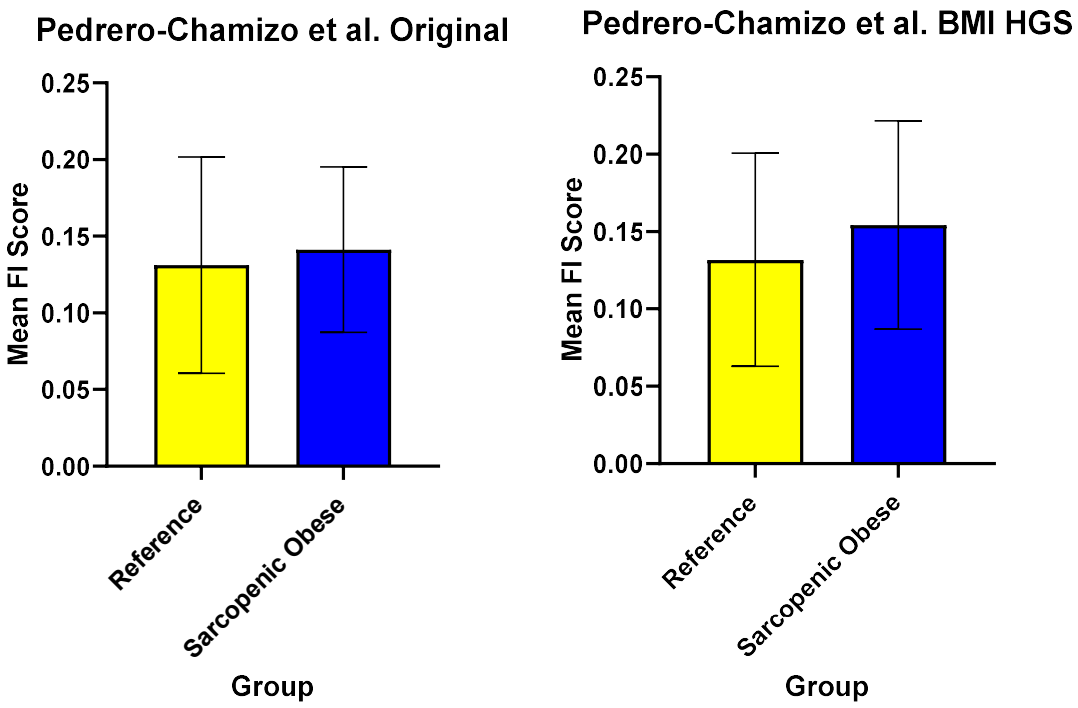

Moreira et al. Original
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group
Moreira et al. BMI HGS
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group

13


Munoz-Arribas et al. Original
Mean FI Score
0.25
0.20
0.15
0.10
0.05
0.00
Reference
Sarcopenic Obese
Group


Munoz-Arribas et al. BMI HGS
Mean FI Score
0.3
0.2
0.1
0.0
Reference
Sarcopenic Obese
Group

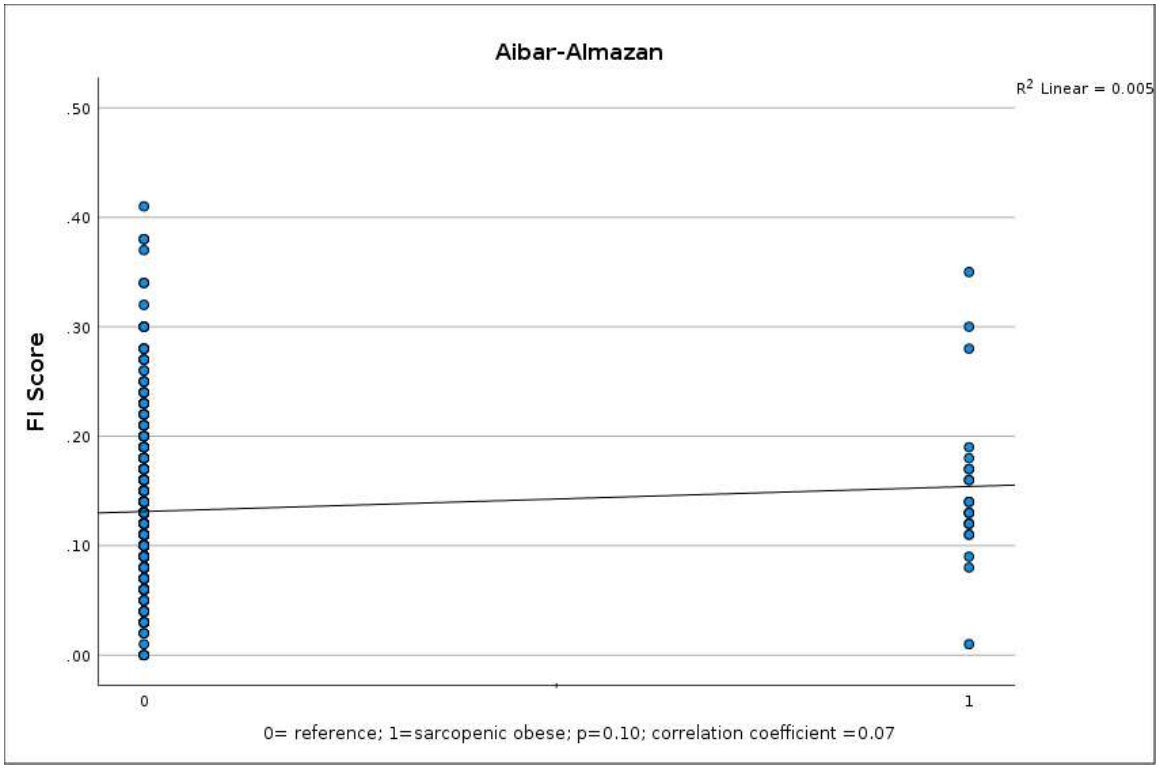
14



1. Aibar-Almazan et al.; 2. Baek et al.; 3. Batsis et al.; 4. Biolo et al.; 5. Chen et al.; 6. Davison et al. (n=1); 7. DeRosa et al.; 8. Ishii et al.; 9. Joppa et al.; 10. Lee et al.; 11. Lu et al.; 12. Moreira et al.; 13. Munoz-Arribas et al.; 14. Pedrero-Chamizo et al.

Appendix E: Spearman correlations scatter plots

1



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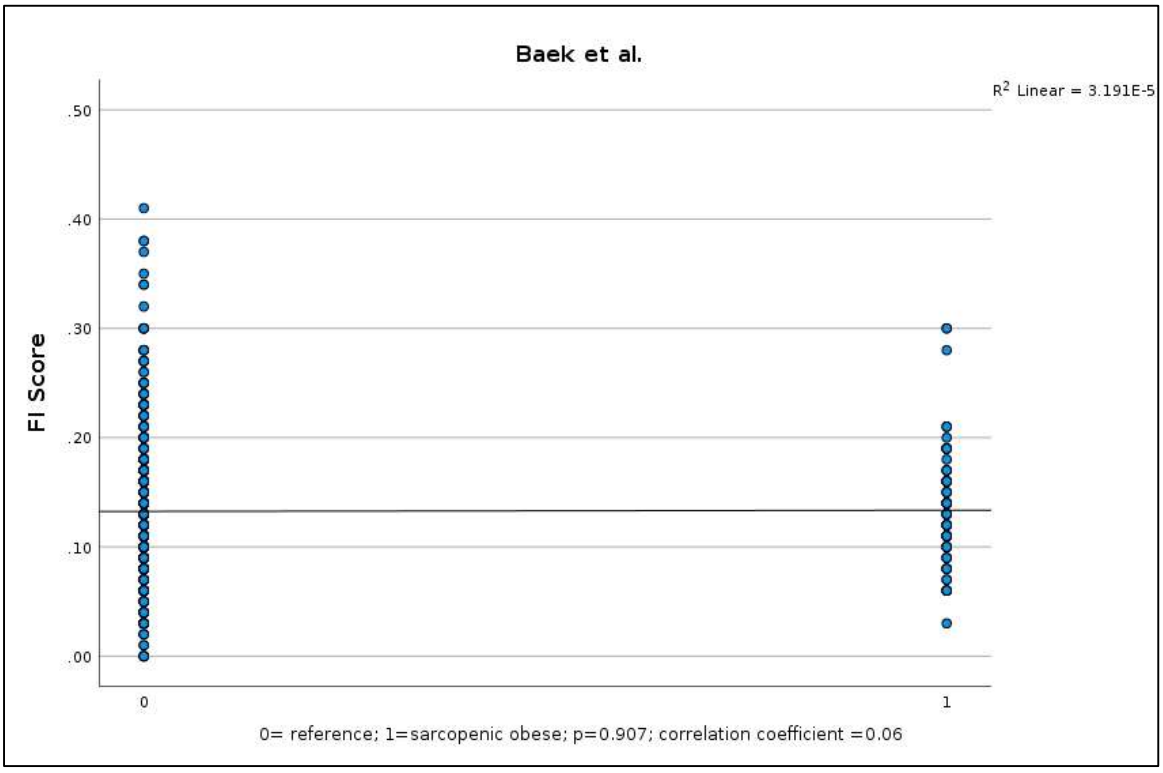

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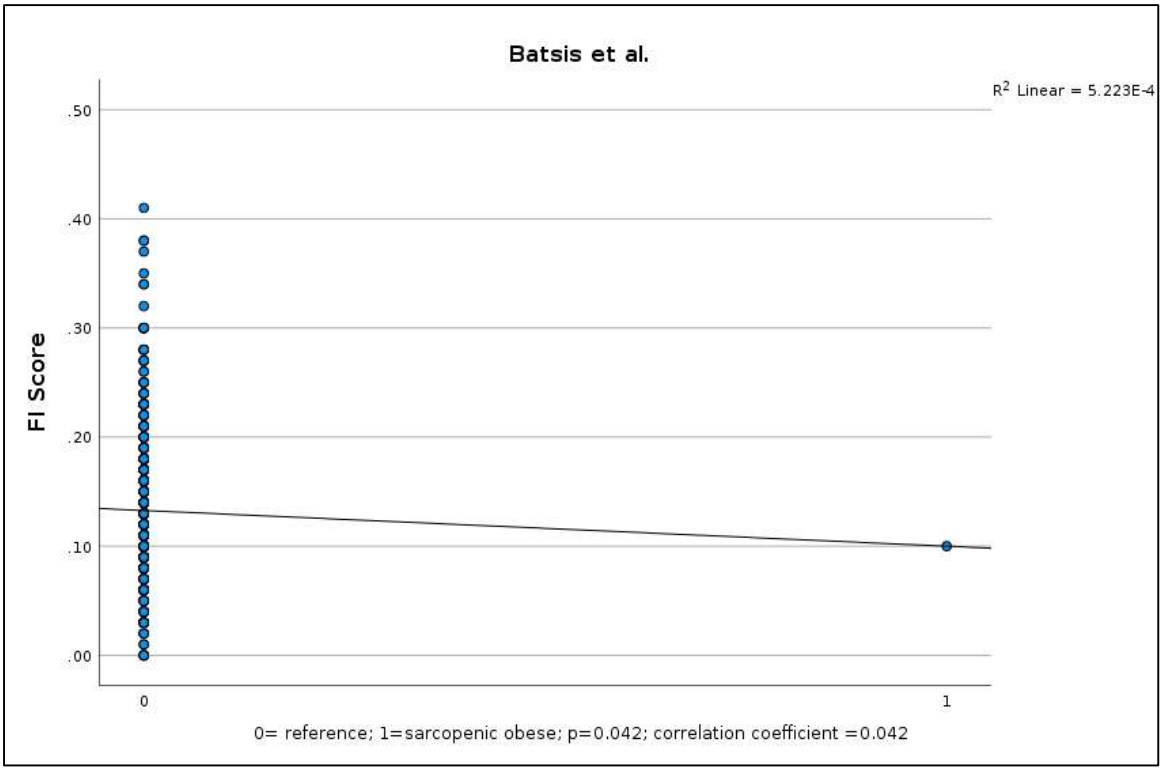
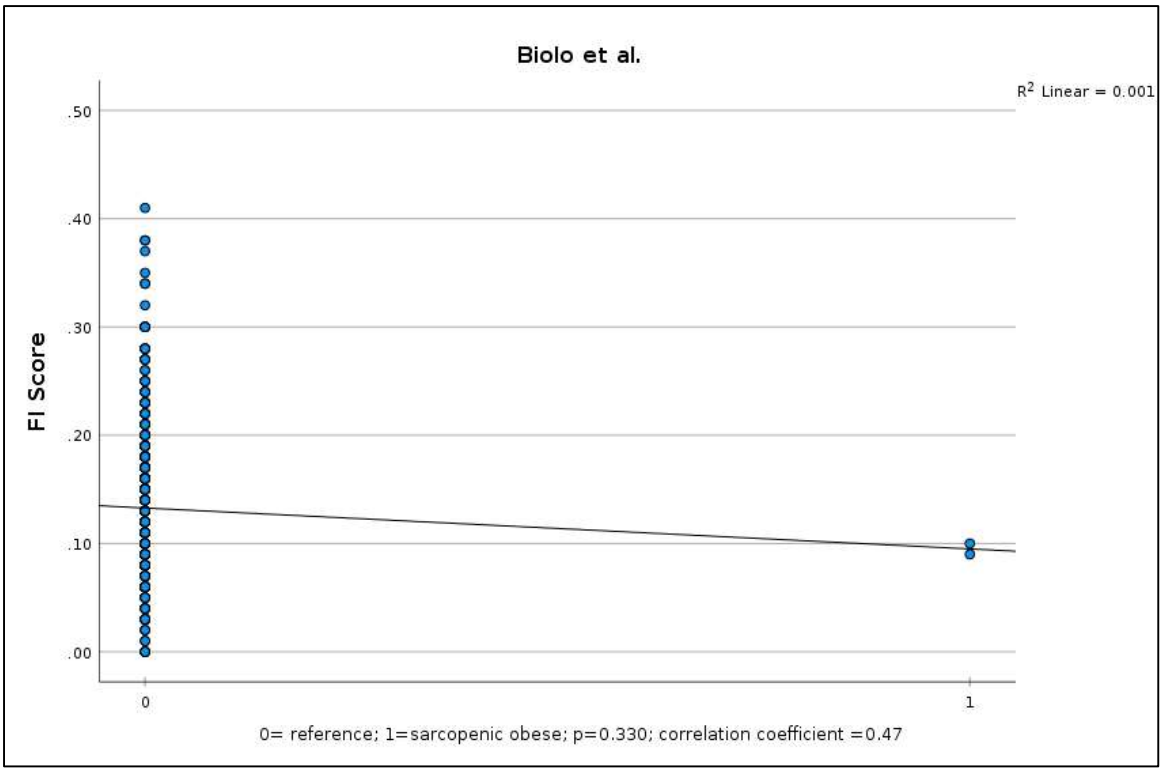
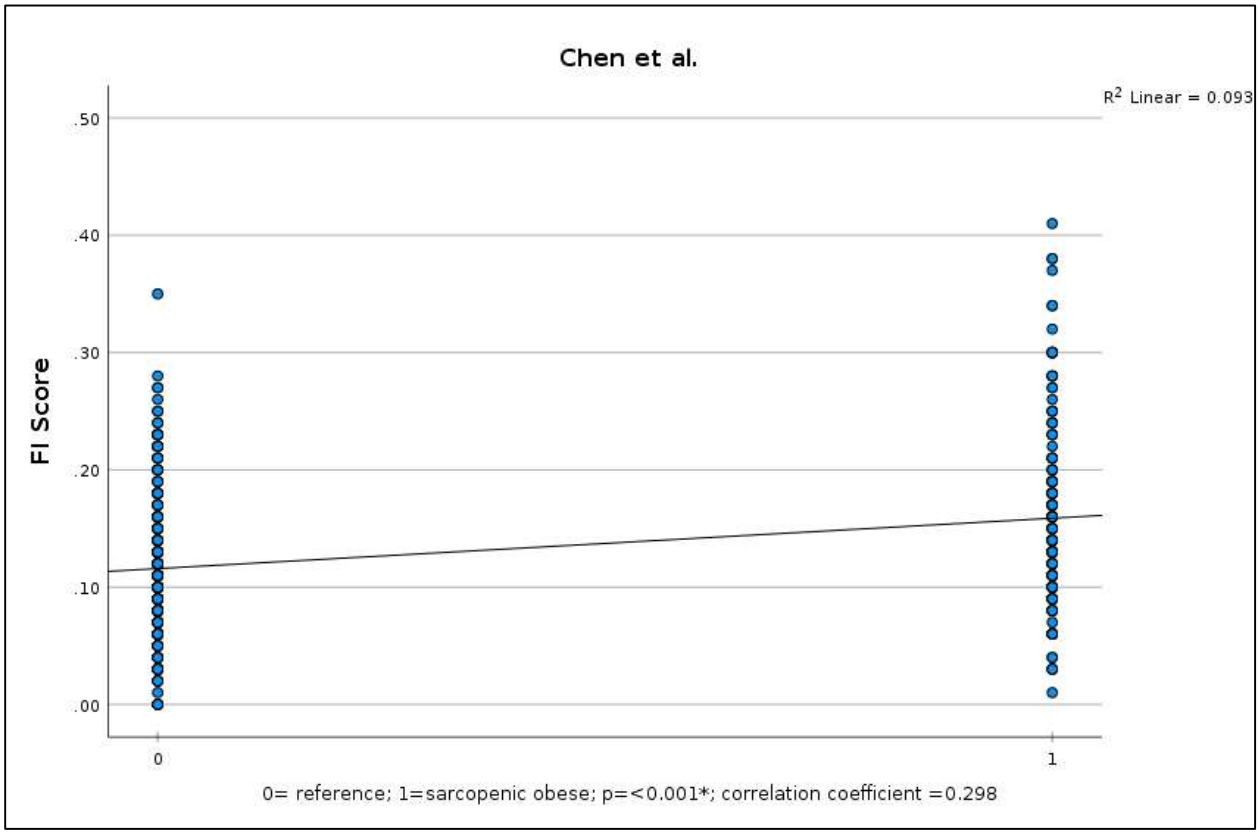

Batsis et al.
R² Linear = 5.223E-4
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.042; correlation coefficient =0.042

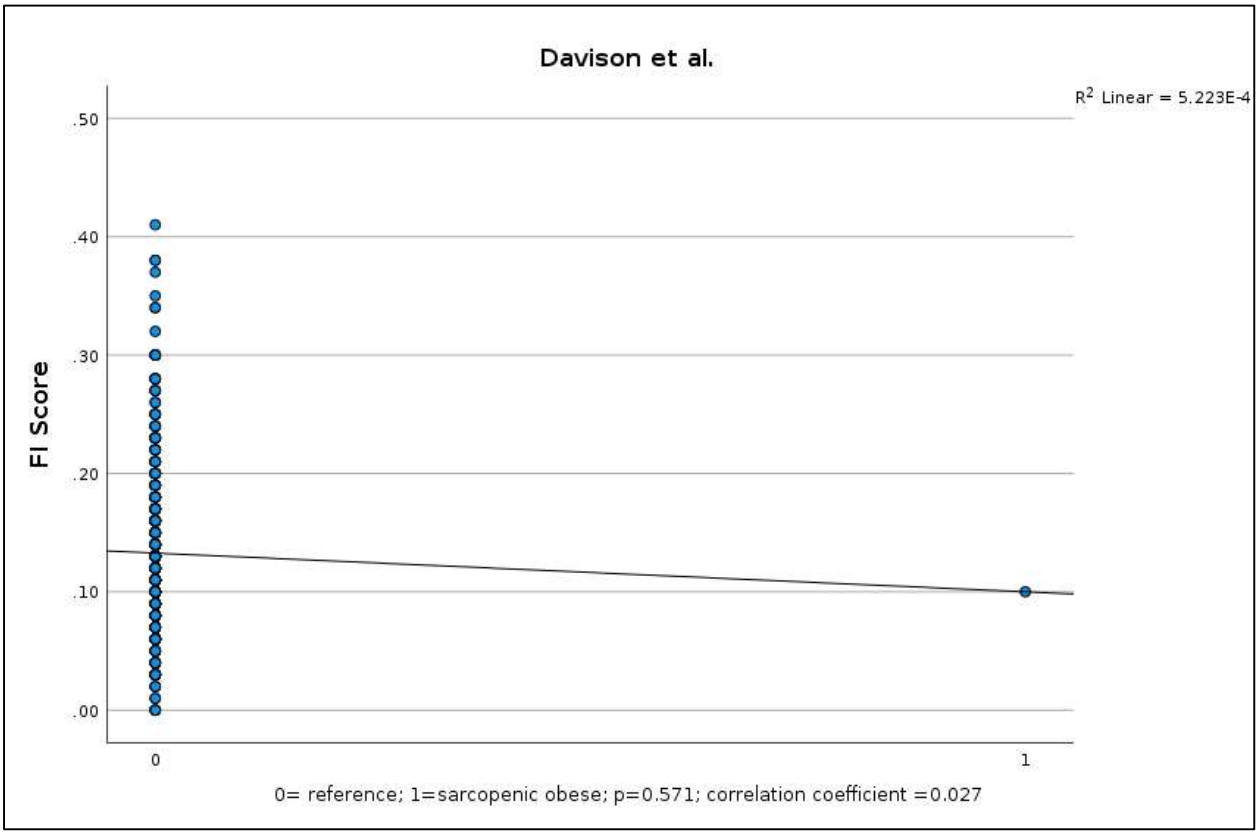
4


Biolo et al.
R² Linear = 0.001
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.330; correlation coefficient =0.47

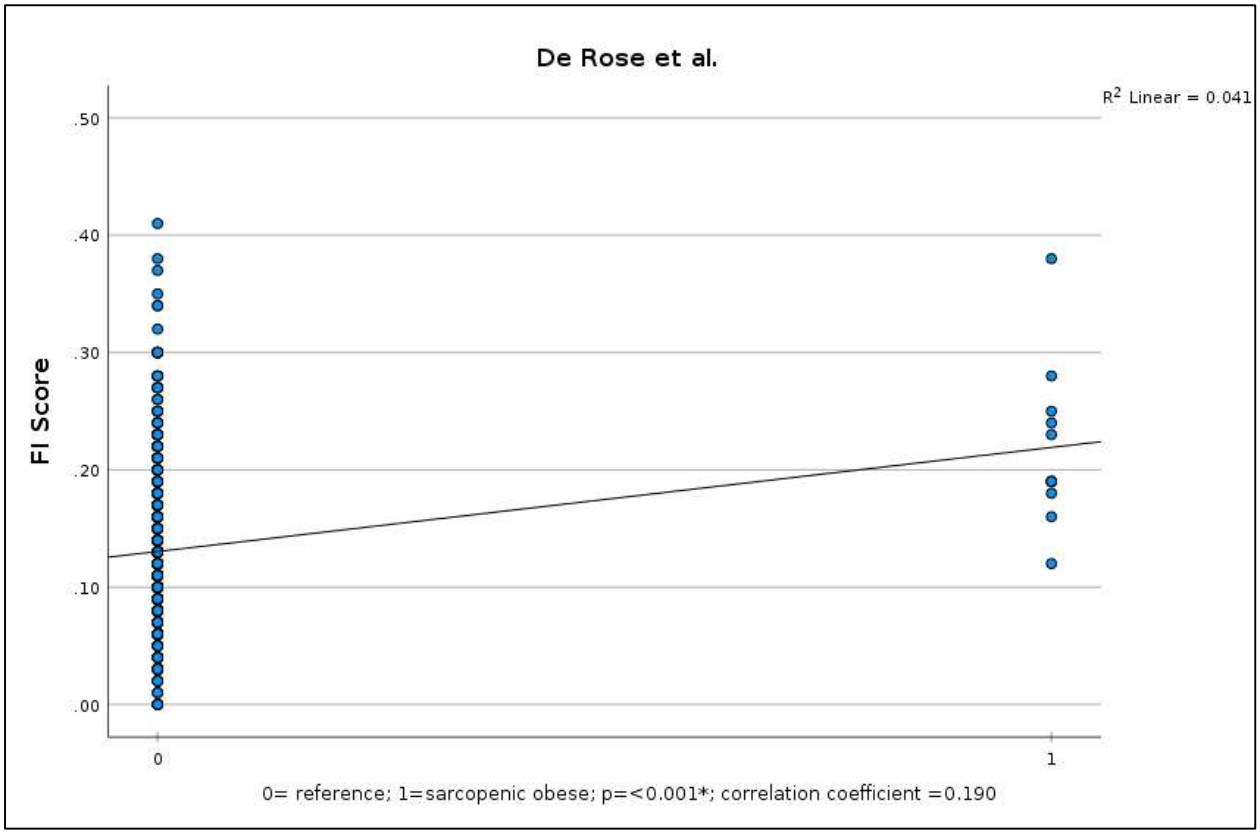
5


Chen et al.
R² Linear = 0.093
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=<0.001*; correlation coefficient =0.298

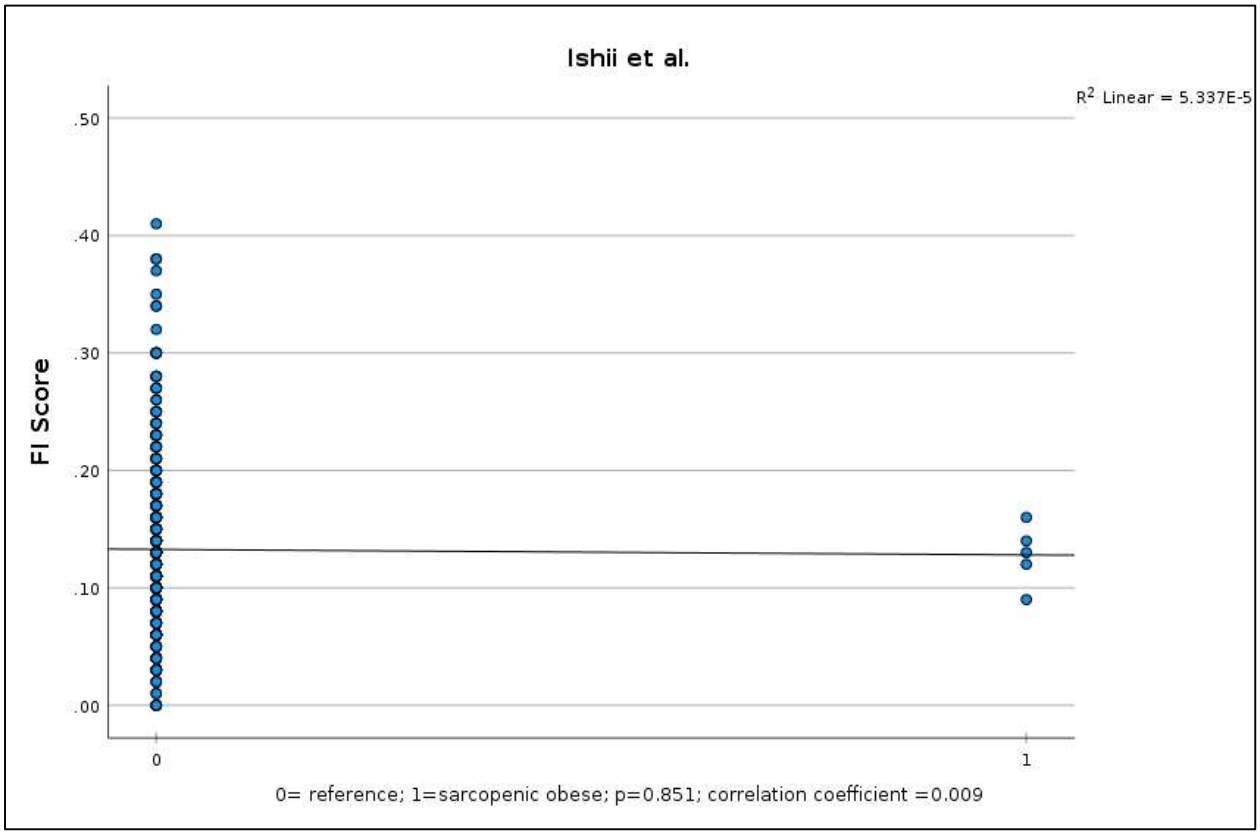
6


Davison et al.
R² Linear = 5.223E-4
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.571; correlation coefficient =0.027

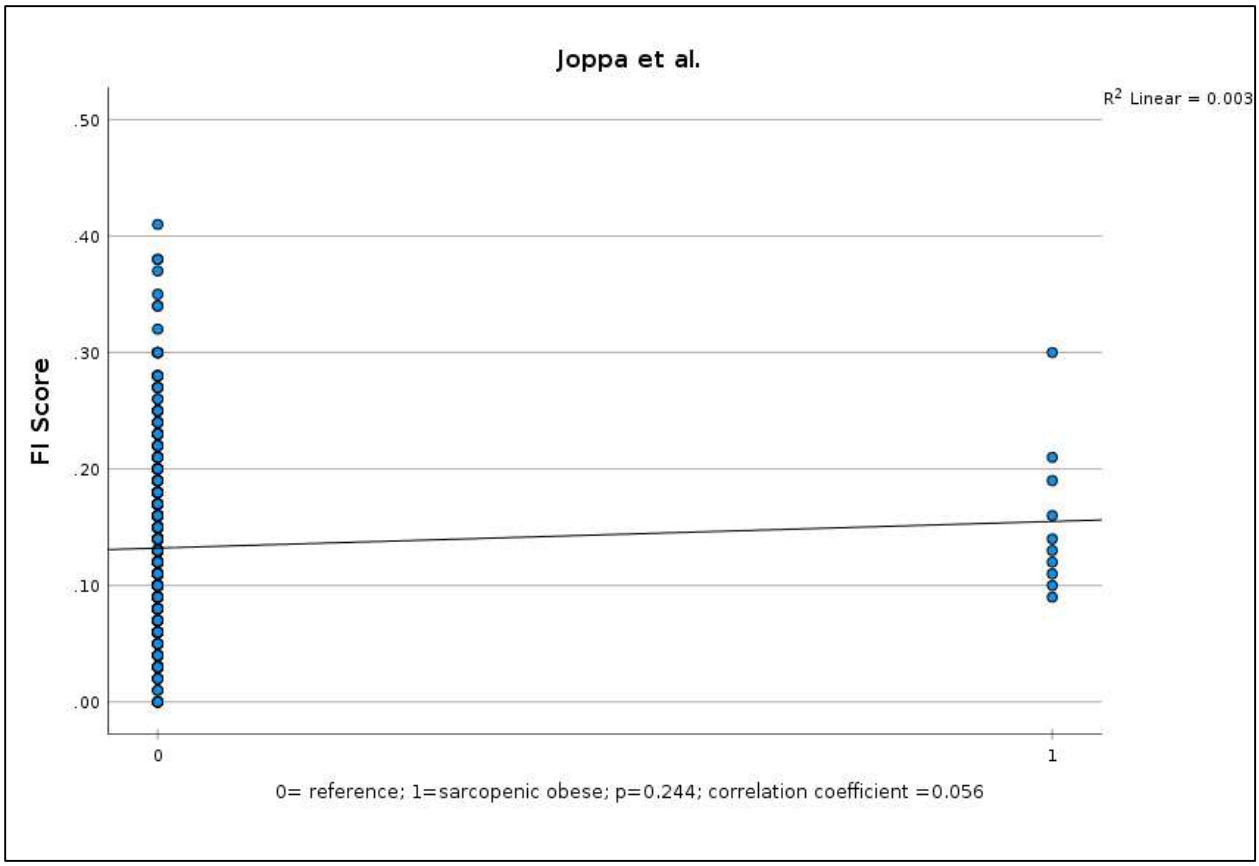
7


De Rose et al.
R² Linear = 0.041
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=<0.001*; correlation coefficient =0.190

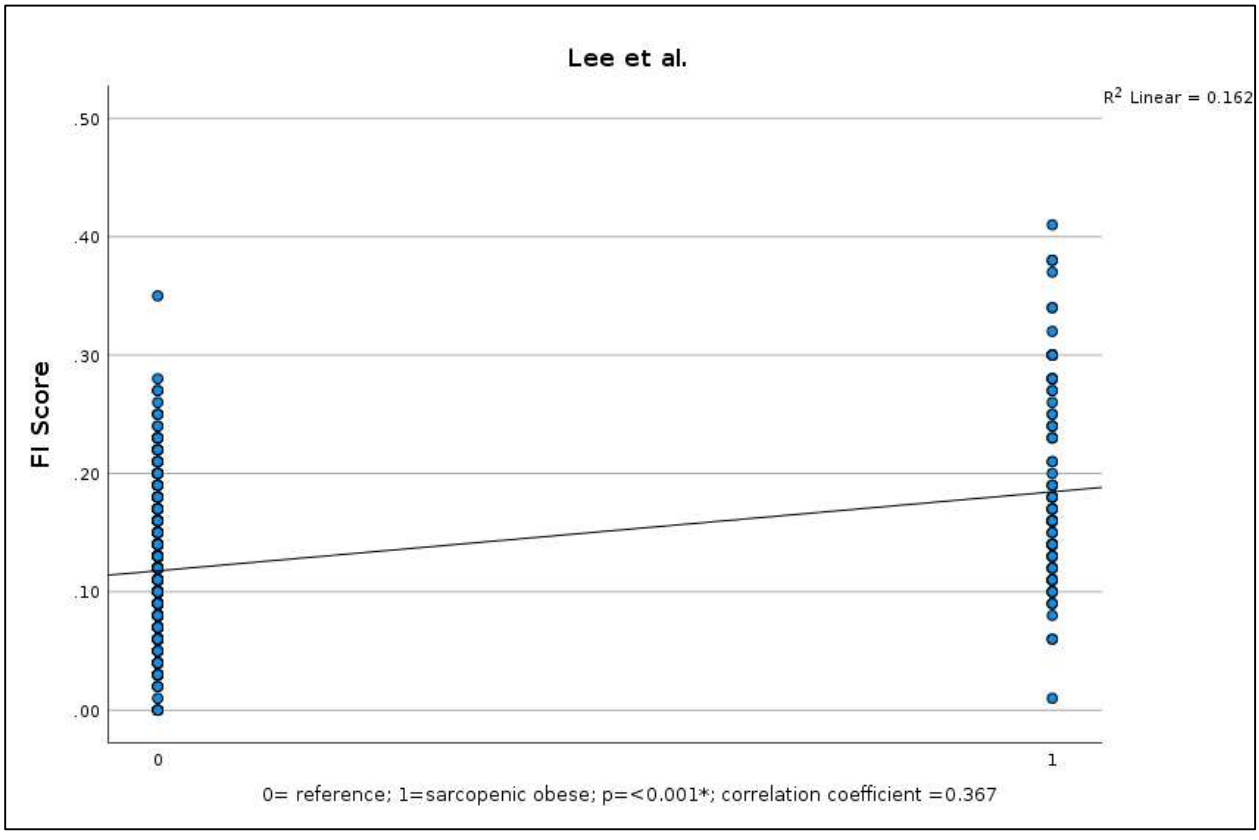
8


Ishii et al.
R² Linear = 5.337E-5
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.851; correlation coefficient =0.009

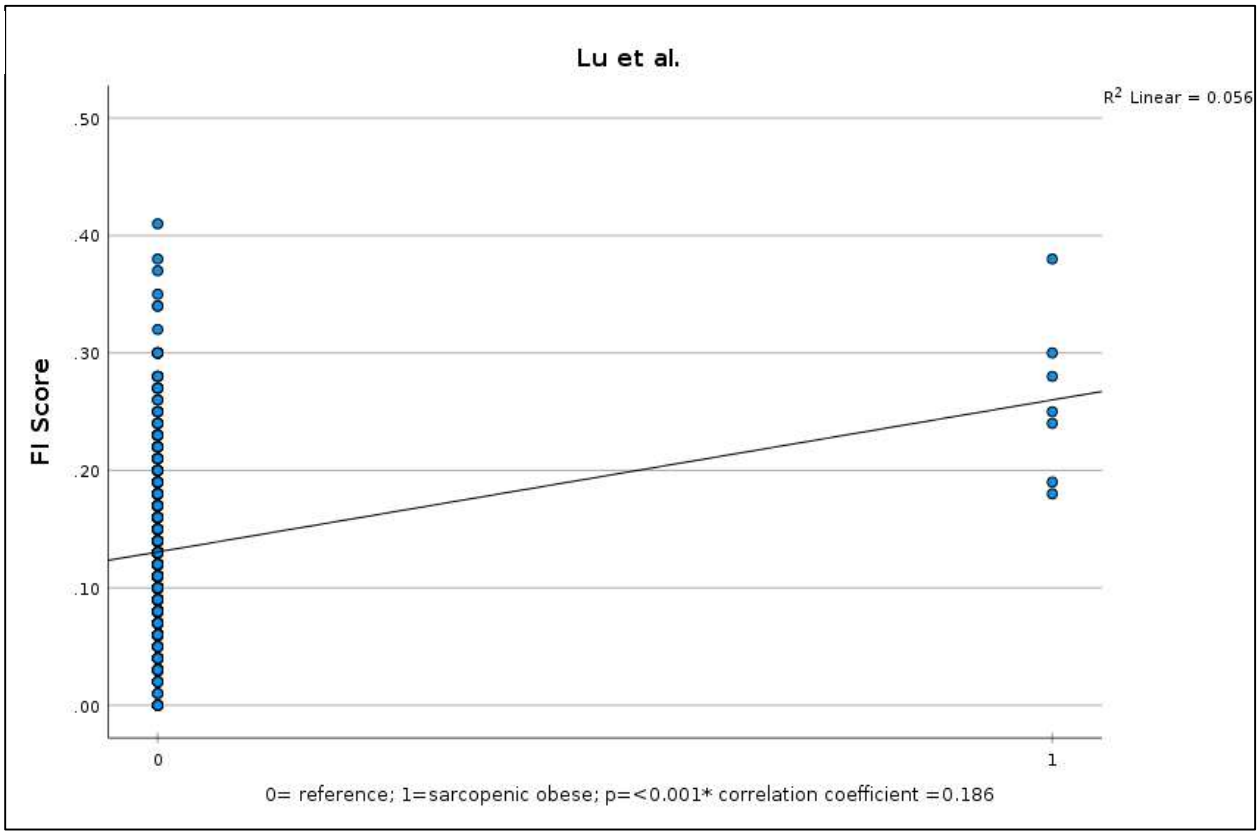
9


Joppa et al.
R² Linear = 0.003
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.244; correlation coefficient =0.056

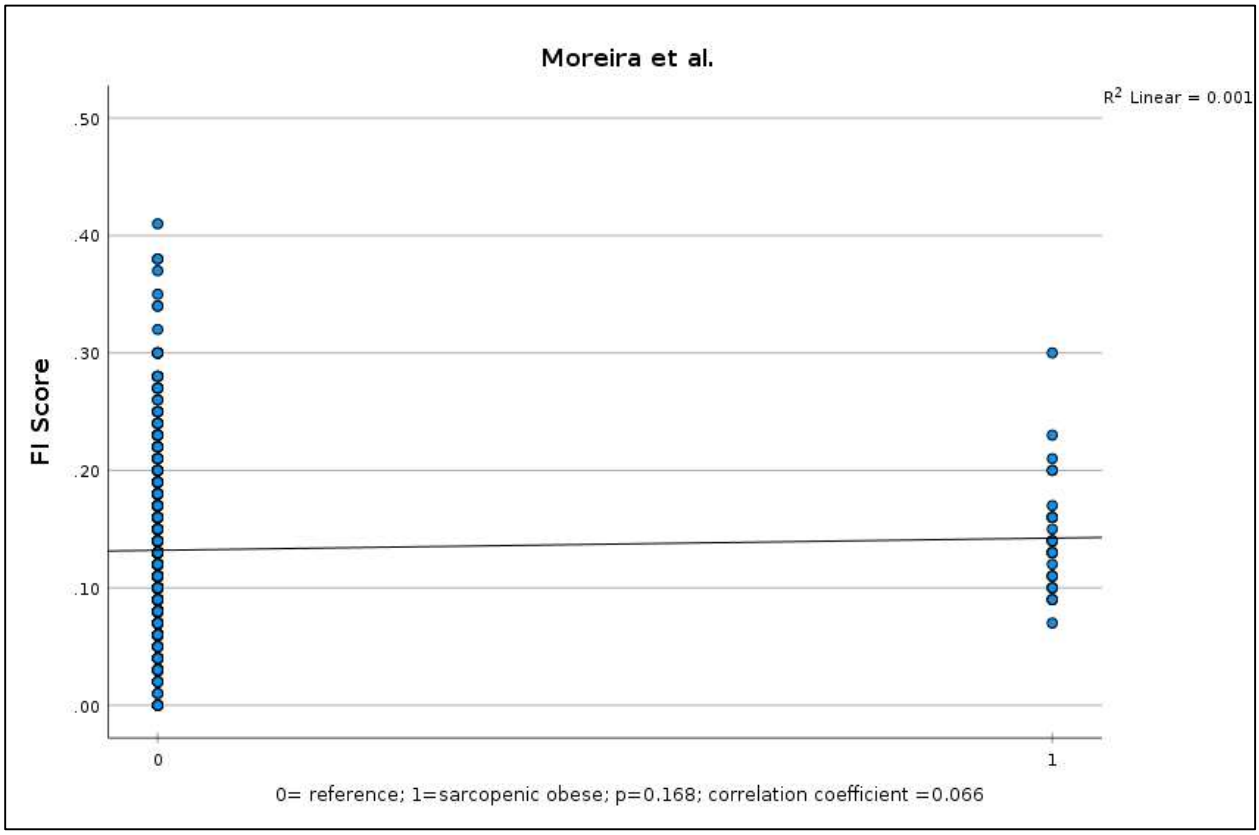
10


Lee et al.
R² Linear = 0.162
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=<0.001*; correlation coefficient =0.367

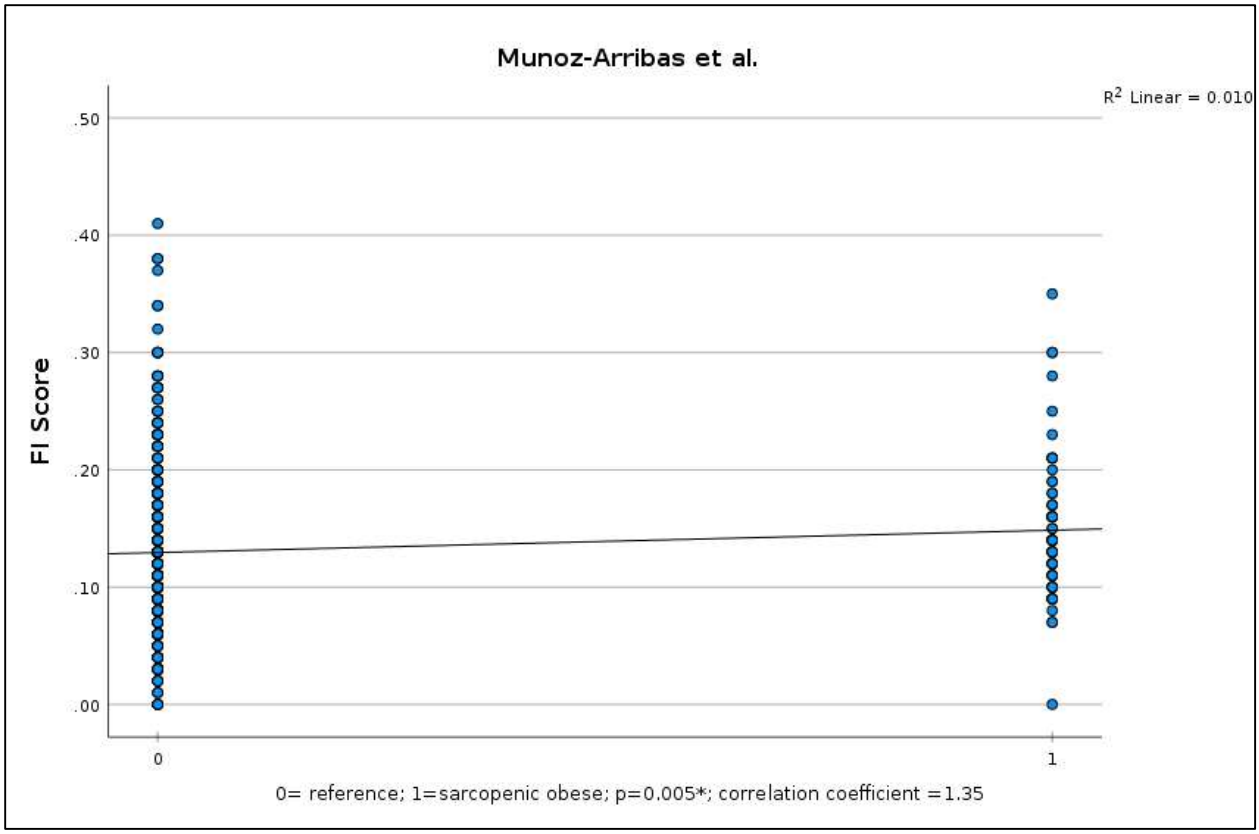
11


Lu et al.
R² Linear = 0.056
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=<0.001* correlation coefficient =0.186

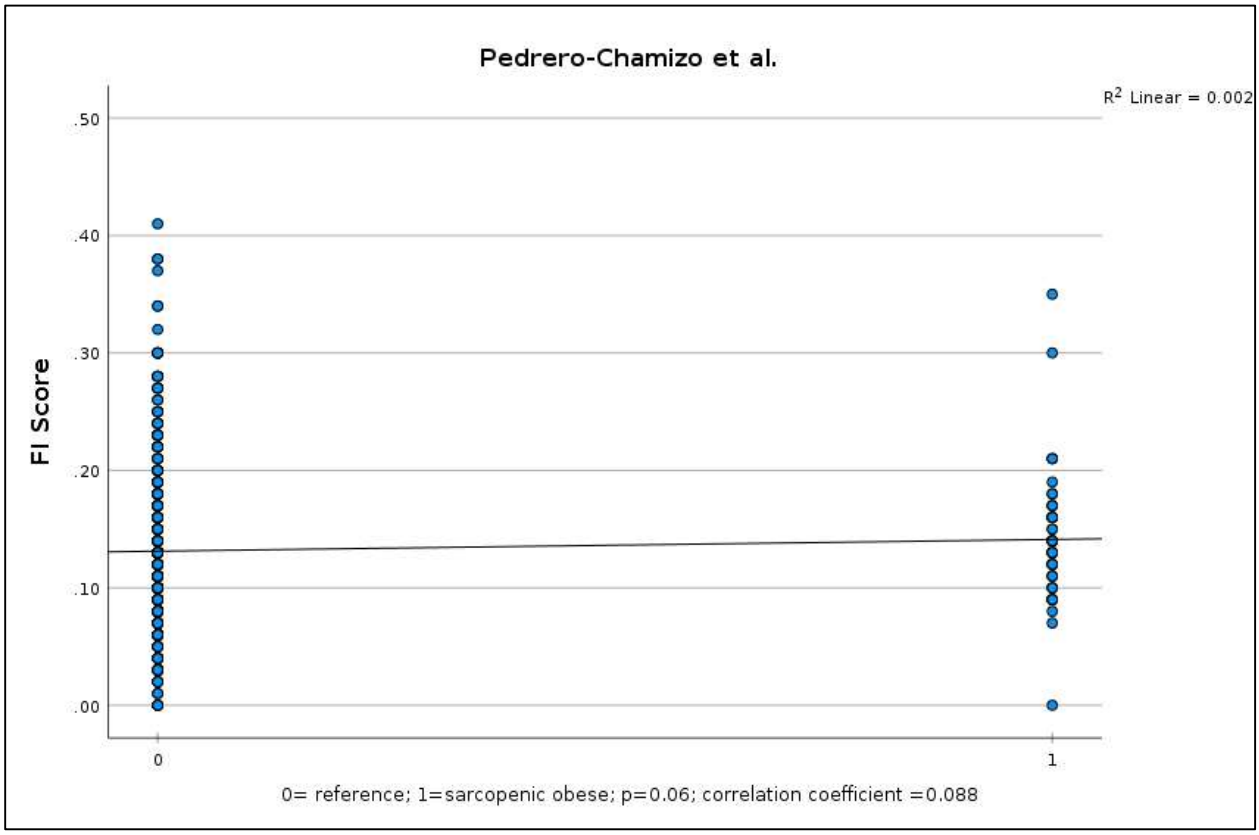
12


Moreira et al.
R² Linear = 0.001
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.168; correlation coefficient =0.066

13


Munoz-Arribas et al.
R² Linear = 0.010
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.005*; correlation coefficient =1.35

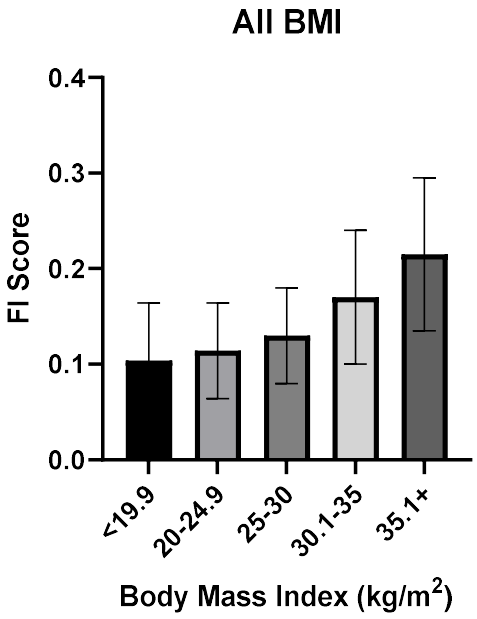
14


Pedrero-Chamizo et al.
R² Linear = 0.002
FI Score
.50
.40
.30
.20
.10
.00
0
1
0= reference; 1=sarcopenic obese; p=0.06; correlation coefficient =0.088

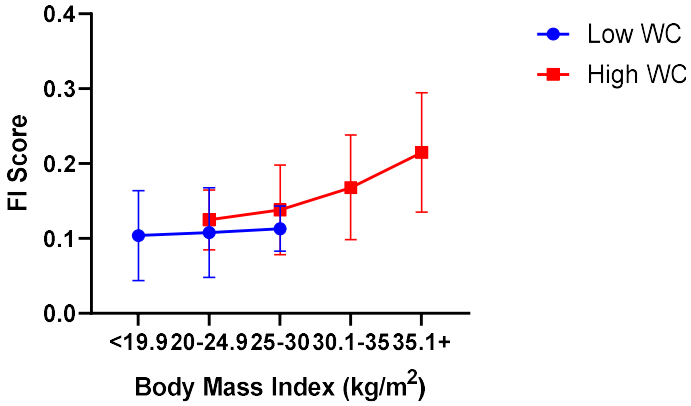
1. Aibar-Almazan et al.; 2. Baek et al.; 3. Batsis et al.; 4. Biolo et al.; 5. Chen et al.; 6. Davison et al.; 7. DeRosa et al.; 8. Ishii et al.; 9. Joppa et al.; 10. Lee et al.; 11. Lu et al.; 12. Moreira et al.; 13. Munoz-Arribas et al.; 14. Pedrero-Chamizo et al.

Appendix F: BMI, WC, and FI scores ANOVA Bar Graphs

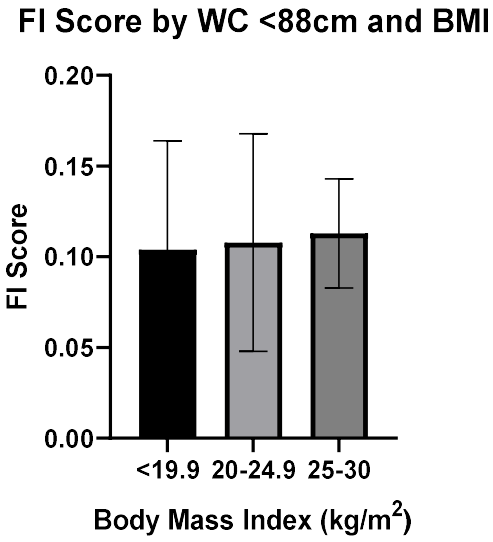
1.



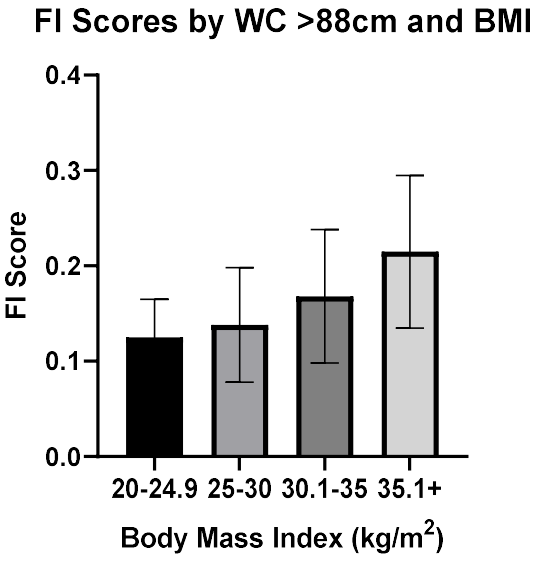
2.



3.



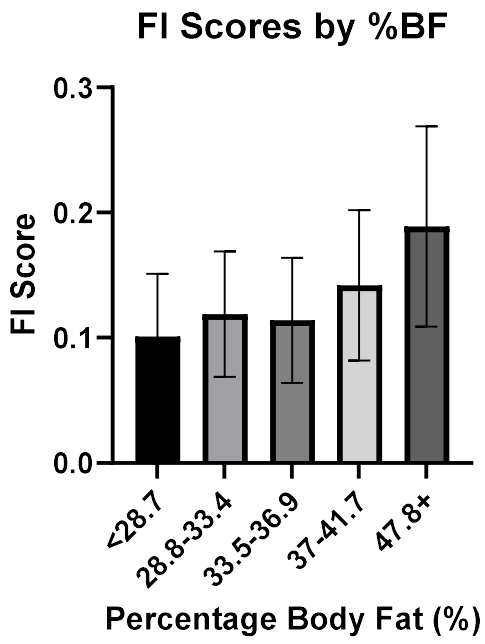
4.



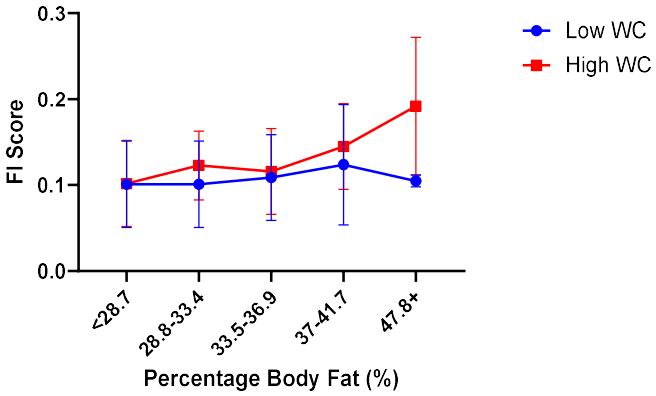
Frailty index scores expressed as mean ± standard deviation. 1. Frailty index scores by body mass index (kg/m^2) categories; 2. Line graph with the frailty index scores by body mass index (kg/m^2) categories and low and high waist circumference groups; 3. Frailty index scores by body mass index (kg/m^2) categories in subjects with a waist circumference (WC) of less than 88 centimetre (<88cm); 4. Frailty index scores by body mass index (kg/m^2) categories in subjects with a waist circumference (WC) of greater than 88 centimetres (>88cm).

Appendix G: %BF, WC, and FI scores ANOVA line graph

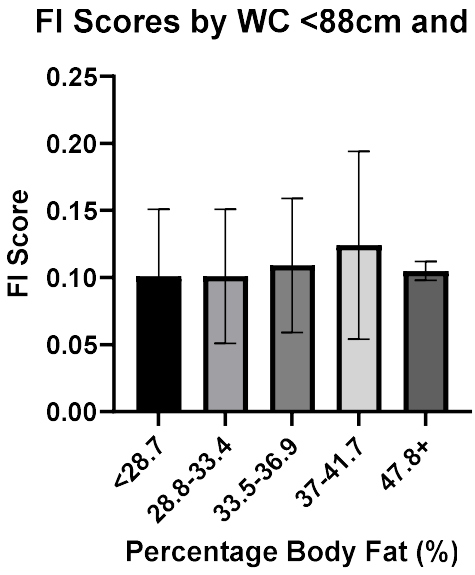
1.



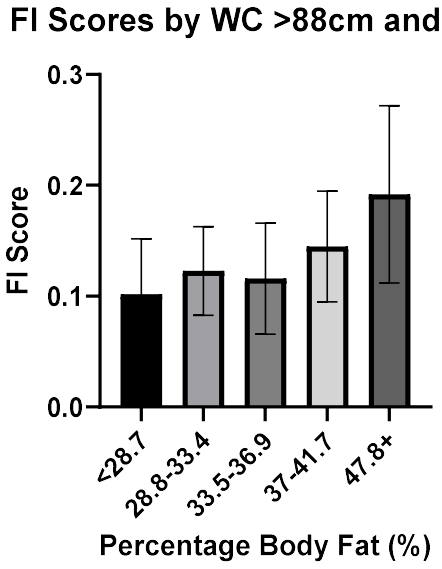
2.



3.



4.



Frailty index scores expressed as mean ± standard deviation. 1. Frailty index scores by percentage body fat (%) quintiles; 2. Line graph with the frailty index scores by percentage body fat (%) quintiles and low and high waist circumference groups; 3. Frailty index scores by percentage body fat (%) quintiles in subjects with a waist circumference (WC) of less than 88 centimetre (<88cm); 4. Frailty index scores by percentage body fat (%) quintiles in subjects with a waist circumference (WC) of greater than 88 centimetres (>88cm).