


BMJ Open Sarcopenia in systemic sclerosis: prevalence and impact – a systematic review and meta-analysis

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ABSTRACT

Objective This review aims to provide an estimate of sarcopenia prevalence and its impact on clinical characteristics in patients with systemic sclerosis (SSc).

Design Systematic review and meta-analysis.

Data sources Embase, Medline, Web of Science and the Cochrane Central Register of Controlled Trials were systematically searched from inception to 24 May 2023.

Eligibility criteria for selecting studies We included observational studies that reported the prevalence of sarcopenia in patients with SSc.

Data extraction and synthesis Two reviewers independently performed study selection and data extraction using standardised methods. Risk of bias was assessed using the Agency for Healthcare Research and Quality Scale and the Newcastle–Ottawa Scale. Meta-analysis was conducted using random effects models.

Results A total of 4583 articles were screened and 9 studies with data from 815 patients were included in the analysis (8 cross-sectional studies and 1 retrospective cohort study). The overall prevalence of sarcopenia in patients with SSc was 22% (95% CI 17% to 28%). Patients with SSc with sarcopenia had a poorer quality of life (mean difference –12.02; 95% CI –19.11 to –4.93) and higher C reactive protein (CRP) levels (standardised mean difference 0.67; 95% CI 0.35 to 1.00).

Conclusions Sarcopenia is common in patients with SSc. Patients with SSc with sarcopenia had a worse quality of life and higher CRP levels, based on our findings. Given the detrimental impact of sarcopenia on quality of life, future efforts aimed at early identification of sarcopenia in the clinical assessment of patients with SSc may have significance.

PROSPERO registration number CRD42022368326.

INTRODUCTION

Systemic sclerosis (SSc) is a rare immune-mediated rheumatic disease that is characterised by inflammation, microvascular damage and progressive fibrosis of both the skin and internal organs, such as the gastrointestinal tract, lung, heart and kidney.^{1 2} Depending on the extent of cutaneous involvement, SSc can be classified as limited cutaneous SSc (lcSSc) or diffuse cutaneous SSc (dcSSc).³ Patients with SSc are at risk for body composition abnormalities, including loss of skeletal

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This is the first systematic review and meta-analysis to evaluate the prevalence and impact of sarcopenia in patients with systemic sclerosis (SSc).
- ⇒ We conducted a comprehensive literature search to ensure that all eligible studies were included in the analysis.
- ⇒ We could not establish a definitive causal relationship between sarcopenia and SSc.
- ⇒ Even though this review included studies from different continents (Europe, South America and Asia), data on participant race were not accessible, limiting its potential applicability to specific patient subgroups.

muscle mass, due to malnutrition resulting from gastrointestinal involvement, chronic inflammation and steroid therapy.^{4–7} In addition, heart, lung and joint involvement in patients with SSc can lead to impaired exercise ability and decreased physical activity.⁸ These factors are closely related to sarcopenia, which is an age-related disease characterised by progressive and generalised loss of skeletal muscle mass and strength.⁹ The coexistence of sarcopenia and SSc can exacerbate the patient's health issues and increase their healthcare costs, posing significant challenges for healthcare professionals.

According to a meta-analysis, the prevalence of sarcopenia in community-dwelling elders aged over 60 years was 11% (95% CI 8% to 13%) in men and 9% (95% CI 7% to 11%) in women.¹⁰ The presence of sarcopenia increases the risk of falling, functional decline, frailty and mortality, leading to poor quality of life and significant healthcare expenses.¹¹ The high prevalence of sarcopenia in older adults, combined with its detrimental consequences, warrants the need for effective prevention and management strategies. In patients with SSc, addressing sarcopenia may improve their functional status and overall health outcomes, highlighting

the importance of early screening and intervention. Healthcare professionals need to recognise the interplay between SSc and sarcopenia to provide optimal care for these patients.

In recent years, the presence of sarcopenia in SSc has garnered attention in several studies.^{4-7 12-16} The documented prevalence of sarcopenia in SSc varies widely from 10.7% to 42% among different studies, which can be attributed to several factors.^{4 5} Differences in diagnostic criteria and assessment methods used in various studies, such as those proposed by the European Working Group of Sarcopenia in Older People (EWGSOP)^{9 17} and the Asian Working Group for Sarcopenia (AWGS),¹⁸ can result in variations in the evaluation of muscle mass in patients. Furthermore, the influence of sarcopenia on the clinical features of patients with SSc has been a topic of debate. For instance, Caimmi *et al*¹² suggested that individuals with SSc and sarcopenia had a longer duration of disease; the longer disease duration means that patients live longer with the disease, while Siegert *et al*⁶ contradicted this claim and found no difference between sarcopenia and disease duration in patients with SSc.

Currently, no comprehensive systematic review or meta-analysis has examined sarcopenia in SSc. Therefore, we conducted a systematic review and meta-analysis to identify the diagnostic criteria for sarcopenia and evaluate the most reliable evidence on the prevalence of sarcopenia in patients with SSc, as well as the effect of sarcopenia on the clinical features of patients with SSc.

METHODS

Data sources and search strategy

This systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline¹⁹ and registered in PROSPERO (CRD42022368326). We systemically searched four electronic databases, including Embase, Medline, Web of Science and the Cochrane Central Register of Controlled Trials, to identify all relevant articles relating to sarcopenia and SSc, without language restrictions. Our search encompassed all records published from inception to 24 May 2023, using the following terms: 'systemic sclerosis', 'scleroderm*', 'SSc', 'muscular atrophy', 'sarcopen*' and 'myopen*' (online supplemental tables S1-S4). Additionally, we conducted a manual search of the reference lists of the included articles to identify potential studies that may have been overlooked by the principal search.

Inclusion and exclusion criteria

The following inclusion and exclusion criteria were employed for this systematic review and meta-analysis: (1) studies conducted exclusively on adult patients (age

>18 years) diagnosed with SSc; (2) studies reporting the prevalence of sarcopenia in patients with SSc; (3) studies defining sarcopenia as low muscle mass (LMM) plus low muscle strength (LMS) and/or low physical performance (LPP) or LMM alone; LMM was evaluated by dividing appendicular skeletal muscle mass (in kilograms) by height in metres squared, LMS by hand grip strength, LPP by gait speed (GS) or Short Physical Performance Battery (SPPB) and diagnostic cut-offs varied depending on the criterion^{9 17 18 20}; (4) studies measuring lean mass or muscle mass using one of the four main techniques: dual-energy X-ray absorptiometry, bioelectrical impedance analysis, MRI and CT and (5) observational studies. Conversely, the exclusion criteria were as follows: repeated studies (defined as either identical data or identical articles).

Outcomes

The main outcomes of this systematic review comprise two aspects: first, the prevalence of sarcopenia among patients with SSc, and second, the clinical features of patients with SSc who suffer from sarcopenia compared with those who do not. These clinical features encompassed a range of factors, namely, the duration of disease, the quality of life assessed by the Short Form-36 (SF-36) survey,²¹ the pulmonary function (the forced vital capacity (FVC)-predicted value) and the C reactive protein (CRP) level. These features are frequently the focus of clinical studies in patients with SSc, and it is of significant interest to understand how sarcopenia impacts them.

Study selection and data extraction

After removing duplicates, the studies identified through the search strategy underwent eligibility assessment by two reviewers (XT and TL), who independently screened the titles and abstracts and assigned them to one of three categories: 'include', 'exclude' or 'maybe'. Subsequently, the full-text articles of those categorised as 'include' or 'maybe' were reviewed to arrive at a final selection, with any discrepancies between the reviewers resolved by a third reviewer (JY). Two reviewers (XT and XS) independently extracted the following variables using a predefined data collection form: first author, publication year, country, study design, sample size, mean age, number of females, disease subtype, mean disease duration, SSc diagnostic criteria, sarcopenia diagnostic criteria, assessment method for detecting sarcopenia and prevalence of sarcopenia. Additionally, we also collected data on clinical features in the form of mean±standard deviation (SD). For those studies that were not expressed as mean±SD, we performed data conversion with the method recommended by Luo *et al*²² and Wan *et al*.²³

Assessment of quality

Two authors (XT and TJ) independently assessed the quality of the included studies using the Agency for

Healthcare Research and Quality (AHRQ)²⁴ Scale in cross-sectional studies. This tool consists of 11 questions, with a 'no' or 'unclear' receiving 0 points and a 'yes' receiving 1 point. Low-quality articles received scores of 0–3, moderate-quality scores of 4–7 and high-quality scores of 8–11. The Newcastle–Ottawa Scale (NOS) was used to judge the quality of the cohort study.²⁵ The NOS scoring system assigns points from 0 to 9. We assigned values ranging from 0 to 3, 4 to 6 and 7 to 9 for low, moderate and high-quality, accordingly. Any discrepancies were resolved through discussion or consensus with a third author (JY).

Statistical analysis

The prevalence of sarcopenia in patients with SSc was determined by calculating the proportion of patients with sarcopenia in each study and conducting a meta-analysis of single proportions. We performed this meta-analysis using Stata/SE (V.12.0, StataCorp, College Station, Texas, USA). Forest plots were used to illustrate the prevalence of sarcopenia, along with the corresponding 95% confidence intervals (CIs) for each study and the overall estimate. Clinical characteristics such as disease duration, the SF-36 value, the FVC-predicted value and the CRP level from studies that compared patients with SSc with and without sarcopenia were also analysed using Review Manager (V.5.4, The Cochrane Collaboration, Oxford, UK) and expressed as mean difference (MD) or standardised mean difference (SMD) with 95% CI. Heterogeneity across studies was assessed via the I^2 statistic, with values of 25% being considered low, 50% moderate and 75% high.²⁶ Considering the variation in the definition of sarcopenia, diagnostic criteria and population characteristics among the included studies, this study employed a random-effects model.

Subgroup analyses were conducted to investigate potential sources of heterogeneity, focusing on sarcopenia definition (1 vs >1 diagnostic criteria), disease subtype and mean age (<60 vs ≥60 years). The reasons for grouping in subgroup analysis are as follows. First, variability in the definition of sarcopenia will result in varied prevalence estimates for patients with SSc. Unsurprisingly, increasing the number of necessary criteria in a sarcopenia definition will eventually diminish sarcopenia prevalence. Additionally, the disease subtype is an important factor that affects the prevalence of sarcopenia. Patients with dcSSc are more prone to develop sarcopenia.¹⁴ Moreover, age is an essential factor that influences the onset and course of sarcopenia, with the prevalence of sarcopenia increasing with age. Meta-regressions were also conducted on sample size, mean age, percentage of female patients and duration of SSc. However, due to limited data on the clinical characteristics of patients with SSc with and without sarcopenia, subgroup analyses and meta-regressions were not conducted. To evaluate the stability of pooled results, sensitivity analysis was performed by excluding one study at a time.

Publication bias was evaluated using Egger's test.²⁷ Statistical significance was set at $p < 0.05$ for all analyses.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

RESULTS

Search results

A comprehensive search of databases yielded 4583 articles. After eliminating duplicates ($n=1523$), the remaining 3060 titles and abstracts were screened. Subsequently, 25 relevant articles underwent full-text reading, and 16 were excluded for reasons specified in the flow chart and online supplemental table S5. Ultimately, nine studies were eligible for inclusion in this meta-analysis (figure 1).

Study characteristics

Online supplemental table S6 provides an overview of the characteristics of the studies included in this meta-analysis. A total of 815 patients with SSc from nine eligible studies^{4–7 12–16} published between 2018 and 2022 were included. The mean age of the patients ranged from 52.5 to 64.1 years, while the mean duration of SSc ranged from 6 to 12.8 years. The majority of the studies (eight out of nine) had a cross-sectional design,^{4–6 12–16} with one being a retrospective cohort study.⁷ The studies were conducted in various regions, with five from Europe,^{5–7 12 16} two from South America^{13 15} and two from Asia.^{4 14}

Risk of bias

According to the AHRQ and NOS ratings, eight of the eligible studies^{4–7 12 14–16} were of moderate quality, with only one article¹³ classified as high quality (online supplemental tables S7 and S8).

Methods used to assess sarcopenia

Online supplemental table S6 provides an overview of the diagnostic criteria used to evaluate sarcopenia across the included studies. Among them, seven studies^{4–7 13 15 16} employed EWGSOP criteria (five EWGSOP 2010 and two EWGSOP 2019) while one¹⁴ used AWGS criteria. Three studies^{5 7 12} solely relied on LMM for sarcopenia diagnosis, while six studies^{4 6 13–16} used LMM combined with LMS and/or LPP. The sarcopenia diagnostic criteria and cut-off values in the studies are summarised in table 1. Muscle mass was measured using dual-energy X-ray absorptiometry in seven studies^{5 7 12–16} and bioelectrical impedance analysis in two studies.^{4 6} Handgrip dynamometry was used to assess muscle strength in six studies,^{4 6 13–16} while GS (three studies^{14–16}) and the SPPB (two studies^{13 16}) were used to evaluate physical performance.

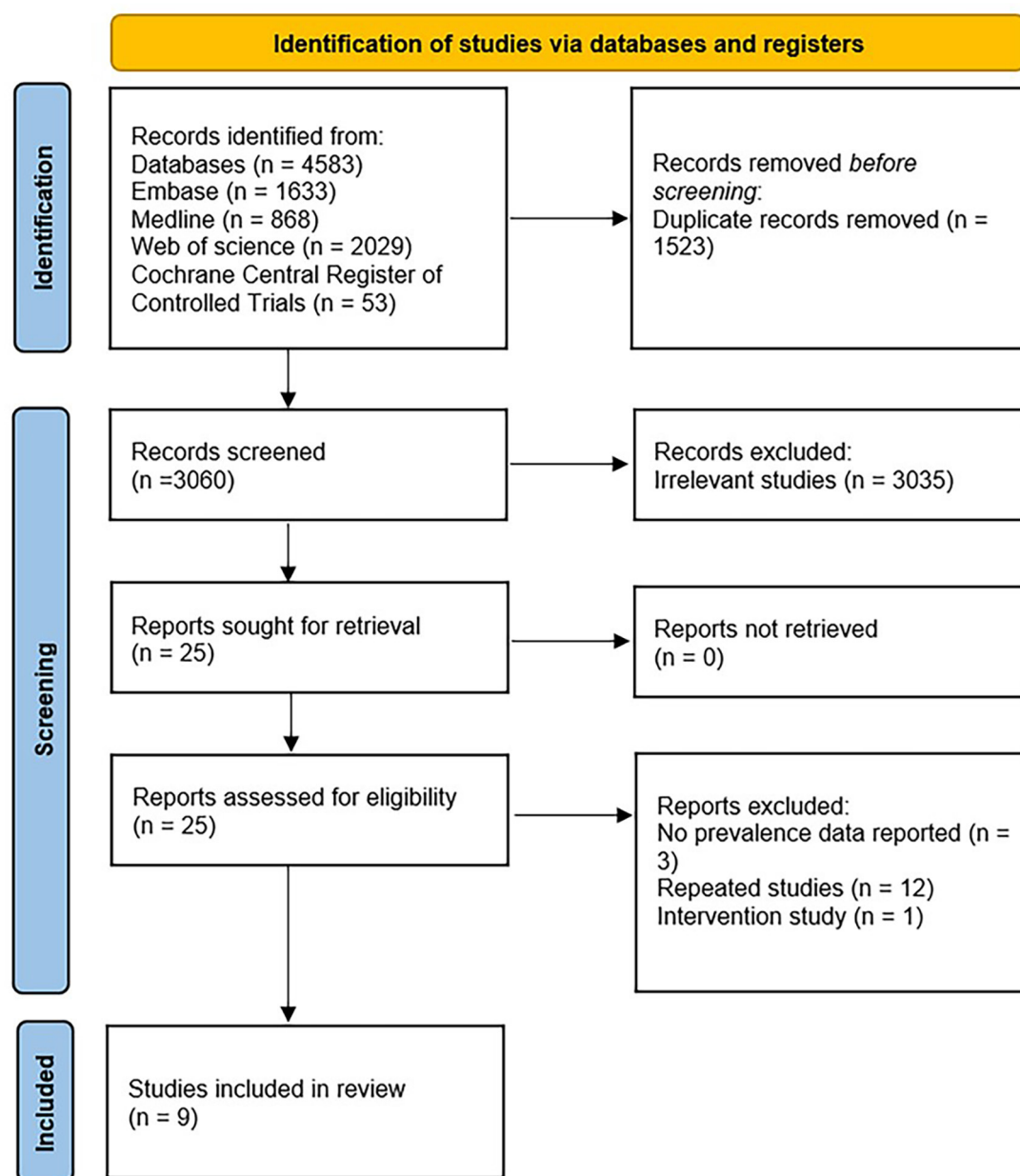


Figure 1 The flow chart of the literature selection.

Sarcopenia prevalence

Overall sarcopenia prevalence

The nine studies included in this review reported the prevalence of sarcopenia in patients with SSc, ranging from 10.7% to 42% (online supplemental table S6). The pooled prevalence of sarcopenia in patients with SSc was estimated at 22% (95% CI 17% to 28%), as shown in figure 2.

Subgroup analysis of sarcopenia prevalence

The prevalence of sarcopenia differed in studies that used a single criterion (LMM; 28% (95% CI 16% to 42%)) versus those that employed >1 criterion (LMM+LMS and/or LPP; 20% (95% CI 15% to 25%)), with no statistically significant difference noted ($p=0.234$, online supplemental figure S1).

Subgroup analysis based on disease subtype revealed that sarcopenia prevalence in dcSSc (30% (95% CI 23% to 37%)) was higher than that in lcSSc (23% (95% CI 12% to 36%)), and the difference was not statistically significant ($p=0.339$, online supplemental figure S2). The United Nations defines an older person as someone above the age of 60. Therefore, we also performed a subgroup analysis stratified by the mean age of the participants, with <60 and ≥ 60 years as the cut-off points. The prevalence of sarcopenia was lower in patients younger than 60 years (20% (95% CI 12% to 29%)) versus those older than 60 years (24% (95% CI 17% to 32%)), but the difference was not of statistical significance ($p=0.539$, online supplemental figure S3).

Table 1 Criteria and cut-off points used to detect sarcopenia in each study

First author and year	Country	Sarcopenia diagnostic criteria	Cut-off points
Caimmi (2018) ¹²	Italy	SMI	LMM: ASM/height ² <7.26 kg/m ² for men and <5.50 kg/m ² for women. ⁴³
Siegert (2018) ⁶	Germany	EWGSOP (2010)	LMM: ALM/height ² <7.26 kg/m ² for men and <5.50 kg/m ² for women. ⁴³ LMS: BMI ≤24, HGS ≤29 kg; 24.1≤BMI≤26, HGS ≤30 kg; 26.1≤BMI ≤28, HGS ≤30 kg; BMI >28, HGS ≤32 kg for men. BMI ≤23, HGS ≤17 kg; 23.1≤BMI≤26, HGS ≤17.3 kg; 26.1≤BMI≤29, HGS ≤18 kg; BMI >29, HGS ≤21 kg for women. ⁴⁴
Corallo (2019) ⁵	Italy	EWGSOP (2010)	LMM: RSMI <7.26 kg/m ² for men and <5.50 kg/m ² for women. ⁴³
Rincón (2019) ¹⁵	Argentina	EWGSOP (2010)	LMM: RSMI <7.26 kg/m ² for men and <5.50 kg/m ² for women. ⁴³ LMS: HGS <30 kg for men and <20 kg for women. ⁴⁵ LPP: GS <0.8 m/s (both genders). ⁴⁵
Paolino (2020) ⁷	Italy	EWGSOP (2010)	LMM: RSMI <7.26 kg/m ² for men and <5.50 kg/m ² for women. ⁴³
Hax (2021) ¹³	Brazil	EWGSOP (2019)	LMM: ASMI <7.0 kg/m ² for men and <5.50 kg/m ² for women. ⁴⁶ LMS: HGS <27 kg for men and <16 kg for women. ⁴⁷ LPP: SPPB ≤8-point score. ⁴⁸
Sari (2021) ⁴	Turkey	EWGSOP (2010)	LMM: ASMI <7.26 kg/m ² for men and <5.50 kg/m ² for women. ⁴³ LMS: BMI ≤24, HGS ≤29 kg; 24.1≤BMI≤26, HGS ≤30 kg; 26.1≤BMI≤28, HGS ≤30 kg; BMI >28, HGS ≤32 kg for men. BMI ≤23, HGS ≤17 kg; 23.1≤BMI≤26, HGS ≤17.3 kg; 26.1≤BMI≤29, HGS ≤18 kg; BMI >29, HGS ≤21 kg for women. ⁴⁴
Efremova (2022) ¹⁶	Russia	EWGSOP (2019)	LMM: ASMI <7.0 kg/m ² for men and <5.5 kg/m ² for women. ⁴⁶ LMS: HGS <27 kg for men and <16 kg for women. ⁴⁷ or Chair stand >15 s for five rises. ⁴⁹ LPP: GS ≤0.8 m/s ⁵⁰ or SPPB ≤8-point score. ⁴⁸
Sangaroon (2022) ¹⁴	Thailand	AWGS (2019)	LMM: ASMI <7.0 kg/m ² for men and <5.4 kg/m ² for women. ²⁰ LMS: HGS <28 kg for men and <18 kg for women. ²⁰ LPP: GS <1 m/s (both genders). ²⁰

ALM, Appendicular Lean Mass; ASM, Appendicular Skeletal Muscle Mass; ASMI, Appendicular Skeleton Muscle Index; AWGS, Asian Working Group for Sarcopenia; BMI, Body Mass Index; EWGSOP, European Working Group of Sarcopenia in Older People; GS, Gait Speed; HGS, Hand Grip Strength; LMM, Low Muscle Mass; LMS, Low Muscle Strength; LPP, Low Physical Performance; RSMI, Relative Skeletal Muscle Mass Index; SMI, Skeletal Muscle Mass Index; SPPB, Short Physical Performance Battery.

Meta-regression analyses

The results of the meta-regression analyses indicated that there was no significant association between the prevalence of sarcopenia and sample size ($p=0.424$), mean age of patients ($p=0.532$), the proportion of female patients ($p=0.449$) or duration of SSc ($p=0.255$). These findings are summarised in online supplemental table S9.

Impact of sarcopenia on the clinical characteristics of patients with SSc

Duration of SSc

Data from a total of four studies comprising 511 patients were included in the meta-analysis of SSc duration, which revealed that individuals with sarcopenia did not

have a longer disease duration than those without sarcopenia (MD 2.97 years (95% CI -0.13 to 6.08); $I^2=90\%$, figure 3A).

Quality of life

The meta-analysis included two studies with a total of 191 patients, which provided data on the SF-36 value. The findings of the meta-analysis indicated that patients with sarcopenia had a lower SF-36 value compared with those without sarcopenia (MD -12.02 (95% CI -19.11 to -4.93); $I^2=71\%$, figure 3B), that is, having sarcopenia was associated with poorer quality of life compared with those without sarcopenia.

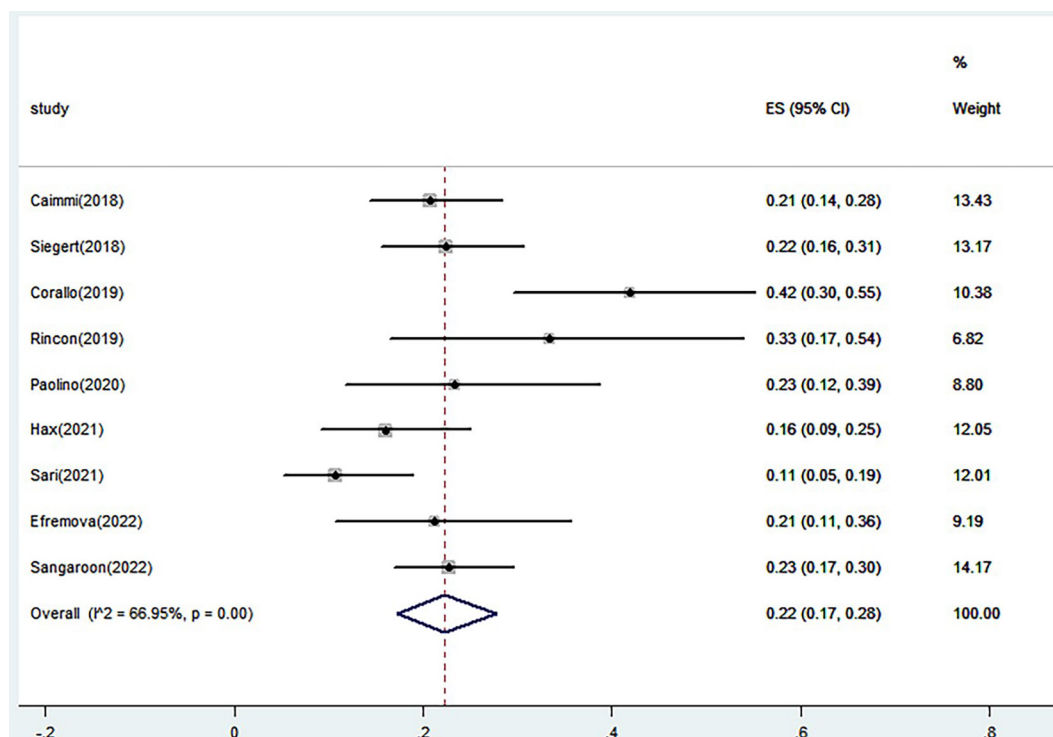


Figure 2 The pooled prevalence of sarcopenia in patients with systemic sclerosis.

Pulmonary function

The meta-analysis incorporated two studies involving a total of 320 patients that reported data on the FVC-predicted value. The results indicated that patients with sarcopenia did not have a lower FVC-predicted value than those without sarcopenia (MD -4.02% (95% CI -8.67 to 0.62); $I^2=0\%$, [figure 3C](#)). Therefore, there was no significant difference in pulmonary function between patients with sarcopenia and non-sarcopenia.

CRP level

Data from two studies comprising 191 patients were analysed to investigate the relationship between sarcopenia and CRP level. The results showed that sarcopenia was associated with a higher CRP level than no sarcopenia (SMD 0.67 (95% CI 0.35 to 1.00); $I^2=0\%$, [figure 3D](#)).

Sensitivity and publication bias analysis

The sensitivity analysis revealed that the overall prevalence of sarcopenia was not significantly affected by any individual study (online supplemental figure S4). In addition, Egger's test suggested no publication bias in this review ($p=0.311$, online supplemental figure S5).

DISCUSSION

Primary results

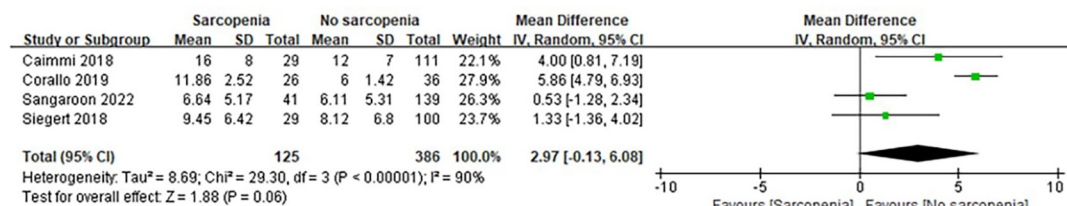
In this meta-analysis encompassing nine studies, the pooled prevalence of sarcopenia among 815 patients diagnosed with SSc was estimated to be 22% , which was significantly greater than that in community-dwelling older adults.²⁸ Notably, patients with SSc diagnosed with sarcopenia had poorer quality of life and a higher CRP

level, while no significant difference was noted for disease duration and FVC-predicted value when compared with patients without sarcopenia.

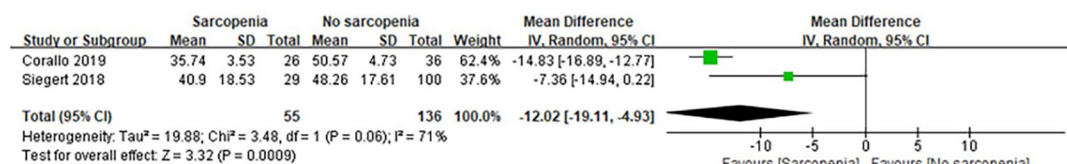
Mechanism basis

Sarcopenia, a condition characterised by loss of muscle mass and function, can be age-associated (primary sarcopenia) or secondary to chronic diseases, including malignant tumours and musculoskeletal diseases.^{29–31} Compared with other chronic inflammatory rheumatic diseases, sarcopenia has not been extensively evaluated in SSc. Recently, some studies have focused on the presence of sarcopenia in SSc. Nevertheless, the pathogenesis of sarcopenia in SSc remains unclear. Possible mechanisms contributing to the development of sarcopenia in SSc include (1) malnutrition: gastrointestinal involvement is the most frequent internal complication of SSc.³² Symptoms such as oesophageal reflux, early satiety, nausea and vomiting may lead to reduced caloric intake.¹² Additionally, fibrosis of the bowel wall and small intestine bacterial overgrowth can result in malabsorption of nutrients. Therefore, malnutrition is prevalent in patients with SSc. One study in community-dwelling older adults demonstrated that malnutrition is an independent predictor of sarcopenia (OR 2.42 ; 95% CI 1.04 to 5.60).³³ (2) Oxidative stress and chronic inflammation: oxidative stress, which is an imbalance in oxidant and antioxidant levels, is commonly observed in patients with SSc.³⁴ Increased oxidative stress disrupts the balance between the degradation and resynthesis of skeletal muscle proteins.³⁵ In addition, chronic low-grade inflammation is detrimental to skeletal muscle in humans.³⁶ Inflammatory cytokines,

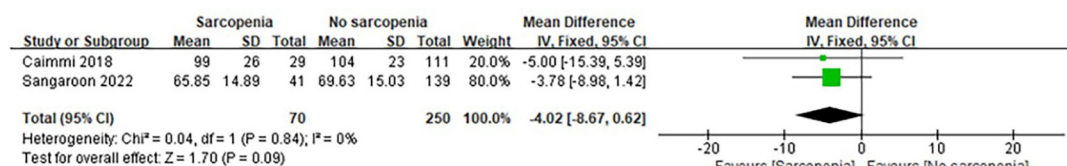
A Effect of sarcopenia on disease duration (years) of SSc patients



B Effect of sarcopenia on quality of life (SF-36 value) in SSc patients



C Effect of sarcopenia on pulmonary function (FVC predicted value) in SSc patients



D Effect of sarcopenia on CRP in SSc patients

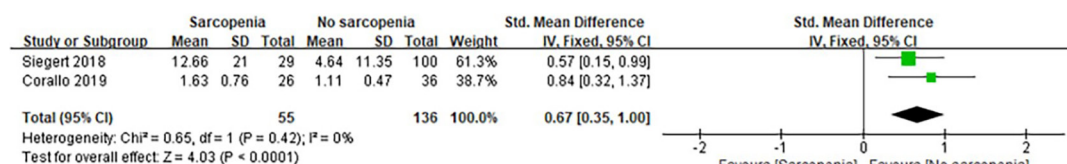


Figure 3 Impact of sarcopenia on clinical characteristics in patients with SSc. CRP, C reactive protein; FVC, forced vital capacity; SF-36, Short Form-36; SSc, systemic sclerosis.

such as tumour necrosis factor- α and interleukin-6, have been reported to contribute to the pathogenesis of SSc.³⁷ These cytokines stimulate protein catabolism and suppress muscle synthesis, ultimately leading to muscle wasting.³⁸ (3) Physical inactivity: due to pain and joint involvement, physical inactivity is common in patients with SSc,³⁹ leading to faster and greater muscle loss.¹¹ However, the mechanism of sarcopenia in patients with SSc remains to be confirmed by future research.

Interpretation of the results

This review offers unique insight into sarcopenia in patients with SSc. It describes the prevalence of sarcopenia in patients with SSc and how it is impacted by the different definitions of sarcopenia. The varying prevalence of sarcopenia may be explained in part by the variety of definitions. However, there was no statistical difference between 1 and >1 diagnostic criteria. This might be due to the lack of robustness of the combined results as a result of the small number of studies using one diagnostic criterion. In addition, discrepancies in sarcopenia diagnostic cut-offs among the included studies may have resulted in differing sarcopenia prevalence.

Furthermore, our meta-analysis indicated no statistically significant variation in the prevalence of sarcopenia between disease subtypes, which is consistent with the results of Sangaroon *et al.*¹⁴ It is important to note that this conclusion needs to be interpreted with caution due to the limited number of studies that could be included in the analysis. Although sarcopenia commonly occurs as an age-related process in older individuals,¹¹ it becomes more common as people get older. Our meta-analysis demonstrated that the difference in the prevalence of sarcopenia was not statistically significant between the patients over 60 years old and the patients under 60 years old. Furthermore, patients younger than 60 years old all used >1 criterion to diagnose sarcopenia, which makes the prevalence of sarcopenia in young people even lower. This suggests that, despite the influence of age on the presence of sarcopenia, the illness itself is responsible for sarcopenia onset and progression in patients with SSc. Therefore, rheumatologists should screen for sarcopenia even in young patients with SSc. However, this conclusion must be confirmed by a large number of high-quality clinical studies.

Our meta-analysis also revealed that patients with SSc diagnosed with sarcopenia had a poorer quality of life. On the one hand, involvement of the heart, lungs and joints in patients with SSc might result in diminished exercise capacity and decreased physical activity,⁸ making patients with SSc vulnerable to sarcopenia. On the other hand, sarcopenia is associated with a variety of negative outcomes, including hospitalisation, functional decline, falls and death.^{40 41} Therefore, it should come as no surprise that patients with SSc with sarcopenia have a higher risk of having a worse quality of life. Furthermore, individuals with SSc who had sarcopenia had higher CRP levels, according to our findings. This result is not surprising given that chronic inflammation is a known contributor to secondary sarcopenia.⁴² However, our review indicated that no significant difference was noted for disease duration or FVC-predicted value between patients with SSc with and without sarcopenia. According to the results of Caimmi *et al*,¹² the longer the disease duration, the greater the risk of sarcopenia. This might be due to the minimal number of studies that could extract data, resulting in false negatives in the pooled study results. Therefore, large prospective cohort studies are required to confirm this conclusion.

Clinical implications

This meta-analysis provides a comprehensive evaluation of the prevalence, diagnostic criteria and impact of sarcopenia in patients with SSc, which has not been previously done. The results of this study provide an up-to-date estimation of the prevalence of sarcopenia, which can guide sample size calculations for future research. While sarcopenia has been relatively understudied in SSc compared with other rheumatic diseases, our findings suggested that neither sarcopenia definition, disease subtype nor age affects the prevalence of sarcopenia. Patients with SSc with sarcopenia had a poorer quality of life, according to our findings. Therefore, early identification and intervention of patients with sarcopenia by clinicians is crucial. The high prevalence of sarcopenia in patients with SSc highlights the importance of early screening and management. Standardised criteria for sarcopenia diagnosis are also essential in patients with SSc to minimise variations in prevalence. These findings have important implications for future research, clinical practice and policy development in managing sarcopenia in patients with SSc and can potentially improve outcomes for these patients.

Strengths and weaknesses

This systematic review undertook a comprehensive and meticulous literature search to ensure that all pertinent studies were included in the analysis. The selection of studies, data extraction and quality assessments were carried out independently by two reviewers, thereby enhancing the accuracy and reliability of the results. Subgroup analyses and meta-regression analyses were also conducted to explore the possible sources of

heterogeneity, while sensitivity and publication bias analyses were performed to ensure robust and dependable conclusions.

Nevertheless, we must acknowledge certain limitations of our study. First, since most of the included studies were cross-sectional, it is impossible to establish a definitive causal relationship between sarcopenia and SSc. Nonetheless, this is a limitation inherent to the original literature and beyond our control. We, therefore, look forward to high-quality prospective cohort studies to provide more conclusive evidence on this matter. Second, there was some heterogeneity among the included studies in terms of factors such as the definition of sarcopenia, measurement approaches and diagnostic cut-offs. Moreover, most of the studies had small sample sizes. Therefore, future studies should aim to use uniform diagnostic criteria for sarcopenia and expand the sample size to improve the quality of research. Finally, even though this review included studies from different continents (Europe, South America and Asia), data on participant race were not accessible, limiting its potential applicability to specific patient subgroups.

CONCLUSIONS

Sarcopenia is common in patients with SSc. Patients with SSc with sarcopenia had a worse quality of life and higher CRP levels, based on our findings. Given the detrimental impact of sarcopenia on quality of life, future efforts aimed at early identification of sarcopenia in the clinical assessment of patients with SSc may have significance.

Contributors All authors conceived and designed this review; YJ, XT and JY developed the search strategy; XT and TL screened studies; XT and XS extracted data; XT and TJ appraised study quality; XT and NG conducted data analysis; XT drafted the manuscript; all authors revised the manuscript for important intellectual content. JY had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. JY is responsible for the overall content as the guarantor. JY accepts full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

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REFERENCES

- Denton CP, Khanna D. Systemic sclerosis. *The Lancet* 2017;390:1685–99.
- Zhong L, Pope M, Shen Y, et al. Prevalence and incidence of systemic sclerosis: a systematic review and meta-analysis. *Int J Rheum Dis* 2019;22:2096–107.
- LeRoy EC, Black C, Fleischmajer R, et al. Scleroderma (systemic sclerosis): classification, Subsets and pathogenesis. *J Rheumatol* 1988;15:202–5.
- Sari A, Esme M, Aycicek GS, et al. Evaluating skeletal muscle mass with ultrasound in patients with systemic sclerosis. *Nutrition* 2021;84:110999.
- Corallo C, Fioravanti A, Tenti S, et al. Sarcopenia in systemic sclerosis: the impact of nutritional, clinical, and laboratory features. *Rheumatol Int* 2019;39:1767–75.
- Siebert E, March C, Otten L, et al. Prevalence of sarcopenia in systemic sclerosis: assessing body composition and functional disability in patients with systemic sclerosis. *Nutrition* 2018;55:56:51–5.
- Paolino S, Goegan F, Cimmino MA, et al. Advanced microvascular damage associated with occurrence of sarcopenia in systemic sclerosis patients: results from a retrospective cohort study. *Clin Exp Rheumatol* 2020;38:65–72.
- Cuomo G, Santoriello C, Polverino F, et al. Impaired exercise performance in systemic sclerosis and its clinical correlations. *Scand J Rheumatol* 2010;39:330–5.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. *Age Ageing* 2010;39:412–23.
- Papadopoulou SK, Tsintavis P, Potsaki P, et al. Differences in the prevalence of Sarcopenia in community-dwelling, nursing home and hospitalized individuals. *J Nutr Health Aging* 2020;24:83–90.
- Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *The Lancet* 2019;393:2636–46.
- Caimmi C, Caramaschi P, Venturini A, et al. Malnutrition and sarcopenia in a large cohort of patients with systemic sclerosis. *Clin Rheumatol* 2018;37:987–97.
- Hax V, do Espírito Santo RC, Dos Santos LP, et al. Practical screening tools for sarcopenia in patients with systemic sclerosis. *PLoS ONE* 2021;16:e0245683.
- Sangaroon A, Foocharoen C, Theerakulpisut D, et al. Prevalence and clinical Association of sarcopenia among Thai patients with systemic sclerosis. *Sci Rep* 2022;12:18198.
- Rincón IDR, Alak M, Alsina G, et al. Sarcopenia in systemic sclerosis. *Arthritis Rheumatol* 2019;71:2957–8.
- Efremova AO, Toroptsova NV, Nikitinskaya OA, et al. The frequency of sarcopenia and factors associated with muscle mass in women with systemic scleroderma (pilot study). *Osteoporos Int* 2022;32:S1–409.
- Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16–31.
- Chen L-K, Liu L-K, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. *J Am Med Dir Assoc* 2014;15:95–101.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71.
- Chen L-K, Woo J, Assantachai P, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc* 2020;21:300–7.
- Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. *Medical Care* 1992;30:473–83.
- Luo D, Wan X, Liu J, et al. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res* 2018;27:1785–805.
- Wan X, Wang W, Liu J, et al. Estimating the sample mean and standard deviation from the sample size, median, range and/or Interquartile range. *BMC Med Res Methodol* 2014;14:135.
- Zeng X, Zhang Y, Kwong JSW, et al. The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review. *J Evid Based Med* 2015;8:2–10.
- Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603–5.
- Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
- Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
- Simsek H, Meseri R, Sahin S, et al. Prevalence of sarcopenia and related factors in community-dwelling elderly individuals. *Saudi Med J* 2019;40:568–74.
- Kawakubo N, Kinoshita Y, Souzaki R, et al. The influence of sarcopenia on high-risk neuroblastoma. *J Surg Res* 2019;236:101–5.
- Matsunaga T, Miyata H, Sugimura K, et al. Prognostic significance of sarcopenia and systemic inflammatory response in patients with esophageal cancer. *Anticancer Res* 2019;39:449–58.
- Laurent MR, Dedeyne L, Dupont J, et al. Age-related bone loss and sarcopenia in men. *Maturitas* 2019;122:51–6.
- Clements PJ, Becvar R, Drosos AA, et al. Assessment of gastrointestinal involvement. *Clin Exp Rheumatol* 2003;21(3 Suppl 29):S15–8.
- Kurose S, Nishikawa S, Nagaoka T, et al. Prevalence and risk factors of sarcopenia in community-dwelling older adults visiting regional medical institutions from the Kadoma Sarcopenia study. *Sci Rep* 2020;10:19129.
- Doridot L, Jelliel M, Chêne C, et al. Implication of oxidative stress in the pathogenesis of systemic sclerosis via inflammation, autoimmunity and fibrosis. *Redox Biol* 2019;25:101122.
- Meng SJ, Yu LJ. Oxidative stress, molecular inflammation and sarcopenia. *Int J Mol Sci* 2010;11:1509–26.
- Howard C, Ferrucci L, Sun K, et al. Oxidative protein damage is associated with poor grip strength among older women living in the community. *J Appl Physiol* (1985) 2007;103:17–20.
- Shima Y. Cytokines involved in the pathogenesis of SSC and problems in the development of anti-cytokine therapy. *Cells* 2021;10:1104.
- Bano G, Trevisan C, Carraro S, et al. Inflammation and sarcopenia: a systematic review and meta-analysis. *Maturitas* 2017;96:10–5.
- Liem SIE, Meessen JMTA, Wolterbeek R, et al. Physical activity in patients with systemic sclerosis. *Rheumatol Int* 2018;38:443–53.
- Tsekoura M, Kastrinis A, Katsoulaki M, et al. Sarcopenia and its impact on quality of life. *Adv Exp Med Biol* 2017;987:213–8.
- Beaudart C, Rizzoli R, Bruyère O, et al. Sarcopenia: burden and challenges for public health. *Arch Public Health* 2014;72:45.
- Wang C, Bai L. Sarcopenia in the elderly: basic and clinical issues. *Geriatr Gerontol Int* 2012;12:388–96.
- Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 1998;147:755–63.
- Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146–56.
- Lauretani F, Russo CR, Bandinelli S, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* (1985) 2003;95:1851–60.
- Gould H, Brennan SL, Kotowicz MA, et al. Total and appendicular lean mass reference ranges for Australian men and women: the Geelong osteoporosis study. *Calcif Tissue Int* 2014;94:363–72.
- Dodds RM, Syddall HE, Cooper R, et al. Grip strength across the life course: normative data from twelve British studies. *PLoS One* 2014;9:e113637.
- Pavasini R, Guralnik J, Brown JC, et al. Short physical performance battery and all-cause mortality: systematic review and meta-analysis. *BMC Med* 2016;14:215.
- Cesari M, Kritchevsky SB, Newman AB, et al. Added value of physical performance measures in predicting adverse health-related events: results from the health. *J Am Geriatr Soc* 2009;57:251–9.
- Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA* 2011;305:50–8.

Sarcopenia in Systemic Sclerosis: Prevalence and Impact - A Systematic Review

and Meta-analysis

1. Table S1 Search strategy by Medline via Ovid SP
2. Table S2 Search strategy by Embase via Ovid SP
3. Table S3 Search strategy by Web of Science
4. Table S4 Search strategy by Cochrane Central Register of Controlled Trials via Ovid SP
5. Table S5 The reasons for the exclusion of full-text articles
6. Table S6 Characteristics of the included studies
7. Table S7 ARHQ Methodology Checklist for Cross-Sectional Study
8. Table S8 Newcastle-Ottawa Scale for Cohort study
9. Table S9 Meta-regression analyses of sarcopenia prevalence
10. Figure S1 Prevalence of sarcopenia by criteria
11. Figure S2 Prevalence of sarcopenia by disease subtype
12. Figure S3 Prevalence of sarcopenia by mean age
13. Figure S4 Sensitivity analysis
14. Figure S5 Egger's test for publication bias

Table S1 Search strategy by Medline via Ovid SP

-
1. exp Scleroderma, Systemic/
 2. ((Systemic or general* or diffus* or progress* or Limit*) adj3 sclerosis).mp.
 3. scleroderm*.tw.
 4. SSc.tw.
 5. 1 or 2 or 3 or 4
 6. exp muscular atrophy/
 7. (sarcopen* or myopen* or dynapon* or amyotroph* or myoatroph* or myophagis* or myodegenerat*).mp.
 8. ((muscle or muscular) adj5 (atroph* or wast* or weak* or loss* or mass or degenerat*)).ti,ab.
 9. 6 or 7 or 8
 10. 5 and 9
 11. exp animals/ not humans.sh.
 12. 10 not 11
-

Table S2 Search strategy by Embase via Ovid SP

-
1. exp systemic sclerosis/
 2. ((Systemic or general* or diffus* or progress* or Limit*) adj3 sclerosis).mp.
 3. scleroderm*.tw.
 4. SSc.tw.
 5. 1 or 2 or 3 or 4
 6. exp muscle atrophy/
 7. (sarcopen* or myopen* or dynapon* or amyotroph* or myoatroph* or myophagis* or myodegenerat*).mp.
 8. ((muscle or muscular) adj5 (atroph* or wast* or weak* or loss* or mass or degenerat*)).ti,ab.
 9. 6 or 7 or 8
 10. 5 and 9
 11. exp animal/
 12. human/
 13. 11 not 12
 14. 10 not 13
-

Table S3 Search strategy by Web of Science

Topic= (((Systemic or general* or diffus* or progress* or Limit*) near/3 sclerosis)
or sclerodem or ssc) and (sarcopen* or myopen* or dynapon* or amyotroph* or
myoatroph* or myophagis* or myodegenerat* or ((muscle or muscular) near/5
(atroph* or wast* or weak* or loss* or mass or degenerat*)))

Table S4 Search strategy by Cochrane Central Register of Controlled Trials via

Ovid SP

-
1. exp Scleroderma, Systemic/
 2. ((Systemic or general* or diffus* or progress* or Limit*) adj3 sclerosis).mp.
 3. scleroderm*.tw.
 4. SSc.tw.
 5. 1 or 2 or 3 or 4
 6. exp muscular atrophy/
 7. (sarcopen* or myopen* or dynapon* or amyotroph* or myoatroph* or myophagis* or myodegenerat*).mp.
 8. ((muscle or muscular) adj5 (atroph* or wast* or weak* or loss* or mass or degenerat*)).ti,ab.
 9. 6 or 7 or 8
 10. 5 and 9
-

Table S5 The reasons for the exclusion of full-text articles

Study	Reason for the exclusion
Norman (2014)	Repeated study
Siegert (2014)	Repeated study
Caimmi (2017)	Repeated study
March (2017)	Repeated study
Doerfler (2017)	Intervention study
Paolino (2018)	Repeated study
Radic (2018)	Not reported sarcopenia prevalence data in SSc patients
Remolina (2019)	Repeated study
Sari (2019)	Repeated study
Veronica (2019)	Repeated study
Hax (2020)	Repeated study
Santo (2020)	Repeated study
Sangaroon (2020)	Repeated study
Peterson (2020)	Not reported sarcopenia prevalence data in SSc patients
Efremova (2021)	Repeated study
Sorokina (2022)	Not reported sarcopenia prevalence data in SSc patients

Table S6 Characteristics of the included studies

First author and year	Country	Study design	Sample size	Mean age(years)	Female, n	Disease subtype	Disease duration (years)	SSc diagnostic criteria	Sarcopenia diagnostic criteria	Criteria (assessment method of detecting sarcopenia)	Prevalence of sarcopenia	
											Total,n(%)	Diffuse,n(%)
Caimmi (2018)	Italy	Cross-sectional study	140	64	118	limited 97 diffuse 43	12.8	2013 ACR/EULAR	SMI	LMM (DXA)	29(20.7%)	11(7.9%)
Siebert (2018)	Germany	Cross-sectional study	129	60	118	-	7	2013 ACR/EULAR	EWGSOP (2010)	LMM (BIA) LMS (HGS)	29(22.5%)	-
Corallo (2019)	Italy	Cross-sectional study	62	62	54	limited 50 diffuse 12	8	2013 ACR/EULAR	EWGSOP (2010)	LMM (DXA)	26(42%)	4(6.4%)
Rincon (2019)	Argentina	Cross-sectional study	27	52.5	20	limited 16 diffuse 11	7.8	2013 ACR/EULAR	EWGSOP (2010)	LMM (DXA) LMS (HGS) LPP (4mGS)	9(33.3%)	3(11.1%)
Paolino (2020)	Italy	Retrospective cohort study	43	64.1	36	-	10.2	2013 ACR/EULAR	EWGSOP (2010)	LMM (DXA)	10(23.3%)	-
Hax (2021)	Brazil	Cross-sectional study	94	60.5	87	-	12.5	2013 ACR/EULAR	EWGSOP (2019)	LMM (DXA) LMS (HGS) LPP (SPPB)	15(15.9%)	-
Sari (2021)	Turkey	Cross-sectional	93	52.6	86	-	10.7	1980ACR	EWGSOP	LMM (BIA)	10(10.7%)	-

First author and year	Country	Study design	Sample size	Mean age(years)	Female, n	Disease subtype	Disease duration (years)	SSc diagnostic criteria	Sarcopenia diagnostic criteria	Criteria (assessment method of detecting sarcopenia)	Prevalence of sarcopenia	
											Total,n(%)	Diffuse,n(%)
Efremova (2022)	Russia	Cross-sectional study	47	53.9	47	limited 29 diffuse 18	6	2013 ACR/EULAR	(2010)	LMS (HGS)	10(21.3%)	6(12.8%)
										LMM (DXA)		
									EWGSOP (2019)	LMS (HGS and Chair rising test)		
Sangaroon (2022)	Thailand	Cross-sectional study	180	58.8	119	limited 86 diffuse 94	6.2	-		LPP (GS and SPPB)	41(22.8%)	30(16.7%)
									AWGS (2019)	LMM(DXA)		
										LMS(HGS) LPP(GS)		

ACR, American College of Rheumatology; EULAR, European League against Rheumatology classification criteria; SMI, Skeletal Muscle Mass Index; EWGSOP, European Working Group on Sarcopenia in Old People; HGS, hand grip strength; 4mGS, 4 m gait speed; SPPB, Short Physical Performance Battery; GS, gait speed; AWGS, Asian Working Group for Sarcopenia.

Table S7 ARHQ Methodology Checklist for Cross-Sectional Study

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total Score
Caimmi (2018)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Unclear	Yes	No	6
Siegert (2018)	Yes	Yes	Unclear	Yes	Unclear	Yes	No	No	No	Yes	No	5
Corallo (2019)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	No	Yes	No	6
Rincon (2019)	Yes	Yes	Unclear	Unclear	Unclear	Yes	No	No	No	Yes	No	4
Hax (2021)	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	No	Yes	Yes	No	8
Sari (2021)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	No	Yes	No	6
Efremova (2022)	Unclear	Yes	Unclear	Unclear	Unclear	Yes	No	No	No	Yes	No	3
Sangaroon (2022)	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	No	Yes	No	6

Item 1. Define the source of information (survey, record review)

Item 2. List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications

Item 3. Indicate time period used for identifying patients

Item 4. Indicate whether or not subjects were consecutive if not population-based

Item 5. Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants

Item 6. Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)

Item 7. Explain any patient exclusions from analysis

Item 8. Describe how confounding was assessed and/or controlled

Item 9. If applicable, explain how missing data were handled in the analysis

Item 10. Summarize patient response rates and completeness of data collection

Item 11. Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained

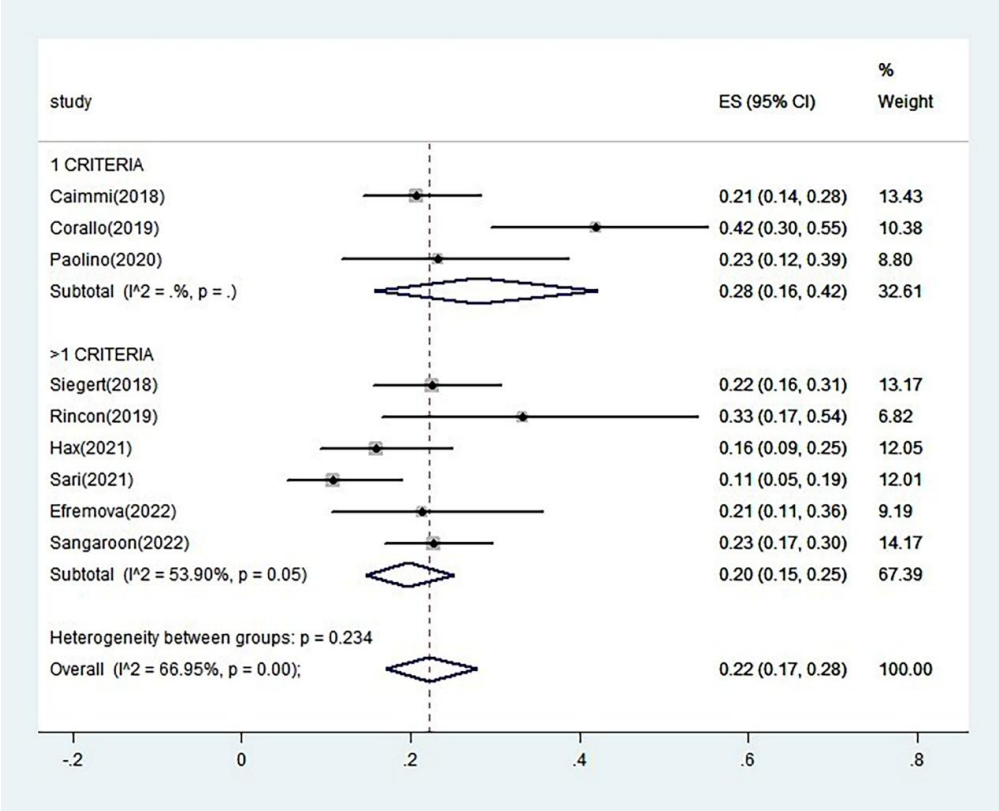
Table S8 Newcastle-Ottawa Scale for Cohort study

Study	Selection				Comparability	Outcome			Total Score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Paolino (2020)	0	1	1	0	1	1	0	0	4

Table S9 Meta-regression analyses of sarcopenia prevalence

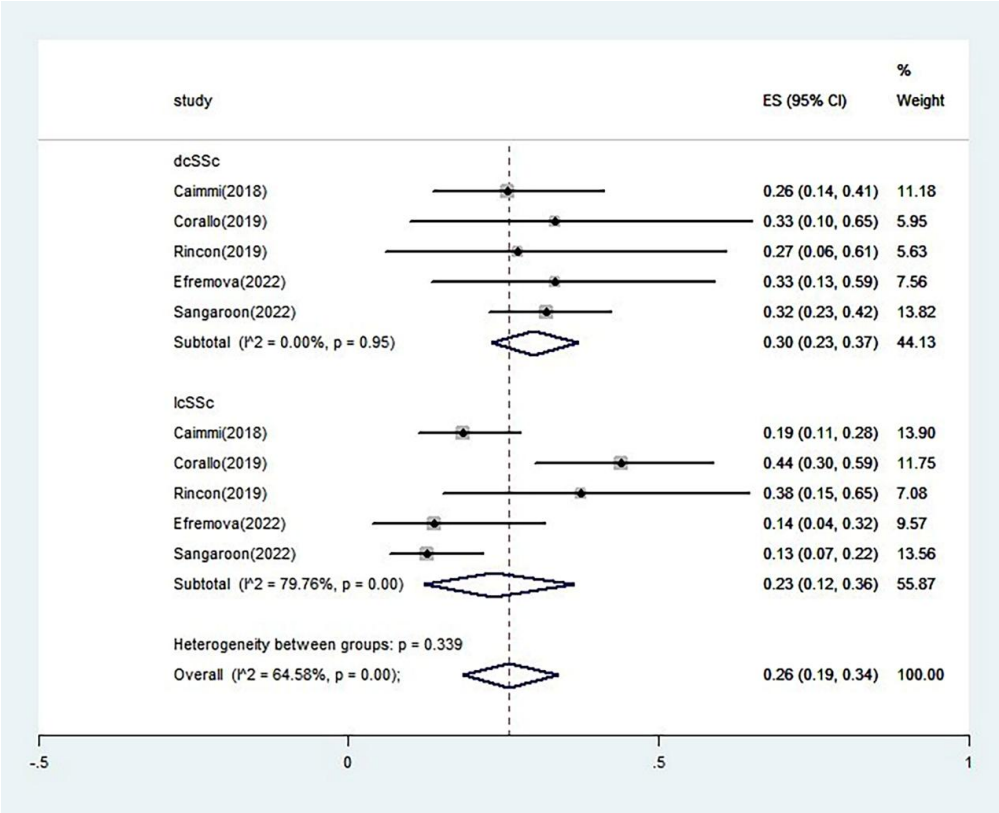
Variables	Coefficient	SE	P value	CI-Lower	CI-Upper
Sample size	-0.0022	0.0026	0.424	-0.0083	0.0039
Average age	0.0210	0.0319	0.532	-0.0545	0.0965
Proportion of female	-1.0603	1.3233	0.449	-4.1893	2.0687
Duration of SSc	-0.0606	0.0488	0.255	-0.1760	0.0549

Figure S1 Prevalence of sarcopenia by criteria



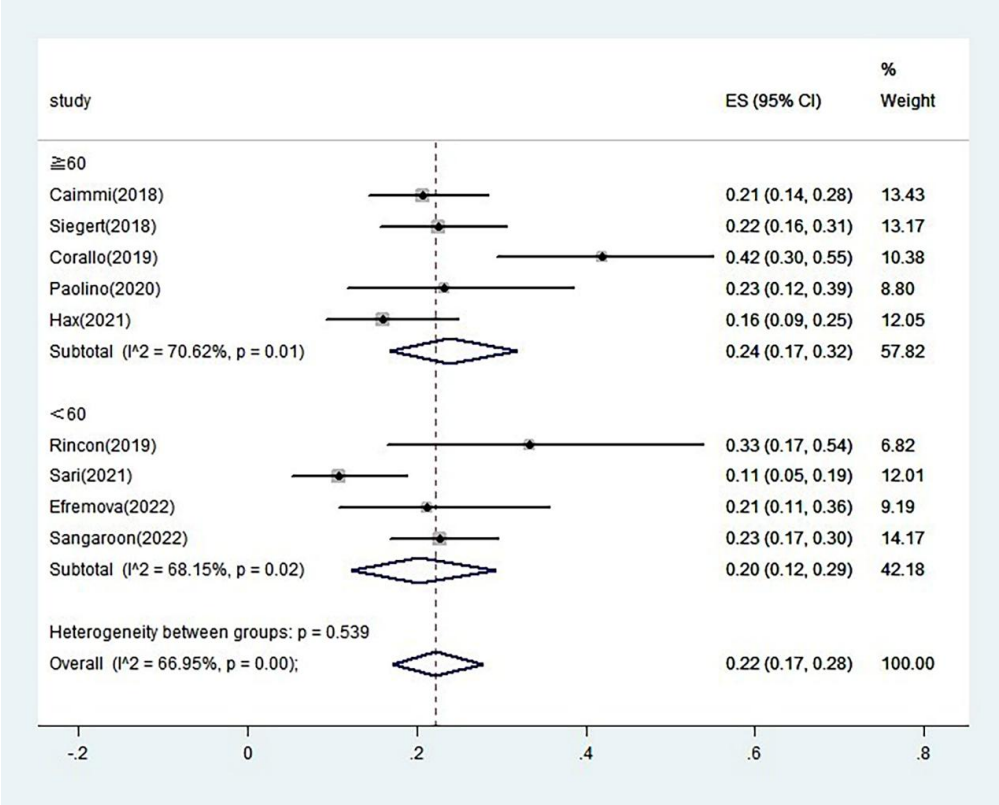
ES = effect size (prevalence); $I^2 = I^2$ heterogeneity statistic. A random effects model was used for analysis, and there was no significant difference between subgroups ($P = 0.234$).

Figure S2 Prevalence of sarcopenia by disease subtype



ES = effect size (prevalence); I² = I² heterogeneity statistic. The random effects model was used for the analysis, and there was no significant difference between the subgroups (P = 0.339).

Figure S3 Prevalence of sarcopenia by mean age



ES = effect size (prevalence); $I^2 = I^2$ heterogeneity statistic. The random effects model was used for the analysis, and there was no significant difference between the subgroups ($P = 0.539$).

Figure S4 Sensitivity analysis

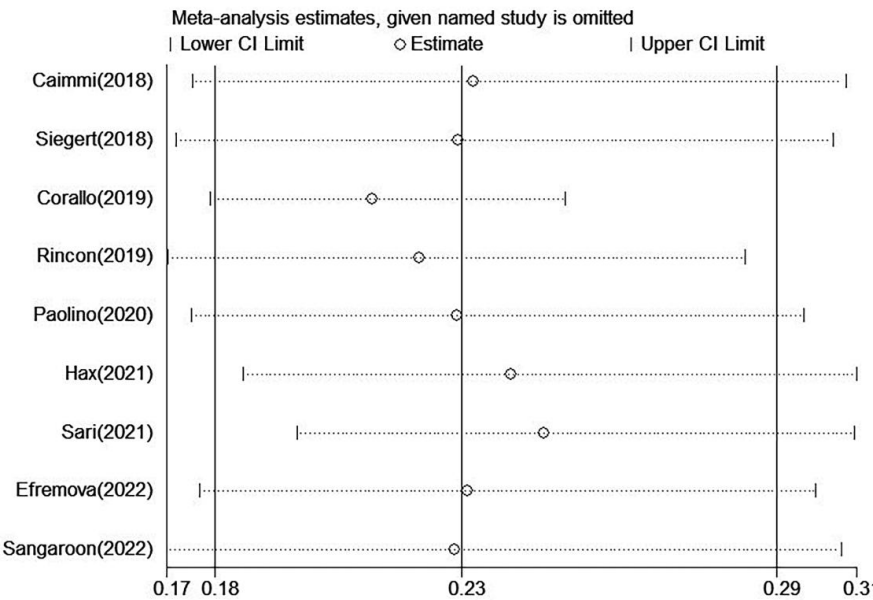


Figure S5 Egger’s test for publication bias

