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Effects of aging on skeletal muscle

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Effects of aging on skeletal muscle

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Correlation between low skeletal muscle index and 3D anthropometric data measured by 3D body scanner: screening sarcopenia

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Background: The screening tools for sarcopenia are measuring calf circumference, SARC-F or SPPB. However, not all of these tools have high sensitivity, specificity, and low margins of error. This research investigates potential of 3D anthropometry of the lower extremities on screening of sarcopenia.

Methods: From October 2022 to February 2023, we retrospectively analyzed results of 3D body scanner and bio-impedance analysis for patients aged 45 to 85 at risk of sarcopenia. The 3D scanner measured the surface and volume values of both thighs and calves. When skeletal muscle index (SMI) is less than 5.7, patients were classified to Low SMI group, indicative of sarcopenia.

Results: A total six out of 62 patients were classified to Low SMI group, showing significantly lower values of right, left, mean calf volumes and mean calf surface than the other patients (right calf volume 2.62 L vs. 3.34 L, $p = 0.033$; left calf volume 2.62 L vs. 3.25 L, $p = 0.044$; mean calf volume 2.62 L vs. 3.29 L, $p = 0.029$; mean calf surface 0.12 m^2 vs. 0.13 m^2, $p = 0.049$). There was no statistical difference in thigh volume and surface. Through AUC-ROC analysis, mean calf volume was the most significant cut-off value (right calf volume 2.80 L, AUC = 0.768; left calf volume 2.75 L, AUC = 0.753; mean calf volume 3.06 L, AUC = 0.774; mean calf surface 0.12 m^2, AUC = 0.747).

Conclusion: The calf volume and surface values have significant relationship with low SMI, and the mean calf volume was the most significant cut-off screening value for Low SMI. The 3D scanner demonstrated its value as a new means for screening sarcopenia.

KEYWORDS

sarcopenia, skeletal muscle index, bio-impedance analysis, screening, 3D scanner, 3D anthropometry

Introduction

Sarcopenia, characterized by the age-related loss of skeletal muscle mass and functional decline, has emerged as a significant health concern in the aging population (1). Sarcopenia is associated with limitations in independent living, diminished physical performance, and increased risks of acute and chronic diseases, ultimately decreasing quality of life and health (2).

The early diagnosis of sarcopenia is crucial for appropriate management and treatment (3). However, the accurate diagnosis of sarcopenia remains challenging, as measurement methods and assessors may vary, allowing sarcopenia to be undiagnosed until significant loss of skeletal muscle mass and functional decline have occurred. The core issue lies in the initial stage of detection and screening processes. Therefore, various screening tools and diagnostic tests have been developed to aid in the identification and confirmation of sarcopenia.

The calf muscle circumference can be measured in the initial screening of sarcopenia, with a cut-off of 34 cm or less for males and 33 cm or less for females (Asian Working Group for Sarcopenia (AWGS) guidelines) (4). The Strength, Assistance with walking, Rising from a chair, Climbing stairs, and Falls (SARC-F) questionnaire and the Short Physical Performance Battery (SPPB), consisting of balance, gait speed, and chair-stand tests that assess specific risk factors, symptoms, or functional limitations associated with sarcopenia, are also used for screening (5, 6).

While these tools are not invasive, easy to administer, provide a quick initial assessment, and help to determine the need for further diagnostic evaluation, they may not always be sufficiently sensitive or specific, leading to potential false negatives or positives, and having disadvantages to use as screening tools (7).

Additionally, diagnoses are based on quantitative muscle measurements with assessments of muscle performance in everyday life. However, current screening tools dominantly assess muscle function and inadequately assess muscle quantity (6). The superiority of any particular tool remains a topic of debate (7–11). Therefore, a diagnosis of sarcopenia may be delayed until muscle mass loss and functional decline have already progressed, limiting the effectiveness of interventions and treatments and negatively impacting patients' quality of life and independent function (12).

We considered using three-dimensional (3D) body scanning as an alternative to calf circumference measurement as a screening tool for evaluating muscle mass and volume in patients with sarcopenia. With the recent advancements in 3D depth camera technology, cameras have become small enough to be integrated into smartphones, their capture speed has increased, and they have become more common. Rapid 3D body measurements have become feasible, enabling 3D reconstruction of the craniofacial skeleton, teeth and teeth atlas, and even forensic applications in the medical field (13).

3D body measurements provide accurate and comprehensive physical measurements, offering values for the volume and surface area of various body parts. To the best of our knowledge, the 3D body scanner has not been previously studied for measuring skeletal muscle mass reductions. In this study, we analyzed the correlation between Skeletal Muscle Index (SMI) values measured by Bio-electrical Impedance Analysis (BIA) with a female sarcopenia cut-off value of 5.7 and limb volume and surface area values measured by a 3D body scanner.

Methods

Materials

This study was approved by the Institutional Board of Seoul National University Boramae Hospital (IRB No. 10-2022-114), and the requirement for patient consent was exempted. This was a single-center retrospective analysis of 3D body scanner measurements (Medi Help Line Co., Seoul, South Korea) and BIA analysis of patients who visited our hospital from October 2022 to February 2023. The patients came for health check-ups, and the BIA and 3D body scans were being conducted free of charge. The BIA and 3D body scanner that were previously available for free use at fitness centers or health centers, had been acquired by our hospital's health screening center. Subsequently, the examinations were conducted targeting patients who volunteered through our outpatient clinic banner advertisements.

3D body scanning

The 3D body scanner measured the surface area and volumes of chest, pelvis, upper extremities, both thighs and calves. The results of 3D body scans can vary due to factors such as the patient's posture and clothing. Therefore, we standardized the scanning procedure as follows:

1. Posture: The position of the patient being scanned can significantly affect the results. Generally, a standard standing pose is adopted, with feet shoulder-width apart, arms slightly raised, and looking forward at a fixed point at eye level. This posture enables a comprehensive 3D body scan, including every aspect of the lower extremities (Figure 1).
2. Clothing: Any clothing or accessories worn by patients being scanned can interfere with the scanner's ability to accurately capture the body's surface. Typically, wearing minimal clothing and accessories, including jewelry, watches, and accessories, that be removed is recommended. Patients were asked to wear form-fitting clothing provided by our department to ensure the most accurate body shape capture. For consistency, all patients in this study were scanned wearing the same type of clothing. Any accessories or bulky items were removed prior to the scan (Figure 2).
3. Body Movement: Body scanning requires the subject to remain completely still throughout the process. Any movement can distort the measurements.
4. Several measurements: If the patient moved during the measurement or the measurement was considered inappropriate for other reasons, the measurement was repeated until it was satisfactory.

Participants

Female patients between the ages of 45 and 85 were included in this study to identify screening cut-off values to exclude gender difference bias. Patients with a history of malignant neoplasia and musculoskeletal disorders, with metal implants in the limbs due to

FIGURE 1
An example of poses for 3D scanner imaging.

orthopedic surgery or other reasons, were excluded. Patients' medical histories were also considered. Individuals with conditions that could cause lower limb swelling, such as heart or kidney disease, varicose veins, lymphedema, lumbar radiculopathy, or lower extremity trauma within the past 6 months, and conditions that could potentially influence 3D body scanner measurements or BIA were excluded.

Methods

We calculated the SMI value using BIA and height. SMI values were calculated by dividing the skeletal muscle mass (total muscle mass of four extremities) by the square of the height. The unit was kilograms per square meter (kg/m^2). SMI values are commonly used as an indicator of muscle mass relative to body size and used in the assessment of sarcopenia and muscle-related conditions. When the SMI value is less than 5.7, the patient is considered to have low skeletal muscle mass, which might indicate sarcopenia. We classified these patients into the Low SMI group and the other patients to the control group.

Statistical analysis

Mann-Whitney U test tests were used to compare nonparametric continuous variables, and Fisher's exact test was used to compare categorical variables between groups. Statistical analyses were performed using Rex (http://rexsoft.org/, Version 3.0.3, RexSoft Inc., Seoul, Korea), an Excel-based statistical analysis software. The p-value < 0.05 was considered statistically significant. Continuous variables were presented as the mean (standard deviations) for parametric data and the median (interquartile range) for nonparametric data. Categorical variables were presented as number of patients (percentage). The factors assessed were age, body mass index (BMI), comorbidities (presence of hypertension, dyslipidemia, diabetes mellitus and osteoporosis), and the surface and volume of body parts.

FIGURE 2
Activewear that adheres to the body was worn during 3D scanner imaging. **(A)** Top, **(B)** Shorts.

Results

Characteristics of participants

A total 62 patients were included in the total group, and 6 patients were classified into the Low SMI group, whom BMI was less than 5.7. The mean age of the entire patients was 65.85 years, with a mean age of 66 years in the Low SMI group and 65.84 years in the control group; however, these differences were not statistically significant. The BMI was 24.9, 21.65 and 25.05, respectively. The comorbidities of the patients (hypertension, diabetes, hyperlipidemia, and osteoporosis) were collected; however, there were no statistically significant associations (Table 1).

Results in 3D body scan

The Low SMI patients showed statistically significantly lower right, left, and mean calf volumes than the control group (right calf volume, 2.62 ℓ vs. 3.34 ℓ, $p = 0.033$; left calf volume, 2.62 ℓ vs. 3.25 ℓ, $p = 0.044$; mean volume of both calves, 2.62 ℓ vs. 3.29 ℓ, $p = 0.029$). Also, the mean calf surface area was significantly lower than in the control group (mean surface of both calves, 0.12 m^2 vs. 0.13 m^2, $p = 0.049$). However, there was no statistical difference between the two groups in volume or surface area of the other body parts (Table 1).

Area under the curve-receiver operating characteristic (AUC-ROC) analysis was conducted for four statistically significant values: right and left calf volume, mean calf volume, and mean calf surface area. The cut-off value for the right calf volume was 2.80 L, and the AUC value was 0.768 (specificity = 85.7%, sensitivity = 66.7%). The cut-off value was 2.75 L for the left calf volume, and the AUC value was 0.753, with the highest specificity and sensitivity (specificity = 82.1%, sensitivity = 83.3%). The cut-off and AUC values for the mean calf volume were 3.06 L and 0.774 (specificity = 67.9%, sensitivity = 83.3%), and for the mean calf surface area, the values were 0.12 m^2 and 0.747, respectively (specificity = 89.3%, sensitivity = 66.7%). The mean calf volume of 3.06 L had the highest AUC value (a "fair" value of 0.774) and could be used as the most significant cut-off value (Figure 3). The specificity and sensitivity were highest for left calf volume.

Discussion

Rapid advancements in 3D scanning and printing technologies capabilities have occurred, particularly over the past decade. 3D scanners have the advantages of high accuracy, high speed, easy manipulation, and low operational costs relative to computed tomography and magnetic resonance imaging (14–16). Moreover, there is minimal risk to the human body, such as radiation exposure, resulting in very few limitations on imaging and making it possible to perform scans outside of hospitals and in everyday spaces.

Many studies have reported applications in medical fields, apart from areas directly related, such as engineering and computer science (13). Research on 3D scanning applications, especially in fields such as dentistry, maxillofacial surgery, and plastic surgery, has been conducted (17, 18). While these prior studies were conducted by 3D scanning of specific body parts, research on full-body 3D scanning has yet to be conducted.

Full-body scanning data is already being collected as big data in some countries. In South Korea, the Ministry of Trade, Industry, and Energy has conducted a Korean anthropometric survey called "Size Korea" since 1979. Direct measurements using a tape measure have been conducted since 1979, and data on 103,254 people have been accumulated, while data on 15,429 people have been collected using a 3D scanner since 2003 and are freely accessible.[1] In the United Kingdom, a survey called "SizeUK" measured 5,500 men and 5,500 women to create a national anthropometric database (19). The United States Centers for Disease Control and Prevention (CDC) periodically compiles and publishes anthropometric data on Americans (20).

Such data collection initiatives were originally commenced due to interests in fields related to body sizing, custom clothing, and virtual shopping. Yet, the potential for medical research based on these data cannot be overlooked. The significance of this study lies in establishing a foundation that associates sarcopenia with whole-body anthropometric data acquired through 3D body scanning. This

1 http://sizekorea.kr

TABLE 1 Comparison of anthropometric data between sarcopenic and non-sarcopenic patients.

Variables	Group			*p*-value[a]
	Total (*n* = 62)	Low SMI (*n* = 6)	Control (*n* = 56)	
Age	65.85 ± 6.58	66 ± 5.18	65.84 ± 6.75	0.9462[a]
BMI (kg/m^2)	24.9 (23.13, 26.05)	21.65 (20.05, 23.55)	25.05 (23.75, 26.25)	0.019[a]
Comorbidities				
Hypertension	19 (30.65%)	2 (33.33%)	17 (30.36%)	>0.99[b]
Dyslipidemia	14 (22.58%)	2 (33.33%)	12 (21.43%)	0.61[b]
Diabetes mellitus	11 (17.74%)	1 (16.67%)	10 (17.86%)	>0.99[b]
Osteoporosis	12 (19.35%)	1 (16.67%)	11 (19.64%)	>0.99[b]
Thigh volume (ℓ)				
Right	3.95 (3.46–4.66)	4.01 (3.47–4.14)	3.92 (3.48–4.70)	0.5281[a]
Left	3.68 (3.29–4.35)	3.62 (3.30–3.86)	3.68 (3.30–4.41)	0.4533[a]
Mean	3.78 (3.37–4.51)	3.82 (3.37–4.00)	3.78 (3.38–4.57)	0.4824[a]
Thigh surface (m^2)				
Right	0.11 (0.1–0.13)	0.12 (0.10–0.12)	0.11 (0.10–0.13)	>0.99[a]
Left	0.11 (0.1–0.12)	0.11 (0.11–0.11)	0.11 (0.10–0.12)	0.9336[a]
Mean	0.11 (0.1–0.13)	0.11 (0.11–0.12)	0.11 (0.10–0.13)	0.9525[a]
Calf volume (ℓ)				
Right	3.29 (2.97–3.59)	2.62 (2.52–3.01)	3.34 (3.03–3.69)	0.0331*[a]
Left	3.16 (2.79–3.43)	2.62 (2.49–2.72)	3.25 (2.88–3.45)	0.0442*[a]
Mean	3.23 (2.88–3.55)	2.62 (2.51–2.98)	3.29 (2.98–3.63)	0.0294*[a]
Calf surface (m^2)				
Right	0.14 (0.13–0.15)	0.13 (0.12–0.13)	0.14 (0.13–0.15)	0.0843[a]
Left	0.13 (0.12–0.14)	0.11 (0.11–0.12)	0.13 (0.12–0.14)	0.0801[a]
Mean	0.13 (0.12–0.14)	0.12 (0.11–0.13)	0.13 (0.12–0.15)	0.0495*[a]

SMI, skeletal muscle index. Values are expressed as the mean ± standard deviation or median (interquartile range) for continuous variables, and number of patients (percentage) for categorical variables.
[a]Derived with Mann-Whitney U test.
[b]Derived with Fisher's exact test.
*p-value < 0.05.

research showed a correlation between sarcopenia and 3D anthropometry by setting cut-off values for calf volume and surface areas in patients with low SMI values (less than 5.7).

However, this study had the following limitations. First, this study did not target patients who were definitively diagnosed with sarcopenia. Additional tests on grip power, physical activity, or DEXA scans are required to diagnose sarcopenia. However, conducting these tests was impossible due to the retrospective study design. Therefore, it is imperative to conduct further research on the 3D anthropometry of patients diagnosed with sarcopenia, especially when integrated with functional assessments, such as grip strength, walking speed, and the SPPB.

Secondly, this study was based on the BIA test results of a small number of patients. However, BIA test results have high variability. Thus, the reliability of these values decreases when based on a small patient group. Therefore, research involving a larger number of patients or based on more reliable tests, such as DEXA scans instead of BIA results, is necessary. Lastly, this study targeted a single gender. While it is true that sarcopenia has a higher prevalence in women, research targeting both genders is required for demographic universality.

Conclusion

Mean calf volume was the most useful 3D scanning result in women aged 45–85 with a low SMI value. The 3D scanner demonstrated its value as a new means for screening sarcopenia.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found at: doi: 10.17632/4ps56b29tm.1.

Ethics statement

The studies involving humans were approved by Seoul Metropolitan Government-Seoul National University Boramae Medical Center Institutional Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived

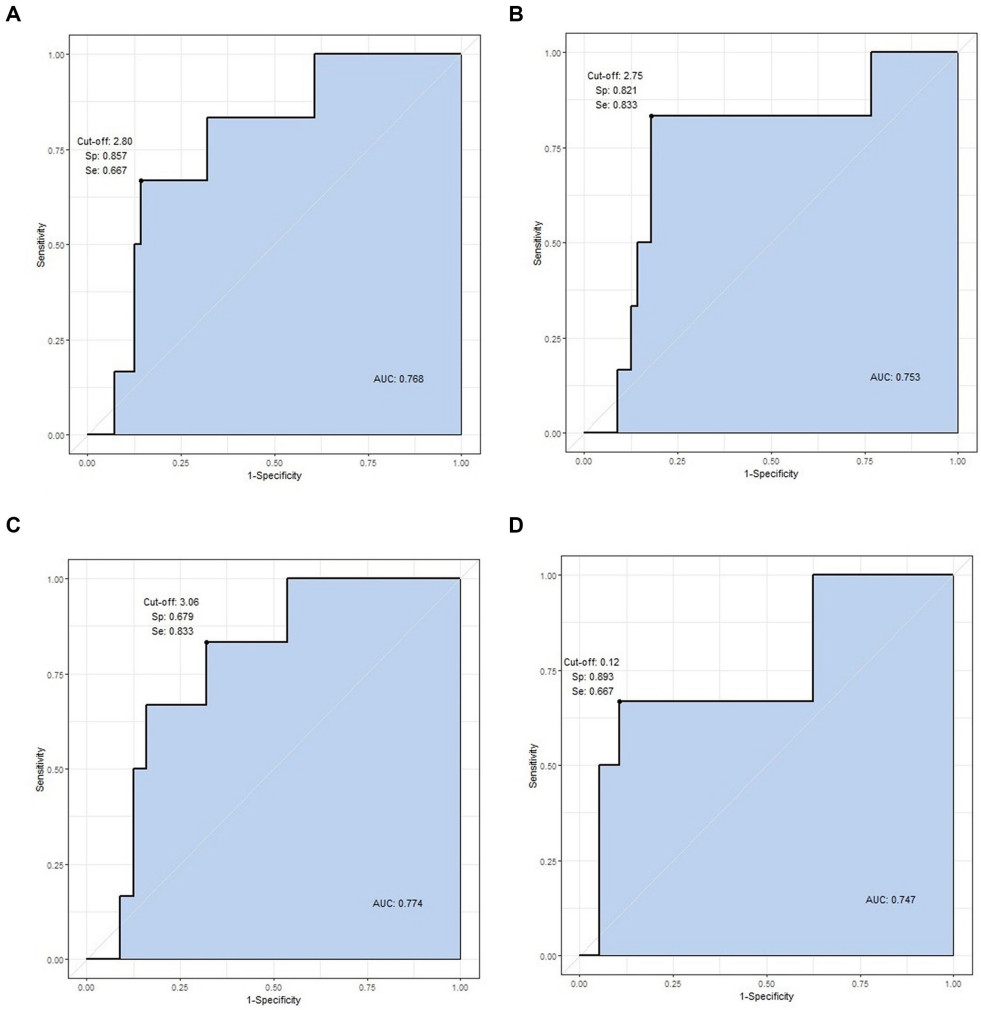

FIGURE 3
ROC curve analysis of statistically significant variables. The four values are cut-off value, specificity, sensitivity, and AUC, respectively. **(A)** Right calf volume (2.80, 0.857, 0.667, and 0.768 L), **(B)** left calf volume (2.75, 0.821, 0.833, and 0.753 L), **(C)** mean calf volume (3.06, 0.679, 0.833, and 0.774 L), and **(D)** mean calf surface area (0.12, 0.893, 0.667, 0.747 m^2).

the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because this study is a retrospective investigation conducted based on the information obtained during health check-ups of patients.

Author contributions

KK: Writing – original draft, Writing – review & editing. YP: Conceptualization, Data curation, Investigation, Writing – review & editing. YL: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. MC: Conceptualization, Investigation, Methodology, Project administration, Writing – review & editing.

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Conflict of interest

YP was employed by Medi Help Line Inc.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Assessing muscular power in older adults: evaluating the predictive capacity of the 30-second chair rise test

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Background: Timed chair rise tests are frequently used as a substitute for assessing leg muscle strength or power. To determine if timed chair rise tests are an indicator of lower extremity muscle power, we examined the relationship between the repetitions completed in a 30-s chair rise test and the power generated during the test.

Methods: Seventy-five individuals participated in this study (n = 30 < 65 years and 45 ≥ 65 years). Participants underwent a 30-s chair rise test while instrumented with a power analyzer. Handgrip strength was also evaluated.

Results: The relationship between chair rise repetitions and *average* chair rise power was R^2 = 0.32 (p < 0.001). Chair rise repetitions when regressed on a *total* (i.e., summed) chair rise power, it yielded R^2 = 0.70 with data from all participants combined (p < 0.001). A mediation analysis indicated that anthropometrics partially mediates the relationship between chair rise repetitions and total chair rise power accounting for 2.8%–6.9% of the variance.

Conclusion: Our findings indicate that in older adults, the overall performance of chair rises offers limited information about the average power per rise but is more indicative of the cumulative power exerted. Thus, the total number of chair rises in a 30-s test is likely a more comprehensive metric of overall muscular power, reflecting endurance aspects as well. Additionally, we found that personal physical attributes, such as height and weight, partially influence the link between chair rise count and total power, highlighting the importance of factoring in individual body metrics in assessments of muscular performance.

KEYWORDS

sarcopenia, muscle strength, muscle power, dynapenia, physical function

Introduction

The population of Americans aged 65 and older is projected to almost double by 2060 (US Census Bureau, 2018). This demographic shift coincides with a consistent decline in muscle strength and mass as people age, a condition known as sarcopenia (Frontera et al., 2000). The subset of Americans aged 85 and above, who are highly susceptible to sarcopenia

(Cao et al., 2022), is expected to more than double in just the next 15 years. Sarcopenia significantly contributes to limitations in mobility, loss of independence, heightened fall risk, and increased mortality rates (Cruz-Jentoft et al., 2019; Bhasin et al., 2020). For instance, reduced leg extensor strength in older adults is linked to a four-fold increase in the risk for mobility limitations (Manini T. M. et al., 2007). Accordingly, the societal impact of sarcopenia affects healthcare planning for patients, families, caregivers, and insurance providers due to the resultant decline in mobility and autonomy, and thus necessitates a multidimensional and multidisciplinary approach for its assessment and management (Fielding et al., 2011; Cruz-Jentoft et al., 2019; Giovannini et al., 2021). Consequently, sarcopenia has garnered considerable attention in recent years, culminating in its recognition as a disease entity with the assignment of an ICD-10 code in 2016 (Anker et al., 2016).

While there's no universally agreed-upon definition of sarcopenia, the most recent definition by the European Working Group on Sarcopenia in Older People (EWGSOP2) characterizes it as "muscle failure" (Cruz-Jentoft et al., 2019). This definition marks a shift in how sarcopenia is conceptualized, moving away from low muscle mass to considering low muscle function, such as weakness, as the primary determinant and core aspect of sarcopenia. The EWGSOP2 definition, along with others, suggests timed chair rise tests (such as the 5x chair rise test or the 30-s chair rise test) as a way to approximate leg muscle strength and endurance (Jones et al., 1999; Cruz-Jentoft et al., 2019). These tests are practical for clinical and home settings. Indeed, the 30-s chair rise test has been reported to correlate with lower body muscle strength in older adults living in the community. This supports the idea that it can serve as a surrogate for assessing leg muscle strength (Jones et al., 1999).

Muscular strength refers to the maximum force exerted, while muscle power is the product of force and the velocity of muscle contraction. Muscle power tends to decline earlier and more rapidly with age compared to muscle strength, suggesting that more research should focus on muscle power as a critical outcome in studies related to sarcopenia (Reid and Fielding, 2012). The timed chair rise test, influenced by factors like height and weight, may not be a reliable surrogate for assessing leg muscle power. Few studies have explored the link between timed chair rise tests and muscle power indicators. These studies typically measure power using a leg extension power rig, which might not reflect the specific tasks involved in a chair rise test, leading to potential task specificity issues (Manini et al., 2005; Manini T. et al., 2007). One study found no correlation between a 5x chair rise test and muscle power (Lindemann et al., 2003). However, later research suggested that peak power in a chair rise test often occurs after the fifth rise, indicating a longer test may better evaluate functional power (Smith et al., 2010). Accordingly, in our brief report, we discuss our findings on the correlation between the number of chair rises completed in 30 s and the average and total power exerted during these chair rises.

Methods

Study participants

The study involved seventy-five participants ranging in age from 25 to 93 years. Among them, 30 were below 65 years old, and 45 were 65 years old or above. Table 1 presents descriptive statistics detailing the characteristics of these participants. To be eligible, individuals had to be 18 years old. Exclusion criteria included the presence of an implanted pacemaker or any other electronic device, self-reported neurological or neuromuscular diseases, or any condition that, in the opinion of the investigators, could affect participant safety or compromise data quality while performing the specified tasks assessing muscle strength and performance in this study. Approval for the study was obtained from the Ohio University Institutional Review Board.

Data acquisition

The data included in this report is a segment of a more extensive study. Specifically, we focus on the data related to lower extremity physical performance and handgrip strength in this report.

Short physical performance battery (SPPB)

The SPPB was conducted through a series of tests.

1) 4-m Normal Gait Speed Test: Participants completed two trials of walking a 4-m distance at their usual pace, and the time taken for each trial, recorded to the nearest 0.01 s, was averaged.
2) Balance Tests: This evaluated the ability to maintain balance in different positions: side-by-side, semi-tandem and the tandem standing tests. Participants were assessed on their ability to hold each position for 10-s, with the time recorded to the nearest 0.01 s.
3) Five-Times (5x) Chair Rise Test: Participants performed this test on a stable chair with a pan height of 45 cm and no seat padding or arm rests. Chair rises were performed by the participants keeping their arms braced across to their shoulders. The time taken to complete five consecutive chair rises was recorded.

The scores from the gait speed, balance, and chair-rise tests were combined calculate the overall SPPB score (Guralnik et al., 1994).

Handgrip strength (HGS)

HGS was measured using a portable Jamar dynamometer (Model 5030 J1; Lafayette Instrument Co.; Lafayette, Indiana), following previously established procedures (Wages et al., 2020). Both dominant and non-dominant handgrips were assessed through alternating three trials on each side, with an option for a fourth trial if the top two trials differed by > 3 kg). The average of the three trials was recorded as the mean HGS for each side.

30-second chair rise test

During the 30-s chair-rise test, participants used the same chair as described previously for the 5x chair test. In this assessment, we recorded the number of repetitions completed during the chair rise test and measured the power output generated throughout the chair rise part of the test. Participants were instructed to perform repeated sit-to-stand movements as fast as possible, ensuring they reached a full standing position before returning to a fully seated position.

TABLE 1 Descriptive statistics for seventy-five study participants in the study stratified by age: <65 years (n = 30) and ≥65 years (n = 45), and disaggregated by sex. All data are presented as mean ± SD, except for the SPPB data which is shown as median ± quartile ranges.

Group	Age (yr)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Dominant HGS (kg)	Non-dominant HGS (kg)	SPPB (0–12 score)	30-s chair rise reps (#)	Chair rise power (watts)
Females <65 years (n = 17)	53.4 ± 9.98	173.68 ± 5.77	68.88 ± 19.95	21.24 ± 5.59	24.86 ± 6.94	23.69 ± 6.59*	12.0 IQR = 1.0	20.00 ± 6.00	401.09 ± 86.27
Males <65 years (n = 13)	46.85 ± 12.83	175.96 ± 6.39	82.54 ± 13.06	22.04 ± 3.21	42.06 ± 8.28	40.74 ± 10.01	12.0 IQR = 0.0	22.31 ± 4.44	558.72 ± 107.47
Females ≥65 years (n = 34)	75.48* ±7.23	160.36 ± 7.22	72.90 ± 15.91	23.24 ± 5.13	17.83 ± 6.36*	17.02 ± 6.86*	10.0 IQR = 4.50*	14.16 ± 4.37*	311.32 ± 91.92*
Males ≥65 years (n = 11)	71.09 ± 4.48*	173.36 ± 7.52	85.37 ± 20.17	25.29 ± 5.68	33.66 ± 8.11*	29.15 ± 8.18*	9.0 IQR = 2.0*	16.55 ± 4.11*	442.51 ± 78.84*

*Denotes significant difference between the respective sexes for the two age groups, at $p < 0.05$.
HGS, Dominant handgrip strength (mean of three trials).

Throughout the test, participants were connected to a low-friction pulley system attached to their waist. This system was linked to a Tendo Power Analyzer (Tendo Power-Tendo Sports Machines, Trencin, Slovak Republic), allowing us to calculate chair rise power during each rise. We used this data to subsequently calculate the average chair rise power as well as the total (i.e., summed) chair rise power. This method broadly aligns with previous descriptions of quantifying chair rise power (Vincenzo et al., 2018).

Statistical analysis

The data was divided into two age groups: those <65 years old and those ≥65 years old. Between-group comparisons were conducted using independent t-tests, which were disaggregated by biological sex. For SPPB data, comparisons were made using a Mann Whitney *U* Test due to the non-normal distribution of this variable.

R-squared values were calculated to examine the relationship between the number of repetitions completed during the 30-s chair rise test and the *average* as well as *total* chair rise power achieved in the same duration. This analysis was conducted for the entire sample and separately for the age-stratified groups. We observed a robust association between chair rise repetitions and the total chair rise power. Thus, a mediation analysis was conducted to examine the mediating effect of individual anthropometric measures (height, weight, and BMI) on the relationship between the number of repetitions completed during the 30-s chair rise test and the total chair rise power. A bias-corrected 95% confidence interval of the indirect effects was obtained with 5,000 bootstrapped resamples. A significant indirect effect *via* the mediator between the dependent and independent variables was determined if the 95% confidence interval did not contain zero.

A *post hoc* power analysis revealed that the power for a one-tailed correlation, with alpha set at 0.05, was 0.99 for the entire sample and 0.76 and 0.89 for the younger and older age-stratified groups, respectively. All statistical calculations were performed using the SPSS software (IBM SPSS Statistics, Version 27, Chicago), and significance was determined at two-tailed *p*-value <0.05.

Results

In Table 1, descriptive statistics of the study participants are presented, stratified by age (<65-year and ≥65-year). The association between chair rise repetitions and *average* chair rise power yielded an R-squared value of 0.32 for the entire sample (i.e., when data from all subjects were combined), with a significant *p*-value of <0.001. When considering age groups, the R-squared value was 0.16 for those under 65 years ($p = 0.031$) and 0.17 for those aged 65 or above ($p = 0.006$) (Figures 1A–C). When chair rise repetitions were regressed on *total* (i.e., summed) chair rise power, an R^2 value of 0.70 was observed as data from all participants were combined ($p < 0.001$). This association was R^2 of 0.70 for individuals under 65 years ($p < 0.001$) and was R^2 0.75 for those aged 65 or above ($p < 0.001$) (Figures 1D–F).

Notably, *average* and *total* chair rise power exhibited a stronger correlation with grip strength compared to chair rise repetitions. Specifically, the R-squared value was 0.64 for *average* chair rise power in relation to both dominant and non-dominant grip strength ($p < 0.001$), while the R-squared values for *total* chair rise power in relation to both dominant and non-dominant grip strength was 0.45 and 0.44, respectively ($p < 0.001$). Conversely, the R^2 values for the relationship between chair rise repetitions and dominant and non-dominant grip strength were only 0.17 and 0.18, respectively ($p < 0.002$)).

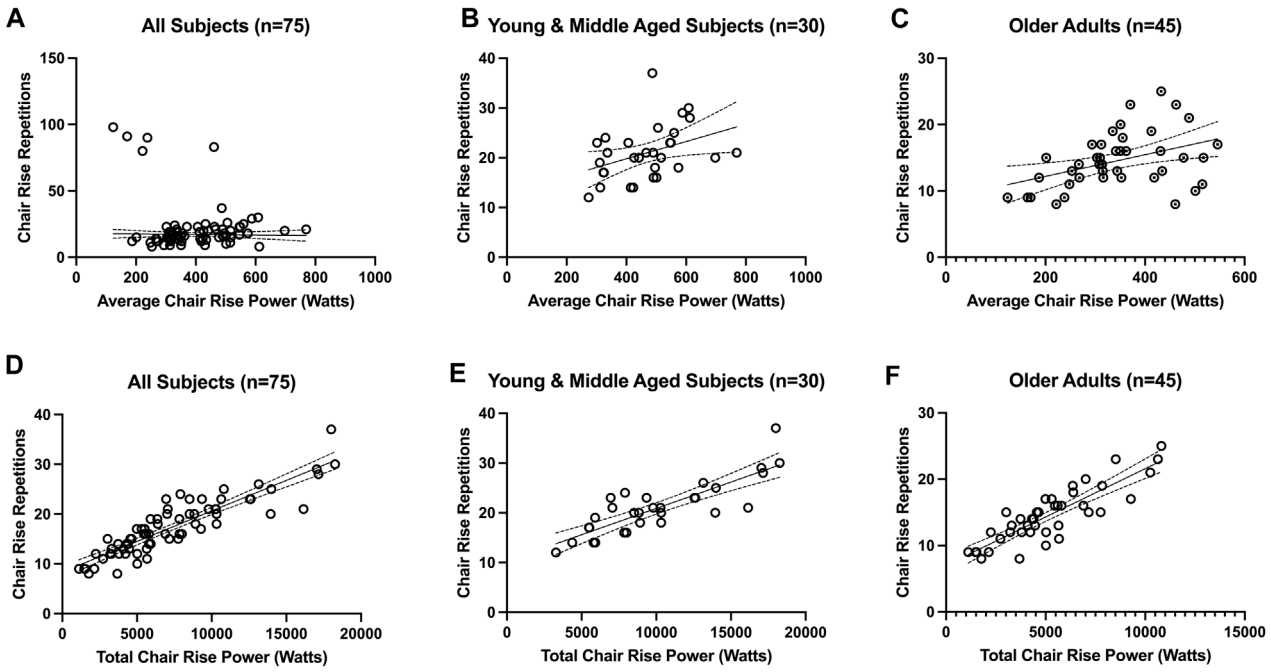

FIGURE 1
Association between timed chair rise test repetitions and average chair rise power **(A-C)** and total (i.e., summed) chair rise power **(D-F)**. The association between chair rise repetitions and average chair rise power was $R^{2=}$0.32 for the entire sample (i.e., when data from all subjects were combined) (panel A; $p < 0.001$), $R^2 = 0.16$ for those under 65 years old (panel B; $p = 0.031$), and $R^2 = 0.17$ for those aged ≥65-year (panel C; $p = 0.006$). The association between chair rise repetitions and total chair rise power was $R^{2=}$0.70 for the entire sample (i.e., when data from all subjects were combined) (panel D; $p < 0.001$), $R^2 = 0.70$ for those under 65 years old (panel E; $p < 0.001$), and $R^2 = 0.75$ for those aged ≥65-year (panel F; $p < 0.001$).

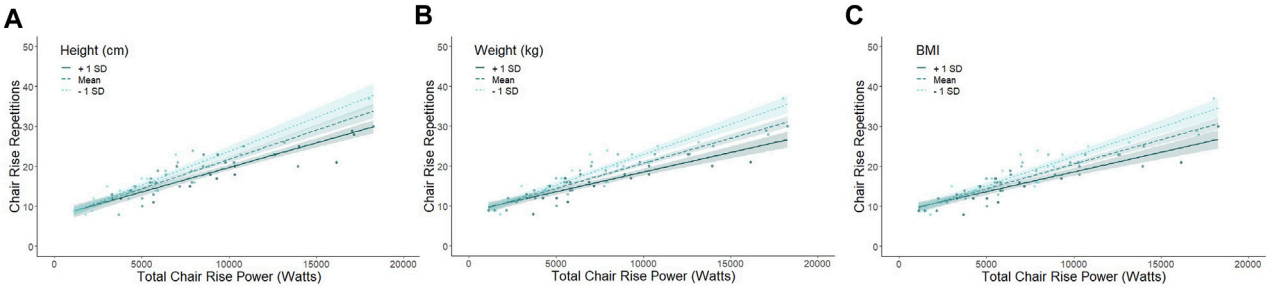

FIGURE 2
Partial mediation of anthropometric measures on the relationship of chair rise repetitions and chair rise power. The association between chair rise repetitions and chair rise power is partially mediated by height (accounts for 6.9% of the variance between chair rise and power; panel A), weight (accounts for 4.5% of the variance between chair rise and power; panel B), and BMI (accounts for 2.8% of the variance between chair rise and power; panel C). For panel **(A)** height mean = 165.99 cm, +1SD = 175.14 cm, and -1SD = 156.84 cm. For panel **(B)** weight mean = 57.41kg, +1SD = 93.62 kg, and -1SD = 57.41 kg. For panel **(C)** BMI mean = 23.12 kg/m^2, +1SD = 28.12 kg/m^2, and -1SD = 18.06 kg/m^2. Overall, the mediation analyses indicate that individuals who are shorter, weigh less, and have a lower BMI have a stronger and positive relationship between total chair rise power and chair rise repetitions (increase in total chair rise power and chair rise repetitions).

Because we observed a robust association between chair rise repetitions and *total* chair rise power, we conducted a mediation analysis to examine the mediating effect of individual anthropometric measures (height, weight, and BMI) on this relationship. There was partial mediation for height ($F_{2,69}$ = 218.83, $p < 0.001$), weight ($F_{2,69}$ = 181.72, $p < 0.001$), and BMI ($F_{2,69}$ = 160.13, $p < 0.001$). The relationship between chair rise repetitions and *total* chair rise power had 6.9%, 4.5%, and 2.8% of the variance being accounted for by height, weight, and BMI, respectively for each mediation analysis (Figure 2). Overall, the mediation analyses indicate that individuals who are shorter, weigh less, and have a lower BMI

have a stronger and positive relationship between total chair rise power and chair rise repetitions (increase in total chair rise power and chair rise repetitions).

Discussion

Timed chair rise tests are commonly employed as a substitute for assessing leg muscle strength or power in sarcopenia studies. Typically, these tests involve measuring the time taken to complete a set number of repetitions or quantifying the number of chair rise stands within a fixed timeframe. Both methods evaluate absolute chair rise performance. However, it remains uncertain whether absolute chair rise performance directly estimates lower extremity muscle strength, power, or endurance because factors like body anthropometrics can influence this performance (e.g., taller or heavier individuals potentially perform more work than their shorter and lighter counterparts). Moreover, factors such as balance and multi-segment movement coordination might also impact absolute chair rise performance. Previous studies have explored the relationship between the time taken for sit-to-stand chair rise tests and indicators of leg muscle strength and power (Bassey et al., 1992; Skelton et al., 1994; Jones et al., 1999; Bean et al., 2002; Bean et al., 2003; Hardy et al., 2010). However, this evaluated power using a leg extension power rig rather than assessing power during the actual chair rise test, potentially introducing issues related to task specificity (Manini et al., 2005; Manini T. et al., 2007). Consequently, our study investigated the relationship between the number of repetitions completed during a 30-s chair rise test and the chair rise power generated with the same duration.

Our primary finding indicates that in older adults, absolute chair rise performance explains merely 17% of the variance in average chair rise power, indicating that measuring absolute chair rise performance alone (through time or repetitions) is insufficient for accurately assessing average lower extremity muscle power (that is, the power of each repetition, particularly in a 30-s chair stand test). However, in these individuals, absolute chair rise performance is associated with 75% of the variance in total chair rise power. This implies that the count of chair rises within a 30-s period is a good indicator of the overall power exerted during the test. Therefore, the frequency of chair rises observed in this time frame is a better measure of the total power, incorporating aspects of muscular endurance, than the power of each individual chair rise. Muscle performance spans a continuum from generating maximal force against maximal resistance (strength) in a specific exercise to performing repetitions until failure at a certain resistance, which is endurance. Therefore, the 30-s chair rise test can be best understood as a measure of muscle performance within this range, effectively integrating the EWGSOP2 assertions with the current findings on muscle power.

Additionally, we found a more substantial correlation between both the average and total chair rise power with hand grip strength, a recognized biomarker for adverse health outcomes in older adults (Bohannon, 2019), compared to the number of chair rise repetitions. These findings suggest that chair rise power is a more relevant measure for evaluating skeletal muscle performance than merely counting chair rises.

Finally, our research indicates that individual anthropometric factors partially mediate the relationship between the number of chair rises and the total chair rise power, pointing to the influence of physical characteristics on this association. This study faces multiple limitations. Firstly, the absence of power data from the 5x chair rise test barred us from directly comparing the two sit-to-stand paradigms. Secondly, the small sample size limits the generalizability of our findings to the broader population of older adults.

In conclusion, our study supports the notion that the 30-s chair rise test is a meaningful measure of lower extremity muscle power. While it partially reflects muscle endurance due to its association with the total number of chair rises, it offers a more comprehensive metric of overall muscular power. Our findings indicate that the 30-s chair rise test is effective in assessing overall muscular performance, blending strength and endurance aspects. This aligns with EWGSOP2's view and addresses the gap in research regarding the relationship between timed chair rise tests and direct measures of chair rise power. Furthermore, we note that individual physical characteristics, such as height and weight, play a role in this association, emphasizing the need for considering personal anthropometrics in muscle performance assessments.

Data availability statement

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Institutional Review Board, Ohio University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

NM: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Writing–original draft, Writing–review and editing. AD: Data curation, Resources, Writing–review and editing. JS: Data curation, Formal Analysis, Visualization, Writing-review–editing, BC: Data curation, Formal Analysis, Resources, Supervision, Writing–original draft, Writing–review and editing, Investigation, Validation, Visualization.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Endurance exercise preserves physical function in adult and older male C57BL/6 mice: high intensity interval training (HIIT) *versus* voluntary wheel running (VWR)

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Exercise has been shown to improve physical function, mitigate aspects of chronic disease and to potentially alter the trajectory of age-related onset of frailty and sarcopenia. Reliable and valid preclinical models are necessary to elucidate the underlying mechanisms at the intersection of age, exercise, and functional decline. The purpose of this study was to compare, head to head, the effects of two common pre-clinical models of endurance exercise: high intensity interval training (HIIT) and voluntary wheel running (VWR). The hypothesis was that a prescribed and regimented exercise program, HIIT, would prove to be a superior training method to unregulated voluntary exercise, VWR. To investigate this hypothesis, we evaluated adult (n = 24, designated 10 m, aged 6 months at the beginning of the study, 10 months at its completion) and older adult (n = 18, designated 26 m, aging from 22 months to 26 months over the course of the study) C57BL/6 male mice. These mice were randomly assigned (with selection criteria) to a 13-week program of voluntary wheel running (VWR), high intensity interval training (HIIT), or sedentary control (SED). The functional aptitude of each mouse was determined pre- and post-training using our composite CFAB (comprehensive functional assessment battery) scoring system consisting of voluntary wheel running (volitional exercise and activity rate), treadmill (endurance), rotarod (overall motor function), grip meter (forelimb strength), and inverted cling (whole body strength/endurance). To measure sarcopenia, we tracked body mass, body composition (with EchoMRI), plantar flexor torque (in 10 m), and measured muscle wet mass post-training. Overall, adult CFAB scores decreased while body mass and percent body fat increased as they matured; however, exercise significantly mitigated the changes ($p < 0.05$) compared to

SED. Older adults demonstrated preservation of function (CFAB) and reduced body fat ($p < 0.05$) compared to SED. To conclude, both types of exercise maintained physical function equally in older mice.

KEYWORDS

sarcopenia, exercise, mice, endurance training, aging

Introduction

Exercise, and increasing physical activity in general, has been well-described as an intervention with efficacy to mitigate a host of chronic diseases and age-related syndromes (Pedersen and Saltin, 2006; Landi et al., 2014). For example, adequate physical activity, such as the minimums (e.g., 150–300 min of moderate activity and 2 day/week of strength training) described by the U.S. Department of Health and Human Services (2023), has been shown to prevent/delay the onset of diabetes, cardiovascular disease, cancer, and metabolic syndrome, including obesity (Pedersen and Saltin, 2006; Medeiros et al., 2008; Garcia-Valles et al., 2013). Exercise also plays a role in maintenance of cognitive function and muting the trajectory of cognitive decline (Klusmann et al., 2010; Theou et al., 2011; Tarazona-Santabalbina et al., 2016).

Sarcopenia is traditionally referred to as the "age-related loss of muscle mass and strength or function" though there are varying definitions among clinicians and researchers (Evans et al., 2024). One clinical definition is "...probable sarcopenia is identified by Criterion 1. Diagnosis is confirmed by additional documentation of Criterion 2. If Criteria 1, 2 and 3 are all met, sarcopenia is considered severe. 1 Low muscle strength, 2 Low muscle quantity or quality, 3 Low physical performance..." (Cruz-Jentoft et al., 2019). Sarcopenia is also now recognized as a disease in the ICD-10 (Vellas et al., 2018). After the age of fifty, muscle mass decreases by 1%–2% annually while muscular strength can decrease 12%–15% every 10 years (Larsson, 1983; Quittan, 2016). Reduced physical function is a major consequence of sarcopenia leading decreased ability to perform activities of daily living (ADLs), loss of independence, onset of disability and frailty, and increased mortality (Reeves et al., 2004; Marzetti et al., 2017). Low muscle mass correlates to weakness in older adults (Newman et al., 2003), while weakness has a strong positive correlation with decreased function (Schaap et al., 2013) and mobility (Visser et al., 2005). Rodent models demonstrate similar sarcopenic outcomes to those mentioned above in humans (Parks et al., 2012; Graber et al., 2013; Liu et al., 2014; Graber et al., 2021). Exercise, however, can help mitigate frailty and preserve physical function in both humans and mice (Koster et al., 2012; Reeves et al., 2004; Graber et al., 2015; Medeiros et al., 2008; Seldeen et al., 2019).

The large-scale MoTrPAC (molecular transducers of physical activity) study financed by the NIH common fund has been initiated to learn more about the mechanisms by which exercise improves health, in humans and rats (Sanford et al., 2020). In humans, endurance exercise programs produce improvements in body composition, endurance, physical function, and to a lesser degree, strength (Wanderley et al., 2015; Henderson et al., 2017; Villareal et al., 2017; Yoo et al., 2018). In contrast, resistance training (e.g., weight lifting) in humans primarily improves strength and muscle mass, with less improvement in aerobic capacity than endurance training (Phillips SM, 2007). Similar results have been observed in mouse models of exercise (Graber et al., 2015; Graber et al., 2019a; Seldeen et al., 2019).

In this study we determined the efficacy of two mouse endurance exercise models, voluntary wheel running (VWR) and high intensity interval training (HIIT), to preserve or improve physical function in older adult and adult male C57BL/6 mice (Liu et al., 2014; Graber et al., 2015; Seldeen et al., 2018; Seldeen et al., 2019). In VWR, the mice choose to exercise at will on a running wheel—which would be similar to a human study where participants are given a pedometer, and their activity rate is tracked without any directed exercise goals. HIIT is a prescribed program of progressively increasing challenge where intervals of intense activity (in this case sprinting on a treadmill) are alternated with a lower intensity (walking on the treadmill) recovery period. In mice, HIIT is designed similarly to how humans would perform the same exercise on a treadmill (Seldeen et al., 2018; Seldeen et al., 2019). We measured exercise capacity and physical function with our previously designed composite scoring system, CFAB (comprehensive functional assessment battery), currently validated only in male C57BL/6 mice (at 6 m, months old, 24 m, and 28 m) and not female mice (Graber et al., 2021). CFAB, the primary outcome measure of the current study, is composed of 5 well-validated determinants: wheel running (volitional activity rate), grip meter (forelimb strength), inverted cling (four-limb strength/endurance), rotarod (overall motor function), and treadmill max-speed test (aerobic capacity) (Graber et al., 2021). *A priori*, we hypothesized that in comparison to VWR, the prescribed, personalized, and regimented HIIT protocol would provide a greater overall improvement in physical function and exercise capacity. To test this hypothesis, we randomized male C57BL/6 mice at two different ages into exercise groups (VWR and HIIT): adults (A) starting training at 6 m (months-old) adults (roughly early to mid-20s human equivalent) and then ending at 10 m (corresponding roughly to early middle age in humans), and older adults (OA) training from 22 m to 26 m (at the study end the mice were roughly equivalent to early 70s in humans). We had two sedentary control groups (SED) that did not exercise: 6m–10 m adults (SEDA) and 24m–28 m (SEDOA). See the online-only Supplemental Discussion for a comparison of human *versus* mouse ages and how we estimate mouse to human month to year calculations. Pre- and post-training, we determined body composition (with MRI), physical function with CFAB, and maximal isometric plantar flexor torque with *in vivo* contractile physiology.

Methodology

Animals

We obtained male C57BL/6 mice from the NIH NIA Aging Rodent Colony and from Charles River Laboratory. The mice were

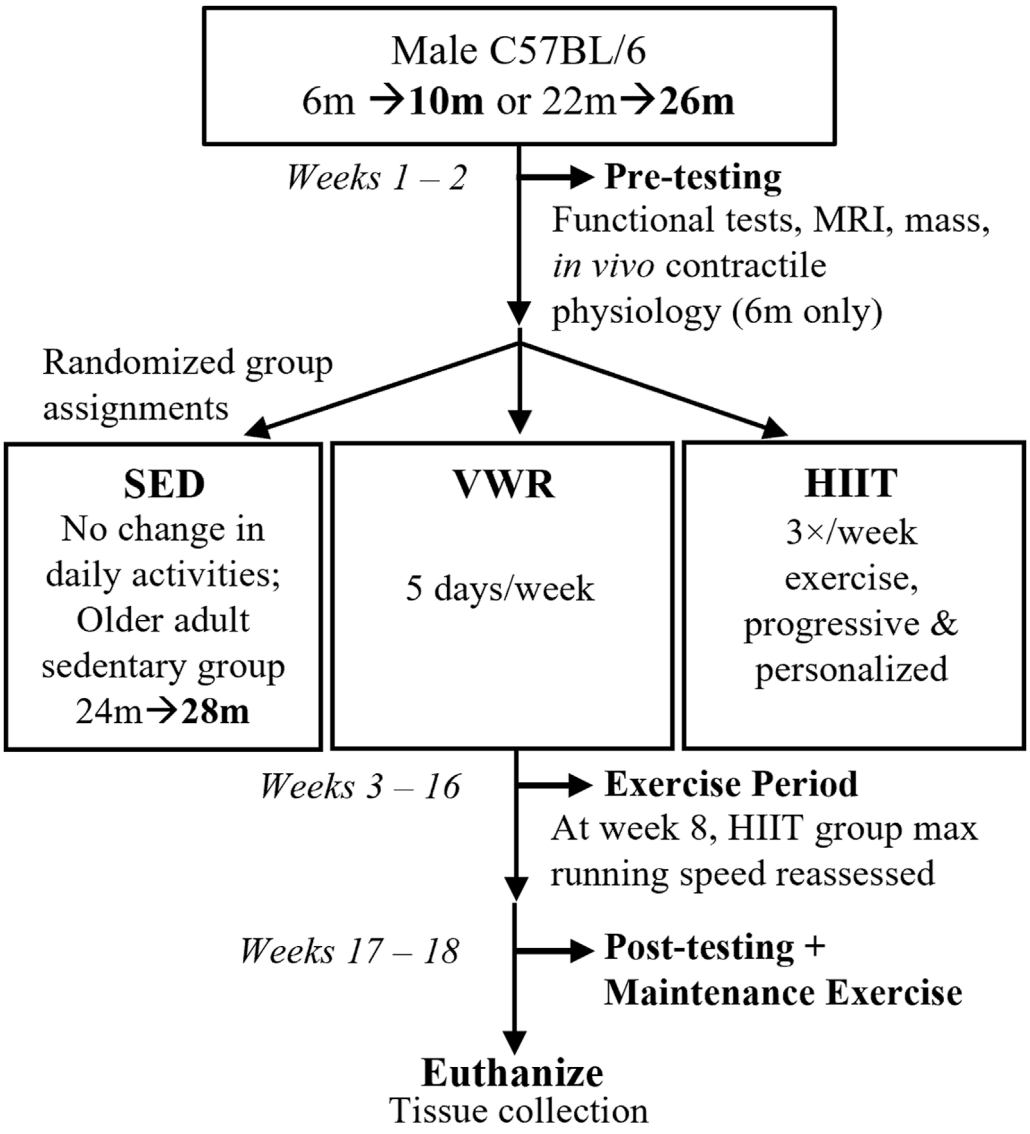

FIGURE 1
Study Design. Prior to exercise assignments, male C57BL/6 mice aged 6 months, m (10 m at study end, n = 24) or 22 months (26 m at study end, n = 18) were pre-tested for functional abilities (voluntary wheel running or VWR, rotarod, treadmill, grip strength, inverted cling), as well as mass, body composition (MRI, magnetic resonance imaging), and *in vivo* contractile physiology (maximum isometric plantar flexor torque). Afterwards, mice were randomized into volitional exercise/VWR (10 m n = 8, 26 m n = 8), HIIT, high intensity interval training (10 m n = 8, 26 m n = 10), or sedentary controls/SED (10 m n = 8). We had an additional slightly older adult SED group (24 m n = 8). For the next 13 weeks, VWR groups spent 5 days/week singly-housed in cages equipped with running wheels (and 2 days group housed with cage mates), HIIT groups trained 3 days/week, and SED groups remained in home cages. HIIT and SED mice (and VWR mice on the 2 days/week) were group housed. After exercise training, the mice post-tested before being euthanized for tissue collection. Maintenance exercise 2 days/week was provided for HIIT groups between the end of the exercise period and euthanasia.

treated humanely under protocols approved by East Carolina University IACUC (protocol #p106). The mice were group housed in large static microisolator mouse cages come from Ancare (N40 cage bottom top hi-temp polycarbonate, N40 micro filter top hi-temp polycarbonate, and the N40SS wire lid stainless steel), unless separated for extreme aggression and fighting. They were kept at 22°C with 12-h light/dark cycles and fed/watered *ad libitum* with standard rodent chow. At the start of the study, we had n = 24 adult mice (aged 6 m), n = 18 older adult mice (22 m) and n = 10 older adult mice (24 m). During the study, four adult and four older adult mice died from natural causes or were euthanized by recommendation of the ECU veterinary staff. Sample size (minimum n = 7) was determined using power analysis based upon the CFAB mean (−5.74) and standard deviation, SD (0.44), for 28-month-old mice from our previous work with the second group to have a predicted minimum difference of 15% (−4.879, assuming equal variance) generated effect size of 1.957 with α = 0.05 and power = 95% in a two-tailed independent samples Student's t-test using the software program G-Power (Faul et al., 2007; Faul et al., 2009; Graber et al., 2021). Furthermore, a power analysis of changes between group CFAB means for a mixed model ANOVA at two time points with three groups (group 1, control, mean as above, and groups 2 and 3, exercise treatments, with predicted 15% equal change of mean = −4.879, and assuming equal standard deviation of

0.44 for all groups) showed a strong effect size of 0.922 with α = 0.029 and power = 97% at n = 7.

Study design

See Figure 1 for study design schematic. We assessed the mice for physical function and then randomly selected them into groups based on age and exercise type. Age groups were defined as: A, adults (10 m at study completion), and OA, older adults (26 m at study completion for both exercise groups, while the sedentary group was 28 m at study completion). We defined the exercise groups as: VWR, voluntary wheel running, HIIT, high intensity interval training; and SED, sedentary control (no exercise). Due to complications during the Covid-19 pandemic shutdown we added an additional control group of slightly older adult sedentary control mice (n = 10, 24 m at start and 28 m at finish, SEDOA) since we were unable to complete a 26 m SED group because of laboratory lockdowns. Only CFAB and mass were measured in the SEDOA group to determine the effect of 4 months of sedentary behavior on older adult mice. See section on Exercise Training for more details.

We established an exclusion criterion to be selected into the VWR exercise group (<500 revolutions per week on the running wheels during pretesting). This exclusion criteria ensured that mice randomized to VWR would actually exercise voluntarily to at least a minimal degree. Without this exclusion, the VWR group may have had mice with no internal voluntary exercise drive, thus invalidating the results (cannot measure exercise results if the subjects do not exercise!). Mice running below the 500 revolution per week pre-testing threshold were randomized into either HIIT or CON. Similar to successful training durations previously established, the mice exercised for 13 weeks (including a 1-week acclimation period), followed by post-training functional assessment and subsequent tissue collection (Graber et al., 2019a).

Functional testing

Neuromuscular Performance

We determined physical function and exercise capacity using the Comprehensive Functional Assessment Battery (CFAB) similar to as previously described (Graber et al., 2021). CFAB is a composite scoring system measuring overall physical function consisting of five common non-colinear well-validated determinants, including grip meter for fore-limb strength (normalized to body mass), inverted cling for overall strength/endurance (log10 transformation to assure normality), rotarod for overall motor function (coordination, balance, endurance, power production), voluntary wheel running (volitional exercise and activity rate, with endurance (log10 transformation to assure normality), and treadmill running (max speed test for aerobic endurance/capacity and running speed). We administered these tests pre- and post-training. Devices used for each test were: grip meter (Bioseb GT3), treadmill max speed test (Columbus Instruments Exer 3/6Treadmill), rotarod (Panlab LE820 from Harvard Apparatus), VWR (Columbus Instruments Mouse Home Cage Running Wheel), and inverted cling (custom built device consisting of a hinged grid top over a 56 cm tall × 29 cm wide × 27 cm deep plexiglass box with a padded bottom). CFAB was derived for each individual mouse as the sum of the individual standardized scores for each of the five determinants (reference group is the mean and standard deviation of the 6 m male C57BL/6 mouse published in Graber et al., 2021). We then compared the pre- and post-CFAB results to determine the effect of the three conditions (HIIT, VWR, or SED) on functional capacity over the 4 month period. A perfectly average 6 m old mouse would rate as a zero CFAB, a positive score indicates function greater than average, whereas a negative CFAB score indicates function worse than the average 6 m mouse, i.e., the more negative the score, the worse the overall functional performance and exercise capacity of the mouse. Further information on the specific Individual testing procedures are discussed briefly in the Online Supplement Methodology Section and have been previously published in detail (Graber et al., 2013; Graber et al., 2015; Graber et al., 2018; Graber et al., 2019a; Graber et al., 2021).

Other tests

In vivo contractile physiology

We measured maximal plantar flexor torque production (1300A: 3-in-1 Whole Animal System–Mouse, Aurora Scientific) in the 10 m HIIT, VWR, and CON, pre- and post-training period. Due to Covid19 restrictions and laboratory limitations we were unable to collect this data for the OA mice. Methods have been published elsewhere (Graber et al., 2019b; Neelakantan et al., 2019; Brightwell et al., 2021; Graber et al., 2021) and see further details in the online supplement. In brief, we anesthetized the mouse using isoflurane (~3% isoflurane and 1.5 L/m of O_2, to effect) to remove conscious control of skeletal muscle. We then shaved the lower limb, and the mouse was situated on a heated platform with the tibia parallel to the platform and the femur condyle clamped to prevent shifting of the leg, forming a 90° angle. The foot was set into a footplate attached to a force transducer adjusted to provide minimum resistance and then we found the optimal placing of the needle electrodes to produce a maximum torque twitch in the plantar flexors (gastrocnemius complex) using 2 mA of current. Next, we determined the optimal current needed to produce the maximum isometric twitch by increasing the amperage applied for sequential twitches in sequence (0.5 mA, 1mq, 2 mA, 3 mA, 4 mA, 5 mA. . .) to find the largest twitch torque prior to decrease or plateau of torque at the minimum needed current (to avoid off target muscle stimulation). Keeping the needles and current set as were determined while finding the maximal twitch torque, we then found maximum isometric tetanic torque (mN*m, milliNewtons multiplied by meters) by constructing a torque-frequency curve from a single pulse, 10 Hz (Hz), 40 Hz, 80 Hz, 100 Hz, 120 Hz, 150 Hz, 180 Hz, 200 Hz, and finally a second single pulse, with a 1 min rest between each stimulus. These contractile values were normalizing to body mass (mN*m/gbm, gbm = grams of body mass).

Body Composition

Body mass was measured during *in vivo* contractile physiology, at the time of tissue collection prior to euthanasia, and once a week during the treadmill and running wheel protocols. EchoMRI-700

(Echo Medical Systems) was used to determine body composition (fat percentage, fat%) at pre- and post-training. Due to Covid19 restrictions and laboratory limitations we were unable to collect this data for SEDOA. We thus substituted, for the sake of comparison, body composition data previously collected using DEXA (dual-energy x-ray absorptiometry) on a different cohort (n = 10) of sedentary mice aged between 23 and 27 months that was previously reported (Graber et al., 2019b).

Muscle Mass

We collected tissue during non-survival surgery just prior to euthanasia (via exsanguination and removal of the heart). The mice were deeply anesthetized with a ketamine/xylazine mix (144 mg/kg ketamine, 16 mg/kg xylazine, to effect). We then collected the hindlimb muscles, including dorsiflexor (tibialis anterior, TA), plantar flexors (gastrocnemius, GAS; soleus, SOL; plantaris, PLANT), and extensor digitorum longus (EDL) (Charles et al., 2016). We recorded the wet mass of muscles (mg). We then combined the total mass of the collected muscles into a parameter we termed *total muscle mass*.

Exercise training

The mice were divided into groups as described above: VWR (both ages n = 8, with 7 OA and 6 A surviving to complete the study, but see below), high intensity interval training (HIIT, A n = 8 all completed the study; and OA n = 10, 9 OA completed training), and sedentary control (SED, A, n = 8, 6 completed; OA, n = 10, 8 completed. Three mice were euthanized as instructed by our veterinary staff due to extreme dermatitis and were unable to complete the study (n = 2 A and n = 1 OA), the other mice died of natural causes prior to study completion. One mouse that was originally randomized into the VWRA group refused to exercise and was thus moved to the SEDA group (final count: VWRA n = 5 and SEDA n = 7).

Sedentary mice (SEDA and SEDOA) were group housed in cages with environmental enrichment but did not exercise. Exercise mice trained as follows:

VWR

VWR training protocols were the same as VWR functional testing, except mice were singly housed in cages equipped with running wheels for 5 days, followed by a two-day period when mice were returned to social housing for rest and recuperation. Each VWR mouse completed one five-day session per week, with mass and total wheel revolutions recorded at the end of the 5 days (converted to km/day). We tracked weekly VWR exercise volume (measured as work done in units of grams body weight × distance ran).

HIIT (prescribed treadmill running)

HIIT protocols were modified from Seldeen and others (2019), differing in that we did not have the mice run at an incline. Using maximum running speed at failure from pre-training treadmill functional testing, HIIT mice were placed in similarly paced groups. The median max speed of each group was used to determine 75%, 80%, and 85% max speed for HIIT intervals. Mice trained three times per week with a two-day rest during weekends. HIIT sessions began with a 1-min 3 m/min warm-up walk, followed by intervals separated by 60 s walk steps (3 m/min). Each interval began with a 30 s acceleration step to running speed (set to 75%, 80%, or 85% max speed), which was maintained for 60 s, before ending with a 30 s deceleration back to walking speed. HIIT sessions ended with a 2-min 3 m/min cool-down walk. Initially, groups trained at lower-intensity, fewer HIIT intervals (three intervals at 75% max speed, or 75-75-75). Over time, interval number and running speed increased according to the abilities of the mice until groups were running 75-80-85-80-75 intervals. This might be considered a typical recommended intensity scheme for HIIT in humans (Mack, 2018; Maillard et al., 2018; Marriott et al., 2021). Halfway through the study, HIIT mice repeated the functional treadmill test with group speeds and assignments changed according to how the maximum running speed of each mouse had improved. We tracked weekly HIIT exercise volume (measured as work done in units of grams body weight x distance ran) and power produced (work/total seconds of exercise session). The HIIT groups were groups housed.

Statistics and data

Unless otherwise noted, we report the mean plus or minus the standard error of the mean (SE). For analysis, experimental groups were assigned number identifiers and statistical tests were performed by a lab member blind to the group ID meanings. Statistical significance was set at $p < 0.05$, and trends are reported where $0.05 < p < 0.10$. One-way ANOVA, or Student's t-test are used to compare means between subjects, as appropriate. We used $3 \times 2 \times 2$ (3 exercise groups, 2 age groups, and 2 time points) mixed model ANOVA, 3×2 (3 exercise groups and 2 time points) mixed model ANOVA and paired t-tests for with-in subject changes and to analyze main effects. Our main outcome was the difference in CFAB from pre-to post-training (normally distributed, and tested with Tukeys's Honest Significant Difference, HSD, posthoc). As we normally do, to minimize type two error from the inherently large variability in CFAB determinants, we used least significant differences (LSD) *post hoc* testing and we report Tukey's HSD alongside for comparison. If tests had outliers (defined *a priori* as greater than >2 standard deviations from the mean), we analyzed both with and without these outliers and report both, if needed, for clarity (i.e., if the outlier changes the statistical test). In addition, we report effect sizes as appropriate (either Cohen's d or η^2 (or partial η^2) in the Supplementary Tables. We specify the statistical test used for each set of data in the results and figures/tables. We report effect size, skew, kurtosis, and results of normality tests in Supplementary Tables S1–S4. Contrary to previous work the VWR measurement in km/day severely violated normality, but was normally distributed with a log10 transformation. We thus used the log10 transformation to construct CFAB. Non-parametric tests were used where violations of normality occurred (e.g., the Kruskal-Wallace 1-Way ANOVA or Wilcoxon Signed Rank Test, see Supplementary Tables S1–S4 for more details). We used SPSS v28 and v29 (IBM) for statistical analyses.

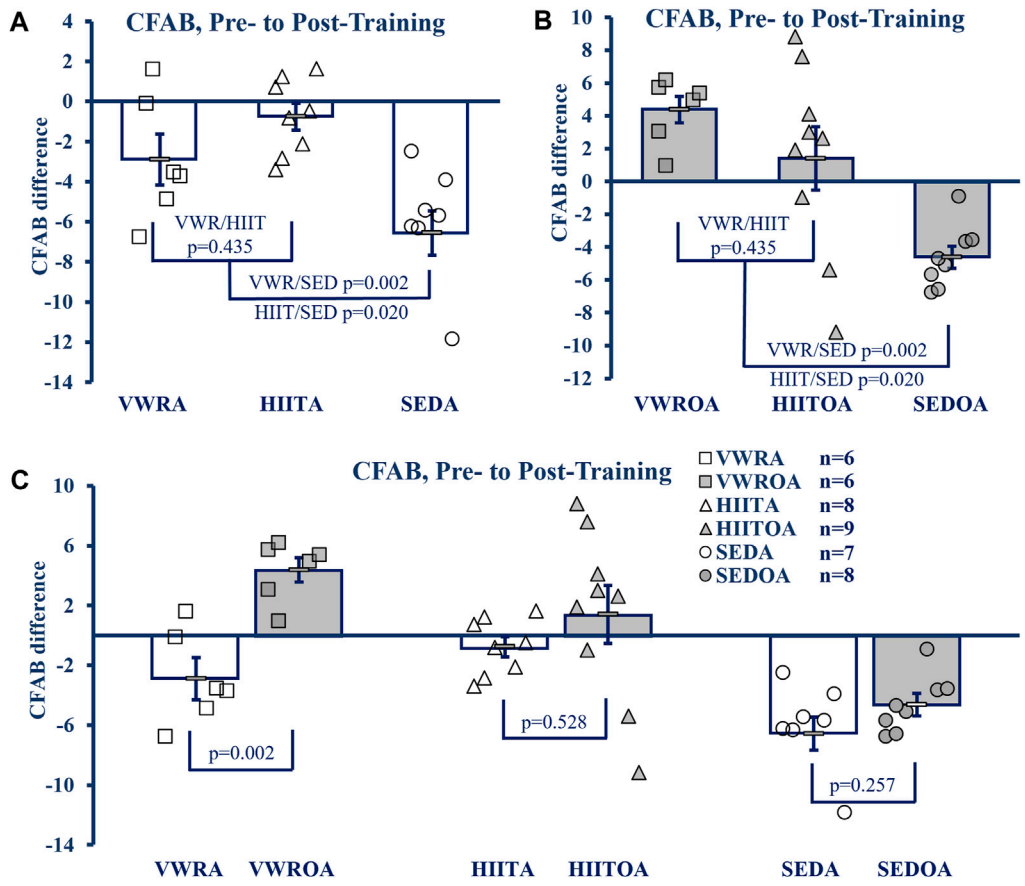

FIGURE 2
CFAB Difference Pre-to Post-Training. **(A)** Comparison of Exercise Groups in Adults **(B)** Comparison of Exercise Groups in Older Adults), **(C)** Comparison of Exercise Groups By Age. KEY: CFAB: comprehensive functional assessment battery composite scoring system. A more negative score means less functional ability and lower exercise capacity. Symbols: Each symbol (square, VWR; triangle, HIIT; or circle, SED) represents the change in CFAB score for one individual male mouse, while bars and error bars represent group mean and standard error. Ages and Groups: Open symbols = adult groups, shaded symbol = older adults. VWR = voluntary wheel running, HIIT = high intensity interval training, SED = sedentary control, A = adults (10 m at study end), OA = older adults (26 m at study end, except SEDOA = 28 m). *Statistical Tests:* Error bars = standard error, *p*-value (*p*), effect size η^2 (partial eta squared) or Cohen's d. Panels A) and B) One-Way ANOVA (panel A: F = 5.768 p = 0.012, η^2 = 0.404; panel B: F = 8.38, p = 0.002, η^2 = 0.456) with Tukey's HSD (honest significant difference) *post hoc* testing, C) p from Student's T-test (age comparison of exercise effects), effect sizes (Cohen's d) = −2.324, −0.605, and −0.736 for VWR, HIIT, and SED respectively.

Results

Physical function (CFAB): improved, maintained or loss mitigated with exercise

To determine exercise efficacy, and age-associated functional loss over the training period, we measured the difference between pre- and post-training CFAB values, producing an intervention assessment value similar to systems used previously (Graber, et al., 2015; Seldeen, et al., 2019). Exercise effects within age groups are shown in Figures 2A,B, while the effect of age on training is shown in Figure 2C.

In the adult groups the mean CFAB difference from pre-to post-training (One-Way ANOVA, F = 8.621, p = 0.002, η^2 = 0.489, Tukey's HSD *post hoc*) did not change with respect to training types (mean difference VWRA -2.873 ± 1.20, HIITA -0.842 ± 0.679, p = 0.341), but both training groups demonstrated preservation of function during aging compared to the sedentary control (SEDA mean difference −6.409 ± 1.126, p = 0.062 compared to VWRA and p = 0.002 compared to HIITA).

Similarly, in the older adult groups the mean CFAB difference from pre-to post-training (F = 7.394, p = 0.004, η^2 = 0.425) were not different between exercise groups (VWROA 3.214 ± 0.919, HIITOA 0.499 ± 1.935; p = 0.426), but both groups again demonstrated significant preservation of function during aging compared to the sedentary control (SEDOA -4.837 ± 0.756, p = 0.004 compared to VWROA and p = 0.034 compared to HIITOA).

To compare the effect of VWR, HIIT and SED based on age, we evaluated the mean CFAB difference pre-to post-training of each exercise type using Student's independent samples t-test. VWROA improved function compared to VWRA (t = 4.027, p = 0.002, Cohen's d = 2.325). However, HIITA and HIITOA did not differ in effect between the ages (t = 0.654, p = 0.528, Cohen's d = 0.302), and SEDA and SEDOA both declined similarly (t = −1.186, p = 0.257, Cohen's d = −0.614).

We used a 3 × 2 × 2 mixed model ANOVA (3 exercise types, 2 ages, 2 time points, pre- and post-training) and compared CFAB measurements with-in subjects directly (F = 15.392, p < 0.001, partial η^2 = 0.288) and both the main effects of exercise type

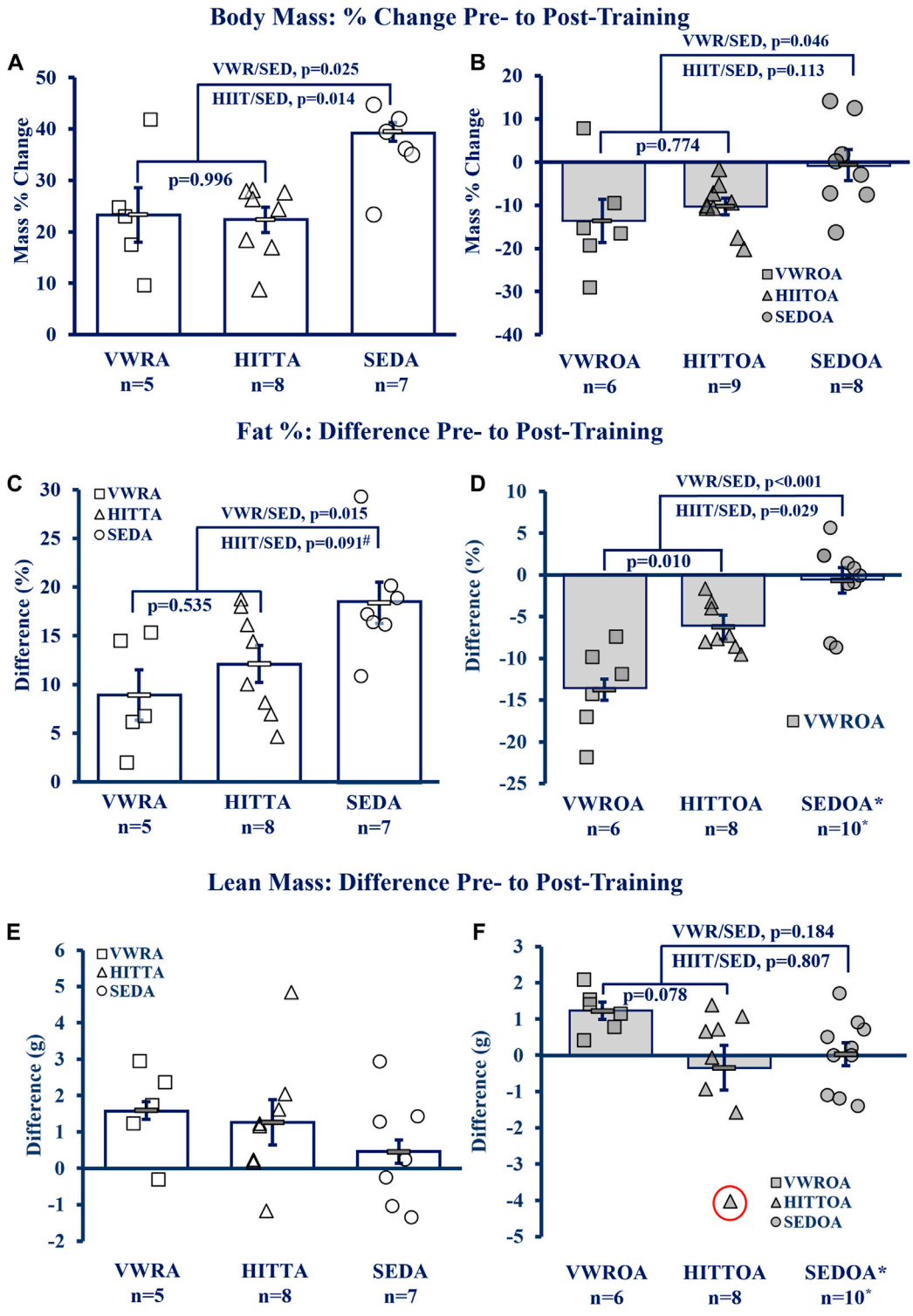

FIGURE 3
Body Composition Improved by Exercise. **(A, B)** Body Mass, **(C, D)** Fat percentage (Fat%), **(E, F)** Lean Mass Difference. KEY: Symbols: Each symbol (square, VWR; triangle, HIIT; or circle, SED) represents the measurement from MRI (magnetic resonance imaging) for one individual male mouse, while bars and error bars represent group mean and standard error. Ages and Groups: Open symbols = adult groups, shaded symbol = older adults. VWR = voluntary wheel running, HIIT = high intensity interval training, SED = sedentary control, A = adults (10 m at study end), OA = older adults (26 m at study end, except SEDOA = 28 m). g = grams. NOTE: *Fat% difference and lean mass change (from DEXA) in SEDOA taken from previously reported study (Graber et al., 2019b) for illustrative purposes only since we were unable to perform MRI on the SEDOA group due to Covid19 lab lockdowns. *Statistical Tests:* Means analysis by One-Way ANOVA with Tukey's HSD (honest significant difference) *post hoc* testing: **(A)** $F = 6.085$, $p = 0.010$, $\eta^2 = 0.417$, **(B)** $F = 3.806$, $p = 0.040$, $\eta^2 = 0.276$, **(C)** $F = 5.236$, $p = 0.016$, $\eta^2 = 0.368$, **(D)** $F = 17.865$, $p < 0.001$, $\eta^2 = 0.630$, # trend ($p = 0.091$) between HITTA and SEDA, **(E)** no significant differences or trends: $F = 1.196$, $p = 0.325$, $\eta^2 = 0.117$, **(F)** $F = 2.810$, $p = 0.083$, $\eta^2 = 0.211$; Circled triangle = significant outlier; without outlier: $F = 3.220$, $p = 0.061$, $\eta^2 = 0.244$, (no difference between VWROA and HIITOA, n = 7, $p = 0.143$; between VWROA and SEDOA, $p = 0.060$).

collapsed across age (F = 12.917, $p < 0.001$, partial $\eta^2 = 0.408$) and age collapsed across exercise type (F = 13.083, $p < 0.001$, partial $\eta^2 = 0.254$) were significant. Between subjects the main effect of age collapsed across exercise was significant (F = 18.618, $p < 0.001$, partial $\eta^2 = 0.329$, mean difference of −3.502 ± 0.812), though collapsing all exercise types across age was not significant (F = 0.367, $p = 0.696$, partial $\eta^2 = 0.019$) and the interaction of age and exercise type tended toward a difference (F = 2.579, $p = 0.089$, partial $\eta^2 = 0.120$).

Mouse performance on individual functional tests can reveal interesting trends in particular physical skills most affected by exercise. See Supplementary Table S1 for pre-training baseline and post-training means, and statistical analysis of the raw data including means testing, skew, kurtosis, and normality testing.

Body composition: improved with exercise

Exercise of either type improved the body composition outcomes of body mass percent change and the difference in pre- to post-training to similar degrees within age-groups, though lean mass difference was largely unchanged (see Figure 3A, B. Body Mass; Figure 3C, D Fat Percentage; Figure 3E, F Lean Mass). Adult exercise mice were resistant to body mass and fat% increases compared to the sedentary controls, whereas in the OA exercise mice both body mass and fat% were reduced compared to the SEDOA (note: values used for SEDOA fat% were taken from and earlier publication (Graber et al., 2019a) of a different population because we were unable to use MRI on the SEDOA mice due to the Covid19 lockdown). See Supplementary Table S2 for pre-training baseline and post-training means, and statistical analysis of the raw data including means testing, skew, kurtosis, and normality testing.

Body mass

Total body mass also altered between pre- and post-training (Figure 3A, B), except for the SEDOA which remained stable. Statistics below for the adult groups are from pair-wise comparisons from pre-to post-training from a 3 × 2 mixed model ANOVA within age groups (3 groups, VWR, HIIT< and SED; two time points, pre- and -post-training; with-in subject pair-wise comparisons). Body mass in all of the adult groups increased over the course of the experiment (with-in subjects effects, interaction of time and groups: F = 3.991, $p = 0.037$, partial η2 = 0.307). VWRA body mass increased 6.607 ± 1.179 g ($p < 0.001$), HIITA increased 6.594 ± 1.201 g ($p < 0.001$), and SEDA increased 10.376 ± 1.091 g ($p < 0.001$). The SEDA gained both overall mass and increased fat percentage by 18.40 points (pre-mean of 13.98% fat to 32.38% fat, post-mean) indicating that the SEDA mice gained primarily fat (mean difference pre-to post-training of 8.65 g ± 1.16 g) and a small amount of lean mass (average 0.46 g ± 0.67 g). Both older adult exercise groups lost mass. Older adult mass violated normality and *p*-values following are from the Wilcoxon Signed Rank test. The VWROA group lost an average of 6.01 ± 2.44 g of body mass ($p = 0.046$) while HIITOA lost 4.01 ± 0.71 g ($p = 0.012$). SEDOA mice did not gain weight and remained indistinguishable to their pre-training mass (mean mass change = −0.26 ± 2.44 g, $p = 0.779$).

Fat % and lean mass

Body composition (Fat%) altered markedly between the start and end of the experiment for all measured groups other than SEDOA (see Figures 3C,D). Statistics below for adult mice are from pair-wise comparisons from pre-to post-training using a 3 × 2 mixed model ANOVA interaction of exercise and groups (3 groups, VWR, HIIT and SED; two time points, pre- and -post-training; with-in subject pair-wise comparisons: F = 5.237, p=<0.001, partial η2 = 0.873). All adult groups gained body fat. VWRA, HIITA, and SEDA all increased body fat percentage: VWRA +8.97 ± 2.20% fat ($p < 0.001$), HIITA +12.14 ± 1.91% fat ($p < 0.001$), SEDA +18.40 ± 2.12% body fat ($p < 0.001$). The older adult mice had normality violations and the with-in subject tests for changes in fat% were performed using the Wilcoxon Signed Rank Test. Both VWROA and HIITOA mice lost body fat: VWROA -13.74% ± 5.03% body fat ($p = 0.028$), HIITOA -6.24% ± 2.88% body fat ($p = 0.012$). SEDOA mice in our prior study (Graber, et al., 2019) did not lose body fat (mass percent change −0.66% ± 1.43%, $p = 0.953$), for illustrative purposes the is data reproduced in Figure 3D. Thus, both exercise types mitigated increases in body fat associated with 6- to 10-month aging and decreased fat% in older adult mice.

Lean mass differences between groups were not significant, though there was a tendency ($p = 0.078$, Tukey's HSD) for VWROA to increase lean mass compared to HIITOA (see Figure 3E, F, and Supplementary Table S2).

Muscle mass

Hindlimb muscles were collected, blotted dry, and weighed following euthanasia (see Figure 4). Statistics for data below from One-Way Univariate ANOVAs, and Student's t-tests. NOTE: Muscles from SEDOA were not collected for this study and so values are only presented for the other five groups. See Supplementary Table S3 in the Supplement for raw data values of the tested muscles: gastrocnemius (GAS), plantaris (PLANT), soleus (SOL), tibialis anterior (TA), extensor digitorum longus (EDL), heart, and total muscle (sum of the other 5 hindlimb muscles) in mg and normalized to body mass including means testing, skew, kurtosis, and normality testing.

In the adult mice there was little overall change in muscle mass. Only SOL normalized to body (1-Way ANOVA, F = 5.037, $p = 0.018$, partial $\eta^2 = 0.359$, Tukey's HSD *post hoc*) mass demonstrated that the VWR increased mass compared to the SED ($p = 0.014$), but VWR was not different than HIIT. HIIT did not change compared to SED.

In the older adult mice, we only compared the two exercise types. VWR tended to improve muscle mass compared to HIIT in the total muscle mass measurement with a strong effect size (Student's t-test, t = 2.134, $p = 0.055$, Cohen's d = 0.974). This was confirmed when the total muscle mass was normalized to body mass (Student's t-test, t = 2.254, $p = 0.043$, Cohen's d = 1.053). GAS mass tended to be larger in VWR compared to HIIT, also with a strong effect size (Student's t-test, t = 2.042, $p = 0.062$, Cohen's d = 1.076), but this advantage was erased when normalized (Student's t-test, t = 0.580, $p = 0.572$, Cohen's d = 0.306).

Plantar flexor peak tetanic torque (*in vivo* contractile physiology)

See Figure 5 for more details and Supplementary Table S4 in the Supplement for raw data values including means testing, skew,

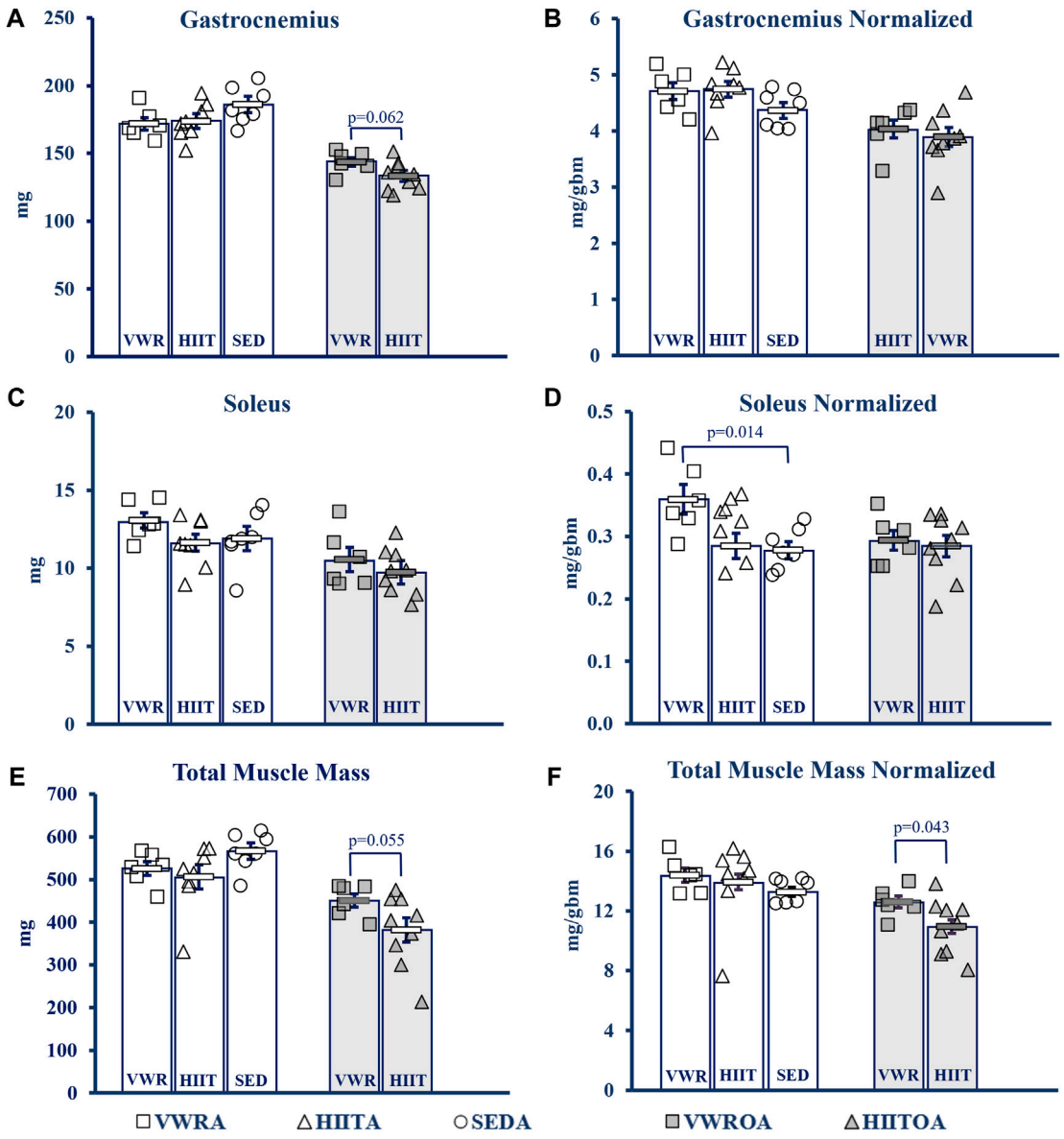

FIGURE 4
Muscle Mass Changes with Exercise. **(A)** Gastrocnemius (GAS). **(B)** GAS normalized to body mass. **(C)** Soleus (SOL). **(D)** SOL normalized to body mass. **(E)** Total muscle mass. Calculated by summing the mass of GAS, SOL, Plant, TA and Edl. **(F)** Total muscle mass normalized to body mass. KEY: Units: mg = milligrams, gbm = grams body mass. Symbols: Each symbol (square, VWR; triangle, HIIT; or circle, SED) represents the measurement for one individual male C57BL/6 mouse, while bars and error bars represent group mean and standard error. Ages and Groups: Open symbols = adult groups, shaded symbols = older adults. VWR = voluntary wheel running, HIIT = high intensity interval training, SED = sedentary control, A = adults (10 m at study end), OA = older adults (26 m at study end, except SEDOA = 28 m). VWRA, open squares (n = 7); HIITA, open triangles (n = 8); SEDA, open circles (n = 6); VWROA, shaded squares (n = 7); HIITOA, shaded triangles (n = 10). *Statistical Tests:* Means analysis by One-Way ANOVA with Tukey's HSD (honest significant difference) *post hoc* testing, effect size η^2 (partial eta squared for adult groups, effect size η^2 (partial eta squared), and Student's independent samples t-test for Older Adult groups: **(A)** F = 1.584, p = 0.232, η^2 = 0.1; t = 2.042, p = 0.620, Cohen's d = 1.076, **(B)** F = 1.584, p = 0.232, η^2 = 0.150; t = 0.951, p = 0.359, Cohen's d = 0.005, **(C)** F = 1.584, p = 0.232, η^2 = 0.150; t = 0.951, p = 0.359, Cohen's d = 0.501, **(D)** F = 5.037, p = 0.018, η^2 = 0.359; t = 0.239, p = 0.815, Cohen's d = 0.126, **(E)** F = 1.971, p = 0.168, η^2 = 0.160; t = 2.14, p = 0.055, Cohen's d = 0.984, **(F)** F = 0.479, p = 0.627, η2 = 0.051; t = 2.254, p = 0.043, Cohen's d = 1.053.

kurtosis, and normality testing. NOTE: Because of technical limitations and the Covid19 global pandemic, we do not have data for the older adult groups (26 m). There was also a significant outlier in the SEDA group (−5.76% change from pre- to post, SD > 3 from the mean) that increased variability and we report both with and without the outlier (Figure 5 has the outlier designated, but the mean and statistics exclude it). With the outlier kept, there was no significant difference in the mean percent change (pre-to post-training) between groups using a one-way Univariate ANOVA (F = 2.605, p = 0.105, partial η2 = 0.246). However, without the outlier VWRA > HIITA > SEDA (F = 4.704, p = 0.026, partial η2 = 0.385), with Tukey's HSD *post hoc* VWRA = HIITA (p = 0.147), VWRA > SEDA (p = 0.023), HIITA = SEDA (p = 0.464). Within the groups from pre-to post-training (3 × 2 ANOVA, F = 63.058,

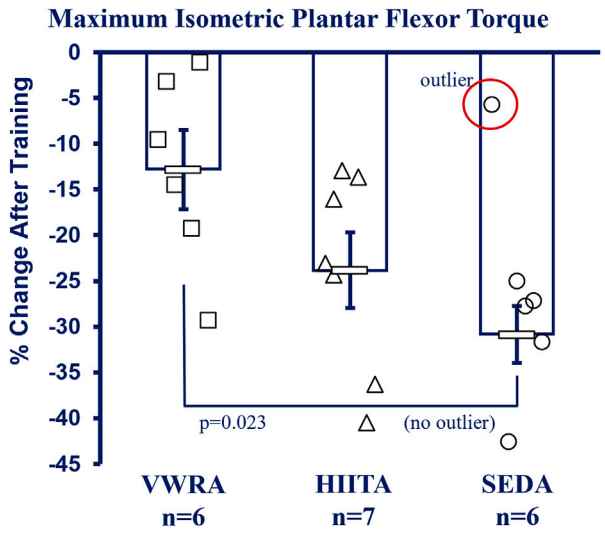

FIGURE 5
In vivo Contractile Physiology. All groups had decreases in maximum plantar flexor (gastrocnemius complex) isometric torque between pre- and post-training (means shown without the outlier in SED, −5.76% change >2.5 SD from the mean—marked as circled open circle symbol, NOTE: with outlier included there is no difference between groups). Maximum tetanic isometric torque was measured (mN*m) and is reported as percent change after correction to body mass (mN*m/gbm). KEY: Units: mN = milliNewtons, m = meters, gbm = grams of body mass. Symbols: Symbols: Each symbol (square, VWR; triangle, HIIT; or circle, SED) represents the measurement for one individual male C57BL/6 mouse, while bars and error bars represent group mean and standard error. Ages and Groups: Open symbols = adult groups (NOTE: older adults data not collected). VWR = voluntary wheel running, HIIT = high intensity interval training, SED = sedentary control, A = adults (10 m at study end). n:VWRA, open squares (n = 6); HIITA, open triangles (n = 7); SEDA, open circles (n = 6). *Statistical Test:* With SED outlier: no statistical difference between groups. 1-Way ANOVA with Tukey's HSD (honest significant difference), Circled circle = significant outlier: F = 2.605, p = 0.105, η2 = 0.246. Without SED outlier: F = 4.704, p = 0.026, η2 = 0.385; VWRA vs. HITTA (p = 0.147), VWRA vs. SEDA (p = 0.023), HIITA vs. SEDA (p = 0.464).

$p < 0.001$, partial η2 = 0.102) all the groups lost torque (normalized to body mass): VWRA -0.047 ± 0.018 mN*m/g (p = 0.018), HIITA -0.089 ± 0.016 mN*m/g ($p < 0.001$), when including the outlier SEDA decreased by 0.102 ± 0.018 mN*m/g ($p < 0.001$) and without outlier SEDA decreasing by 0.118 ± 0.009 mN*m/g ($p < 0.003$).

Exercise volume

See the Online Only Supplemental Results section and Supplementary Figures S1, S2 for more details.

Discussion

As we grow older, declining physical function is associated with loss of muscular strength, endurance, and mobility (McPhee et al., 2016; Nascimento et al., 2019). This decline leads to reduced ability to perform activities of daily living and a lower quality of life (McPhee et al., 2016; Marzetti et al., 2017). Consequently, older adults with greatly declined functional capacity lose independence and require assisted living (Marzetti et al., 2017). Exercise, while not a cure for sarcopenia, is a promising therapy to potentially retard the slope of age-related functional loss while improving quality of life. Exercise increases functional ability in older adults while also improving biomarkers of physical fitness such as strength, muscle mass, and VO_{2max} (Fiatorone et al., 1990; Bonnefoy et al., 2003; McPhee et al., 2016).

In this study we originally hypothesized that HIIT would prove to be a universally more efficacious exercise paradigm than VWR. The data supported partly supported our hypothesis in the adult 10 m male mice, but this did not hold true in the older 26 m male mice, which seemed to benefit equally from either type of exercise.

Exercise: VWR or HIIT?

Our results complement existing literature findings that exercise improves or preserves measurements of health and function in both humans and rodents (Peterson et al., 2009; Garcia-Valles et al., 2013; Graber et al., 2015; Steffl et al., 2017; Feito et al., 2018; Seldeen et al., 2018; Ben-Zeev and Okun, 2021). In work from our lab and others, both VWR and HIIT protocols have demonstrated attenuated frailty and mitigated functional loss in mice (Graber et al., 2015; Gomez-Cabrera et al., 2017; Seldeen et al., 2018; Graber et al., 2019a; Seldeen et al., 2019; Gioscia-Ryan et al., 2021; Bisset et al., 2022). However, to date, there is little information in the literature regarding side-by-side comparisons of the efficacy of these two pre-clinical exercise paradigms, thus our current study focus.

VWR

Voluntary wheel running in mice improves both body composition and physical function (Graber et al., 2015; Manzanares et al., 2019). VWR design is voluntary in nature--an individual mouse chooses their running volume and intensity. Most (but not all) mice will run on wheels, though the volume run varies widely between individuals. To ensure that mice randomized to the VWR group would run enough to be beneficial, we instituted an *a priori* exclusion criteria cut-off of <500 revolutions per week during pre-randomization CFAB testing. Mice excluded from the VWR trial were randomized into the HIITor SED groups. In retrospect, this may have unavoidably ensured the VWR group was home to more naturally active mice.

VWR is a common endurance exercise mouse model. Comparing VWR to a human exercise trial is problematic because the mice have no proscribed volume or intensity. A comparable human model to VWR would be one of tracking physical activity rates. Clinical studies incorporating self-reported activity levels indicate that, like the mice in this study, more frequent daily activity is associated with improved frailty scores (Manini et al., 2012; Savela et al., 2013; Tak et al., 2013). Thus, one might think of voluntary wheel running as translatable to a clinical trial where older adults are encouraged to start walking or jogging (tracked by pedometer), at a self-determined intensity and volume (Cheatham et al., 2018; Teixeira et al., 2021). Additionally, we must note that the size and type of wheels used influence the amount of running. Larger mice may run less on smaller in-cage style wheels designed for use in specific pathogen free environments,

such as the ~30 cm circumference wheels we use (Graber et al., 2021; Manzanares et al., 2019). This may partially account for why the 10 m mice in our study had a larger drop-off in VWR distance totals over time than we expected (with an average VWR group body mass gain of 22.7% from 6 to 10 months).

HIIT

Both human and animal models of HIIT make use of standardized protocols accounting for the principles of exercise physiology such as progressive difficulty, intensity and volume. With mice, perceived exertion is detected by third party observation (how easily are the mice keeping up with the treadmill).

Seldeen et al. have previously shown that HIIT in 24-month-old mice resulted in improved frailty scores (Seldeen et al., 2018) and that long-term HIIT training (16 weeks) increased maximal treadmill time in older adult mice.

Prescribed high-intensity exercise has been previously shown to improve measures of frailty in elderly humans, including improvements in strength and flexibility (Hess et al., 2006; Buckinx et al., 2018; Losa-Reyna et al., 2019), stair climbing (Bonnefoy et al., 2003), walking time (Bonnefoy et al., 2003; Losa-Reyna et al., 2019), chair rising (Bonnefoy et al., 2003; Buckinx et al., 2018), and hand grip strength (Jimenez-Garcia et al., 2019). Additionally, high-intensity exercise in humans has long been shown to improve markers of frailty and sarcopenia, including oxygen consumption, cardiovascular function, blood pressure, and inflammation (Fiatorone et al., 1990; Bonnefoy et al., 2003; McPhee et al., 2016; Buckinx et al., 2018).

One of the hallmarks often touted as a benefit of HIIT for humans is the time-saving nature—more exercise for equal or better benefit in a shorter time period than traditional long distance endurance training. This holds true for mice as well. In our study the adult mice eventually worked up to a 3x/week training period of 6–10 min of intense activity with 6–7 min of lower intensity recovery/warm-up/cool-down time per exercise bout; with the older adult mice having a little less. The VWR mice, on the other hand, spread out their exercise bouts over multiple time periods accounting for a greater expenditure of time during their 4 days per week of training in that their average time spent running on the wheel (which is measured in 10-min increments) account for 13–17 h total. Please see Supplementary Figures S1, S2 in the Supplement for more details.

From the standpoint of amount of time spent exercising in comparison to benefits gained by attenuating functional loss, HIIT clearly shows superiority to VWR. However, maximal benefit in the older mice is less clearly defined, and VWR is equivalent to HIIT (albeit with a greater time investment). However, HIIT exercise significantly increased older adult work-out intensity compared from pre-to post-training, while VWR does not (see Supplementary Figure S1, S2). Overall, though, functional benefits are similar, contrary to our original primary hypothesis. We now suggest that endurance exercise training of any type improves or preserves physical function in untrained older adult male mice, although based on our results from the adult groups, HIIT may better mitigate functional loss in early middle age male mice (see Supplementary Figure S1B, C; Supplementary Figure S2D).

Both older adult groups maintained or improved physical function following exercise training. There was wide variation in individual results, suggesting that for older adults mice, after a lifetime of sedentary living, starting any program of physical activity successfully prevented functional loss, though, for any given individual, the specific type of exercise may matter. In contrast, all adult groups decreased overall function. These mice aged from young adult males (6-months old) to early middle-age males (10-months old) during the study. The onset of middle age is associated with reduced physical function and reduced physical function in mice aging from 6-10 months has been reported previously (Yanai and Endo, 2021). However, the pre-to post-training decrease in exercise capacity (CFAB) shown by both adult exercise groups was significantly mitigated compared to the sedentary mice, indicating that early adoption of a lifestyle including regular exercise may slow age-related deterioration of physical function.

Age and exercise

Contrary to our hypothesis, HIIT did not universally improve outcomes compared to VWR. The effects of the exercise types depended, in part, on the age of the exercising group (exercise type * age interaction). Both groups of older adult exercise mice had similar improvements in overall motor function (CFAB change, Figure 2), and body composition (Figure 3). The older exercisers differed in grip strength, with the VWR mice having improved forelimb strength (Supplementary Table S1), a surprising result potentially related to the running wheels having small ridges that the mice might grip with their front feet as they run. In addition, as we expected, the HIIT mice greatly increased their treadmill capability compared to the VWR group. Notably, total muscle mass and normalized SOL mass in both older adult exercise groups were similar to SEDA—suggesting an age-reversing rescue effect from exercise. This occurred most strikingly in the soleus, a postural and locomotive muscle with a large percentage of type 1 muscle fibers, which, of the muscles we measured, should respond the most to endurance training (Graber et al., 2015; Graber et al., 2023).

The results suggest that for older age sedentary individuals, any type of physical activity will result in improved functional performance; however, what happens after the initial activity increase overcomes the effect of detraining remains to be investigated. Commonly, “any exercise is better than no exercise” is a mantra used to encourage exercise participation by sedentary older adults, and the current study has demonstrated this in the context of older mice.

In contrast, compared to VWRA the HIITA benefited in rotarod, treadmill, and mitigated loss of overall function (CFAB). However, as with the older mice; VWRA had significantly stronger forelimbs than HIITA. Notably, exercise types did not differ in their effect on adult body composition.

Overall, while adult male mice all experienced a decrease in physical function between pre- and post-testing, older adult male exercise groups maintained performance. This may be because prior to entering the study at 22 months of age, both HIITOA and VWROA were sedentary (detrained) for their entire lives, potentially leaving them with more room for improvement compared to the adult mice at their 6-month prime-of-life point.

It would be enlightening to follow a HIIT exercise group during a lifespan longitudinal study to observe how HIIT effects functional abilities, or whether training for a longer period (6 m or more) in older adult mice would demonstrate greater efficacy as the mice became more highly trained. There have been a number of long-term exercise trials in mice that determined VWR improved healthspan including physical and cognitive function (Garcia-Valles et al., 2013; Robison et al., 2018; Gioscia-Ryan et al., 2021). Retrospective studies in humans of master endurance athlete humans have shown that maintaining an endurance exercise program over time is essential to preserving cardiorespiratory fitness, since rapid linear degradation of VO_{2max} begins even after a few days of detraining whether in highly trained athletes or not (Burtscher, et al., 2022). Lifelong master athletes retain lean mass compared to less active older adults (Walker et al., 2023). Increased activity rate itself in humans is also linked to a plethora of positive outcomes, and both intense exercise as well as moderate activity promotes retention of muscle and physical function (Crane et al., 2013; Steffl et al., 2017). However, likely due to the labor-intensive aspects, randomized controlled trials of lifespan exercise with treadmill running, whether moderate or high-intensity, are understudied in both humans and rodents.

Caveats

One major caveat is because of restrictions related to the SARS-CoV-2 global pandemic and the ensuing laboratory shut-downs, we were unable to supervise a 26 m SEDOA group or perform *in vivo* contractile physiology on the 26 m exercise groups. We did include data on a slightly older (age 24m–28 m) sedentary group as a substitute SEDOA, demonstrating an overall loss of function over a four-month time period that was not observed in either exercise group. There is also data in the literature demonstrating the increased functional capacity of mice exercised with both HIIT and VWR compared to age-matched controls (Graber et al., 2015; Seldeen et al., 2018; Seldeen et al., 2019).

Secondly, we may have erred on the side of caution in advancing the HIIT protocol intensity in the older mice. It is possible that we did not stimulate them to the highest degree possible as we were concerned about injuries. As we based the HIIT program for the adult mice to match that of the older mice, the amount of stimulation may have been suboptimal to ensure maximum exercise adaptations. In future work, a dose-response study is warranted to determine if greater intensity would increase gains. Never-the-less, it was clear from the study that exercise either improved or preserved functional performance relative to the sedentary control groups.

Third, as we have addressed previously (Graber et al., 2021), the small (30 cm circumference) VWR wheels designed to fit inside home cages and permissible in specific pathogen free facilities may encourage less running by larger mice who may find the wheels smaller than would be optimal. This results in fewer overall revolutions, which may be of less import when the goal is to measure volitional exercise/activity rate than if the VWR is being utilized as an exercise protocol. Thus, a major consideration when designing future exercise should be the size/type of running wheels and the sizes of the mice.

Finally, this study includes only information on male C57BL/6 mice. Our major outcome measure CFAB has to date only been validated in male mice. Future work should address potential sexual dimorphisms in exercise response, and any differences in other strains of mice.

Conclusion

As the world population ages, it will become increasingly necessary to determine and evaluate therapeutic strategies to maintain physical function and independence for as long as possible. Exercise of all types is a critical component of this, but more information is needed to understand exactly how different exercise modalities affect functional capacity, sarcopenia and frailty. Eventually uncovering exercise mimetics may help provide these positive effects in individuals who are unable to participate in a standard exercise program (e.g., older adults in the hospital restricted to bedrest can lose 1 kg of lean leg muscle in just a week—which is very hard to regain) (Galvan et al., 2016). Furthermore, more research is needed on how to improve exercise response in older adults.

We have shown that exercise improves or preserves overall physical function, or mitigates functional loss, in both adult and older adult male C57BL/6 mice, but the pattern of improvement differs according to age. Younger adult male mice benefit more from high-intensity interval training while older adult male mice receive similar functional benefits from either high-intensity exercise or lower-intensity voluntary exercise. Thus, to extrapolate to humans, for untrained sedentary older male adults, getting started in any type of exercise program will improve physical function, though whether exercise type does influence adaptations after the initial training period (i.e., after counteracting the effects of detraining) remains to be investigated. Importantly, HIIT provided similar benefits to older male mice as VWR with a vastly reduced time commitment for exercise. This is a critical point when considering how best to structure exercise programs for individuals who may have multiple time constraints or limits on participation.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The animal study was approved by East Carolina University IACUC protocol p106. The study was conducted in accordance with the local legislation and institutional requirements.

Author contributions

MP: Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Writing–original draft, Writing–review and editing. CB: Formal Analysis, Investigation, Writing–original draft, Writing–review and editing. NN: Investigation, Writing–original draft, Writing–review and editing. ES: Investigation, Writing–original draft, Writing–review and

editing. AS: Investigation, Writing–original draft, Writing–review and editing. AE: Investigation, Writing–original draft, Writing–review and editing. TG: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing–original draft, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fragi.2024.1356954/full#supplementary-material

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Skeletal muscle index based on CT at the 12th thoracic spine level can predict osteoporosis and fracture risk: a propensity score-matched cohort study

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Background: Multiple studies have shown that skeletal muscle index (SMI) measured on abdominal computed tomography (CT) is strongly associated with bone mineral density (BMD) and fracture risk as estimated by the fracture risk assessment tool (FRAX). Although some studies have reported that SMI at the level of the 12th thoracic vertebra (T12) measured on chest CT images can be used to diagnose sarcopenia, it is regrettable that no studies have investigated the relationship between SMI at T12 level and BMD or fracture risk. Therefore, we further investigated the relationship between SMI at T12 level and FRAX-estimated BMD and fracture risk in this study.

Methods: A total of 349 subjects were included in this study. After 1:1 propensity score matching (PSM) on height, weight, hypertension, diabetes, hyperlipidemia, hyperuricemia, body mass index (BMI), age, and gender, 162 subjects were finally included. The SMI, BMD, and FRAX score of the 162 participants were obtained. The correlation between SMI and BMD, as well as SMI and FRAX, was assessed using Spearman rank correlation. Additionally, the effectiveness of each index in predicting osteoporosis was evaluated through the receiver operating characteristic (ROC) curve analysis.

Results: The BMD of the lumbar spine (L1-4) demonstrated a strong correlation with SMI ($r = 0.416$, $p < 0.001$), while the BMD of the femoral neck (FN) also exhibited a correlation with SMI ($r = 0.307$, $p < 0.001$). SMI was significantly correlated with FRAX, both without and with BMD at the FN, for major osteoporotic fractures ($r = -0.416$, $p < 0.001$, and $r = -0.431$, $p < 0.001$, respectively) and hip fractures ($r = -0.357$, $p < 0.001$, and $r = -0.311$, $p < 0.001$, respectively). Moreover, the SMI of the non-osteoporosis group was significantly higher than that of the osteoporosis group ($p < 0.001$). SMI effectively predicts osteoporosis, with an area under the curve of 0.834 (95% confidence interval 0.771–0.897, $p < 0.001$).

Conclusion: SMI based on CT images of the 12th thoracic vertebrae can effectively diagnose osteoporosis and predict fracture risk. Therefore, SMI can make secondary use of chest CT to screen people who are prone to osteoporosis and fracture, and carry out timely medical intervention.

KEYWORDS

osteoporosis, skeletal muscle index, fracture risk assessment tool, propensity score matching, computed tomography, bone mineral density

Introduction

The loss of bone mass and skeletal muscle is often one of the important triggers of falls and prolonged bed rest in the elderly population (1, 2). Studies have shown that the body loses muscle mass at a rate of 1% per year by the age of 40 and older (3). Sarcopenia is an age-related decline in overall muscle mass and strength or physical muscle function—a degenerative disease resulting in a marked decrease in balance and mobility (4). The primary diagnostic approach for sarcopenia in clinical guidelines involves assessing participants' skeletal muscle index (SMI) using methods like dual-energy X-ray absorptiometry (DXA) and bioelectrical impedance analysis (BIA) (5). In addition, many studies have shown that SMI can be well reflected by calculating the area of a single chest or abdominal CT image (6–8). Shen et al. (6) demonstrated that SMI based on T12 levels can predict in-hospital mortality in elderly patients. In addition, Tan et al. (7) demonstrated that SMI of the T12 thoracic vertebrae contributes to the diagnosis of sarcopenia in the Chinese population. Based on the above studies, SMI at the T12 level may be a potential indicator to predict osteoporosis and fracture risk propensity.

Osteoporosis is a bone metabolic disorder in which the loss of bone mass causes changes in the microstructure of bone, resulting in decreased mechanical structural properties and increased fragility of bone (9, 10). Risk factors for osteoporosis include aging, sex (more common in women), family genetics, poor diet, lack of exercise, and certain chronic diseases (11). Similarly, these risk factors are strongly associated with changes in muscle mass (12). Bone mineral density (BMD) assessment via DXA serves as the gold standard for diagnosing osteoporosis (13). The Fracture risk assessment tool (FRAX) is often applied to predict the risk of osteoporotic fracture in individuals, such as a femoral neck (FN) fracture in the elderly, using risk factors associated with osteoporosis (14, 15). In addition, FRAX is widely used worldwide because of the reliability and ease of use of its predictive results.

There have been several studies showing that osteoporosis is strongly associated with sarcopenia (16, 17). Multiple studies have shown that SMI measured on abdominal computed tomography (CT) is strongly associated with BMD and fracture risk (18, 19). Although the authors demonstrated that SMI measured on CT images at the level of the 12th thoracic vertebra (T12) can be used to diagnose sarcopenia (7), no subsequent studies have delved into the correlation between SMI and BMD at the T12 level, or the connection between SMI and fracture risk. In addition, chest CT has been more and more widely used in physical examination and hospitalization, such as follow-up of lung nodules and screening of lung cancer.

In summary, in this study, our team explored the relationship between SMI and BMD at the T12 level and the relationship between SMI and fracture risk. When patients undergo a chest CT examination (for other clinical reasons), clinicians have the opportunity to use these imaging data to screen for osteoporosis and fracture risk.

Abbreviations: BMI, body mass index; FN, femoral neck; SMA, skeletal muscle area; BMD, bone mineral density; L1-4, lumbar spine 1–4; T12, the 12th thoracic vertebra; DXA, dual-energy x-ray absorptiometry; ROC, Receiver operating characteristic; BIA, bioelectrical impedance analysis; NRS, nutritional risk screening; CT, computed tomography; AUC, area under the curve; FRAX, Fracture Risk Assessment Tool; PSM, propensity score matching; SMI, skeletal muscle index.

Methods

Study participants

With the approval of the review board of Affiliated Yueqing Hospital of Wenzhou Medical University, patients who completed DXA and chest CT examinations in the database of the Yueqing Hospital of Wenzhou Medical University from January 1, 2023 to December 1, 2023 were retrospectively collected. The inclusion criteria for this study were (1) Unenhanced chest CT scan was performed, (2) DXA was performed, and (3) Complete medical records. The exclusion criteria for this study were (1) The interval between DXA and chest CT examination was >3 months, (2) Artifacts on CT images, and (3) Lack of medical records. A total of 349 subjects were enrolled in this study, and 162 of them were finally included after propensity score matching (PSM) analysis. Table 1 presents the demographic and clinical baseline characteristics of the study participants.

SMI measurements

A 120 kV, 250 mA, 5 mm slice thickness picture archiving and communication system was used to collect CT image data. Moreover, the CT images were obtained within 3 months after DXA examination to keep bone mass and muscle mass data in the same period as possible. Skeletal muscle cross-sectional area at the middle level of the T12 vertebral body was calculated using Image J (NIH Image J version 1.52c) software (Figure 1). Relevant studies (20) have shown that the skeletal muscle threshold ranges from −29HU to 150HU, and the skeletal muscle area was measured within this threshold range in this study. SMI was derived by dividing the calculated area value by the square of the patient's height (m^2).

BMD and diagnosis of osteoporosis

BMD at the entire lumbar (lumbar spine 1–4, L1-4) and FN were measured by DXA. According to relevant clinical guidelines, patients with osteoporosis are diagnosed based on the T or Z scores of the femoral neck and lumbar spine measured by DXA.

The FRAX tool

A questionnaire survey on the risk factors of fracture was conducted by face to face or telephone. History of fractures, secondary osteoporosis, glucocorticoid use, parents with hip fractures, excess alcohol intake, gender, current smoking, age, systemic rheumatoid arthritis, height, weight, and FN of BMD were included. Through the https://www.sheffield.ac.uk/FRAX/?lang=chs website login Chinese version FRAX model, and the clinical data of patients after PSM is applied to the model. The 10-year probability of osteoporotic fracture was calculated on whether to include FN BMD in the FRAX model.

TABLE 1 Comparison of clinical characteristics between two groups: before and after the propensity matching score.

	Overall series			Propensity score–matched pairs		
	Non-osteoporosis (249)	Osteoporosis(100)	*P*-value	Non-osteoporosis (81)	Osteoporosis(81)	*P*-value
Age (years)	63(57–71)	67(63–74)	<0.001	64(59–72)	68(63–74)	0.028
Height (cm)	161(156–168)	156(153–161)	<0.001	157(153–162)	156(153–161)	0.672
Weight (kg)	63.60 ± 8.96	57.19 ± 9.31	<0.001	60.23 ± 8.86	59.26 ± 8.58	0.153
BMI (kg/m^2)	24.29 ± 3.58	23.17 ± 3.63	0.010	24.12 ± 3.53	23.58 ± 3.47	0.320
Gender			<0.001			0.693
Female, n(%)	137(55.0)	84(84.0)		64(79.0)	66(81.5)	
Male, n(%)	112(45.0)	16(16.0)		17(21.0)	15(18.5)	
Hypertension, n(%)	159(63.9)	59(59.0)	0.397	47(58.0)	51(63.0)	0.520
Diabetes, n(%)	238(97.9)	84(92.3)	0.033	79(97.5)	78(96.3)	1.000
Hyperlipidemia, n(%)	147(59.0)	56(56.0)	0.603	51(63.0)	48(59.3)	0.629
Hyperuricemia, n(%)	30(12.0)	7(7.0)	0.166	5(6.2)	5(6.2)	1.000

BMI, body mass index.

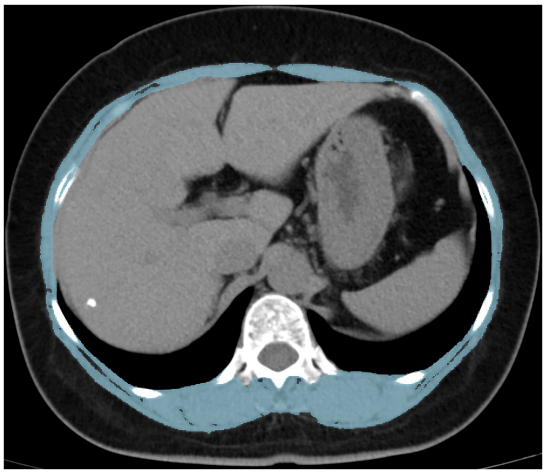

FIGURE 1
Measurement of the skeletal muscle index using computed tomography at the T12 level. T12 the 12th thoracic vertebra.

Statistics

The Shapiro–Wilk test assessed data distribution. Subject baseline characteristics were described using medians (interquartile range), means ± standard deviations, frequencies, and percentages. Nonparametric tests were employed for non-normally distributed or heteroscedastic data. Categorical variables were analyzed using the Pearson Chi-squared test. Spearman rank correlation was used to assess the correlation between SMI and BMD, as well as SMI and FRAX. The receiver operating characteristic curve (ROC) was utilized to evaluate the predictive efficacy of each index for osteoporosis. Statistical analyses were conducted using SPSS software (version 26.0; SPSS Inc., Chicago, IL, United States).

Propensity Score Matching (PSM) is frequently employed in observational studies to address covariate imbalances between groups. It involves employing specific statistical methods to screen the experimental and control groups, facilitating a more equitable comparison between them (21). In addition, some studies have shown that the results of PSM analysis are close to those of prospective random cohort studies (22). Nine covariates were included in this study, including age, height, hypertension, weight, diabetes, body mass index (BMI), hyperlipidemia, gender, and hyperuricemia. On the basis of these covariates, using propensity scores based on logistic regression, the nearest neighbor matching was applied to generate pairs of subjects in the osteoporosis and non-osteoporosis groups. A preset caliper width of 0.1 was used and no cases were replaced. PSM was calculated using Statistical Package for Social Science software version 26.0 (SPSS, Chicago, Illinois, United States).

Results

Table 1 displays clinical characteristics data for the eligible patients. This study included 349 subjects, with 249 in the non-osteoporosis group and 100 in the osteoporosis group. Significant differences were observed between the two groups in terms of age, gender, height, weight, BMI, and diabetes (p-values were all <0.05). However, there were no significant differences in hypertension, hyperlipidemia, and hyperuricemia between the two groups. After PSM analysis, 162 subjects were enrolled in the study, including 81 in the non-osteoporosis group and 81 in the osteoporosis group. Furthermore, age was the only significant difference between the two groups (64 versus 68 $p = 0.028$), while height, weight, BMI, sex, hypertension, hyperlipidemia, diabetes, and hyperuricemia were not. Patients obtained from PSM analysis were evaluated for fracture risk, and their fracture risk factors are shown in Table 2. Among the 162 patients, 22 had a history of brittle fractures, 18 had a history of smoking, 3 had a history of parental hip fractures, 4 had a history of

TABLE 2 Prevalence of factors associated with the FRAX after propensity score matching analysis

Fracture-related factor	n (%)
Prior fragility fracture	22(13.6)
Parental hip fracture	3(1.9)
Smoking	18(11.1)
Systemic glucocorticoid use	4(2.5)
Rheumatoid arthritis	4(2.5)
Other cases of secondary osteoporosis	27(16.7)
Excess alcohol intake	13(8.0)

FRAX, Fracture Risk Assessment Tool.

TABLE 3 The measurement results after propensity score matching analysis

Characteristic	Value
SMI (cm^2/m^2)	32.46 ± 6.64
BMD (g/cm^2)	
L1-L4	0.91 ± 0.13
Femoral neck	0.74 ± 0.11
FRAX (10-year probability of fracture), %	
Major osteoporotic fracture (with BMD at femoral neck)	6.59 ± 5.14
Hip fracture (with BMD at femoral neck)	2.33 ± 3.55
Major osteoporotic fracture (without BMD at femoral neck)	6.63 ± 4.11
Hip fracture (without BMD at femoral neck)	2.48 ± 3.61

BMD, bone mineral density; SMI, skeletal muscle index; FRAX, Fracture Risk Assessment Tool.

systemic glucocorticoid use, 4 had a history of rheumatoid arthritis, 27 had a history of risk factors for secondary osteoporosis, and 13 had a history of excess alcohol intake.

The measurement results after propensity score matching analysis are presented in Table 3. The SMI was 32.46 ± 6.64 cm^2/m^2. L1-4 and FN BMD were 0.91 ± 0.13 g/cm^2 and 0.74 ± 0.11 g/cm^2, respectively. Moreover, the probability of major osteoporotic fractures was 6.59 ± 5.14% and 2.33 ± 3.55% for hip fractures when the femoral neck BMD was included. The probability of major osteoporotic fractures was 6.63 ± 4.11% and 2.48 ± 3.61% for hip fractures when the femoral neck BMD was not included.

The BMD of L1-4 exhibited a strong correlation with SMI ($r = 0.416$, $p < 0.001$, as shown in Figure 2A). Additionally, BMD of the FN showed a correlation with SMI ($r = 0.307$, $p < 0.001$, as depicted in Figure 2B). SMI also displayed correlations with FRAX, both with and without BMD at the FN. For major osteoporotic fractures, these correlations were as follows: $r = -0.431$, $p < 0.0001$, and $r = -0.416$, $p < 0.001$, respectively. For hip fractures, the correlations were: $r = -0.311$, $p < 0.001$, and $r = -0.357$, $p < 0.001$ (refer to Figure 3). Furthermore, Figure 4A illustrates that the SMI of the non-osteoporosis group was significantly higher than that of the osteoporosis group ($p < 0.001$). SMI proved to be an effective predictor of osteoporosis, with an area under the curve of 0.834 (95% confidence interval 0.771–0.897, $p < 0.001$). In order to visualize the prediction performance of SMI, the ROC curve was drawn, as shown in Figure 4B.

Discussion

Our findings indicate that SMI, measured at the T12 level, demonstrates a robust correlation with both lumbar spine and femoral neck (FN) BMD. Moreover, SMI serves as a reliable predictor of osteoporosis. Additionally, our results show a strong association between SMI and fracture risk as calculated by FRAX.

Osteoporosis is closely related to skeletal muscle; the two interact to make older people prone to falls and brittle fractures. Reduced muscle mass, strength, and function increase the risk of osteoporosis, and similarly, reduced bone mass increases the risk of sarcopenia (23). The bone and skeletal muscle relationship is not just a simple mechanical one. Bone and muscle are endocrine target organs and secretory organs interacting with each other through paracrine and endocrine signals. The skeletal muscle is the largest endocrine organ in the human body, secreting factors that regulate bone metabolism. These muscle-secreting factors mainly include myostatin, β-aminoisobutyric acid and irisin, and so on. In addition, circadian rhythm s, nutritional deficiencies, aging, and nervous system networks also affect bone and muscle (24–26). Therefore, maintaining skeletal muscle mass can prevent sarcopenia and osteoporosis. In this study, SMI based on T12 was closely related to BMD of the FN and lumbar spine. Similar to previous studies, SMI measured by DXA or BIA was strongly associated with BMD (27, 28). In addition, we found that low-quality SMI was effective in predicting osteoporosis, with moderate predictive power after ROC analysis. These results further support the close relationship between SMI and BMD.

Due to the lack of awareness of osteoporosis in the general population, the first diagnosis of osteoporosis is usually found at the time of fracture using DXA examination. However, when patients develop osteoporotic fractures, they have a poorer prognosis and higher mortality than non-osteoporotic fractures (29, 30). Therefore, more and more research is devoted to using a more convenient method to detect osteoporosis, treat osteoporosis in time and prevent osteoporosis fractures. Among them, Kajiki et al. (18) proved that psoas muscle index, as measured by abdominal CT, is strongly associated with the BMD and is a valuable predictor of osteoporosis. However, most patients do not have a specific reason to undergo abdominal CT. Chest CT has been more and more widely used, especially for the follow-up of lung nodules and screening of lung cancer in middle-aged and elderly people. This study found that SMI based on chest CT measurements can predict osteoporosis, providing a new way to more easily screen for osteoporosis. Therefore, when patients undergo chest CT examination (for other clinical reasons), doctors have the opportunity to use these image data for osteoporosis screening, thereby reducing the waste of medical resources to a certain extent.

In this study, SMI exhibited a strong association with fracture risk, as evaluated using FRAX. This outcome aligns with previous research findings that demonstrated a higher fracture risk assessed by FRAX in individuals with low muscle mass (31–33). FRAX effectively improves patient lifestyles and prevents fractures, reducing fracture-related mortality (34). Our study suggests that SMI can be used as an indicator to assess a patient's risk of fracture. SMI based on chest CT measurement is helpful for early detection of high-risk patients and timely intervention.

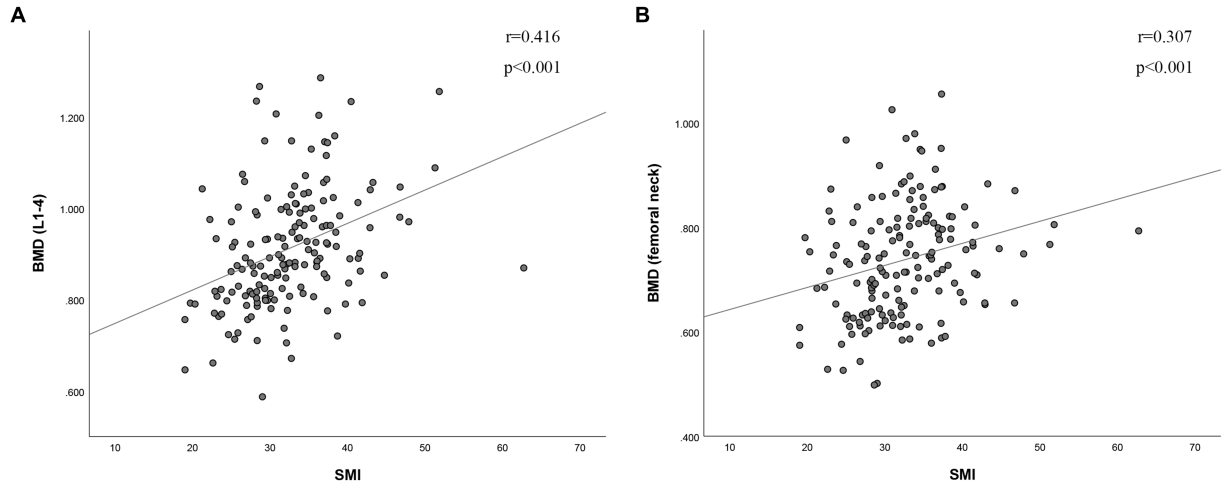

FIGURE 2
The correlation between skeletal muscle index and **(A)** bone mineral density of L1-4 and **(B)** bone mineral density of femoral neck. BMD (g/cm^2), bone mineral density; SMI (cm^2/m^2), skeletal muscle index; L1-4, lumbar spine 1–4.

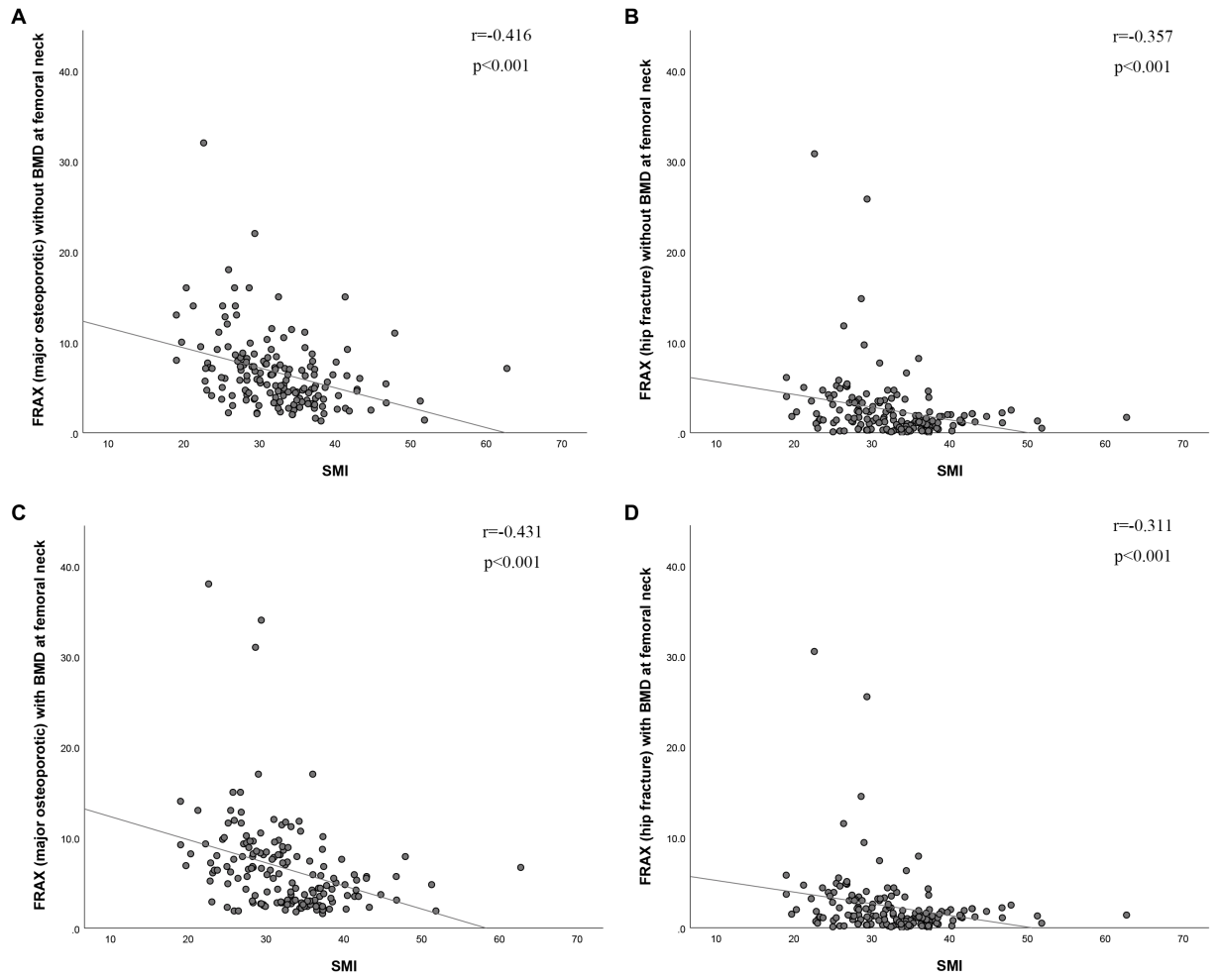

FIGURE 3
The correlation between skeletal muscle index and risk of **(A,C)** major osteoporotic fractures and **(B,D)** hip fractures (with or without BMD of the femoral neck). BMD (g/cm^2), bone mineral density; SMI (cm^2/m^2), skeletal muscle index; FRAX, fracture risk assessment tool.

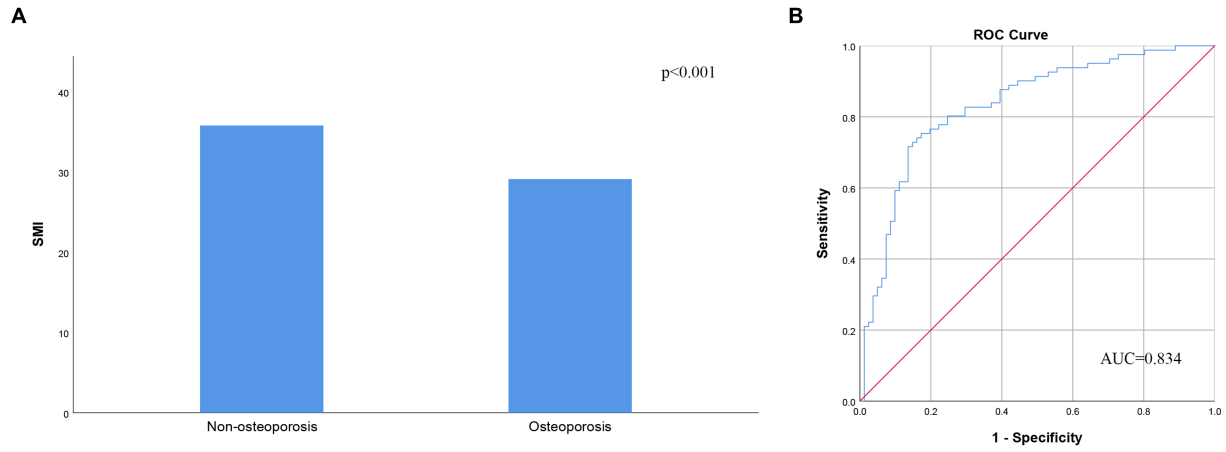

FIGURE 4
(A) Skeletal muscle index according to the presence of osteoporosis. **(B)** Receiver operating characteristic analysis of skeletal muscle index's ability to diagnose osteoporosis. AUC, area under the curve; SMI, skeletal muscle index.

This study found that SMI based on chest CT measurements can be used to predict osteoporosis and fracture risk. With the development of medical technology, chest CT has been widely used, especially in routine physical examination. With clinicians' secondary use of these chest CT images to detect osteoporosis early through SMI, patients can benefit from timely intervention and improved management, potentially reducing the risk of fractures and other related complications. Patients can both improve their quality of life and reduce subsequent medical costs.

Limitations

This study mainly has the following limitations. First of all, the study is a retrospective study, so there may be a series of selection and recall biases. However, this study used PSM analysis, which can effectively reduce these biases and may even approximate the results of prospective studies. Secondly, the PSM analysis method was used, which resulted in a small number of participants in this study. Therefore, large-scale prospective cohort studies are needed to further support this study. Third, although the FRAX score was used in this study as a predictor of osteoporotic fractures, the relationship between SMI and actual osteoporotic fractures has not been elucidated. Therefore, relevant research is urgently needed in the future.

Conclusion

SMI based on CT images of the 12th thoracic vertebrae can effectively diagnose osteoporosis and predict fracture risk. Therefore, SMI can make secondary use of chest CT images to screen people who are prone to osteoporosis and fracture, and carry out timely medical intervention to reduce the waste of medical resources to a certain extent.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Department of Orthopedics, Affiliated Yueqing Hospital of Wenzhou Medical University, Wenzhou, China. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin because this study is a retrospective study and does not involve any impact on patient health and safety.

Author contributions

J-sH: Data curation, Formal analysis, Writing – original draft. Y-pJ: Data curation, Writing – original draft. J-kW: Data curation, Writing – original draft. J-gN: Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Efficacy of lumbar and abdominal muscle rehabilitation training on degree of osteoporosis, pain and anxiety in elderly patients with osteoporotic vertebral compression fracture after PKP and compliance analysis

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Purpose: To explore the rehabilitation effect and compliance of lumbar and abdominal muscle rehabilitation training in patients with osteoporotic vertebral compression fracture (OVCF) after percutaneous balloon vertebroplasty (PKP).

Methods: A total 177 elderly patients with OVCF were divided into rehabilitation group ($n = 104$) and control group ($n = 73$) according to whether they received psoas and abdominal muscle rehabilitation training for 3 months after PKP. The differences of general data, orthopaedic rehabilitation, prognosis and bone metabolism were compared between the two groups. All the patients were divided into compliance group (68 cases) and non-compliance group (36 cases) according to compliance. Orthopaedic rehabilitation indicators, prognostic indicators of PKP, and bone metabolism-related parameters were collected for analysis of Chi-square test and Logistic regression. ROC curve was used to analyze the predictive value of bone metabolism related indicators in the compliance of lumbar and abdominal muscle rehabilitation training.

Results: There was no significant difference in the general data between the rehabilitation training group and the control group (All $p > 0.05$). Compared with the control group, the Berg balance scale score was significantly increased, while the Visual Analogue Scale (VAS) score, Oswestry Disability Index (ODI) score and the proportion of new fractures were significantly decreased in the rehabilitation training group (All $p < 0.05$). Compared with the control group, the bone mineral density (BMD) T value, osteocalcin (OCN) and 25-hydroxyvitamin D (25 (OH) D) levels were significantly increased and the levels of type I N-propeptide (P1NP) and β-isomerized C-terminal telopeptides (β-CTX) were significantly decreased in the rehabilitation training group compared with the control group (All $p < 0.05$). Chi-square test and Logistic regression analysis showed that age > 75 years, severe anxiety, severe pain and postoperative complications were significantly associated with the compliance of psoas and abdominal muscle rehabilitation training in patients with OVCF after PKP. ROC curve analysis showed that BMD T

value, OCN, P1NP, β-CTX, or 25-OH-D levels predicted the AUC of rehabilitation training compliance in patients with OVCF after PKP were 0.821, 0.835, 0.736, 0.715, and 0.748, respectively.

Conclusion: Rehabilitation training of lumbar and abdominal muscles can significantly improve the efficacy of PKP, reduce the degree of osteoporosis and improve the prognosis of patients with OVCF. Age, anxiety, pain and postoperative complications were independent risk factors affecting the compliance of psoas and abdominal rehabilitation training in patients with OVCF after PKP.

KEYWORDS

osteoporotic vertebral compression fracture, percutaneous vertebroplasty with balloon dilatation, rehabilitation training, compliance, PKP

1 Introduction

Osteoporosis is a systemic disorder of bone metabolism characterized by damage of bone tissue microstructure, decreasing proportion of bone mineral composition and bone matrix, and increased bone fragility (1). With the aggravation of population aging, osteoporotic fracture has become one of the main diseases endangering the health of the elderly, leading to a significant decrease in the quality of life of patients (2). Osteoporotic fractures are usually caused by low-energy or nonviolent injuries and are a serious consequence of osteoporosis (2). Among them, osteoporotic vertebral compression fractures (OVCF) are common types of spinal fractures. The incidence of OVCF is generally higher in patients with osteoporosis. Improper treatment can easily cause severe deformation of the spine, which affects spinal function. Patients generally see a doctor with severe pain in the waist and mobility disturbance (3). Without prompt treatment, the progression of fracture collapse can lead to kyphosis, and chronic persistent pain will seriously affect the quality of life of the elderly (4).

Patients with OVCF generally have poor surgical tolerance due to advanced age and multiple underlying diseases (5, 6). Current treatment modalities for elderly patients with OVCF include conservative treatment, open surgery and minimally invasive surgery (4, 7, 8). Conservative treatment mainly includes bed rest (for at least 3 months), traditional reduction methods (e.g., manual reduction, traction reduction), external fixation of braces, and functional exercise, which are mainly applicable to those with mild symptoms or difficult to undergo surgical treatment (9). However, long-term bed rest is not only accompanied by an exacerbation of osteoporosis, but also a greatly increased risk of bedridden complications (e.g., hypostatic pneumonia, bedsore, venous thrombosis of lower extremities, etc.) (9). In addition, open surgical treatment has the disadvantages of high risk, large incision and large amount of bleeding, which leads to a long recovery time after open fracture surgery (10). Therefore, the main treatment modality for elderly patients with OVCF is minimally invasive surgery (11). Percutaneous kyphoplasty (PKP) is a minimally invasive procedure performed under C-arm fluoroscopy (12). The surgical incision is only about 0.5 cm, with the advantages of less bleeding, short operation time and rapid postoperative pain relief (12). In addition, early recovery of activity after PKP is the preferred treatment option for patients with OVCF in recent years.

Patients with osteoporosis tend to have balance dysfunction and a higher risk of falls (13). Of these, more than half of patients with OVCF still experience a second fall leading to a secondary fracture (13). Although PKP can provide some degree of reduction and fixation for collapsed vertebral bodies, most patients still have soft tissue injury and partial kyphosis after surgery (13). These factors are prone to decrease spinal structural stability and bias in the center of gravity, ultimately leading to pain, poor mobility and falls in patients with OVCF (14). Early postoperative rehabilitation exercise, as an important part of rehabilitation therapy, has become a routine treatment item after PKP (15–17). Early postoperative rehabilitation training based on strength training principles can improve postural control and muscle strength, increase postural stability, improve balance ability, relieve pain, and significantly improve patients' activities of daily living (18). However, the elder patient may exhibit the lower acceptance for lumbar and abdominal muscle rehabilitation training, and difficult to complete the daily arrangement of lumbar and abdominal muscle rehabilitation training. In addition, the higher the degree of postoperative pain, the lower the acceptance of lumbar and abdominal muscle rehabilitation training. Therefore, there were large differences in compliance with early postoperative rehabilitation exercises. In order to improve the compliance of patients and improve the effectiveness of rehabilitation exercise, the purpose of this study was to investigate the effect of psoas and abdominal muscle rehabilitation training on the prognosis of patients with OVCF after PKP and the influencing factors affecting the compliance of rehabilitation exercise. Meanwhile, the effect of lumbar and abdominal muscle rehabilitation training on the rehabilitation of OVCF patients after PKP were also analyzed by different evaluation scales.

2 Data and methods

2.1 Clinical data

A total of 177 patients with OVCF who visited Zhejiang Provincial People's Hospital from January 2022 to August 2023 were retrospectively collected. All patients with OVCF were divided into rehabilitation group (104 cases) and control group (73 cases) according to whether they received lumbar and abdominal muscle rehabilitation training. In addition, patients receiving psoas and abdominal muscle rehabilitation training were further divided into

compliance group (68 patients) and noncompliance group (36 patients) according to compliance.

Inclusion criteria: (1) OVCF was diagnosed by X-ray, CT or MRI; (2) Received PKP treatment; (3) Age ≥ 60 years old; (4) Non-violent or low-energy injury was the causative factor.

Exclusion criteria: (1) Patients with incomplete clinical data; (2) Those who cannot cooperate with rehabilitation training in the whole course; (3) Patients with mental illness; (4) Patients with malignant tumors; (5) Patients with relevant diseases that have an impact on bone metabolism. The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance with the tenets of the Helsinki Declaration, and has been approved by the ethnical committee of Zhejiang Provincial People's Hospital.

2.2 Treatment regimen

All patients received 3 months of lumbar and abdominal muscle rehabilitation training after PKP. Rest in supine position 8 h after PKP. From the first postoperative day, patients in both groups were able to start walking with waistlines. The psoabdominal muscle function training was started on the first day after PKP, and the training was continued for 3 months. Routine incision dressing change was performed after operation, and the anterolateral radiographs of thoracolumbar spine were reexamined. Depending on the time of discharge, waist circumference was continued until 3 months after discharge.

Self-management of rehabilitation was arranged by patients according to training before and after discharge. In addition, the physician regularly followed up the patients every week and recorded the completion of rehabilitation training for the patients. Lumboabdominal muscle rehabilitation training methods are as follows:

1) Lumbodorsal muscle training: the patient lies on the bed top, take the supine position, place the pillow back, both elbow and both soles on the bed surface as the supporting point, so that the axis of the lower leg is as 90° as possible from the bed surface, and naturally separated as wide as the shoulder. Lumbodorsal muscle strength mainly caused the two parts of the back and buttocks to leave the bed slowly, and the abdomen and knee were kept at the same level as much as possible. After the movement was in place for 5 s, then slowly placed on the bed. The rest interval between the two actions was 5 s, 20 times/group, and completed 5 groups per day (total of 100).
2) Abdominal muscle training 1: the patient lies on the bed, takes the supine position, puts his hands crossed over the abdomen, slowly contracts the abdominal muscles when exhales, feels the internal abdominal muscles slowly close to the spine, maintains the action for 20 s, then relaxes the muscles, and then relaxes the muscles one time. The rest interval of the two movements was 5 s, 20 times/group, and 5 groups (100 in total) were completed daily.
3) Abdominal muscle training 2: lie on the bed, take the supine position, hold the shoulders with both hands, then flex the hips and knees 90°, with abdominal muscle strength as the main starting point, so that the neck above the neck is slowly lifted out of the bed surface about 15 cm, conscious abdominal tighten, keep it in this position for 5 s, then slowly put it slowly to the bedside, and relax the whole body. The two movements were rested at an interval of 5 s, 20 times/group, and 5 groups (100 in total) were completed daily.

2.3 Observation measure

2.3.1 Baseline data

Data including smoking history, alcohol consumption history, fracture site, fracture course, previous fracture history, and whether falls occurred in the past month were collected after admission.

2.3.2 Relevant indicators of orthopaedic rehabilitation

All patients received Berg Balance Scale, Visual Analogue Scale (VAS) and Oswestry Disability Index (ODI) Scale at 3 months after surgery. At the same time, the occurrence of falls and clinical efficacy were statistically analyzed. Berg balance scale score: the balance function was assessed with Berg balance scale. The total score of Berg balance scale was 56. The higher the score indicated that the better the balance function. VAS: draw a straight line 10 cm long on the paper surface, and the patient marks the corresponding points on the line according to their current pain perception. The physician scored the location. The scores ranged from 0 to 10, and 0 to 4, 4 to 7, and 7 to 10 according to no/mild, moderate, and severe pain, respectively. The higher the score indicated the more severe the pain. ODI: a total of 10 questions were included, including the degree of low back pain and leg pain, personal self-care, weight lifting, walking, sitting, standing, sleep, sexual, social and travel. Each topic was subdivided into 5 grades, with higher scores indicating more pronounced dysfunction. All rating scale results were collected in a double-blind fashion by a physician.

Criteria for judging clinical efficacy: (1) Effective: fracture healing, basically no occurrence of low back pain, patients basically resumed daily life; (2) Ineffective: there was still some pain, unfavorable lumbar activity, no obvious improvement or even aggravation of the condition.

2.3.3 Prognostic indicators of PKP

During the follow-up period of lumbar and abdominal muscle rehabilitation training, the new fracture of adjacent vertebral body, whether the patient needed further anti-osteoporosis treatment, and the situation of bone cement leakage were counted. New fractures were defined as nonoperative vertebral fractures occurring within 3 months of surgery. The patient's cement leakage was assessed by CT. Leakage was judged if the cement exceeded the vertebral boundary.

2.3.4 Bone metabolism-related parameters

Bone mineral density (BMD) T value was measured using GE Lunar-DPX-MD DXA. The T value of BMD of L1-L4 vertebrae in each patient was measured in anteroposterior position. According to WHO diagnostic criteria, T value > −1.0 SD was normal, −2.5 SD < T value ≤ −1.0 SD was osteopenia, and bone mineral density T value ≤ −2.5 SD was osteoporosis. Serum osteocalcin levels (OCN) were measured by ELISA. The bone metabolism indexes including procollagen of type I N-propeptide (P1NP), β-isomerized C-terminal

telopeptides (β-CTX), 25-hydroxyvitamin D (25-OH-D) and parathyroid hormone (PTH) were measured by Swiss Roche electrochemiluminescence analyzer Cobas e602.

2.3.5 Compliance-related indicators

The early rehabilitation training compliance evaluation form was used to evaluate the compliance of rehabilitation training at 3 months after surgery. The contents of the evaluation form included 3 items, including the degree of knowledge of rehabilitation, the mastery of psoas and abdominal muscle exercise methods, and whether to complete the functional exercise program according to the guidance of medical staff. Compliance: Patients can take the initiative to complete the early functional exercise program developed by medical staff with high quality every day; Non-compliance: patients occasionally carry out rehabilitation training or do not follow the guidance of medical staff or refuse to carry out lumbar and abdominal muscle rehabilitation exercise. Lumbar and abdominal muscle rehabilitation training program for patients after PKP and patient compliance evaluation scale were referred to Supplementary Tables S1, S2. Self-rating Anxiety Scale (SAS) was used to evaluate the negative emotions of the patients.50–59 points were classified as no or mild anxiety, 60–69 as moderate anxiety, and ≥ 70 as severe anxiety. Higher scores represent more severe anxiety. Glasgow Soma Scale (GCS) was used to assess the degree of consciousness disturbance. GCS totaled 15 points, 11 to 15 as no or mild disturbance of consciousness, 6 to 10 as moderate disturbance of consciousness, and 0 to 5 as severe disturbance of consciousness. The lower the score, the worse the patient's state of consciousness.

2.4 Statistical analysis

Statistical analysis was performed using SPSS 27.0 soft. Measurements that meet the normal distribution are expressed as mean ± SD, and the inter-group comparison is performed using an independent sample T-test. Measurements that did not meet the normal distribution were expressed as median (quartile), and nonparametric rank sum test was used for group comparisons. Enumeration data were expressed as rate (%) or constituent ratio, and chi-square test was used for comparison between groups. Binary Logistic regression was used for influencing factor analysis. $p < 0.05$ was statistically significant.

3 Results

3.1 Analysis of general data of OVCF patients

According to the inclusion criteria and exclusion criteria, 177 patients with OVCF who underwent PKP were included in this study. According to whether they received lumbar and abdominal muscle rehabilitation training, all patients were divided into rehabilitation training group (104 cases) and control group (73 cases). The patients in the rehabilitation training group received postoperative anti-osteoporosis treatment and rehabilitation training, while the control group received only postoperative anti-osteoporosis treatment. There were no dropouts after 3 months of follow-up. Baseline data for patients with OVCF are presented in Table 1. Compared with the control group, there was no statistically significant difference in sex composition, age, height, weight, diabetes, hypertension, previous regular exercise, smoking history, alcohol consumption history, fracture site, disease course, previous fracture history, and the number of patients with falls in the past month between the rehabilitation training group (All $p > 0.05$).

3.2 Effect of lumboabdominal muscle rehabilitation training on postoperative efficacy of PKP in patients with OVCF

The efficacy of psoabdominal muscle rehabilitation training in patients with OVCF after PKP is shown in Table 2. The score of Berg balance scale in the rehabilitation training group was significantly higher than that in the control group ($p < 0.001$), indicating that the balance function was significantly improved in patients with OVCF after lumbar and abdominal muscle rehabilitation training. In addition, the VAS and ODI scores in the rehabilitation training group were significantly lower than those in the control group (Both $p < 0.001$), suggesting that the pain degree and self-care ability of the rehabilitation training group were significantly improved. The frequency of falls in patients with OVCF within 3 months after PKP was statistically analyzed. The results showed that the frequency of falls in the rehabilitation training group was significantly lower than that in the control group ($p < 0.05$). In addition, the overall clinical efficacy of OVCF patients after 3 months of lumbar and abdominal muscle rehabilitation training was significantly better than that of the control group ($p < 0.001$). In summary, lumbar and abdominal muscle rehabilitation training can significantly improve the clinical efficacy of PKP in patients with OVCF.

TABLE 1 Analysis of general data of OVCF patients.

Parameters	Rehabilitation training group (n = 104)	Control group (n = 73)	t/Z/X^2	p value
Gender (male/female)	48/56	34/39	0.003	0.956
Age	71 (67, 77)	71 (68, 75)	−0.428	0.669
Height (cm)	162.71 ± 6.64	163.63 ± 6.94	−0.889	0.375
Weight (kg)	57.78 ± 9.31	59.82 ± 6.11	−1.763	0.080
Diabetes	4 (3.85%)	2 (2.74%)	0.160	0.689
Hypertension	27 (25.96%)	15 (20.55%)	0.695	0.405
Previous regular exercise	11 (10.58%)	8 (10.96%)	0.007	0.936
Smoking history	43 (41.35%)	34 (46.58%)	0.477	0.490
Drinking history	27 (25.96%)	15 (20.55%)	0.695	0.405
Fracture site (thoracic/lumbar)	61/43	45/28	0.160	0.690
Illness course (days)	6 (5, 6)	5 (5, 6)	−0.867	0.386
Fracture history	52 (50.00%)	36 (49.32%)	0.008	0.929
Fall in the past month	49 (47.12%)	30 (41.10%)	0.629	0.428

3.3 Effect of lumboabdominal muscle rehabilitation training on prognosis of patients with OVCF

To further analyze the effect of lumbar and abdominal muscle rehabilitation training on the prognosis of patients with OVCF after PKP. As shown in Table 3, only 19 (18.27%) or 15 (14.42%) patients in the rehabilitation group experienced fracture or cement leakage after PKP compared with 23 (31.51%) or 19 (26.03%) patients in the control group, respectively. Chi-square test showed that the proportion of new fractures in the rehabilitation training group was significantly lower than that in the control group ($p < 0.05$), but there was no significant difference in the proportion of bone cement leakage ($p > 0.05$). In addition, 64 patients (61.54%) in the rehabilitation group and 61 patients (83.56%) in the control group still needed further anti-osteoporosis treatment after 3 months of psoas and abdominal muscle rehabilitation training. Chi-square test showed that the proportion of patients who still needed anti-osteoporosis treatment in the rehabilitation training group was significantly lower than that in the control group ($p < 0.01$). The above results showed that psoas and abdominal muscle rehabilitation training could significantly improve the prognosis of patients with OVCF after PKP.

3.4 Effect of lumboabdominal muscle rehabilitation training on osteoporosis-related indexes in OVCF patients

The degree of osteoporosis in patients with OVCF is an important factor to evaluate the efficacy of PKP. Therefore, we further evaluated the effect of lumbar and abdominal muscle rehabilitation training on osteoporosis-related indicators in patients with OVCF. As shown in Table 4, the BMD T value of the rehabilitation training group was significantly higher than that of the control group ($p < 0.001$), indicating that the overall degree of osteoporosis was significantly improved after OVCF rehabilitation training via the psoas and abdominal muscles. In addition, both OCN and PTH in the rehabilitation group were significantly higher than those in the control group (Both $p < 0.05$). In contrast, Both P1NP and beta-CTX were significantly lower in the rehabilitation group than in the control group (Both $p < 0.001$). The above results showed that the lumbar and abdominal muscle rehabilitation training could significantly improve the degree of osteoporosis in patients with OVCF after PKP.

TABLE 2 Comparison of orthopaedic rehabilitation-related indicators in different groups of OVCF patients.

Parameters	Rehabilitation training group ($n = 104$)	Control group ($n = 73$)	Z/X^2	p value
Berg balance scale	48.50 (46.18, 50.26)	28.32 (26.00, 30.85)	−11.312	<0.001
VAS	2.81 (2.29, 3.55)	4.12 (2.81, 5.62)	−4.269	<0.001
ODI	17.46 (16.40, 18.29)	20.54 (19.48, 21.94)	−9.664	<0.001
Postoperative fall	4 (3.85%)	10 (13.70%)	5.716	0.017
Clinical efficacy (effective/ ineffective)	98/6	54/19	14.513	<0.001

3.5 Analysis of influencing factors of lumboabdominal muscle rehabilitation training compliance in OVCF patients

The compliance of 3 months after PKP was evaluated according to the compliance evaluation form of early rehabilitation training and divided into compliance group (68cases) and non-compliance group (36 cases). The analysis of factors influencing compliance with lumbar and abdominal muscle rehabilitation training in patients with OVCF after PKP is shown in Table 5. There were 34 males and 34 females in the compliance group, while 14 males and 22 females in the noncompliance group, the difference was not statistically significant ($p > 0.05$). In addition, the proportion of patients>75 years of age was 23.53% in the compliance group, which was significantly lower than that in the noncompliant group (44.44%) ($p < 0.05$), suggesting that the older the age, the higher the frequency of noncompliance. Moreover, the postoperative anxiety, postoperative pain and the frequency of osteoporosis in the compliance group were significantly lower than those in the non-compliance group (All $p < 0.05$). However, there was no significant difference in the frequency of postoperative disturbance of consciousness between the two groups ($p > 0.05$). In terms of the prognosis of PKP, the proportion of patients requiring further anti-osteoporotic treatment and the proportion of patients with cement leakage were significantly lower in the compliance group than in the non-compliance group (Both $p < 0.05$), while the proportion of patients with new fractures was not statistically different between the two groups ($p > 0.05$).

3.6 Logistic regression analysis of lumboabdominal muscle rehabilitation training compliance in patients with OVCF

Logistic regression analysis was performed with patient compliance as dependent variable and factors with statistically significant differences in univariate analysis as independent variables, and the results are shown in Figure 1 and Table 6. Age > 75 years, postoperative complications, severe postoperative anxiety, severe postoperative pain, osteoporosis, anti-osteoporosis treatment and bone cement leakage were independent risk factors for poor compliance in patients with OVCF after PKP (All $p < 0.05$), and the probability of noncompliance increased 1.600, 1.292, 2.352, 9.806, 1.514 and 2.444 times, respectively.

3.7 Predictive efficacy of serum bone metabolism indicators on the compliance of rehabilitation training in OVCF patients

The occurrence of osteoporosis after PKP is one of the important factors affecting patient compliance. Therefore, we analyzed the

TABLE 3 Comparison of prognosis in patients with different OVCF.

Parameters		Rehabilitation training group (n = 104)	Control group (n = 73)	X^2	p value
New fracture	Yes	19	23	4.153	0.042
	No	85	50		
Cement leakage	Yes	15	19	3.722	0.054
	No	89	54		
Anti-osteoporosis therapy	Yes	64	61	10.027	0.002
	No	40	12		

TABLE 4 Comparison of osteoporosis-related indicators in different OVCF patients.

Parameters	Rehabilitation training group (n = 104)	Control group (n = 73)	t value	p value
BMD T value	−2.41 ± 0.55	−3.12 ± 0.48	8.872	<0.001
OCN (μg/L)	5.59 ± 1.27	5.20 ± 1.33	1.987	0.048
P1NP (μg/L)	41.76 ± 8.06	59.00 ± 10.47	−11.829	<0.001
β-CTX (ng/L)	478.39 ± 75.74	594.81 ± 77.79	−9.955	<0.001
25(OH)D (μg/L)	15.12 ± 4.02	9.86 ± 2.79	10.281	<0.001
PTH (ng/L)	71.10 ± 19.82	56.57 ± 15.90	5.198	<0.001

predictive efficacy of different serum bone metabolism-related indicators on rehabilitation training compliance in patients with OVCF after PKP by ROC curves. As shown in Figure 2 and Table 7, BMD T value, OCN, P1NP, β-CTX, or 25-OH-D levels predicted rehabilitation training compliance in patients with OVCF after PKP for AUC greater than 0.7, suggesting that these serum bone metabolism parameters have high predictive power. Of these, OCN had the highest AUC of 0.835. When the cut-off value was 5.44 μg/L, the sensitivity and specificity of OCN in rehabilitation training compliance were 72.1 and 88.9%, respectively. However, the AUC at PTH level was only 0.589 and was not statistically different ($p > 0.05$). These results suggest that BMD T value, OCN, P1NP, β-CTX or 25-OH-D levels can be used as predictors of rehabilitation compliance in patients with OVCF after PKP.

4 Discussion

The bone quality of the elderly is poor, so the leading cause of osteoporotic fractures is usually non-violent or low-energy injury (19). Osteoporotic fractures are most common in the elderly, with an incidence of approximately 49% of osteoporotic fractures (20). Fractures tend to occur at the thoracolumbar junction, often manifesting as loss of vertebral height, involving the anterior and middle columns of the vertebral body (2). Currently, the main modalities of minimally invasive treatment of OVCF are percutaneous vertebroplasty (PVP) and percutaneous balloon-expandable vertebroplasty (PKP) (21). PKP is the development and extension of PVP, and the main points of operation between the two are mainly different from balloon dilatation resulting in endplate collapse and partial correction of vertebral Cobb angle (22). Studies have demonstrated that PKP has a lower incidence of cement leakage, reduced progression of Cobb angle, and is more durable in terms of pain relief than PVP (23). In addition, PKP has a wide range of indications, except for vertebral compression fractures, but also has therapeutic effects on invasive intraspinal hemangiomas or vertebral metastases (24).

PKP provides some degree of reduction and internal fixation for fracture. Functional exercise and anti-osteoporosis therapy are the direction of perioperative and even long-term treatment for OVCF. Because patients lack sufficient attention to dysfunction after PKP, very few patients will choose further rehabilitation, greatly increasing the risk of falls and secondary fractures (16). Functional exercise as early as possible after surgery can accelerate the recovery of muscle strength, avoid muscle atrophy, and promote fracture healing through the stress stimulation of the muscle on the skeleton (25). In addition, local blood circulation can be accelerated by muscle movement and edema absorption can be promoted (25). Moreover, rehabilitation exercise is of great significance to prevent bone loss, fall and fracture recurrence after operation, and is beneficial to the recovery of postoperative function and the improvement of quality of life. Elderly patients are characterized by a high risk of falls, nonviolent injury as a contributing factor, and a high risk of recurrence after fracture surgery (26). The trunk is the core of motor control. The level of trunk control determines walking ability (including walking speed, efficiency balance, etc.). Therefore, the prevention of falls in patients after PKP should be mainly based on the training of the function of the abdominal muscles of the lower back muscles. Therefore, the aim of this study was to investigate the efficacy of lumboabdominal muscle functional training in patients with OVCF after PKP. In addition, there was a large difference in compliance among patients with OVCF after PKP. Therefore, this study will further explore the factors influencing the compliance of patients with psoas and abdominal muscle rehabilitation training.

A total of 104 patients in the rehabilitation training group and 73 in the control group were included in this study. There was no statistically significant difference in sex composition, age, smoking history, alcohol consumption history, fracture site, disease course, previous fracture

TABLE 5 Univariate analysis of compliance with lumbar and abdominal muscle rehabilitation training in patients with OVCF.

Parameters		Compliance group (n = 68)	Non-compliant group (n = 36)	X^2	p value
Age	>75	16	16	4.834	0.028
	≤75	52	20		
Gender	Male	34	14	1.169	0.280
	Female	34	22		
Postoperative anxiety	No or mild	9	1	7.236	0.027
	Moderate	52	25		
	Severe	7	10		
Postoperative disturbance of consciousness	No or mild	52	21	3.713	0.156
	Moderate	12	11		
	Severe	4	4		
Degree of postoperative pain	No or mild	59	24	8.446	0.015
	Moderate	8	7		
	Severe	1	5		
Degree of osteoporosis	Osteopenia	47	15	7.367	0.007
	Osteoporosis	21	21		
New fracture	Yes	9	10	3.334	0.068
	No	59	26		
Anti-osteoporosis therapy	Yes	37	27	4.215	0.040
	No	31	9		
Cement leakage	Yes	6	9	4.990	0.025
	No	62	27		

history, and the number of patients with falls in the past month between the two groups (All $p > 0.05$), and the overall data were comparable. Studies have shown that osteoporosis can cause low back pain and scoliosis, with poor posture control relative to normal subjects, increasing the risk of falls and leading to new vertebrae (26). Decreased lumbar and back muscle strength in patients with osteoporotic compression fractures can lead to sagittal kyphosis deformity of the patient's spine. The magnitude of left–right sway at the center of gravity is significantly increased while walking, and the anterior–posterior movement distance is decreased (2). Patients with OVCF have a progressive decline in their ability to maintain body homeostasis, and abnormal gait is accompanied by an increased risk of falls and a significantly increased risk of fractures (2). Moreover, falls are the main predisposing factor leading to the occurrence of first fragility fractures and re-fractures in patients (27). In addition, it has been shown that the primary cause of falls is imbalance (28). This suggests that the prevention of falls is essential to reduce the risk of osteoporotic vertebral fractures and re-fractures in the elderly (27). In this study, patients had significant improvements in balance function, pain severity, and risk of falls after 3 months of psoas and abdominal function training. Moreover, psoas and abdominal muscle rehabilitation training further improved the prognosis of patients with OVCF after PKP compared with controls, mainly including reducing the incidence of postoperative re-fractures and cement leakage, and reducing the proportion of patients still requiring further anti-osteoporotic treatment.

The degree of osteoporosis is a major factor in the development of OVCF (29). Current screening for fracture risk and the diagnosis of osteoporosis are usually based on BMD results (30). However, radiographic measurements of bone mass are not sensitive, and the physiological changes of bone respond slowly and do not reflect the state of bone metabolism early (31). Therefore, BMD measurements alone do not adequately predict fracture risk early (31). Bone turnover markers are a series of breakdown products released by osteoblasts and osteoclasts during bone remodeling and reflect their activity, including bone resorption marker β-CTX, which evaluates osteoclast activity and bone formation markers OCN and P1NP reflecting osteoblast activity (32). These indicators are able to early judge bone metabolic status and predict the risk of osteoporotic fracture (33). In addition, serum 25 (OH) D is a commonly used indicator reflecting the nutritional status of vitamin D in humans and plays a promoting role in maintaining homeostasis of bone homeostasis and bone mineral content (34). In addition, PTH can act on osteoblasts and promote osteoclast maturation, increased bone resorption, etc. (35). Therefore, serum 25 (OH) D and PTH levels also reflect the state of bone metabolism to some extent. Fluctuations in bone metabolism indicators can affect the activity of osteocytes and osteoclasts through multiple pathways. The rate of bone formation lags behind bone loss, resulting in decreased bone quality, which then leads to osteoporosis, leading to an increased risk of fracture (36). In this study, psoas and abdominal muscle rehabilitation training significantly increased BMD T value, OCN, and PTH levels, while reducing P1NP and β-CTX levels. The above results showed that the lumbar and abdominal muscle rehabilitation training could significantly improve the degree of osteoporosis in patients with OVCF after PKP.

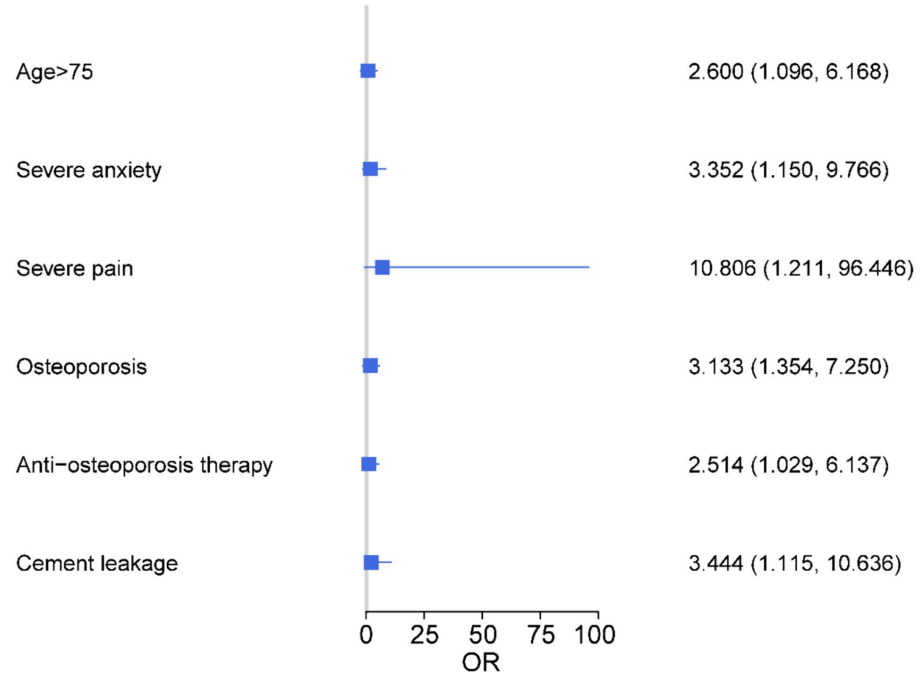

FIGURE 1
Analysis of influencing factors for compliance of OVCF patients after PKP surgery.

TABLE 6 Logistic regression analysis of lumboabdominal muscle rehabilitation training compliance in patients with OVCF.

Parameters	β	S.E	Wald	*p*	OR	95%CI
Age > 75	0.956	0.441	4.701	0.030	2.600	1.096 ~ 6.168
Severe postoperative anxiety	1.089	0.550	3.926	0.027	3.352	1.150 ~ 9.766
Severe postoperative pain	1.743	1.212	2.070	0.033	10.806	1.211 ~ 96.446
Osteoporosis	1.142	0.428	7.121	0.008	3.133	1.354 ~ 7.250
Anti-osteoporosis therapy	0.922	0.455	4.095	0.043	2.514	1.029 ~ 6.137
Cement leakage	1.237	0.575	4.622	0.032	3.444	1.115 ~ 10.636

At present, there is no study on the compliance of early rehabilitation exercise after PKP. Therefore, we further evaluated compliance and its influencing factors in 104 patients undergoing lumboabdominal muscle rehabilitation training. Elderly patients have weak immunity, poor nutritional status, more underlying diseases and weak self-recovery capacity. The results showed that patients >75 years of age in the compliance group were significantly lower than those in the noncompliant group, suggesting a significant association between age and patient compliance. Logistic regression analysis showed that patients aged >75 years had a 1.6-fold higher probability of poor compliance with psoas and abdominal muscle rehabilitation training. The occurrence of postoperative complications will hinder or delay the occurrence of early rehabilitation exercise to some extent (37). In addition, the occurrence of complications will, to a certain extent, limit the early rehabilitation exercise of patients, increase the psychological and physiological burden of patients, further cause patients' anxiety and reduce patient compliance (38). In this study, postoperative complications (new fractures, cement leakage) and the proportion of patients requiring further antiosteoporotic treatment were significantly lower in the compliance group than in the noncompliant group. In addition, patients with severe postoperative anxiety had a 2.352-fold increased probability of poor compliance. On the other hand, standardized pain management can effectively promote early postoperative rehabilitation exercises and promote the recovery of patients' early function (39). Pain management is beneficial to reduce postoperative pain and reduce the burden of postoperative rehabilitation exercises (40). At the same time, good pain management is an important means to promote rehabilitation exercise (41). The results of this study showed that the degree of postoperative pain was significantly lower in the compliance group than in the noncompliant group. Furthermore, severe postoperative pain is the most important factor affecting patient compliance. The risk of non-compliance with lumbar and abdominal muscle rehabilitation training in patients with severe postoperative pain was significantly increased by 9.806-fold. In summary, age, postoperative anxiety, postoperative pain, and postoperative complications were independent risk factors affecting the compliance of lumbar and abdominal rehabilitation training in patients with OVCF after PKP. Therefore, it is still necessary to further

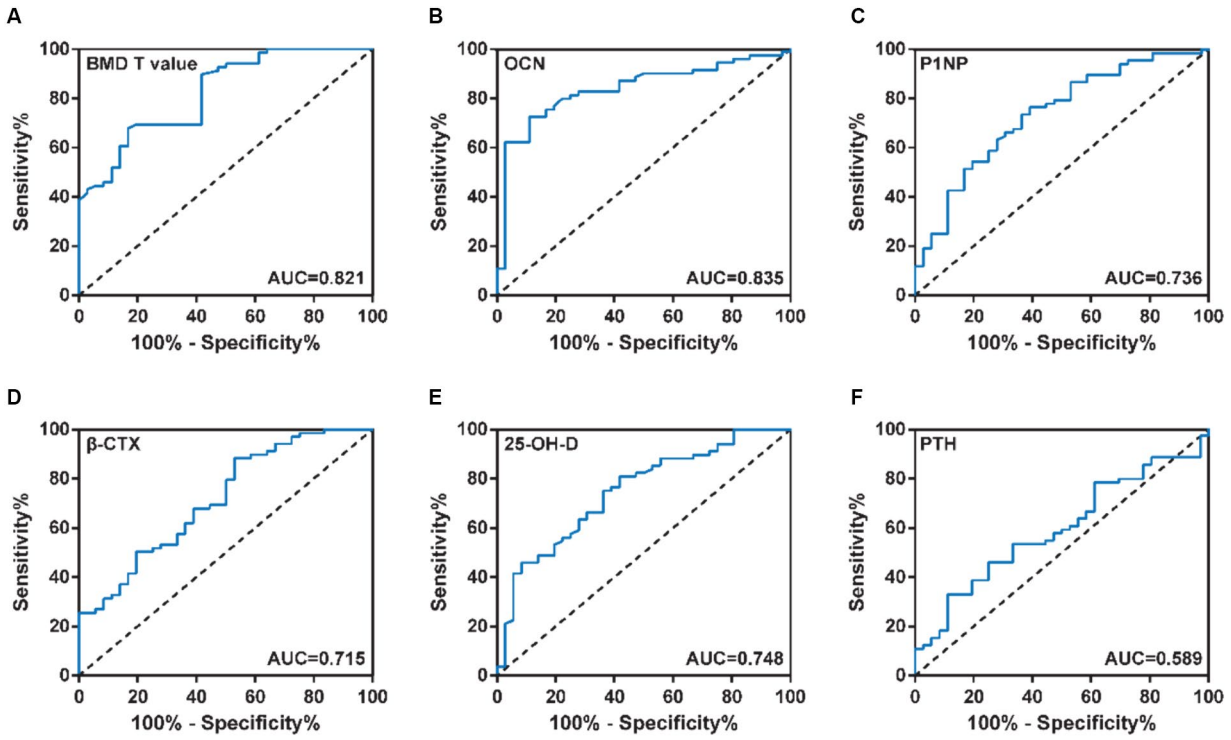

FIGURE 2
(A) BMD T value, **(B)** OCN, **(C)** P1NP, **(D)** β-CTX, **(E)** 25-OH-D and **(F)** PTH levels predicted rehabilitation training compliance in patients with OVCF after PKP for AUC.

TABLE 7 Diagnostic efficacy of serum bone metabolic indicators for compliance with rehabilitation training in patients with OVCF.

Parameters	AUC (95% CI)	Cut-off	Sensitivity	Specificity	*p* value
BMD T value	0.821 (0.739, 0.902)	−2.35	67.6%	83.3%	<0.001
OCN	0.835 (0.754, 0.915)	5.44 μg/L	72.1%	88.9%	<0.001
P1NP	0.736 (0.636, 0.837)	45.85 μg/L	76.5%	61.1%	<0.001
β-CTX	0.715 (0.612, 0.818)	527.40 ng/L	88.2%	47.2%	<0.001
25-OH-D	0.748 (0.650, 0.846)	13.16 μg/L	80.9%	58.3%	<0.001
PTH	0.589 (0.478, 0.700)	85.30 ng/L	32.4%	88.9%	0.136

develop a personalized program for lumbar and abdominal muscle rehabilitation training according to the patient's condition.

The limitations of lumbar and abdominal muscle rehabilitation training are mainly reflected in compliance. The compliance of rehabilitation training refers to the degree to which the patient's training behavior is consistent with the doctor's order. Poor compliance can lead to failure of the treatment effect to meet the expected criteria, thereby accelerating the course of the disease, increasing the risk of complications, and thus affecting the patient's prognosis. Therefore, early and accurate assessment of rehabilitation compliance and intervention of poor compliance in patients with OVCF after PKP is of great significance in promoting the effect of rehabilitation training of psoas and abdominal muscles and improving the prognosis of patients. At present, the compliance of patients after PKP can only be evaluated by subjective feelings of patients and compliance evaluation scales. Therefore, we further analyzed the predictive efficacy of different bone metabolism indices on the compliance of rehabilitation training patients, with the aim of assessing the degree of osteoporosis, and at the same time preliminarily predicting the compliance of patients with psoas and abdominal muscle rehabilitation training. The results showed that the AUCs of BMD T value, OCN, P1NP, β-CTX or 25-OH-D levels in predicting rehabilitation compliance in patients with OVCF after PKP were 0.821, 0.835, 0.736, 0.715 and 0.748, respectively, suggesting that these serum markers of bone metabolism have high predictive power. Among them, OCN had the highest predictive power, and the diagnostic sensitivity and specificity were 72.1 and 88.9%, respectively.

The study has the following limitations: (1) The sample size of this study is small, and the results may be biased; (2) All the included cases were from a single center, which limited the universality of the study results to some extent; (3) The compliance of the patients is derived from the subjective answers of the patients, while the patients tend to choose the positive choices expected to be achieved by their own behavior when answering the subjective questions, which may lead to the evaluation results different from their true level.

In conclusion, lumbar and abdominal muscle rehabilitation training in patients with OVCF can significantly improve the efficacy

of PKP, reduce the degree of osteoporosis and improve the prognosis. In addition, age, anxiety, pain and postoperative complications were independent risk factors for compliance with psoas and abdominal rehabilitation training in patients with OVCF after PKP. In addition, bone metabolism can be used as an effective method to predict the compliance of psoas and abdominal muscle rehabilitation training in patients after PKP. In the future, the sample size and scope of the study can be expanded, and longitudinal studies can be conducted to further evaluate the predictive value of compliance assessment indicators of lumbar and abdominal muscle rehabilitation training in patients with OVCF after PKP, so as to better guide clinical work.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the ethical committee of Zhejiang Provincial People's Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

YX: Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing. DL: Formal analysis, Methodology, Validation, Writing – original draft, Writing – review & editing. QZ: Resources, Visualization, Writing – original draft, Writing – review & editing. LT: Project administration, Supervision, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

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Association between sarcopenia and hemoglobin level: a systematic review and meta-analysis

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Background: Sarcopenia is a disease characterized by decreased skeletal muscle mass and function in elderly individuals. Decreased hemoglobin levels is a marker of anemia. According to reports, there may be an association between anemia and sarcopenia, but research is inconsistent. Therefore, this meta-analysis aims to explore the association between sarcopenia and low hemoglobin levels.

Methods: We searched PubMed, Embase, the Cochrane Library, Web of Science, Ovid, China National Knowledge Infrastructure (CNKI), and Wan Fang databases until September 2022. The present study included cross-sectional and case-control studies regarding low hemoglobin levels and sarcopenia. The studies were selected using inclusion and exclusion criteria. Studies were meta-analyzed by Review Manager 5.4 and Stata 16.0. We performed the heterogeneity test using the I^2 test. Subgroup analysis was carried out to explore the cause of heterogeneity. Egger test was used to evaluate publication bias.

Results: Out of 1,550 initial studies, 16 studies were meta-analyzed. Sarcopenia participants had significantly lower levels of hemoglobin than controls (MD=−0.53, 95% CI: −0.68 to −0.37, p<0.001). Subgroup analysis, performed in China population reported lower hemoglobin levels in the sarcopenia population (MD=−0.49, 95% CI: −0.65 to −0.33, p<0.001). And sarcopenia based on AWGS criteria reported lower hemoglobin levels (MD=−0.49, 95% CI: −0.65 to −0.33, p<0.001). Among the population from hospitals and communities, patients with sarcopenia have lower hemoglobin levels.

Conclusion: Our meta-analysis found evidence that sarcopenia is associated with low hemoglobin levels. However, further large-scale prospective studies should be conducted in the future to further confirm our conclusions.

Systematic review registration: PROSPERO, CDR42024532252.

KEYWORDS

anemia, hemoglobin level, sarcopenia, aging, muscle mass

1 Introduction

Sarcopenia, defined as the age-related reduction in lean muscle mass and muscle function (1), is linked to falls, fractures, disabilities, diminished quality of life, and imposes a greater economic burden along with increased healthcare expenses (2). Epidemiological surveys indicate that the global prevalence of sarcopenia varies between 10 and 27% (3), with the prevalence rate among

elderly people in Asia ranging from 2.5 to 45.7% (4). With the development of an aging society, the prevalence of sarcopenia is increasing. Due to the serious harm and high incidence of sarcopenia, it has brought a heavy burden to an aging society.

Sarcopenia's risk factors are diverse, including aging, illness, malnutrition, and sedentary lifestyle, among others (5). The nutritional status of the elderly declines over time, leading to reduced physical activity and a subsequent decline in muscle mass and function, consequently heightening the risk of sarcopenia. Likewise, persistent chronic inflammation, characterized by muscles experiencing oxidative stress, can further worsen the weakening of muscle strength (6).

Anemia presents a well-established hazard for frailty, reduced quality of life, and increased mortality among older individuals (7). The occurrence of anemia in the elderly can result from various factors including iron deficiency, chronic inflammation, or chronic kidney disease (8). Research has shown that anemia is associated with diminished muscle strength, physical dysfunction, reduced mobility, heightened disability risk, and mortality increase (9, 10). Decreased hemoglobin levels may impair the transportation of oxygen to skeletal muscles, thus compromising muscle strength (11). Chronic inflammation frequently leads to anemia, potentially impacting muscle mass and physical function negatively (6). Given the shared underlying mechanisms of sarcopenia and anemia, a correlation between the two is plausible.

However, there has been controversy over the relationship between sarcopenia and anemia in current research. Tseng's et al. (12) study had analysis 730 patients that there was a significant association between anemia and sarcopenia; but Kitamura et al. (13) and Ko's et al. (14) studies have shown that there is no discernible correlation between anemia and sarcopenia. These studies showed a controversial relationship between hemoglobin and sarcopenia, which prompted us to explore the relationship. Therefore, we investigated the association between low hemoglobin level and sarcopenia by conducting a thorough meta-analysis, with diverse subgroup analyses to elucidate. The results will provide enhanced insights for the prevention and management of sarcopenia, thereby contributing to the amelioration of elderly health conditions.

2 Methods

This research was conducted according to the Preferred Reporting Items for Meta-Analysis (PRISMA) guidelines. It is registered in the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CDR42024532252.

2.1 Literature search

Two researchers independently searched PubMed, Embase, the Cochrane Library, Web of Science, Ovid, China National Knowledge Infrastructure (CNKI), and Wan Fang to identify relevant papers published before March 2024. The search terms included sarcopenia, anemia, hemoglobin, hyphemia, and low-level hemoglobin. To ensure comprehensive coverage, we carefully reviewed all eligible studies for inclusion and examined referenced reviews to avoid any potentially missed papers. In cases where multiple publications existed for the same clinical trial, we included only the most informative or up-to-date publication.

2.2 Selection criteria

In this systematic review, we employed the following inclusion criteria: (1) diagnosis of sarcopenia based on European Working Group on Sarcopenia in Older People (EWGSOP), Asian Working Group for Sarcopenia (AWGS), consensuses, or any other definition provided by original studies' author; (2) the variables of the studies including serum or plasmatic levels of hemoglobin in both sarcopenia and control group (non-sarcopenic population) reported. Exclusion criteria comprised: (1) unclear reporting of sarcopenia diagnosis; (2) literature reviews, case reports, animal studies, or conference abstracts; (3) absence of quantitative hemoglobin level data.

2.3 Data extraction and confirmation

Two researchers independently extracted the following variables from the included studies: first author, publication year, location or nationality, study design, total number of individuals included in the study, gender distribution, applied definition of sarcopenia, method used for sarcopenia identification, mean muscle mass, handgrip strength, and gait speed in sarcopenia and group, hemoglobin levels in sarcopenia and non-sarcopenia population. Data verification was conducted by two researchers to reduce errors, with any discrepancies resolved through discussion or consultation with external sources.

2.4 Literature quality evaluation

We assessed the methodological quality of the included studies using the Newcastle–Ottawa scale (NOS) (15) for case-control studies and a modified version of the NOS for cross-sectional studies. This scale assessed studies based on three key dimensions: selection of study population, comparability of groups, and description of the outcome. The scale scores varied depending on the study design. For case-control studies, it ranged from 0 to 9 points with ≥7 points classified as high quality. For cross-sectional studies, it ranged from 0 to 7 points with ≥4 points considered as high quality. When any disagreement arose during data extraction and quality assessment, the two reviewers reached a consensus through negotiation.

2.5 Statistical analysis

All statistical analyses were performed by Review Manager 5.4 and Stata 16.0. The heterogeneity of the studies was analyzed using the I^2 test. When I^2 was higher than 50%, the random effect model was used; when I^2 was less than 50%, the fixed effect model was performed. Subgroup analysis was carried out to explore the cause of heterogeneity. In addition, funnel plots were used initially to evaluate visual publication bias while Egger's regression test was used to inferentially evaluate publication bias. p-values <0.05 was considered statistically significant (two-sided).

3 Results

3.1 Search results

After a comprehensive search, 1,555 published studies were identified from 7 databases. After removal of duplicates, 946 studies remained. After reading the title and abstracts, 38 studies were eligible for full-text review and data assessment. From these, 6 studies did not find full text, 12 studies did not report quantitative expression of hemoglobin level in sarcopenic and non-sarcopenic subjects, other 4 studies reported diagnostic criteria for sarcopenia were not clear or absent. Finally, we included 16 studies in the meta-analysis. Figure 1 shows the study flow-chart.

3.2 Study characteristics

Table 1 shows the study characteristics of the included studies. A total of 35,746 individuals with 18,187 male and 17,541 female, 10,836 sarcopenia and 24,910 control. Studies were conducted in various countries, including China, Istanbul, and the United States of America. Fifteen studies employed a cross-sectional study (16–28), and one study was case control study (29). Seven studies (12, 14, 16, 18, 21, 23, 26) included community-dwelling individuals, while nine studies included hospitalized patients (17, 19, 20, 22, 24, 25, 27–29). Ten of the selected studies used the Asian Working Group for Sarcopenia (AWGS) definition of sarcopenia (12, 14, 16, 18, 19, 23–27), two studies identified sarcopenia through European Working Group on Sarcopenia in Older People (EWGSOP) (17, 21), and four studies identified sarcopenia by skeletal muscle mass index (SMI) (20, 22, 28, 29).

3.3 Quality assessment of included studies

Table 2 shows the methodological quality of the included studies based on the NOS. The overall quality of the literature was considered strong, as the NOS score for case-control studies was 7, while the NOS scores for cross-sectional studies were all more than 4.

3.4 Hemoglobin expression and meta-analysis findings

All 16 studies reported the levels of hemoglobin in patients with sarcopenia and in control subjects. The heterogeneity between the included studies was significant, so the random-effects model was applied. Meta-analysis of all included studies revealed that individuals with sarcopenia ($n = 10,836$), compared to individuals without sarcopenia ($n = 24,910$), were more likely to have significantly lower hemoglobin levels: (MD = −0.47, 95% CI: −0.69 to −0.24, $p < 0.0001$)

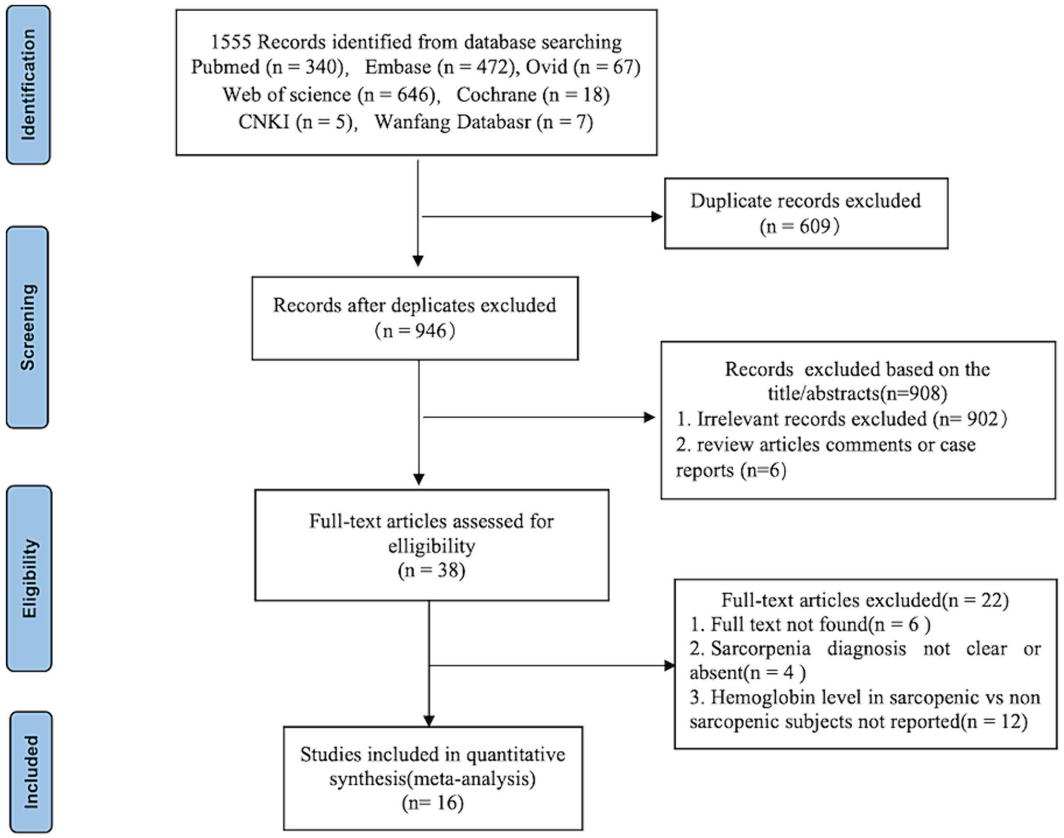

FIGURE 1
PRISMA flowchart of study selection.

TABLE 1 Main characteristics of studies included in the meta-analysis.

Study	Study region	Study design	Setting	Age	Sample size	Sex (male/female)	Definition of sarcopenia	Diagnostic criteria
Dai (2023)	China	Cross-sectional	Community dwelling	≥60	5,016	2,575/2,441	Low muscle mass coupled with low muscle strength or poor physical performance	AWGS
Gulcicek (2023)	Istanbul	Cross-sectional	Hospital	≥18	220	117/103	Low grip strength, low muscle mass	EWGSOP
Hai (2017)	China	Cross-sectional	Community dwelling	≥60	836	415/421	Low muscle mass with low muscle strength or low physical performance	AWGS
He (2020)	China	Cross-sectional	Hospital	≥50	1,125	586/539	Low muscle strength	AWGS
Hu (2024)	China	cross-sectional	Hospital	≥18	212	153/59	SMI-L3 <44.77 cm^2/m^2 in men and SMI-L3 <32.5 cm^2/m^2	SMI-L3
Kin (2018)	USA	Cross-sectional	Community dwelling	≥20	11,761	5,965/5,796	Lower muscle mass, lower walking speed	EWGSOP
Ko (2021)	China, Taiwan	Cross-sectional	Community dwelling	≥65	500	235/265	Low muscle mass, low grip strength, a slow walking speed	AWGS
Lee (2020)	Korea	Cross-sectional	Hospital	≥18	79	58/21	SMI-L3 <49 cm^2/m^2 in men and SMI-L3 <31 cm^2/m^2	SMI-L3
Liu (2023)	China	Cross-sectional	Community dwelling	≥60	3,055	1,572/1,483	Low muscle mass, low muscle strength, low physical performance	AWGS
Lu (2022)	China	Cross-sectional	Hospital	≥60	441	262/161	Loss of muscle mass plus low muscle strength and/or low physical performance	AWGS
Sun (2023)	China	Cross-sectional	Hospital	≥60	543	269/274	Low muscle mass and low muscle strength or low physical performance	AWGS
Tseng (2021)	China, Taiwan	Cross-sectional	Community Dwelling	≥50	730	386/344	Low muscle mass in combination with reduced muscle strength and/or low physical performance	AWGS
Wu (2021)	China	Cross-sectional	Community Dwelling	≥60	6,172	3,070/3,102	Low muscle mass plus low muscle strength or low physical performance	AWGS
Yao (2022)	China	Case control study	Hospital	18–80	259	179/80	Both decreased muscle mass and strength	AWGS

(Continued)

TABLE 1 (Continued)

Study	Study region	Study design	Setting	Age	Sample size	Sex (male/female)	Definition of sarcopenia	Diagnostic criteria
Zeng (2022)	China	Cross-sectional	Hospital	≥20	4,673	2,271/2,271	ASMI <7.23 kg/m^2 in men and ASMI <5.67 kg/m^2 in women	SMI
Zhang (2021)	China	Cross-sectional	Hospital	≥18	124	74/50	SMI <41 cm^2/m^2 in women; <43 cm^2/m^2 in men with BMI <25 kg/m^2; <53 cm^2/m^2 in men with BMI ≥ 25 kg/m^2	SMI-L3

AWGS, Asian Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; SMI, skeletal muscle index; ASM, appendicular skeletal muscle mass; ASMI, appendicular skeletal muscle mass index.

(Figure 2). Meanwhile, subgroup analysis was performed to analyze the origin of the heterogeneity.

3.5 Subgroup analysis

Thirteen studies reported the hemoglobin levels in Chinese patients with sarcopenia and in control subjects. The heterogeneity between the included studies was significant, so the random-effects model was applied. The data suggested that Chinese patients with sarcopenia had lower hemoglobin levels (MD = −0.53, 95% CI: −0.68 to −0.37, $p < 0.001$) (Figure 3). Seven studies in community-dwelling and nine studies in hospitalized reported the hemoglobin levels patients with sarcopenia and in control subjects. The data suggested that among the population from hospitals and communities, patients with sarcopenia have lower hemoglobin levels (Figure 4).

The subgroup analysis showed that the MD between hemoglobin and sarcopenia was −0.49 (95% CI: −0.65 to −0.33, $p < 0.001$) in the group diagnosed with sarcopenia according to AWGS guidelines. However, the subgroup analysis of studies based on AMI evaluation of sarcopenia did not report significantly different hemoglobin levels (MD = −0.47, 95% CI: −0.69 to −0.24, $p = 0.07$) (Figure 5).

3.6 Publication bias

Asymmetry was observed by visual inspection of funnel plots. However, Egger's regression test ($p = 0.259$) indicated no statistically significant publication bias among the studies in this meta-analysis.

4 Discussion

In this meta-analysis, we incorporated 16 studies encompassing 35,746 individuals, comprising 10,836 with sarcopenia and 24,910 controls. Our analysis revealed that hemoglobin levels were lower in individuals with sarcopenia in contrast to those in non-sarcopenia patients.

We conducted a subgroup analysis involving 13 studies on Chinese individuals, revealing lower hemoglobin levels in Chinese patients diagnosed with sarcopenia. However, there is an insufficient number of studies conducted in the United States or Istanbul to allow for additional subgroup analysis. The meta-analysis incorporated studies from both community residents (7 studies) and hospitalized patients (9 studies). Subgroup analysis revealed that the characteristics of the study population did not influence the association between sarcopenia and hemoglobin levels.

In subgroup analysis, we found that individuals diagnosed with sarcopenia according to AWGS criteria exhibited a decline in hemoglobin levels. Conversely, no significant variances in hemoglobin levels were observed among those diagnosed with AMI in the subgroup analysis. This phenomenon may be ascribed to the comprehensive nature of AWGS definitions, which encompass not only diminished muscle mass but also reduced physical performance and/or grip strength. In a prior cross-sectional investigation on the Taiwanese population, it was found that low hemoglobin levels correlated solely with muscle strength and walking speed, rather than muscle mass (12). The human skeletal muscle expresses the erythropoietin receptor (30). The body's sensitivity to erythropoietin stimulating agents is independently correlated with skeletal muscle mass (31). It is possible that inadequate skeletal muscle mass resulted in reduced hemoglobin production, potentially introducing reverse causality in cross-sectional studies. In addition, since only 2 studies employed the EWGSOP diagnostic criteria, a subgroup analysis was not performed.

Diminished hemoglobin levels are an independent risk factor for increased mortality and decreased quality of life in elderly individuals. Previous research has shown a significant correlation between hemoglobin levels and reduced muscle mass and muscle strength in patients undergoing kidney transplantation (32). This is consistent with the results of our meta-analysis that the hemoglobin levels of sarcopenia patients were significantly reduced compared to the control group.

The impact of low hemoglobin on sarcopenia may be multifaceted. As is well known, hemoglobin is mainly responsible for binding with oxygen in the human body and transporting oxygen to various tissues throughout the body. Diminished hemoglobin levels may reduce oxygen delivery to cells or tissues, leading to skeletal muscle hypoxia and impacting muscle strength and functionality (33). Anemia can also reflect the nutritional level of the human body. Low hemoglobin indicates insufficient nutrient intake, hindering protein synthesis,

TABLE 2 Results of the Newcastle-Ottawa Scale quality assessment.

Case-control studies									
Author, year	Selection				Comparability (comparability of cases and controls on the basis of the design or analysis)	Exposure			Total
	Adequate definition of case	Representativeness of the cases	Selection of controls	Definition of controls		Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate	
Yao (2022)	1	1	1	1	1	1	1	0	7

Cross-sectional studies							
Author, year	Selection			Comparability (confounding factors are controlled)	Exposure		Total
	Representativeness of the sample	Selection of the non-exposed subjects	Ascertainment of exposure		Assessment of outcome	Response rate	
Dai (2023)	1	1	1	1	1	0	5
Gulcicek (2023)	1	1	1	1	1	0	5
Hai (2017)	1	1	1	2	1	0	6
He (2020)	1	1	1	2	1	0	6
Hu (2024)	1	1	1	1	1	0	5
Kin (2018)	1	1	1	1	1	0	5
Ko (2021)	1	1	1	1	1	0	5
Lee (2020)	1	1	1	2	1	0	6
Liu (2023)	1	1	1	2	1	0	6
Lu (2022)	1	1	1	1	1	0	5
Sun (2023)	1	1	1	1	1	0	5
Tseng (2021)	1	1	1	1	1	0	5
Wu (2021)	1	1	1	0	1	0	4
Zeng (2022)	1	1	1	1	1	0	5
Zhang (2021)	1	1	1	0	1	0	4

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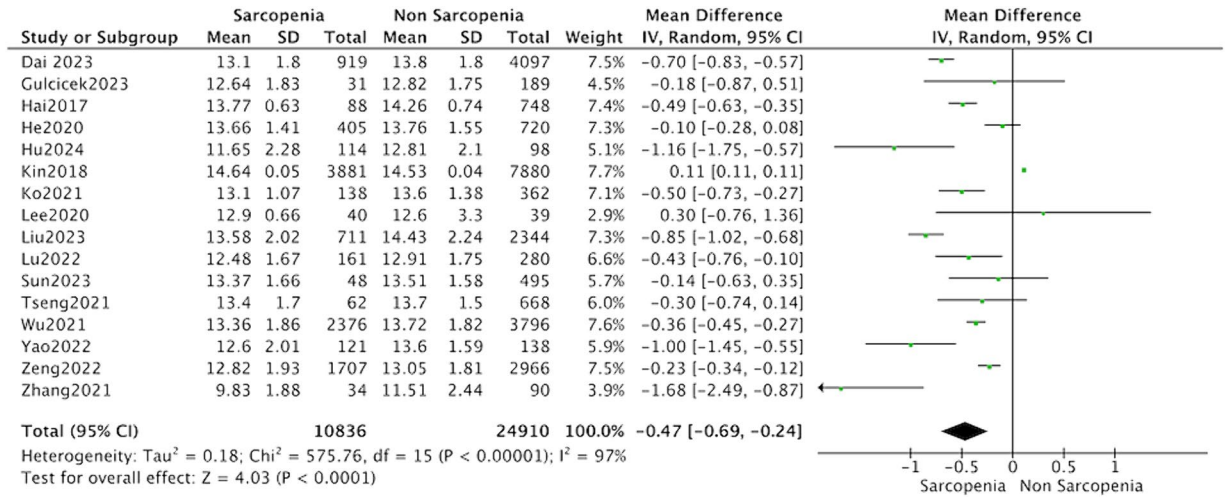

FIGURE 2
Forest plot of serum hemoglobin levels in sarcopenic vs. no sarcopenic subjects. SD, standard deviation; CI, confidence interval.

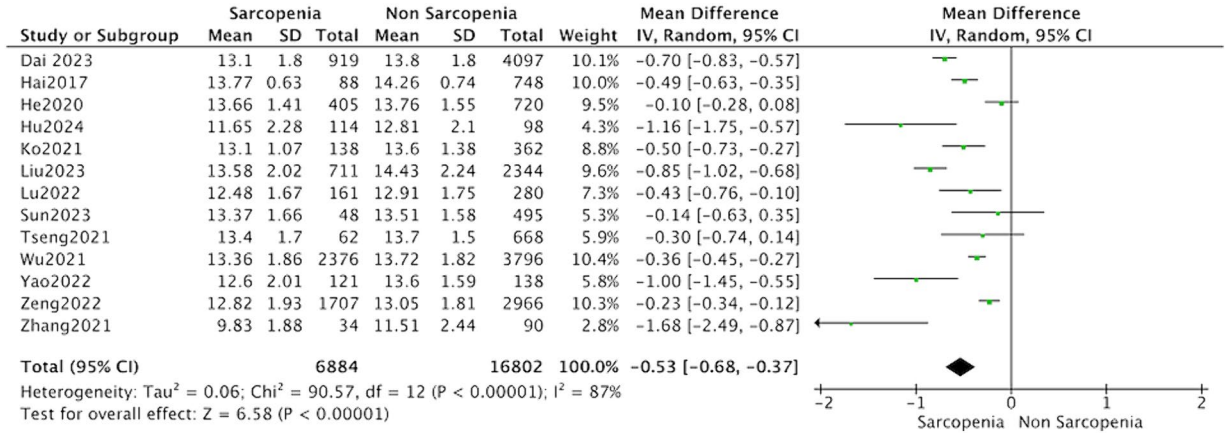

FIGURE 3
Forest plot of serum hemoglobin levels in sarcopenic vs. no sarcopenic subjects. Studies performed on China population. SD, standard deviation; CI, confidence interval.

leading to a decrease in muscle mass and strength, and hastening sarcopenia progression (34). In addition, anemia patients are prone to fatigue, leading to reduced physical activity and muscle function (35). The decrease in iron content in anemia patients affects mitochondrial metabolism and myoglobin synthesis, consequently impairing muscle performance (36, 37).

Chronic inflammation plays an important role in both anemia and sarcopenia. Studies have shown that pro-inflammatory cytokines are associated with loss muscle mass and decreased physical function in elderly individuals (38–40). The sustained inflammation can activate the NF-kB and TNF-α signaling pathways, promoting the pro-inflammatory cytokine like TNF-α, interleukin-6 (IL-6) mediates catabolism, leading to disrupted muscle protein balance, promoted cell apoptosis, and imped muscle repair and regeneration (41, 42). In addition, animal studies have revealed a negative correlation between cytokine levels and the extent of muscle atrophy (43). Scientific investigations have found that inflammatory cytokines such as IL-1, IL-6, and TNF-α in the body upregulate ferritin transcription through different signaling pathways, disturbing iron metabolism. This disruption inhibits red blood cell production, ultimately leading to anemia (44).

This study still has certain limitations. Firstly, we observed heterogeneity in all cross-sectional studies. However, the Meta-analysis of Observational Studies in Epidemiology guidelines indicate that heterogeneity is expected when analyzing observational data. Secondly, the incorporated research, comprising cross-sectional and case-control studies, lacks the capacity to establish causal relationships. Finally, there are differences in the diagnostic criteria for sarcopenia included. Despite our efforts in conducting subgroup analyses, the number of studies included in the subgroup analysis is relatively small, which may have caused false-negative results. In the future, it is imperative to conduct more longitudinal studies of high quality to delve into the correlation and potential mechanisms linking sarcopenia and anemia.

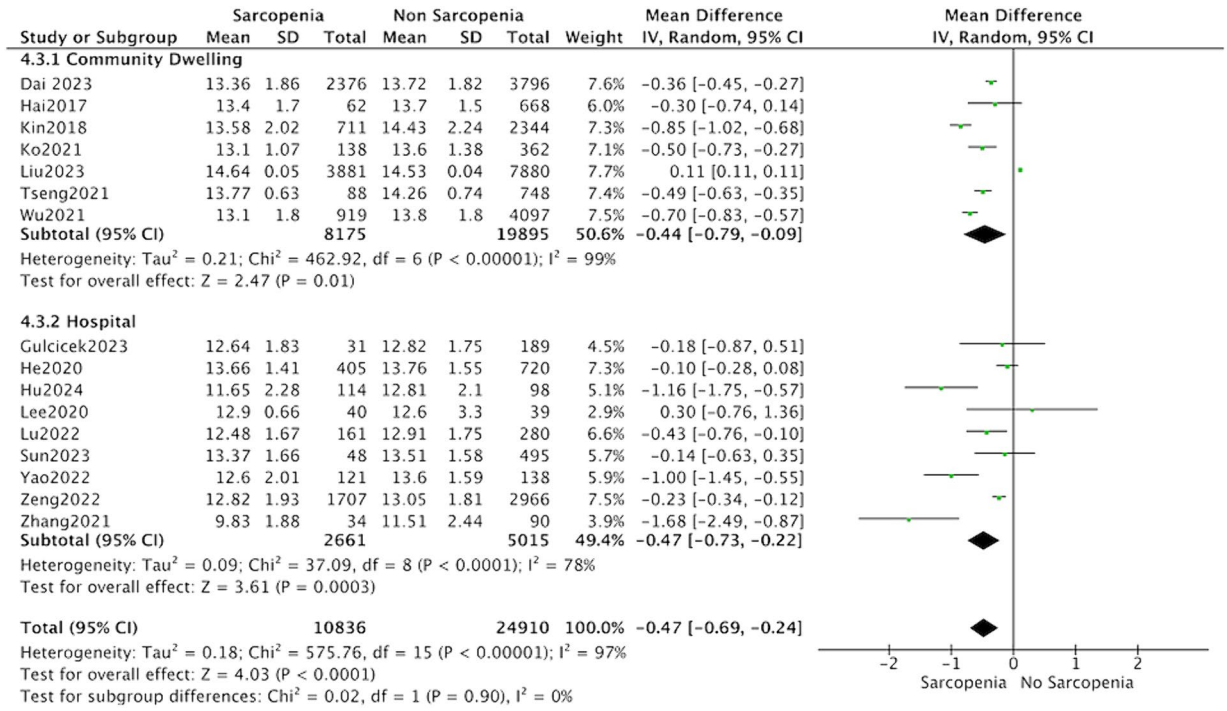

FIGURE 4
Forest plot of serum hemoglobin levels in sarcopenic vs. no sarcopenic subjects. Studies based on different study population. SD, standard deviation; CI, confidence interval.

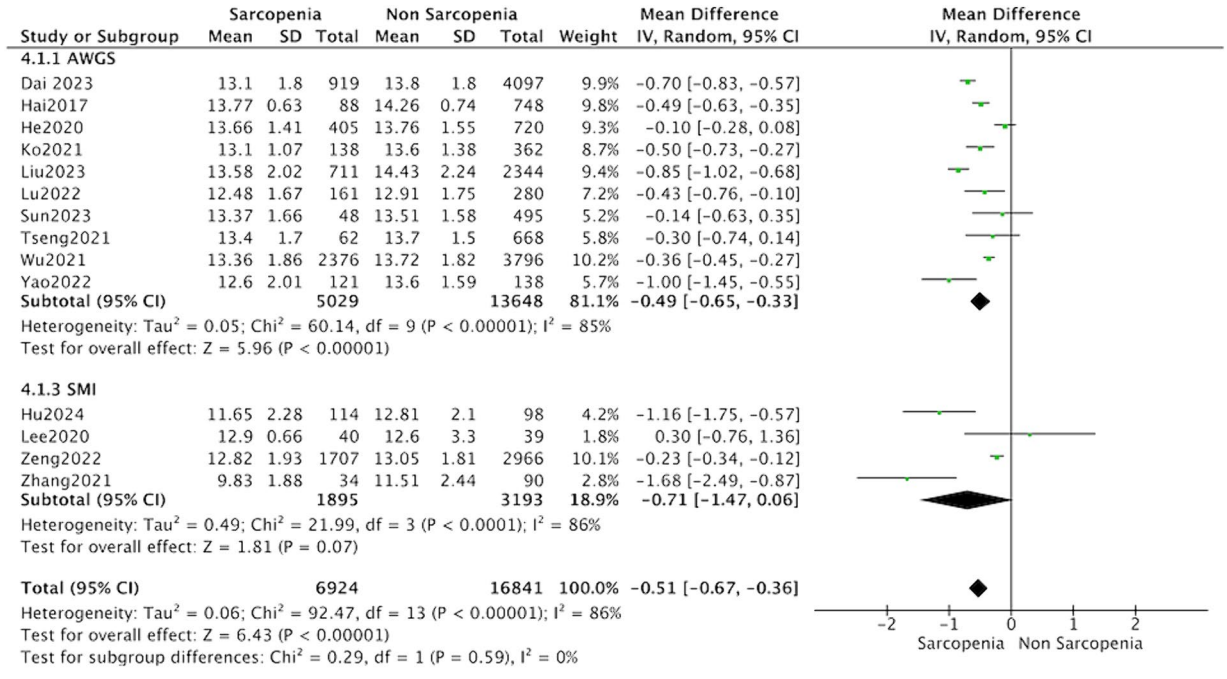

FIGURE 5
Forest plot of serum hemoglobin levels in sarcopenic vs. no sarcopenic subjects. Studies based on different diagnostic criteria for sarcopenia. SD, standard deviation; CI, confidence interval.

Despite these limitations, the current research finds suggest that sarcopenia appears to be linked to low hemoglobin level. These findings emphasize the importance of addressing both sarcopenia and hemoglobin levels in the elderly population to optimize health outcomes. Therefore, our findings may have significant implications for preventing sarcopenia and promoting healthy aging.

5 Conclusion

Our study shows that sarcopenia patients had significantly lower levels of hemoglobin than healthy people. Based on our subgroup analyses, we found that sarcopenia population in China had lower hemoglobin levels. And the characteristics of the study population did not influence the association between sarcopenia and hemoglobin levels. Nevertheless, considering the limitations of the included studies, further large-scale prospective investigations are warranted to validate these findings and elucidate the underlying mechanisms. These findings underscore the importance of addressing both sarcopenia and hemoglobin levels in the elderly population to optimize health outcomes.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

HW: Data curation, Formal analysis, Methodology, Writing – original draft. PL: Conceptualization, Data curation, Funding acquisition, Investigation, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The association between weight-adjusted-waist index and muscle strength in adults: a population-based study

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Background: The relationship between the weight-adjusted-waist index (WWI) and grip strength, a crucial marker in assessing sarcopenia, lacks clarity. We aimed to explore the relationship between WWI and muscle strength across genders.

Methods: The cross-sectional study involved adults with complete data on WWI and grip strength from the 2011–2014 National Health and Nutrition Examination Survey. WWI was derived by dividing waist circumference by the square root of weight. Weighted multivariable logistic regression and smooth curve fitting techniques were used to examine the independent association and potential non-linear relationship between WWI and grip strength. A two-piecewise linear regression model was utilized to determine the threshold effect. Additionally, subgroup analyses and interaction tests were conducted.

Results: The study encompassed 9,365 participants, including 4,661 males and 4,704 females. Multivariate logistic regression analysis revealed a negative correlation between WWI and grip strength among males ($\beta = -11.49$, 95% CI: −12.38, −10.60, $p < 0.001$) as well as females ($\beta = -2.53$, 95% CI: −2.98, −2.08, $p < 0.001$). Subgroup analysis showed that the negative correlation of WWI with grip strength remained consistent across various age groups and levels of obesity for both males and females.

Conclusion: An increase in WWI correlates with reduced muscle strength in both males and females. WWI was negatively associated not only with muscle mass but also with muscle strength. WWI may serve as an assessment tool for sarcopenia, but further large-scale studies are needed to clarify causality.

KEYWORDS

cross-sectional studies, muscle strength, NHANES, obesity, sarcopenia, weight-adjusted-waist index

1 Background

Sarcopenia is delineated as the gradual and progressive reduction in skeletal muscle mass and strength, often accompanied by a decline in physical function (1, 2). This condition stands as a significant aging-related syndrome, independently foretelling multiple clinically consequential adverse outcomes, encompassing an elevated susceptibility to fractures, reduced quality of life, impaired mobility, and heightened mortality rates (3–5). In Asian countries, the

prevalence of sarcopenia varies between 5.5 and 25.7%, with a higher occurrence among males (5.1–21.0% in male compared to 4.1–16.3% in female), leading to significant socioeconomic implications (6, 7). Throughout the revision of sarcopenia guidelines, there is an increased emphasis on muscle strength. This shift stems from the acknowledgment that, in anticipating negative outcomes, muscle strength surpasses muscle mass in predictive accuracy (1, 8). Grip strength, acknowledged as a dependable proxy for overall muscle strength, has garnered considerable attention in numerous guidelines as a pivotal marker for assessing and diagnosing sarcopenia (1, 7, 9).

The weight-adjusted-waist index (WWI) is a recently introduced anthropometric measure derived by standardizing waist circumference (WC) to body weight, computed as the WC in centimeters divided by the square root of weight in kilograms (10). Similar to body mass index (BMI), a higher WWI score signifies increased levels of obesity. Previous studies demonstrated an independent association between WWI and sarcopenic obesity in specific populations like type 2 diabetes mellitus patients and males undergoing maintenance hemodialysis (11, 12). Notably, WWI exhibits a stronger correlation with sarcopenic obesity in older men compared to other anthropometric indices such as waist-to-height ratio, BMI, and WC (13).

Previous studies have demonstrated an inverse correlation between WWI and both appendicular lean mass and abdominal muscle mass among middle-aged and older adult populations (14–16). The association between WWI and sarcopenia has been initially explored. However, the association between WWI and grip strength, a crucial component in assessing sarcopenia, lacks clarity.

The objectives of this study are as follows: Firstly, it aims to investigate the relationship between WWI and grip strength in the adult population. Secondly, the study aims to explore the potential of WWI as a predictive indicator for sarcopenia. It is assumed that there exists a negative correlation between WWI and grip strength.

2 Methods

2.1 Data source and study population

Data were sourced from National Health and Nutrition Examination Survey (NHANES), a nationally conducted cross-sectional survey aimed at gathering information on potential health risk factors and the nutritional status of non-institutionalized civilians in the United States, conducted by the National Center for Health Statistics. A complex, stratified, multistage probability cluster sampling design was employed to obtain a representative sample of the entire the United States population (17). The NHANES study protocols were sanctioned by the Research Ethics Review Board of the NCHS. Written informed consent was acquired from all survey participants or from a parent/legal guardian for those under 16 years of age. Comprehensive details regarding the NHANES study design and data can be accessed publicly at https://www.cdc.gov/nchs/nhanes/.

Our study utilized data from the NHANES survey cycles spanning 2011 to 2014, as only these cycles encompassed information on grip strength and WWI. Initially, 19,932 participants were enrolled; however, following the exclusion of those lacking grip strength data ($n = 5,191$), missing WWI data ($n = 561$), and those under 20 years of age ($n = 4,815$), our final analysis comprised 9,365 participants. The cohort consisted of 4,661 males and 4,704 females (Figure 1).

2.2 Assessment of WWI

The WWI, an anthropometric index combining WC and weight, serves as an estimation tool for obesity. A higher WWI score indicates a higher level of obesity. Body measurement data pertaining to WC and weight were gathered within the mobile examination center by proficient health technicians. The WWI for each participant was computed as the WC in centimeters divided by the square root of weight in kilograms, rounded to two decimal places. In our analysis, we regarded WWI as a continuous variable, subsequently grouping participants according to WWI quartiles for further investigation. WWI was utilized as an exposure variable in our study.

2.3 Assessment of grip strength

Grip strength measurements were conducted during the NHANES 2011–2014 survey, following the protocol specified for that period. The assessment of grip strength adhered to the guidelines outlined in the Muscle Function Procedures Manual and utilized the Takei Digital Grip Strength Dynamometer, Model T.K.K.5401 (Takei Scientific Instruments Co., Niigata, Japan). Beforehand, the dynamometer was adjusted to fit each participant's hand size while they stood with their arm straight down and wrist in a neutral position. Participants were

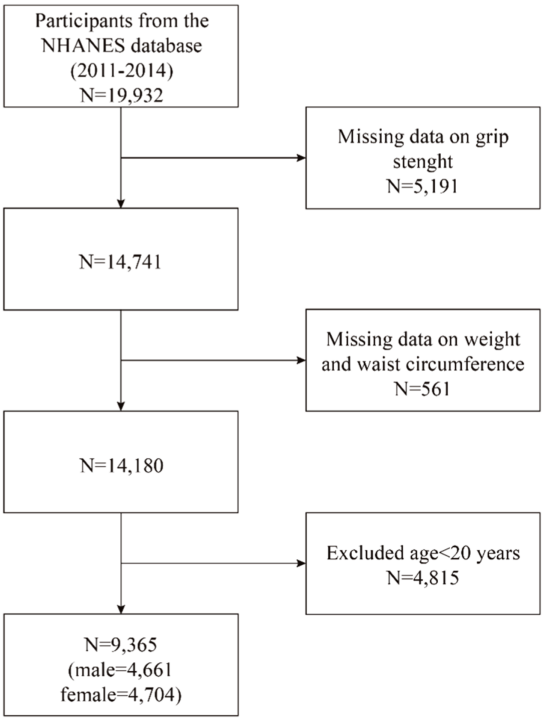

FIGURE 1
Flowchart of population included in our final analysis.

Abbreviations: WWI, Weight-adjusted-waist index; WC, Waist circumference; BMI, Body mass index; NHANES, National Health and Nutrition Examination Survey.

instructed to exert maximum force while squeezing the dynamometer using one hand, repeating the test three times on alternate hands with a 60-s interval between measurements of the same hand. The NHANES recorded the combined handgrip strength by summing the highest readings from each hand, expressed in kilograms.

2.4 Covariates

Our study incorporated covariates that might influence the relationship between WWI and grip strength. These included gender (male/female), age (year), race (non-Hispanic White/non-Hispanic Black/Mexican American/other races), education level (less than high school/high school/more than high school), height (cm), weight (kg), BMI (kg/m^2), WC (cm), intake of energy (kcal/day), intake of protein (gm/day), smoking status (yes/no), alcohol status (yes/no), hypertension (yes/no), diabetes (yes/no) and hypercholesterolemia (yes/no). Energy and protein intake were calculated by averaging the intake across day 1 and day 2. Smoking status was determined based on whether one had smoked at least 100 cigarettes in life. Participants who had at least 12 alcohol drinks per year were considered drinkers. Hypertension, diabetes, and hypercholesterolemia were identified based on self-reported diagnoses of these conditions. Subgroup analysis categorized BMI as <25, 25–29.9, and ≥30 kg/m^2, representing normal weight, overweight, and obese categories, respectively, for the participants. Further details were accessible at www.cdc.gov/nchs/nhanes.

2.5 Statistical analysis

The statistical analyses adhered to Centers for Disease Control and Prevention guidelines, and an adjusted NHANES sampling weight was utilized, considering the intricate multistage cluster survey design during analysis. Significant disparities in grip strength were observed between male and female (18). Consequently, this study was segregated into male and female groups to investigate the correlation between WWI and grip strength. Continuous variables were expressed as mean ± standard deviation, while categorical variables were displayed as percentages. Group differences based on WWI quartiles were assessed using either a weighted Student's *t*-test (for continuous variables) or a weighted chi-square test (for categorical variables). Three models of multivariable logistic regression were employed to assess the association between WWI and grip strength. In model 1, no covariates were adjusted. In model 2, age, race, and education level were adjusted. Model 3 was adjusted for age, race, education level, BMI, intake of energy, intake of protein, smoking status, alcohol status, hypertension, diabetes, and hypercholesterolemia. Subgroup analyses examining the associations between WWI and grip strength were performed, stratified by gender (male/female), age groups (20–39/40–59/≥60 years), and BMI categories (normal weight/overweight/obesity). These stratified factors were considered as predetermined potential effect modifiers. An interaction term was introduced to assess the diversity of associations among the subgroups. Additionally, smooth curve fittings were employed to identify potential non-linear relationships between WWI and grip strength, and a two-piecewise linear regression model was employed to further explore their threshold effects. Missing values for continuous variables were imputed using the mean, and for categorical variables, the mode was used, limited to existing cases of those variables. All analyses were performed using R version 3.4.3 (http://www.R-project.org, The R Foundation) and Empower software (www.empowerstats.com; X&Y solutions, Inc., Boston, MA). Statistical significance was set at a two-sided *p*-value <0.05.

3 Results

3.1 Baseline characteristics of participants

The demographic characteristics of the study cohort categorized by gender-specific quartiles of WWI were presented in Tables 1, 2. Among males, the mean WWI was 10.82 ± 0.81, with quartile ranges of 8.37–10.25, 10.25–10.82, 10.82–11.39, and 11.39–14.79 for Quartiles 1 through 4, respectively. Grip strength exhibited a mean of 87.23 ± 18.92 kg, with values of 95.79 ± 17.45, 90.86 ± 16.98, 85.30 ± 17.62, and 76.98 ± 18.29 kg for Quartiles 1, 2, 3, and 4, respectively. Among females, the mean WWI was 11.22 ± 0.83, with quartile ranges of 8.38–10.63, 10.63–11.20, 11.20–11.79, and 11.79–14.20 for Quartiles 1 through 4, respectively. Grip strength exhibited a mean of 55.63 ± 11.92 kg, with values of 59.52 ± 10.64, 57.33 ± 11.39, 54.85 ± 11.55, and 50.84 ± 12.27 kg for Quartiles 1, 2, 3, and 4, respectively.

3.2 The association between WWI and grip strength

Table 3 illustrated the relationship between WWI and grip strength in males and females using three weighted generalized linear regression models. In the fully adjusted model (Model III), a negative correlation between WWI and grip strength was evident in males ($\beta = -11.49$, 95% CI: −12.38, −10.60, $p < 0.001$). Similarly, females displayed a negative correlation between WWI and grip strength ($\beta = -2.53$, 95% CI: −2.98, −2.08, $p < 0.001$). Regardless of gender, compared to the lowest quartile of WWI, the second, third, and fourth quartiles of WWI exhibited a statistically significant association with grip strength (Male: Q2: $\beta = -4.24$, 95% CI: −5.59, −2.89, $p < 0.001$; Q3: $\beta = -9.35$, 95% CI: −10.91, −7.80, $p < 0.001$; Q4: $\beta = -19.84$, 95% CI: −21.72, −17.96, $p < 0.001$; Female: Q2: $\beta = -1.25$, 95% CI: −2.06, −0.45, $p = 0.002$; Q3: $\beta = -2.33$, 95% CI: −3.22, −1.45, $p < 0.001$; Q4: $\beta = -5.18$, 95% CI: −6.18, −4.18, $p < 0.001$). Sensitivity analysis confirmed this trend (p for trend <0.001).

3.3 Subgroup analysis

To investigate the relationship between WWI and grip strength in the general population, subgroup analyses and interaction tests were conducted based on age and BMI for both males and females (Table 4). In males, the negative correlation between WWI and grip strength endured across all age groups. When stratified by BMI, the negative relationship between WWI and grip strength remained consistent across the normal weight, overweight, and obese populations. Similarly, in females, the negative correlation between WWI and grip strength was stable across different age groups and levels of obesity. Interaction analyses indicated that in females, the association between WWI and grip strength was influenced by BMI rather than age, while in males, neither age nor BMI appeared to affect this association.

TABLE 1 Basic characteristics of participants by WWI quartile in male.

Characteristics	Overall	Weight-adjusted-waist index quartile (cm/$\sqrt{kg}$)				*P*-value
	N = 4,661	Q1 (8.37–10.25) *N* = 1,165	Q2 (10.25–10.82) *N* = 1,165	Q3 (10.82–11.39) *N* = 1,165	Q4 (11.39–14.79) *N* = 1,166	
Age (years)	47.93 ± 17.53	34.78 ± 13.08	44.44 ± 14.71	52.32 ± 15.75	60.18 ± 15.47	<0.001
Race/ethnicity, *N* (%)						<0.001
Non-Hispanic White	1898(40.72)	409 (35.11)	444 (38.11)	457 (39.23)	588 (50.43)	
Non-Hispanic Black	1,086(23.30)	416 (35.71)	251 (21.55)	238 (20.43)	181 (15.52)	
Mexican American	543(11.65)	58 (4.98)	154 (13.22)	161 (13.82)	170 (14.58)	
Other race	1,134(24.33)	282 (24.21)	316 (27.12)	309 (26.52)	227 (19.47)	
Education level, *N* (%)						<0.001
Less than high school	1,044(22.41)	182 (15.62)	219 (18.80)	309 (26.55)	334 (28.67)	
High school	1,073(23.03)	254 (21.80)	267 (22.92)	281 (24.14)	271 (23.26)	
More than high school	2,542(54.56)	729 (62.58)	679 (58.28)	574 (49.31)	560 (48.07)	
Height (cm)	174.38 ± 7.71	177.41 ± 7.32	175.24 ± 7.40	173.43 ± 7.45	171.45 ± 7.41	<0.001
Weight (kg)	86.49 ± 20.60	76.83 ± 14.60	84.50 ± 17.72	88.54 ± 19.46	96.06 ± 24.46	<0.001
Body Mass Index (kg/m^2)	28.34 ± 6.02	24.31 ± 3.77	27.37 ± 4.56	29.26 ± 5.18	32.43 ± 6.96	<0.001
Waist Circumference (cm)	100.23 ± 15.97	85.34 ± 9.14	96.53 ± 10.12	103.86 ± 11.32	115.19 ± 15.27	<0.001
Intake of Energy (kcal/day)	2371.50 ± 904.05	2614.61 ± 1018.46	2412.32 ± 859.36	2297.28 ± 868.31	2161.95 ± 794.64	<0.001
Intake of Protein (gm/day)	94.85 ± 39.99	104.28 ± 47.56	96.98 ± 37.76	91.57 ± 36.65	86.56 ± 34.57	<0.001
Smoking status, *N* (%)						<0.001
YES	2,428(52.13)	521 (44.72)	591 (50.77)	625 (53.74)	691 (59.26)	
NO	2,230(47.87)	644 (55.28)	573 (49.23)	538 (46.26)	475 (40.74)	
Alcohol status, *N* (%)						0.129
YES	3,718(84.34)	906 (83.81)	952 (86.47)	919 (82.94)	941 (84.17)	
NO	690(15.65)	175 (16.19)	149 (13.53)	189 (17.06)	177 (15.83)	
Hypertension, *N* (%)						<0.001
YES	1,604(34.41)	178 (15.31)	317 (27.23)	488 (41.89)	621 (53.35)	
NO	3,052(65.48)	985 (84.69)	847 (72.77)	677 (58.11)	543 (46.65)	
Diabetes, *N* (%)						<0.001
YES	685(14.70)	38 (3.26)	103 (8.85)	192 (16.48)	352 (30.19)	
NO	3,975(85.30)	1,127 (96.74)	1,061 (91.15)	973 (83.52)	814 (69.81)	
Hypercholesterolemia, *N* (%)						<0.001
YES	1,627(35.13)	180 (15.49)	355 (30.71)	500 (43.18)	592 (51.26)	
NO	3,004(64.87)	982 (84.51)	801 (69.29)	658 (56.82)	563 (48.74)	
WWI (cm/$\sqrt{kg}$)	10.82 ± 0.81	9.77 ± 0.37	10.55 ± 0.16	11.10 ± 0.17	11.84 ± 0.38	<0.001
Grip strength (kg)	87.23 ± 18.92	95.79 ± 17.45	90.86 ± 16.98	85.30 ± 17.62	76.98 ± 18.29	<0.001

Continuous variables were presented as mean ± SD, and the *P*-value was derived using a weighted linear regression model, Categorical variables were presented as percentages, and the *P*-value was derived through a weighted chi-square test. WWI, weight-adjusted-waist index.

3.4 Non-linear relationship between WWI and grip strength

As depicted in Figure 2, a non-linear inverse relationship between WWI and grip strength was observed in both males and females. Table 5 illustrated that the inflection points (K), determined through the two-piecewise linear regression model, were calculated at 10.83 for males and 11.43 for females. Both genders exhibited a significant negative correlation between WWI and grip strength on either side of the inflection point. Among males, on the left side of the inflection point, a unit increased in WWI corresponded to a reduction of grip strength by 7.59 kg, while on the right side, each unit rose in WWI resulted in a decrease of grip strength by 15.16 kg. Similarly, among females, on the left side of the inflection point, a unit increased in WWI corresponded to a reduction of grip strength by 1.45 kg, and on the right side, each unit rose in WWI led to a decrease of grip strength

TABLE 2 Basic characteristics of participants by WWI quartile in female.

Characteristics	Overall	Weight-adjusted-waist index quartile (cm/$\sqrt{kg}$)				*P*-value
	N = 4,704	Q1 (8.38–10.63) *N* = 1,176	Q2 (10.63–11.20) *N* = 1,176	Q3 (11.20–11.79) *N* = 1,176	Q4 (11.79–14.20) *N* = 1,176	
Age (years)	48.32 ± 17.26	38.47 ± 14.63	46.20 ± 15.94	51.81 ± 16.00	56.81 ± 16.80	<0.001
Race/ethnicity, *N* (%)						<0.001
Non-Hispanic White	1925(40.92)	499 (42.43)	479 (40.73)	432 (36.73)	515 (43.79)	
Non-Hispanic Black	1,098(23.34)	301 (25.60)	281 (23.89)	296 (25.17)	220 (18.71)	
Mexican American	521(11.08)	75 (6.38)	102 (8.67)	168 (14.29)	176 (14.97)	
Other race	1,160(24.66)	301 (25.60)	314 (26.70)	280 (23.81)	265 (22.53)	
Education level, *N* (%)						<0.001
Less than high school	926(19.69)	116 (9.86)	188 (16.00)	270 (22.96)	352 (29.93)	
High school	957(20.35)	181 (15.39)	213 (18.13)	286 (24.32)	277 (23.55)	
More than high school	2,820(59.96)	879 (74.74)	774 (65.87)	620 (52.72)	547 (46.51)	
Height (cm)	160.79 ± 7.19	164.21 ± 6.71	161.40 ± 6.54	159.73 ± 6.67	157.80 ± 7.26	<0.001
Weight (kg)	76.17 ± 20.90	67.17 ± 15.89	73.72 ± 18.67	79.02 ± 21.21	84.78 ± 22.97	<0.001
Body Mass Index (kg/m^2)	29.40 ± 7.55	24.84 ± 5.35	28.16 ± 6.35	30.80 ± 7.27	33.81 ± 7.91	<0.001
Waist Circumference (cm)	97.35 ± 16.80	82.77 ± 10.34	93.15 ± 11.68	101.35 ± 13.29	112.13 ± 15.62	<0.001
Intake of Energy (kcal/day)	1783.42 ± 662.25	1878.92 ± 735.12	1786.23 ± 612.91	1764.28 ± 649.81	1704.28 ± 633.49	<0.001
Intake of Protein (gm/day)	69.36 ± 27.73	72.56 ± 29.51	69.84 ± 26.78	68.70 ± 27.76	66.36 ± 26.45	<0.001
Smoking status, *N* (%)						<0.001
YES	1,625(34.56)	341 (29.05)	398 (33.84)	416 (35.37)	470 (39.97)	
NO	3,077(65.44)	833 (70.95)	778 (66.16)	760 (64.63)	706 (60.03)	
Alcohol status, *N* (%)						<0.001
YES	2,763(63.11)	785 (72.55)	698 (64.33)	677 (61.60)	603 (54.23)	
NO	1,615(36.89)	297 (27.45)	387 (35.67)	422 (38.40)	509 (45.77)	
Hypertension, *N* (%)						<0.001
YES	1,695(36.06)	194 (16.51)	353 (30.04)	505 (42.98)	643 (54.72)	
NO	3,005(63.94)	981 (83.49)	822 (69.96)	670 (57.02)	532 (45.28)	
Diabetes, *N* (%)						<0.001
YES	670(14.26)	42 (3.57)	97 (8.26)	202 (17.18)	329 (28.02)	
NO	4,029(85.74)	1,133 (96.43)	1,077 (91.74)	974 (82.82)	845 (71.98)	
Hypercholesterolemia, *N* (%)						<0.001
YES	1,577(33.71)	199 (17.02)	340 (29.01)	477 (40.63)	561 (48.24)	
NO	3,101(66.29)	970 (82.98)	832 (70.99)	697 (59.37)	602 (51.76)	
WWI (cm/$\sqrt{kg}$)	11.22 ± 0.83	10.16 ± 0.36	10.93 ± 0.16	11.49 ± 0.17	12.28 ± 0.40	<0.001
Grip strength (kg)	55.63 ± 11.92	59.52 ± 10.64	57.33 ± 11.39	54.85 ± 11.55	50.84 ± 12.27	<0.001

Continuous variables were presented as mean ± SD, and the *P*-value was derived using a weighted linear regression model, Categorical variables were presented as percentages, and the *P*-value was derived through a weighted chi-square test. WWI, weight-adjusted-waist index.

by 4.18 kg. Both groups exhibited logarithmic likelihood ratio test *p*-values <0.001.

4 Discussion

The objective of this study was to assess the correlation between WWI and grip strength. In our cross-sectional analysis encompassing 4,661 male and 4,704 female, a notable adverse correlation between WWI and grip strength was observed. This correlation persisted even subsequent to adjustments for all potential confounding variables. Subgroup analysis showed that the negative correlation of WWI with grip strength remained consistent across various age groups and levels of obesity for both males and females. Our findings indicated a negative association between WWI and grip strength in the adult population of the United States, which held true across various age groups and levels of obesity.

To our knowledge, this study was the inaugural exploration into the association between WWI and muscle strength. The diagnostic

TABLE 3 The associations between WWI and grip strength.

	Model 1 β (95% CI) *p*-value	Model 2 β (95% CI) *p*-value	Model 3 β (95% CI) *p*-value
Male			
WWI (continuous)	−8.29 (−8.90, −7.67) <0.001	−4.04 (−4.77, −3.32) <0.001	−11.49 (−12.38, −10.60) <0.001
WWI (quartile)			
Quartile 1	Reference	Reference	Reference
Quartile 2	−3.52 (−4.87, −2.17) <0.001	0.66 (−0.68, 1.99) 0.336	−4.24 (−5.59, −2.89) <0.001
Quartile 3	−8.53 (−9.90, −7.15) <0.001	−1.40 (−2.85, 0.04) 0.057	−9.35 (−10.91, −7.80) <0.001
Quartile 4	−16.87 (−18.27, −15.47) <0.001	−7.35 (−8.93, −5.77) <0.001	−19.84 (−21.72, −17.96) <0.001
P for trend	<0.001	<0.001	<0.001
Female			
WWI (continuous)	−3.58 (−3.96, −3.19) <0.001	−0.81 (−1.19, −0.43) <0.001	−2.53 (−2.98, −2.08) <0.001
WWI (quartile)			
Quartile 1	Reference	Reference	Reference
Quartile 2	−2.42 (−3.28, −1.56) <0.001	0.11 (−0.67, 0.89) 0.783	−1.25 (−2.06, −0.45) 0.002
Quartile 3	−4.26 (−5.14, −3.37) <0.001	−0.03 (−0.86, 0.80) 0.942	−2.33 (−3.22, −1.45) <0.001
Quartile 4	−7.77 (−8.68, −6.87) <0.001	−1.84 (−2.72, −0.97) <0.001	−5.18 (−6.18, −4.18) <0.001
P for trend	<0.001	<0.001	<0.001

Model 1: no covariates were adjusted. Model 2: age, race, and education level were adjusted. Model 3: age, race, education level, body mass index, intake of energy, intake of protein, smoking status, alcohol status, hypertension, diabetes, and hypercholesterolemia were adjusted. WWI, weight-adjusted-waist index.

criteria for sarcopenia, as proposed by the European Working Group on Sarcopenia in Older People, comprise three elements: low muscle strength, low physical performance and low muscle mass (1). Prior investigations have shown an inverse relationship between WWI and both abdominal muscle mass and appendicular lean mass in middle-aged and older adult cohorts (14–16). However, no research has explicitly elucidated the correlation between WWI and muscle strength which is more associated with poor outcomes. This study filled this gap. Similar to muscle mass, our findings revealed a negative correlation between WWI and muscle strength.

The association between WWI and bone and muscle mass has been partially substantiated. Studies indicated a negative correlation between WWI and bone mineral density in the lumbar spine, pelvis, femoral neck, and total (19). And, previous research on WWI and muscle mass primarily concentrated on middle-aged and older adult individuals (14–16) and even people with characteristic diseases (11, 12), and noted gender disparities. However, through subgroup analysis, the correlation between WWI and muscle strength remained consistent across young, middle-aged, and older adults, encompassing both males and females. BMI stratification indicated that the negative correlation between WWI and grip strength applies consistently across different levels of obesity. The prevalence of obesity is rising worldwide (20). Data sourced from the World Health Organization indicates that 39% of the global adult population are overweight, of which 13% fall under the category of obesity, with a persistent increase in the count of obese individuals (21, 22). The relationship between WWI and grip strength also existed in the obese population. Given this context, WWI shows a growing potential to predict muscle strength.

The association between other obesity indices (BMI, body fat rate, waist-to-hip ratio) and muscle strength remained contentious. In several studies, conflicting results have emerged. Agtuahene et al. (23) showed a positive link between BMI and grip strength in youth, while Alahmari et al. (24) suggested no correlation between BMI and grip strength in grown men. Moreover, Siqueira revealed no substantial relationship between BMI and leg strength in active older adult individuals, except concerning grip strength (25). The sample sizes in these studies were relatively small, ranging from 64 to 304 participants. Nevertheless, a substantial cross-sectional study with a sample size exceeding 7,000 middle-aged individuals uncovered a positive association between BMI and grip strength (26). Variations in sample sizes and age group differences among the studies might explain these inconsistencies in research findings. In the context of body fat percentage, a comprehensive study revealed a positive correlation between body fat percentage and grip strength among middle-aged participants (26). Conversely, a separate study

TABLE 4 Subgroup analysis of the association between WWI and grip strength.

Subgroup	β (95% CI)	*P*-value	*P* for interaction
Male			
Age			0.506
20–39 years	−12.13 (−13.49, −10.76)	<0.001	
40–59 years	−11.33 (−12.71, −9.96)	<0.001	
60–80 years	−12.50 (−14.04, −10.96)	<0.001	
BMI			0.819
Normal weight	−9.66 (−11.31, −8.01)	<0.001	
Overweight	−10.15 (−11.51, −8.80)	<0.001	
Obese	−10.32 (−11.64, −9.01)	<0.001	
Female			
Age			0.702
20–39 years	−2.72 (−3.46, −1.98)	<0.001	
40–59 years	−2.98 (−3.73, −2.24)	<0.001	
60–80 years	−3.17 (−3.95, −2.39)	<0.001	
BMI			0.029
Normal weight	−2.81 (−3.62, −2.00)	<0.001	
Overweight	−3.06 (−3.90, −2.22)	<0.001	
Obese	−1.78 (−2.43, −1.13)	<0.001	

Age, race, education level, body mass index, intake of energy, intake of protein, smoking status, alcohol status, hypertension, diabetes, and hypercholesterolemia were adjusted. BMI, Body Mass Index.

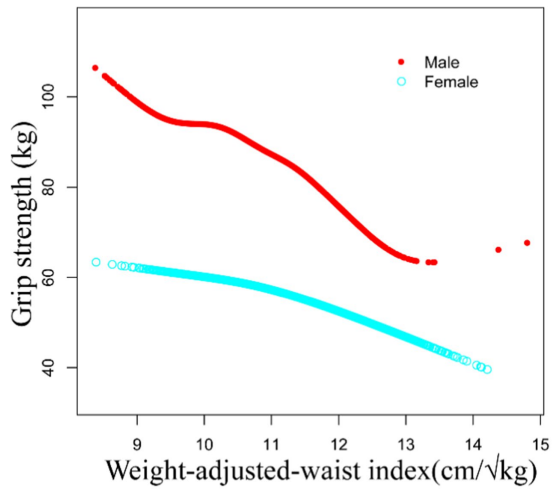

FIGURE 2
The non-linear associations between WWI and grip strength.

demonstrated a negative correlation between body fat percentage and abdominal strength. Notably, there was no observed correlation between waist-to-hip ratio and either grip strength or abdominal strength (26, 27).

However, as an index indicating increased obesity with higher values, BMI either lacks correlation or shows a positive one with muscle strength. Conversely, this study illustrated that WWI, also employed as an obesity indicator, displayed a negative correlation with muscle strength. The relationship between obesity and muscle is intricate. In the progression of obesity and muscle mass decline, a phenomenon of fat redistribution occurs. This presents as the transfer of fat from subcutaneous regions to the abdominal cavity (visceral fat) and its infiltration into muscles (28–30). This results in diminished muscle strength and functionality. Fat infiltration into muscles heightens the risk of advancing toward obesity, while obesity hampers muscle regeneration, initiating pre-sarcopenia. This synergistic interaction between muscle loss and fat infiltration could initiate and worsen sarcopenic obesity. While valuable for illustrating trends in obesity prevalence at a population level, BMI offers a rudimentary assessment of overall adiposity. Because BMI cannot differentiate between fat and muscle mass, the ratio of lean mass to fat mass may differ despite similar BMI values (31, 32). The reduction in muscle mass leading to weight loss is offset by an augmentation in visceral fat, leading to a circumstance wherein, despite diminished muscle strength, the BMI shows no alteration. This observation was also employed to elucidate the phenomenon of the obesity paradox (28, 31, 33). Additionally, the relocation of fat from subcutaneous to visceral areas does not necessarily imply weight gain, but it may enlarge WC (34), thus increasing WWI while BMI remains unchanged. This might be the reason behind the inconsistency in the correlation between WWI and BMI, two obesity indicators, with muscle strength.

The SARC-F scale is utilized for the identification of individuals potentially affected by sarcopenia. However, its sensitivity is limited, frequently resulting in the omission of certain patients (35). And the suggested techniques for assessing muscle strength and mass necessitate specialized tools such as computed tomography, magnetic resonance imaging, and ultrasound (1). Nevertheless, these methods entail substantial expenses and time commitments. The estimation of muscle strength and muscle mass without such specialized tools poses

TABLE 5 Threshold effect analysis of WWI on grip strength using a two-piecewise linear regression model.

	Fitting by the standard linear model	Fitting by the two-piecewise linear model			
		Inflection point (K)	<K-segment effect	>K-segment effect	Log likelihood ratio
Male					
WWI	−11.49 (−12.38, −10.60) <0.001	10.83	−7.59 (−8.90, −6.27) <0.001	−15.16 (−16.43, −13.88) <0.001	<0.001
Female					
WWI	−2.53 (−2.98, −2.08) <0.001	11.43	−1.45 (−2.10, −0.79) <0.001	−4.18 (−5.03, −3.32) <0.001	<0.001

Age, race, education level, body mass index, intake of energy, intake of protein, smoking status, alcohol status, hypertension, diabetes, and hypercholesterolemia were adjusted. WWI, weight-adjusted-waist index.

a challenge, and presently, no anthropometric index adequately reflects both these parameters. Previous studies and this study have demonstrated that WWI is correlated with both muscle strength and muscle mass. As a result, WWI holds promise as a simple screening tool for identifying sarcopenia or to complement the SARC-F scale for better detection of sarcopenia cases.

The study possesses several strengths. Primarily, it relied on NHANES data and conducted analyses while accounting for the appropriate NHANES sample weights. Secondly, we meticulously adjusted confounding covariates, enhancing the reliability of our results and their applicability to a broader spectrum of individuals. Nevertheless, the study also presents certain limitations. Initially, owing to the cross-sectional design, establishing a causal relationship was unattainable. Therefore, further prospective studies involving larger sample sizes remain imperative to elucidate causality. Furthermore, despite our adjustment for several potential covariates, the influence of other conceivable confounding factors could not be entirely ruled out.

5 Conclusion

Increased WWI correlated with reduced muscle strength in both male and female. As the WWI index rises, the strength of this negative correlation intensifies. The negative correlation of WWI with grip strength remained consistent across various age groups and levels of obesity. WWI may serve as an assessment tool for sarcopenia. Nonetheless, additional large-scale prospective studies are required to elucidate the precise causal link in this association.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by Research Ethics Review Board of the National Center for Health Statistics. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LX: Conceptualization, Data curation, Investigation, Methodology, Software, Supervision, Writing – original draft, Writing – review & editing. HZ: Formal analysis, Funding acquisition, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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The prevalence of sarcopenia and risk factors in the older adult in China: a systematic review and meta-analysis

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Background: Understanding the epidemiological information of a certain disease is the first step in related prevention and control work. This article aims to understand the prevalence and associated risk factors of sarcopenia among the older adult (≥60 years old) in China and to provide an evidence-based basis for early identification, management, and prevention of sarcopenia patients.

Methods: We searched seven databases: CNKI, Wanfang, VIP, PubMed, Web of Science, Embase, and Cochrane Library databases from the establishment of the database until January 31, 2024. The Quality evaluation criteria of cross-sectional studies recommended by the Agency for Healthcare Research and Quality (AHRQ) were used for literature quality evaluation. Stata 18.0 software was used for statistical analysis.

Results: We finally included 45 studies, involving a total of 37,571 cases. After statistical analysis, we found that the prevalence of sarcopenia among the older adult in China was 20.7% [95% CI (18.3, 23.0%)]. The results of subgroup analysis suggest that: ① According to gender, the prevalence rate of sarcopenia in women (21.6%) is higher than that in men (19.2%); ② According to age, the prevalence rate of older adult people aged ≥80 (45.4%) was the highest, followed by 70–79 (27.2%) and 60–69 (15.7%). ③ According to region, the prevalence rate of the older adult in the south (21.7%) is higher than that in the north (19.0%); ④ According to the time of publication, the prevalence of sarcopenia among the older adult in China has increased (from 19.2% in 2014–2018 to 21.4% in 2019–2024); ⑤ According to the diagnostic criteria, the detection rate of AWGS (2019) is higher than that of AWGS (2014) (24.5% vs. 19.3%). Finally, aging, low BMI, low leg circumference, smoking, depression, osteoporosis, malnutrition and malnutrition risk are all risk factors for sarcopenia among the older adult in China.

Conclusion: The prevalence of sarcopenia in the older adult in China was higher (20.7%), which should be paid attention to by relevant health authorities. In addition, aging, low BMI, low calf circumference, smoking, depression, osteoporosis, malnutrition and malnutrition risk are risk factors for the development of sarcopenia in the older adult in China. For these high-risk populations, early identification, prevention, and intervention can be carried out to delay the occurrence and progression of sarcopenia.

KEYWORDS
sarcopenia, prevalence, risk factors, older adult, Chinese, meta-analysis

1 Introduction

Sarcopenia is a common senile disease, which refers to the symptoms of a decline in skeletal muscle mass and muscle strength caused by aging (1). Sarcopenia is highly associated with a variety of adverse outcomes (such as fractures, cognitive decline, metabolic disorders, etc.), and its development process is generally hidden and not easily detected by patients until the occurrence of the above-mentioned adverse consequences (2, 3). Sarcopenia not only seriously affects the quality of life of the older adult, but the follow-up medical care will also bring a heavy economic burden to the family and society (4). An epidemiological study in South Korea showed that the prevalence of sarcopenia in the older adult aged 60 years and above was about 13.1% (5); Japan also reported that the prevalence of sarcopenia in the older adult aged 60 years and above was 9.9% (6). A global epidemiological study of sarcopenia shows that: sarcopenia seriously affects the quality of life of 10–16% of the older adult worldwide (7).

Sarcopenia is an aging disease, and with the global trend of the aging population, the phenomenon of sarcopenia in the older adult will become increasingly common (8, 9). As is well known, China has entered a stage of rapid population aging. According to the results of the 7th National Population Census (10): the population aged 60 and above in China is approximately 264 million, accounting for 18.7% of the total population. At present, sarcopenia has received attention from various countries, but a unified diagnostic standard has not yet been established (8, 11). Among them, the most commonly used diagnostic criteria include the European Working Group on Sarcopenia in Older People (EWGSOP), the Asian Working Group on Sarcopenia (AWGS), and the International Working Group on Sarcopenia (IWGS) (12–15). These diagnostic criteria all recognize that muscle mass, muscle strength, and daily activity ability are the three important factors for diagnosing sarcopenia. However, due to significant differences in factors such as country, region, diet, environment, and race, accurately assessing the epidemiological situation of sarcopenia and carrying out related prevention and treatment work still pose certain challenges (16).

Collecting epidemiological evidence of sarcopenia in the older adult is the first step to formulating preventive procedures or health care services. In the case of insufficient literature reports, systematic evaluation of prevalence and risk factors data is becoming more and more important for policy formulation and implementation of preventive measures. At present, we find that China has begun to pay attention to the epidemiological information of sarcopenia in the older adult, but the conclusions on its epidemiological characteristics, risk factors, and complications are not satisfactory (17–19). At the same time, in the past few years, several large-scale sample studies have been published at home and abroad, which can be used for systematic review and meta-analysis. Therefore, we plan to assess the prevalence and risk factors of sarcopenia among the older adult in China aged 60 and above in China, and provide evidence-based evidence for early identification, management and prevention of sarcopenia among the older adult in China.

2 Methods

2.1 Search strategy

This study is based on the PRISMA statement (20). Because this study is an epidemiological survey, ethical approval is not required. The systematic review and meta-analysis have been registered in PROSPERO with the number CRD42023494338. We used the following principles of the PICOS algorithm to guide the initial retrieval:

P (population): China older adult people over 60 years old;

I (intervention): no intervention;

C (comparison): no comparison;

O (outcome): the prevalence and risk factors of sarcopenia among the older adult in China;

S (study): cross-sectional study/retrospective study.

2.2 Literature search

We searched seven databases: CNKI, Wanfang, VIP, PubMed, Web of Science, Embase, and Cochrane Library from the establishment of the database until January 31, 2024. The method of "subject word + the free word" was used to search, and the Chinese search terms were "sarcopenia"; "prevalence, incidence, epidemiology"; "Influencing factors, related factors, risk factors"; English search terms are: "sarcopenia"; "prevalence, incidence, epidemiology"; "risk factor, correlation factor, affecting factor"; "China, Chinese."

The literature retrieval strategy takes PubMed as an example. The detailed retrieval formula of PubMed is as follows: ("sarcopenia"[MeSH Terms] OR "sarcopenia"[All Fields] OR "sarcopenia s"[All Fields]) AND ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "prevalence"[All Fields] OR "prevalence"[MeSH Terms] OR "prevalance"[All Fields] OR "prevalences"[All Fields] OR "prevalence s"[All Fields] OR "prevalent"[All Fields] OR "prevalently"[All Fields] OR "prevalents"[All Fields] OR ("epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "incidence"[All Fields] OR "incidence"[MeSH Terms] OR "incidences"[All Fields] OR "incident"[All Fields] OR "incidents"[All Fields]) OR ("epidemiologies"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "epidemiology"[MeSH Terms] OR "epidemiology s"[All Fields])) AND (("risk factors"[MeSH Terms] OR ("risk"[All Fields] AND "factors"[All Fields]) OR "risk factors"[All Fields]) AND (("correlate"[All Fields] OR "correlated"[All Fields] OR "correlates"[All Fields] OR "correlating"[All Fields] OR "correlation"[All Fields] OR "correlation s"[All Fields] OR "correlations"[All Fields] OR "correlative"[All Fields] OR

Retrieval Procedure	Term
#1	sarcopenia [All Field]
#2	prevalence
#3	incidence
#4	epidemiology
#5	#2 OR #3 OR #4
#6	risk factor
#7	correlation factor
#8	affecting factor
#9	#6 OR #7 OR #8
#10	China
#11	Chinese
#12	#10 OR #11
#13	#1 AND #5 AND #9 AND #12

FIGURE 1
PubMed retrieval procedure flowchart.

"correlatives"[All Fields]) AND ("factor"[All Fields] OR "factor s"[All Fields] OR "factors"[All Fields])) AND (("affect"[MeSH Terms] OR "affect"[All Fields] OR "affects"[All Fields] OR "affected"[All Fields] OR "affecteds"[All Fields] OR "affecting"[All Fields]) AND ("factor"[All Fields] OR "factor s"[All Fields] OR "factors"[All Fields]))) AND ("china"[MeSH Terms] OR "china"[All Fields] OR "china s"[All Fields] OR "chinas"[All Fields] OR ("chineses"[All Fields] OR "east asian people"[MeSH Terms] OR ("east"[All Fields] AND "asian"[All Fields] AND "people"[All Fields]) OR "east asian people"[All Fields] OR "chinese"[All Fields])). (For the specific search process, see Figure 1 and Supplementary File 1).

2.3 Literature inclusion and exclusion criteria

2.3.1 Inclusion criteria

① According to the author's language ability, literature in English, and Chinese were eligible; ② The study subjects include the older adult population aged ≥60 in China; ③ The study includes risk factors that may lead to sarcopenia in the older adult; ④ The definition and diagnostic criteria for sarcopenia were proposed in the study; ⑤ The study provided data on the prevalence of sarcopenia, or data that can be used to calculate the prevalence; ⑥ OR values and 95% CI were provided in the study; and ⑦ Cross-sectional or retrospective studies.

2.3.2 Exclusion criteria

① Repeated published research; ② Research published in the form of reviews, conference abstracts, etc.; ③ Research that cannot obtain full text or extract complete data; ④ The sample size of the older adult is too small (≤100 studies); and ⑤ Low-quality research (AHRQ score < 6 points).

2.4 Literature screening and data extraction

We import the retrieved literature into EndNoteX9.1 software and first remove the duplicate literature. The second step is to make a preliminary screening by reading the titles and abstracts of the literature. Finally, read the rest of the literature in full, and make the final inclusion and exclusion in strict accordance with the inclusion and exclusion criteria. In this process, two evaluators (W.L. and X.Z.) independently cross-checked the included literature repeatedly. If

there is any dispute, it will be resolved through discussion between the two parties or the introduction of the third researcher (XL.F.) for review.

In the data extraction stage, two researchers (W.L. and X.Z.) independently used Excel tables to extract data. The main contents of the extraction are as follows: (1) Basic information included in the literature: first author, publication year, investigation place, etc. (2) Calculate the prevalence rate of sarcopenia and related data of risk factors; (3) Key information of biased risk assessment. After the data is extracted, it shall be summarized, exchanged, and reviewed. If there is disagreement, it shall be submitted to the third researcher (XL.F.) for review.

2.5 Literature quality evaluation

We adopt the cross-sectional study quality evaluation criteria recommended by the Agency for Healthcare Research and Quality (AHRQ) for literature quality evaluation (21). The evaluation criteria consist of 11 items, with a rating scale of 1 point for "yes" and 0 points for "no/unclear." A total score of 8–11 indicates high quality, 4–7 indicates moderate quality, and 0–3 indicates low quality (see Table 1 for details).

2.6 Statistics

We used Stata18.0 software to statistically analyze the data on the prevalence rate and risk factors of sarcopenia and analyzed the heterogeneity of the included studies through the Q test and I^2 value. If $I^2 > 50\%$, and $p < 0.1$, it shows that there is high heterogeneity among the studies, and the random effect model is used for analysis. Otherwise, the fixed effect model will be used for statistical analysis (22). If the heterogeneity between the included research results is large, it is necessary to further analyze the sources of heterogeneity, and the subgroup analysis method can be used to try to find out the obvious sources of heterogeneity. The subgroups set in this paper include: gender, age, region, publication time, and diagnostic criteria, and the statistical significance p-value in all statistical analyses is set to 0.05.

In this study, we did not check the publication bias. The reasons are as follows: publication bias is a phenomenon in which studies with significant results are easier to publish than those with insignificant results, which may lead to systematic differences between published and unpublished studies (23). However, in the observational study of prevalence, there are no significant or insignificant results, and it is not recommended to use mature methods to test this deviation in the systematic evaluation of prevalence research. Therefore, we did not check the publication bias.

3 Results

3.1 Literature screening process and results

After a preliminary search, we obtained a total of 5,733 related articles, and after a layer-by-layer screening, we finally included 45 studies, with a total of 37,571 subjects. (For the process and results of literature screening, see Figure 2).

3.2 Basic characteristics and quality evaluation results of included literature

To ensure the quality of the included literature, we set the inclusion quality standard (AHRQ Score ≥ 6). A total of 45 literatures were included in this study, involving 37,571 older adult people over 60 years old in China in 31 provinces and cities. The general situation and quality evaluation results of the included literature are shown in Table 2. (For the detailed results of literature evaluation, see Supplementary File 2; for the general information of literature, see Supplementary File 3).

TABLE 1 AHRQ cross-sectional study quality evaluation standard table.

	Item content	Yes	No/Unclear
1	Define the source of information (survey or record review?)		
2	List inclusion and exclusion criteria for exposed and unexposed subjects (cases and control) or refer to previous publications		
3	Indicate period used for identifying patients		
4	Indicate whether or not subjects were consecutive if not population-based		
5	Indicate if evaluators of subjective components of the study were masked to other aspects of the status of the participants		
6	Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements)		
7	Explain any patient exclusions from the analysis		
8	Describe how confounding was assessed and/or controlled		
9	lf applicable, explain how missing data were handled in the analysis		
10	Summarize patient response rates and completeness of data collection		
11	Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained		

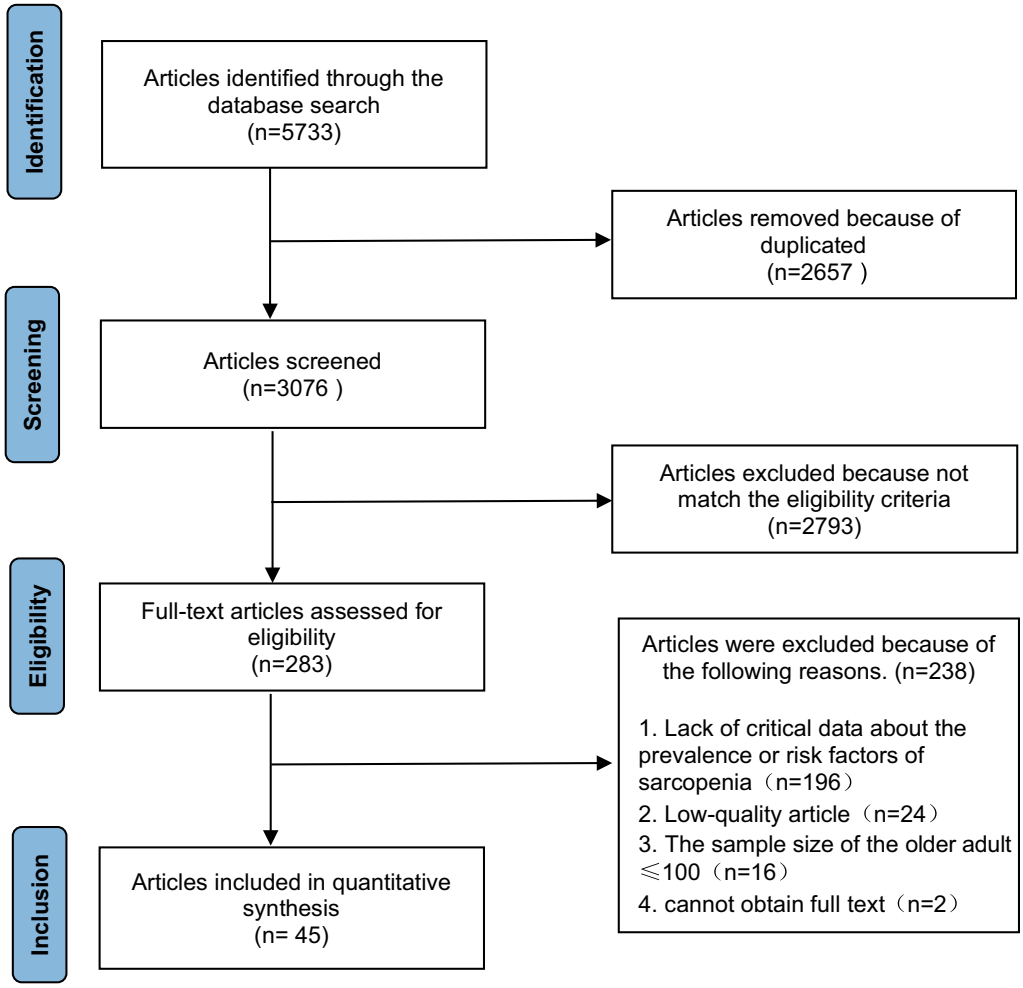

FIGURE 2
Literature retrieval process diagram.

3.3 Meta-analysis results

3.3.1 Meta-analysis of the prevalence of sarcopenia among the older adult in China

We studied the prevalence of sarcopenia in the older adult in 45 literatures. The result of the meta-analysis showed that $I^2 = 97.8\%$, $p < 0.001$, which indicated that the heterogeneity among the studies was high. The sensitivity analysis was carried out by the one-by-one elimination method, and no literature that had a significant impact on the overall results was found, so the random effect model was used for combined analysis. Meta-analysis shows that the prevalence of sarcopenia among the older adult (≥60) in China is 20.7% [95% CI (18.3, 23.0%)], as shown in Figure 3 and Table 3.

3.3.2 Subgroup analysis of the prevalence of sarcopenia among the older adult in China

Meta-analysis of the prevalence of sarcopenia suggests that there is high heterogeneity among studies. We intend to use subgroup analysis to try to identify the source of clinical heterogeneity. The subgroups in this study included: gender (male; Female), age range (60–69; 70–79; ≥80), region (South/North; With Qinling Mountains and Huaihe River as the boundary, north of Qinling Mountains and Huaihe River is north, and south of Huaihe River is south), publication time (2014–2018; 2019–2024), diagnostic criteria (AWGS2019; AWGS2014). The results of the subgroup analysis are shown in Table 3.

3.3.3 Meta-analysis of the risk factor of sarcopenia among the older adult in China

We included 45 articles related to the risk factors of sarcopenia. After extraction, induction, and data processing by relevant personnel, we found that there were 10 risk factors involved in 2 or more studies. We made a meta-analysis of these risk factors of sarcopenia, and the results showed that aging, low BMI, low leg circumference, smoking, depression, osteoporosis, malnutrition and malnutrition risk were all risk factors of sarcopenia among the older adult in China. The results of the meta-analysis of influencing factors of sarcopenia are shown in Table 4.

4 Discussion

4.1 The prevalence of sarcopenia in Chinese older adult

In October 2016, sarcopenia was officially included in the International Classification of Diseases (ICD-10) disease code, marking that sarcopenia has been recognized as a new type of geriatric

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TABLE 2 General information and quality evaluation results of the included literature.

	Study	Region	Population source	Diagnostic criteria	Muscle mass assessment methods	Sarcopenia size	Sample size	AHRQ score
1	Wang et al. 2024 (24)	Yunnan-guizhou Plateau region*	Community population	AWGS (2019)	BIA	194	1,327	8
2	Dai et al. 2023 (25)	China	Community population	AWGS (2019)	BIA	919	5,016	6
3	Wan et al. 2023 (26)	Gansu	Inpatients	AWGS (2019)	BIA	232	540	6
4	Zou et al. 2023 (27)	Anhui	Community population	AWGS (2019)	BIA	214	1716	6
5	Ma et al. 2023 (28)	Shandong	Inpatients	AWGS (2019)	BIA	143	606	6
6	Chen et al. 2023 (29)	Xiangtan	Community population	AWGS (2019)	BIA	87	556	7
7	Musha et al. 2023 (30)	Xinjiang	Community population	AWGS (2019)	BIA	184	1,561	7
8	He et al. 2022 (31)	Shanghai	Community population	AWGS (2019)	BIA	275	1,407	9
9	Zhong et al. 2022 (32)	Hunan	Community population	AWGS (2019)	BIA	282	1,040	7
10	Tang et al. 2022 (33)	Inner Mongolia	Community population	AWGS	——	92	526	7
11	Han et al. 2022 (34)	Urumqi	Inpatients	SARC-F Scale	——	113	695	6
12	Li et al. 2022 (35)	Tianjin	Community population	IWGS (2011)	BIA	115	475	7
13	Zhang et al. 2022 (36)	Dali	Community population	AWGS (2019)	BIA	21	103	8
14	Li et al. 2022 (37)	Zhejiang	Community population	AWGS (2014)	BIA	278	1,420	6
15	Ko et al. 2021 (38)	Taiwan	Health examination population	AWGS (2019)	BIA	138	500	8
16	Chang et al. 2021 (39)	Taiwan	Nursing home population	AWGS (2019)	BIA	88	170	7
17	Pan et al. 2021 (40)	Xining	Inpatients	AWGS (2014)	BIA	30	150	6
18	Zhang et al. 2021 (41)	Jiangsu	Inpatients	AWGS (2019)	BIA	173	445	7
19	Liu et al. 2020 (42)	Western China*	Community population	AWGS	BIA	556	1712	7
20	Yang et al. 2020 (43)	Urumqi	Community population	EWGSOP (2018) EWGSOP (2014) AWGS (2014) IWGS (2011)	BIA	483	22 76 44 78	6
21	Chen et al. 2020 (44)	Nanjing	Community population	EWGSOP	DXA	27	249	7
22	Xu et al. 2020 (45)	Chengdu	Inpatients	AWGS (2014)	DXA	63	142	6
23	Liang et al. 2020 (46)	Beijing	Inpatients	AWGS (2014)	DXA	80	180	8
24	Meng et al. 2020 (47)	Xinxiang	Community population	AWGS (2014)	BIA	131	1,004	7
25	Che et al. 2020 (48)	Urumqi	Community population	Ishii Scale	–	287	740	8
26	Tian et al. 2020 (49)	Urumqi	Community population	AWGS (2014)	BIA	35	395	8
27	Yang et al. 2019 (50)	Suzhou	Nursing home population	AWGS (2014)	BIA	91	316	8
28	Yao et al., 2019 (51)	Xiangtan	Inpatients	AWGS	BIA	47	378	7
29	Liu et al. 2019 (52)	Chongqing	Community population	AWGS (2014)	BIA	14	247	7
30	He et al. 2019 (53)	Beijing	T2DM patients	AWGS (2014)	BIA	75	650	6
31	Hao et al. 2018 (54)	Chengdu	Inpatients	AWGS	BIA	127	407	7
32	Zeng et al. 2018 (55)	Chengdu	Nursing home population	EWGSOP AWGS IWGS	BIA	277	90 95 106	7
33	Zhang et al. 2018 (56)	Shanghai	Community population	AWGS	BIA	164	1,148	8
34	Wang et al. 2018 (57)	Chengdu	Community population	AWGS (2014)	BIA	71	915	7
35	Yang et al. 2018 (58)	Suzhou	Community population	AWGS	DXA	91	316	8
36	Liao et al. 2018 (59)	Chongqing	Nursing home population	AWGS (2014)	BIA	86	225	6

(Continued)

TABLE 2 (Continued)

	Study	Region	Population source	Diagnostic criteria	Muscle mass assessment methods	Sarcopenia size	Sample size	AHRQ score
37	Wang et al. 2018 (60)	Nantong	Outpatient	AWGS (2014)	BIA	92	407	8
38	Hai et al. 2017 (61)	Chengdu	Community population	AWGS	BIA	88	836	8
39	Hu et al. 2017 (62)	Sichuan	Community population	AWGS (2014)	DXA	112	607	7
40	Han et al. 2016 (63)	Tianjin	Community population	AWGS (2014)	BIA	99	1,069	6
41	Xia et al. 2016 (64)	Beijing	Community population	AWGS (2014)	BIA	137	683	6
42	Gao et al. 2015 (65)	Sichuan	Community population	AWGS	—	60	612	9
43	Meng et al. 2015 (66)	Taiwan	Community population	EWGSOP	DXA	44	771	7
44	Wu et al. 2014 (67)	Taiwan	Community population	EWGSOP	BIA	39	549	6
45	Yu et al. 2014 (68)	Hong Kong	Community population	EWGSOP	—	361	4,000	8

AWGS, Asian Working Group on Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; IWGS, International Working Group on Sarcopenia; SARC-F Scale, a simple five-item scoring questionnaire for sarcopenia; Ishii Scale, a simple three-item scoring questionnaire for sarcopenia; BIA, bioelectrical impedance method; DXA, dual-energy X-ray absorption method; AHRQ, Agency for Healthcare Research and Quality; T2DM, type 2 diabetes. Yunnan-guizhou Plateau region*, specifically Liupanshui City and Kunming City; Western China*, specifically Yunnan, Guizhou, Sichuan and Xinjiang.

syndrome and has attracted worldwide attention (69). In 2021, Petermann-Rocha et al. reported on the global prevalence of sarcopenia (4): the prevalence of sarcopenia in people aged 60 and above in the world is about 10–27%. A Korean meta-analysis reported that (5): the prevalence of sarcopenia in the older adult aged 60 years and older in Korea was 13.1%. A similar study in Japan reported that the prevalence of sarcopenia in the older adult (≥60) in Japan was 9.9% (6). Diz et al. (70) reported that the overall prevalence of sarcopenia in older adult people aged 60 years and above in Brazil was 17.0% [95%CI (13.0, 22.0%)]. Our results show that the prevalence of sarcopenia in the older adult in China is 20.7%, which is much higher than in similar Asian countries such as Japan (9.9%) (6) and South Korea (13.01%) (5). The specific reason may be that these Asian countries entered the aging society earlier than China, and have gradually established medical security systems that adapt to their national conditions. In general, there are differences in diet, environment, culture, and ethnically specific genetics among countries and regions, which may be the main reasons for the differences in the prevalence of sarcopenia among countries.

Subgroup analysis showed that there was an association between gender and the incidence of sarcopenia, and the prevalence of sarcopenia was higher in women than in men. Our results are consistent with Dai, Yang et al. (25, 43). The specific reasons may be related to the following reasons: First, the ovarian function of older adult women after menopause decreases, and the content of metabolic hormones (such as estradiol and androgen) in the body will also decrease, which seriously affects the generation of muscle cells and protein synthesis (71). On the other hand, women are more focused on body image management, leading to inadequate nutrient intake, which may also be related to the higher prevalence of sarcopenia in women. However, Chinese scholars Ren, Chen et al. reported the opposite result (17, 19): the prevalence of sarcopenia in older adult Chinese men was higher. They suggest that this difference may be related to the unhealthy lifestyle of men (such as smoking and drinking). As we age, the effects of an unhealthy lifestyle may significantly increase, and these factors can all contribute to sarcopenia (5). In addition, a 12-year cohort study in Japan showed that (72): men were more likely to experience muscle mass loss than women. About this difference, we suggest that future multi-center, large-sample prospective studies can be conducted to continue to explore the relationship between gender and the occurrence of sarcopenia in the older adult, to better implement precise prevention.

Sarcopenia is a well-recognized age-related degenerative condition. With the global rise in aging populations, the prevalence of sarcopenia is expected to increase significantly. This was also confirmed in our study: by age, the prevalence was highest in the older age group ≥80 years (45.4%), followed by 70–79 years (27.2%), and finally 60–69 years (15.7%). Under normal physiological conditions, human skeletal muscle mass reaches its peak at around 25 years of age, and then the number and volume of skeletal muscle fibers begin to decline, and the decline rate gradually accelerates with the increase of age, which is the result of synergistic regulation of multiple aging mechanisms in the human body (1). In addition, with the growth of age, the incidence of various basic diseases in the older adult will also increase, which will also affect the regulation of various hormones and the absorption of nutrients, thereby indirectly affecting the decline of muscle mass (73). Compared with the north (19.0%), the prevalence of sarcopenia was higher in the older adult in the south (21.7%). Our study was consistent with Mao et al. (74), but some studies reported the opposite result (17). China's vast territory, the climate environment, and the dietary habits of different regions are quite different, which may be the main reason for the difference in prevalence. The climate in the north is mostly cold. Due to the influence of climate, the local people's diet mainly includes "beef and mutton, dairy products and nuts," and the incidence of malnutrition and malnutrition risk is relatively low (75). So far, there are few studies on regional differences in the prevalence of sarcopenia in China, which can be further verified with more relevant epidemiological studies in the future.

In addition to the differences in demographic characteristics, the different diagnostic criteria of sarcopenia also directly affect the detection rate of sarcopenia. Based on the fact that China is in Asia, and to ensure the comparability of this study in Asian populations, we selected AWGS for subgroup analysis in terms of diagnostic criteria. Compared with AWGS (2014), the latest AWGS (2019) has

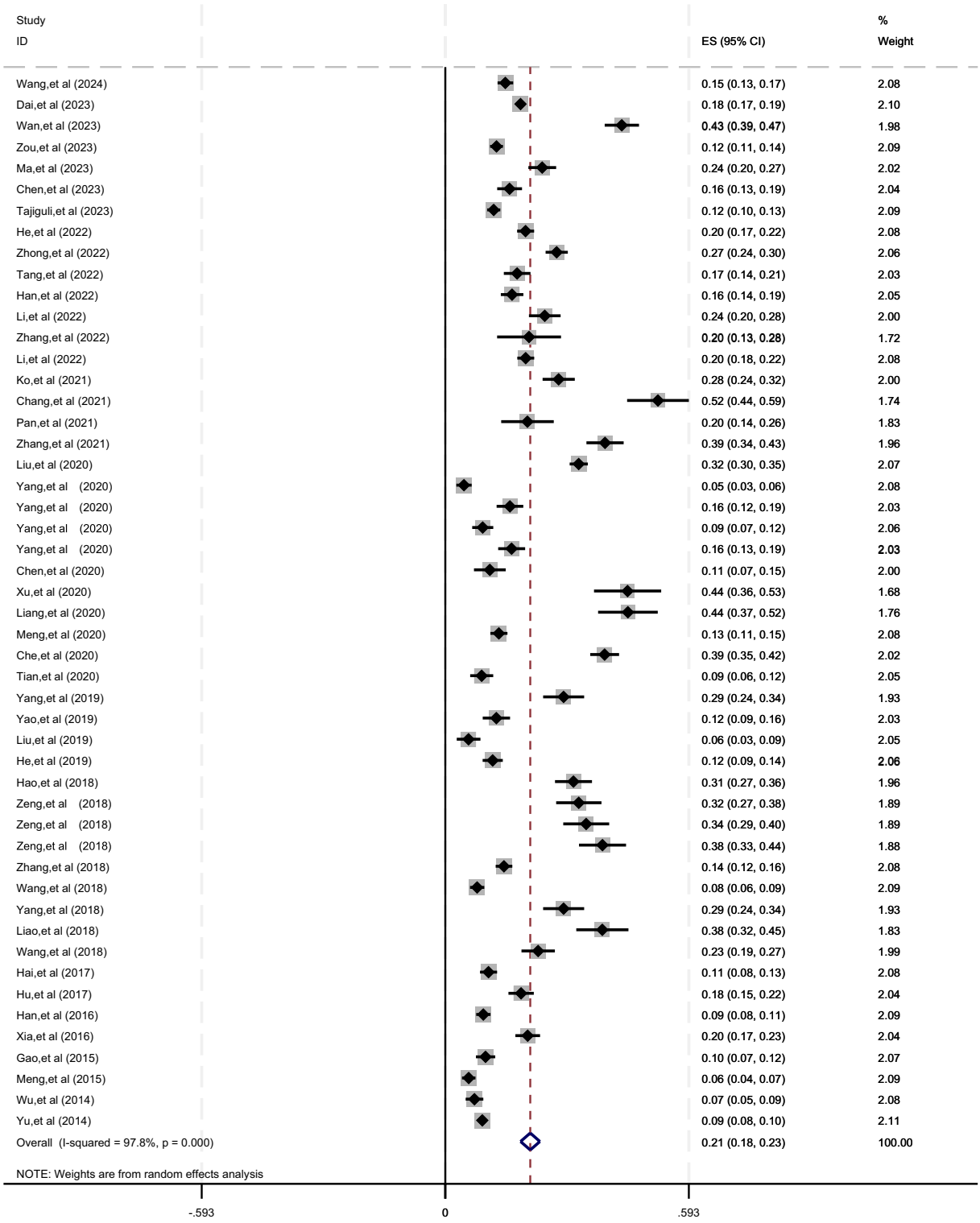

FIGURE 3
Meta-analysis forest figure of the prevalence of sarcopenia among the older adult in China.

significantly improved the evaluation criteria of walking speed and male grip strength (among which, walking speed has been increased from 0.8 m/s to 1.0 m/s, and male grip strength has been increased from 26 kg to 28 kg). As a result, the AWGS (2019) will have a higher rate of sarcopenia detection, and our study also confirms this result. Domestic studies on the evaluation of sarcopenia in the older adult based on AWGS (2014) criteria also generally reported a low incidence [Xinxiang 13.1% (47), Chengdu 10.6% (61), Tianjin 9.3% (63)]. Finally, in the last 5 years, the prevalence of sarcopenia in the older adult in China has been on

TABLE 3 Summary table of meta-analysis results of prevalence of sarcopenia in the older adult in China.

Subgroup	Number of included literature	Results of heterogeneity test		Effect model	The prevalence % (95%CI)
		I^2	p		
Total prevalence rate (24–68)	45	99.2%	<0.001	Random effect model	20.7 (18.3, 23.0)
Sex					
Men (24, 25, 27, 29–33, 35, 37–41, 43–45, 47, 48, 50, 51, 54–64, 66, 67)	34	94.7%	<0.001	Random effect model	19.2 (16.6, 21.8)
Women (24, 25, 27, 29–33, 35, 37–41, 43–45, 47, 48, 50, 51, 54–64, 66, 67)	34	96.5%	<0.001	Random effect model	21.6 (18.7, 24.5)
Age					
60–69 (26, 27, 31–33, 35, 41, 48, 64, 65)	10	96.0%	<0.001	Random effect model	15.7 (10.6, 20.7)
70–79 (26, 27, 31–33, 35, 41, 48, 64, 65)	10	95.4%	<0.001	Random effect model	27.2 (20.2, 34.3)
≥80 (26, 27, 31–33, 35, 41, 48, 64, 65)	10	88.8%	<0.001	Random effect model	45.4 (35.9, 54.9)
Region					
South (24, 29, 31, 32, 36–39, 41, 44, 45, 50–52, 54–62, 65–68)	27	97.7%	<0.001	Random effect model	21.7 (18.5, 24.9)
North (26, 28, 30, 33–35, 40, 43, 46–49, 53, 63, 64)	15	97.6%	<0.001	Random effect model	19.0 (14.9, 23.1)
Publication year					
2014–2018 (54–68)	15	97.3%	<0.001	Random effect model	19.2 (15.8, 22.7)
2019–2024 (24–53)	30	97.6%	<0.001	Random effect model	21.4 (18.4, 24.3)
Diagnostic criteria					
AWGS (2019) (24–32, 36, 38, 39, 41)	13	97.6%	<0.001	Random effect model	24.5 (20.3, 28.7)
AWGS (2014) (37, 40, 43, 45–47, 49, 50, 52, 53, 57, 59, 60, 62–64)	16	96.4%	<0.001	Random effect model	19.3 (15.5, 23.1)

the rise. It increased from 19.2% in 2014–2018 to 21.4% in 2019–2024. We infer that this difference may be due to past and present differences in health and medical resources. At the same time, the widening of diagnostic criteria may also be one of the reasons for the significant increase in the prevalence of sarcopenia reported in China in recent years.

4.2 The risk factor of sarcopenia in Chinese older adult

The occurrence of sarcopenia in the older adult is related to many factors. Our study shows that aging, low BMI, low calf circumference, smoking, depression, osteoporosis, malnutrition and malnutrition risk are risk factors for sarcopenia in the older adult in China.

There is no doubt that aging is one of the risk factors for sarcopenia. Pang et al. reported the epidemiology of sarcopenia in the Singapore community population (76): the prevalence of sarcopenia was 13.6% in the community as a whole (21–90 years), but 32% in people over 60 years of age. A study in Thailand also found that (77): older adult people (≥80 years old) had the highest prevalence of sarcopenia (68%). A 12-year prospective population study in Sweden showed that (78): even subjects without sarcopenia had a 5.1% probability of developing suspected sarcopenia over 10 years. This is consistent with our findings that the older people get, the higher their risk of sarcopenia.

Secondly, bad lifestyle habits can also affect the prevalence of sarcopenia, of which smoking is considered to be a risk factor for sarcopenia. Previous studies have reported that the risk of sarcopenia in older adult smokers in Asia is 2.69 times that of non-smokers (79). The risk of sarcopenia among older smokers in Europe is 2.36 times that of non-smokers (80). We speculate that the reason may be related to the following reasons: on the one hand, smoking directly damages the health of skeletal muscle. Smoking can damage muscle metabolism, increase inflammation and oxidative stress, increase the overexpression of genes related to muscle atrophy, and activate various intracellular signaling pathways, thus causing skeletal muscle injury (81). On the other hand, smoking will increase the risk of cancer, respiratory diseases, and cardiovascular and cerebrovascular diseases (82), thus increasing energy consumption and reducing the activity capacity of the older adult, indirectly leading to the occurrence of sarcopenia. Therefore, not smoking or quitting early may be important for the prevention and treatment of sarcopenia.

There is also a link between depression, osteoporosis, and sarcopenia. Turkish scholar Olgun-Yazar et al. pointed out that (83): depression and sarcopenia are closely related. Symptoms associated with depression, such as weakness, loss of appetite, and decreased activity, may contribute to the onset and progression of sarcopenia (84). Meanwhile, some inflammatory cytokines secreted by the musculoskeletal system are closely related to the occurrence of depression, such as IL-6, TNF-a, and 5-HT (85). In the early

TABLE 4 Summary table of meta-analysis results of risk factors of sarcopenia in the older adult in China.

Risk factor	Number of included literature	Results of heterogeneity test		Effect model	Result	
		I^2	*p*		OR (95%CI)	*p*
Sex (women vs. men) (24–26, 31, 36, 38, 39, 43, 47, 54, 65–68)	14	94.3%	<0.001	Random effect model	1.056 (0.936, 1.191)	0.376
Age (Continuous variable) (24, 25, 29, 32, 38, 43, 45, 49–51, 56, 59, 65, 67, 68)	15	67.5%	<0.001	Random effect model	1.128 (1.117, 1.139)	<0.001*
BMI (Continuous variable) (27, 29, 31, 33, 38, 45, 47, 49–52, 54, 59, 66, 67)	15	82.0%	<0.001	Random effect model	0.706 (0.686, 0.727)	<0.001*
Leg circumference (Continuous variable) (29, 47, 48, 55)	4	89.3%	<0.001	Random effect model	0.743 (0.702, 0.786)	<0.001*
Smoking (Yes vs. NO) (24, 47, 54)	3	66.8%	0.049	Random effect model	2.092 (1.469, 2.977)	<0.001*
Depression (Yes vs. NO) (31, 36, 41, 47)	4	0.0%	0.508	Fixed effect model	2.432 (1.716, 3.447)	<0.001*
Osteoporosis (Yes vs. NO) (34, 41, 49, 59)	4	0.0%	0.980	Fixed effect model	2.778 (1.918, 4.026)	<0.001*
Malnutrition (Yes vs. NO) (32, 55)	2	0.0%	0.587	Fixed effect model	2.656 (1.679, 4.200)	<0.001*
Malnutrition risk (Yes vs. NO) (28, 32, 39)	3	36.9%	0.205	Fixed effect model	2.224 (1.712, 2.891)	<0.001*
Malnutrition and malnutrition risk (Yes vs. NO) (36, 37, 65)	3	89.5%	<0.001	Random effect model	1.641 (1.334, 2.019)	<0.001*

prevention and treatment of sarcopenia, it is necessary to pay attention to and care for the depressed older adult.

Osteoporosis is a systemic bone metabolic disease characterized by low bone mass and mass, which can increase susceptibility to sarcopenia (86). Sarcopenia and osteoporosis are both associated with aging, low quality of life, and low condition of health, and they often occur together. At present, some scholars have shown that there is a close relationship between muscle and bone, namely, osteosarcopenia, and sarcopenia-osteoporosis (87, 88). Maurel et al. (89) investigated the relationship between sarcopenia and osteoporosis and showed that osteoporosis increases the risk of developing sarcopenia. Our study also found that osteoporosis is a risk factor for sarcopenia. Specific reasons may be related to the connection between muscle and bone. For example, Bone cells secrete osteocalcin, insulin-like, etc., affecting muscle quality and function, and the decrease of bone cells will lead to the decline of muscle mass and function (90). Therefore, we should pay attention to the role of bone health in the occurrence of sarcopenia, and reduce the incidence of sarcopenia while maintaining bone health in the older adult.

Finally, there is also a close relationship between the nutritional status of the body and sarcopenia (91). BMI and calf circumference can be used to evaluate the nutritional status of the older adult. Among them, calf circumference is currently recognized as an alternative marker of muscle mass and is used as one of the diagnostic criteria for sarcopenia (92, 93). To a certain extent, BMI can also reflect the nutritional status of the body. A higher BMI is a protective factor for sarcopenia and is positively correlated with muscle mass (94). It is worth noting that there is a special condition here, that is, sarcopenic obesity. This is a condition that occurs based on excessive obesity, with decreased muscle tissue and increased fat infiltration between muscle fibers and muscle cells (10, 12). Medical and health workers should pay attention to health education: the older adult can properly maintain a high BMI level under the premise of not obesity. In addition, physiological evidence shows that when the body is in poor nutritional condition, amino acids, and muscles are broken down and oxidized to produce energy to maintain normal life functions. If sustained for a longer period, it will result in a negative nitrogen balance, as well as a gradual loss of muscle mass and function (95). In addition, poor nutritional status can also lead to micronutrient deficiencies (such as vitamin D and vitamin B12), which further leads to muscle loss and decreased function (96, 97). In conclusion, timely screening and assessment of the nutritional status of the older adult may be an effective strategy for early detection, diagnosis, and management of patients with sarcopenia. Proven and easy-to-use nutrition screening tools are necessary, such as a simple nutritional assessment profile (Mini Nutritional Assessment Short Form, MNA – SF) can be used to determine the nutritional status of the older adult and the poor nutrition risk (98).

So far, this study is currently the most geographically diverse and has the highest number of subjects in the epidemiological study of sarcopenia in older adult people in China, and involves risk factors for sarcopenia. We reported the latest data and risk factors for sarcopenia in older adult people aged 60 and above in China. We conducted differences in gender, age, region (southern/northern), diagnostic criteria, and other factors through subgroup analysis. These works provide more information and evidence-based evidence for the epidemiology of sarcopenia and are the first step in developing preventive measures or health services for the older adult. In addition, our study also found that aging, low BMI, low calf circumference, smoking, depression, osteoporosis, malnutrition and malnutrition risk are risk factors for the development of sarcopenia in the older adult in China. For the older adult population with high-risk factors, timely prevention and screening is very necessary.

There are some limitations to the study. First, we collected representative data for each region but were limited by the characteristics of individual studies and differences between different cities, which may affect comparisons between included studies.

Secondly, some studies reported prevalence rates for different age groups and different risk factors, and relevant data could not be included in subgroups, resulting in fewer studies included in some subgroups (such as smoking, malnutrition, and malnutrition, etc. risk factors), which may also affect comparisons between included studies. Finally, this study is based primarily on evidence from observational studies that cannot provide information about causation for the observed associations. Currently, there is a lack of high-quality prospective cohort studies on sarcopenia, especially in exploring the risk factors for sarcopenia. In addition to focusing on clinical patients susceptible to sarcopenia, cohort studies with accurate measurements of muscle quantity and function in the general healthy population are needed to provide evidence for developing primary prevention strategies.

5 Conclusion

The results of this study show that the overall prevalence of sarcopenia in the older adult aged 60 and above in China is relatively high (20.7%), and it shows a gradual increasing trend in the past 5 years. This phenomenon should arouse the attention and concern of public health departments. Finally, we suggest that the public health sector should carry out early screening, intervention, and management of sarcopenia promptly, especially for the older adult population with high-risk factors (such as osteoporosis and depression).

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

SM: Writing – original draft, Writing – review & editing, Data curation, Formal analysis, Investigation, Project administration, Software. XH: Writing – original draft, Data curation, Investigation, Software, Writing – review & editing. XF: Conceptualization, Writing – review & editing, Data curation, Formal analysis, Software. XZ: Writing – review & editing, Data curation, Software. MT: Writing – review & editing, Data curation, Project administration, Software, Supervision, Validation. WL: Writing – original draft, Writing – review & editing, Data curation, Methodology, Software. WZ: Writing – original draft, Conceptualization, Data curation, Formal analysis, Software. XS: Writing – original draft, Writing – review & editing, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision. KL: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1415398/full#supplementary-material

SUPPLEMENTARY FILE 1
The detailed information of literature retrieval strategy.

SUPPLEMENTARY FILE 2
The detailed results of literature evaluation.

SUPPLEMENTARY FILE 3
The general information of included literature.

SUPPLEMENTARY FILE 4
The corresponding PRISMA checklist.

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Exploring the relationship between ultrasound parameters and muscle strength in older adults: a meta-analysis of sarcopenia-related exercise performance

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Introduction: Ultrasound (US) imaging has emerged as a promising tool for assessing age-related muscle changes. This meta-analysis aimed to comprehensively evaluate the associations between US parameters and muscle strength, as well as sarcopenia-related functional performance in older adults by integrating data from multiple studies.

Methods: A systematic literature search was conducted in PubMed, Web of Science, and Embase until June 2023. Studies reporting Pearson's correlation coefficients between US parameters [echo intensity (EI), muscle thickness (MT), cross-sectional area (CSA), pinnations angle (PA), fascicle length (FL)] and measures of muscle strength or physical performance in older adults were included. Effect sizes were pooled using a random-effects model and presented in forest plots. Heterogeneity was assessed using I^2, and publication bias was evaluated using Egger's test.

Results: Twenty-eight studies met the inclusion criteria. Meta-analysis revealed moderate to strong correlations between EI, MT, and CSA with muscle strength. However, no significant associations were found between US parameters and gait speed. For chair stand tests, the strength of associations varied by test type, with weak correlations observed between echo intensity and muscle thickness with sit-to-stand tests. US parameters did not exhibit significant correlations with the Timed Up and Go test.

Conclusion: Ultrasonographic measurements of echo intensity (EI) and muscle thickness (MT) demonstrated moderate to strong correlations with muscle strength and functional assessments related to sarcopenia. To enhance the accuracy of sarcopenia diagnosis and the effectiveness of management strategies, there is a need for larger, longitudinal studies that evaluate a comprehensive range of ultrasonographic parameters.

Systematic review registration: https://inplasy.com, identifier INPLASY202410086.

KEYWORDS

ultrasonography, sarcopenia, muscle strength, physical functional performance, older adult

1 Introduction

Sarcopenia, characterized by the age-related loss of muscle mass, strength, and function, has emerged as a significant clinical concern impacting the health and wellbeing of older adults worldwide (1). The European Working Group on Sarcopenia in Older People (EWGSOP) reports a prevalence ranging from 9.9 to 40.4% among community-dwelling older individuals, (2) highlighting the urgency for effective diagnostic and therapeutic strategies. This geriatric syndrome is associated with an increased risk of adverse outcomes, such as falls, fractures, physical disability, and a diminished quality of life (3, 4). In response to this clinical challenge, researchers have increasingly explored the potential of ultrasound (US) imaging as a non-invasive, cost-effective, and readily accessible tool for assessing muscle quality and morphology in older adults.

It is important to note that while there is a global recognition of sarcopenia as a significant health issue, there are notable differences in its definition and diagnostic criteria across regions (1). The EWGSOP and the Asian Working Group for Sarcopenia (AWGS) have both established guidelines, but with some distinct features. The EWGSOP emphasizes muscle strength as the primary parameter for identifying sarcopenia, followed by muscle quantity or quality, and physical performance (2). In contrast, the AWGS recommends simultaneous measurement of both muscle strength and muscle mass as the core diagnostic elements, with physical performance as an indicator of severity (5). These differences reflect the potential influence of ethnic and cultural factors on sarcopenia manifestation and highlight the need for population-specific approaches in its assessment and management (6).

Given the complexity and variability in sarcopenia definitions and manifestations across populations, there is a pressing need for reliable, accessible, and versatile diagnostic tools. In response to this clinical challenge, researchers have increasingly explored the potential of US imaging as a non-invasive, cost-effective, and readily accessible tool for assessing muscle quality and morphology in older adults. US imaging offers a non-invasive, cost-effective, tolerable, rapid, real-time, and portable method for evaluating muscle characteristics, rendering it a valuable asset in the clinical assessment and management of sarcopenia. Its ability to accurately and reliably measure muscle quality, with high repeatability, has been well-established (4). Commonly utilized US parameters, including muscle thickness (MT), cross-sectional area (CSA), pennation angle (PA), fascicle length (FL), and echo intensity (EI), provide insights into muscle morphology, structure, and quality, finding extensive application in sarcopenia research (6, 7). Notably, the updated EWGSOP consensus recommends US as an effective and reliable tool for measuring muscle quality, affirming its utility in sarcopenia diagnosis (2).

Our previous meta-analysis, (8) focused solely on the association between EI and muscle strength/functional performance. The present study aims to conduct a comprehensive examination of multiple US parameters in relation to sarcopenia-related outcomes in older adults. Unlike most previous studies that explored specific US parameters and muscle strength or functional performance separately, this review systematically investigates the collective associations across various US measurements. By combining data across studies through meta-analysis, we aim to provide a quantitative synthesis of the correlations, offering more robust evidence to guide the clinical application of US in sarcopenia assessment and management.

Previous studies have indicated a potential correlation between US measurements and muscle function. For instance, quadriceps MT (r = 0.41) (9) and CSA (r = 0.78) (10) have demonstrated correlated with knee extension isometric strength. Additionally, quadriceps MT (r = 0.52) and EI (−0.33) have shown correlations with handgrip strength in older adults (11). Moreover, evidence indicates significant associations between US parameters and sarcopenia-related exercise performance. Studies identified negative correlations between lower limb muscle FL (r = −0.29) and PA (r = −0.30) with gait speed. (12) Furthermore, the EI of the vastus lateralis muscle and Timed Up and Go (TUG) (r = 0.48), (13) as well as the 5 times sit-to-stand test (5TSTS) (r = 0.36) (14), demonstrate significant associations. These studies strongly suggest that structural parameters obtained through US may be associated with muscle strength and functional performance in older adults. However, the findings are limited by the individual study designs, sample sizes, and population characteristics. A meta-analytic approach is needed to provide a more comprehensive and reliable understanding by quantitatively synthesizing and consolidating these associations across multiple studies.

Therefore, this meta-analysis aims to comprehensively examine the associations between US parameters, muscle strength, and sarcopenia-related exercise performance in older adults by synthesizing data across studies. The findings will guide clinical application of US assessments for evaluating muscle health and function, facilitating personalized sarcopenia management to mitigate its impacts and promote healthier aging.

2 Materials and methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (15). Additionally, the review has been registered on Inplasy.com (INPLASY202410086).

2.1 Search strategy

A systematic search strategy was employed using Boolean operators on several databases including PubMed, Web of Science, and Embase up until June 2023. Keywords and Boolean operators were modified according to each database's search strategy, and searches were restricted to studies involving humans, written in English, and reported in peer-reviewed journals. The search strategy is presented in Supplementary Table 1.

2.2 Selection criteria

Inclusion criteria Studies must meet the following criteria.

(a) Participants were healthy community residents aged 60 years or older without major neurological and musculoskeletal disorders (b) Muscle mass testing using US and reporting at least one direct assessment of muscle strength or Sarcopenia-related

exercise performance (c) Observational studies, including cross-sectional studies, cohort studies, and few case-control (d) Published studies (English).

Articles were excluded if: (a) The participant was currently on medication or had an injury that limited physical activity and independence in daily living (b) The study was conducted in an animal model (c) Received interventions other than usual care or placebo and studies used RCTs experiment (d) The result is partially unable to extract the correlation coefficient (e) Reviews, abstracts, case reports or duplicate published articles (f) Non-English articles.

The selection process was carried out by two independent researchers who screened titles and abstracts of all studies based on the inclusion and exclusion criteria, then reviewed the full text of the remaining studies. Any disagreements were resolved through discussion.

2.3 Data extraction

The data extraction process involved coding for author information, year of publication, and population characteristics (sample size, sex, and mean age). The correlation coefficient *r* or standardized beta coefficient between US parameters and two continuous muscle strength or physical function variables were extracted. The test modality/results in the assessment of muscle strength and Sarcopenia-related exercise performance were also coded. Muscle strength was categorized into lower extremity maximum strength (i.e., maximal voluntary force/torque of the force-/torque-time curve [MVC]), explosive force (i.e., rate of force/torque development [RFD/RTD]), handgrip strength (i.e., assessed with a handheld dynamometer [HGS]), while exercise performance indicators was divided into gait speed and mobility. Gait speed (e.g., usual gait speed [UGS] and maximum gait speed [MGS]), chair stand test [e.g., 30-s sit-to-stand test (30SS), 5 times sit-to-stand test (5TSTS), and Timed Up and Go (TUG) test, respectively] were used to classify physical function. If no correlation results were reported, the authors were contacted to obtain the missing information. If the author did not respond, the study was excluded.

2.4 Data quality

The risk of bias in the included studies was assessed using the Joanna Briggs Institute (JBI) Analytic Cross-Sectional Study Quality Checklist (Supplementary Table 2). The methodological quality of the selected studies was evaluated based on eight items that assessed inclusion criteria, study participants and setting, criteria for condition measurement, validity and reliability of exposure and outcome measures, confounding factors and resolution strategies, and statistical analysis. Two authors evaluated each item, which was rated as "yes," "no," "unclear," or "not applicable."

2.5 Statistical analysis

The meta-analysis was conducted using Comprehensive Meta-Analysis (CMA) software, version 3.3.070, to analyze the Pearson Product Moment correlation coefficients (*R*-value) obtained from the included studies. The *R*-values were converted into normally distributed variables (z-transformed *Rz*-value) using Fisher's z transformation (16). The conversion formula is:

$$r_z = 0.5\left[ln\,(1+r) - ln\,(1-r)\right]$$

where ln is the natural logarithm.

The beta coefficient (β) is converted to a value of *r* using the following formula (17).

$$r = 0.98\beta + 0.5\gamma \begin{cases} \text{if} & \beta \geq 0, \gamma = 1; \\ & \beta < 0, \gamma = 0. \end{cases}$$

The weights of the study were calculated based on the standard errors (SE). The calculation formula is:

$$SE = \frac{1}{\sqrt{(N-3)}}$$

where *n* is the sample size.

The method of inverse variance using random-effect models was chosen, and meta-analysis of the transformed *r* values was then conducted. To interpret the results, pooled r_z values were retransformed to *r* values with inverse Fisher *z* transformation:

$$r = \left(\frac{e^{2rz}-1}{e^{2rz}+1}\right)$$

where e is approximately equal to 2.718 and r_z is Fisher-z transformed *r* value (17).

A random-effects model was selected for the meta-analysis.

Correlations (positive or negative) were classified as small ($r < 0.3$), medium ($0.3 \leq r \leq 0.5$), or large ($r > 0.5$) (18). Forest plots were used to display studies with 95% confidence intervals and the combined coefficients. The *r z* values were reverse converted to *r* values to classify and interpret the relevant sizes. The heterogeneity of the results between studies was evaluated using the I^2 index, where $I^2 \leq 25\%$ was considered to indicate low heterogeneity, $25\% < I^2 < 75\%$ was considered to indicate moderate heterogeneity, and $I^2 \geq 75\%$ was considered to indicate high heterogeneity (19). Finally, to address the possibility of publication bias, we examined funnel plots and used Begg and Mazumdar rank correlations. The Trim and Fill procedure (20) was applied if evidence of publication bias was noted.

3 Results

3.1 Search characteristics

During the initial database search until June 2023, a total of 9,591 articles were retrieved. After removing duplicates ($n = 4{,}974$) and excluding 4,617 articles based on title/abstract, 174 articles remained and were assessed for eligibility. Eventually, 28 articles were included in the meta-analysis (Figure 1). A total of 3,599 individuals were included in this review, and the mean age was 73.3 ± 4.6. Sample sizes ranged from 12 to 1,239. Supplementary Table 3 details the baseline characteristics of the included studies.

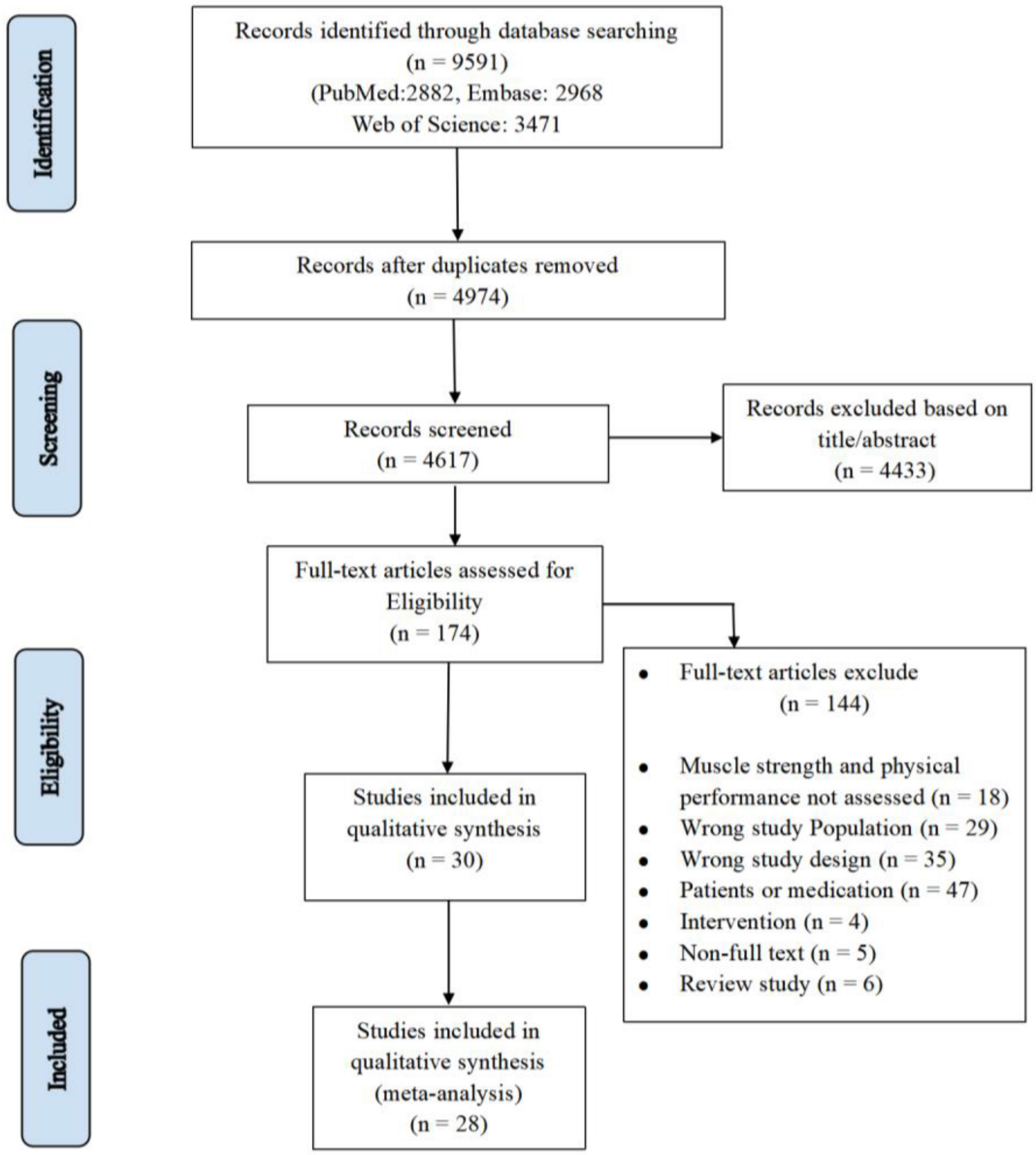

FIGURE 1
Flow chart selection process.

3.2 Association between US parameters and muscle strength

3.2.1 Maximal strength

Fifteen studies (involving 1,861 participants) analyzed the association between EI and maximal strength in older persons with healthy issues (9, 11, 14, 21–32). The results detected a significant strong correlation negative between EI and maximum strength (r = −0.56, 95% CI: −0.75 to −0.29, P < 0.001, I^2 = 38.92). There was no indication of publication bias (t = 1.22, p = 0.24; Supplementary Figure 1A).

Thirteen studies (involving 2,836 participant) analyzed the association between MT and maximal strength in healthy older persons (9, 11, 14, 21–26, 28, 30, 32, 33) and a significant moderate correlation was detected between MT and maximal strength (r = 0.43, 95% CI: 0.35 to 0.50, P < 0.001, I^2 = 59.20). Given indication of publication bias (t = 4.58, p < 0.01; Supplementary Figure 1B), the Trim and Fill procedure was applied, yielding a mean effect size of 0.47 (95% CI = 1.13 to 3.22).

Three research studies (comprising 58 participants) examined the link between CSA and maximal strength (10, 27, 31). The results indicated a significant strong correlation between CSA and maximal strength (r = −0.67, 95% CI: 0.35 to 0.85, P < 0.001, I^2 = 50.38). Two research studies (comprising 62 participants) examined the link between PA and maximal strength (23, 33). The results indicated a weak correlation between PA and maximal strength (r = 0.06, 95% CI: −0.50 to 0.59, P = 0.827, I^2 = 71.73) (Figure 2). There was also no indication of publication bias (t = 1.48, p = 0.37; Supplementary Figure 1C).

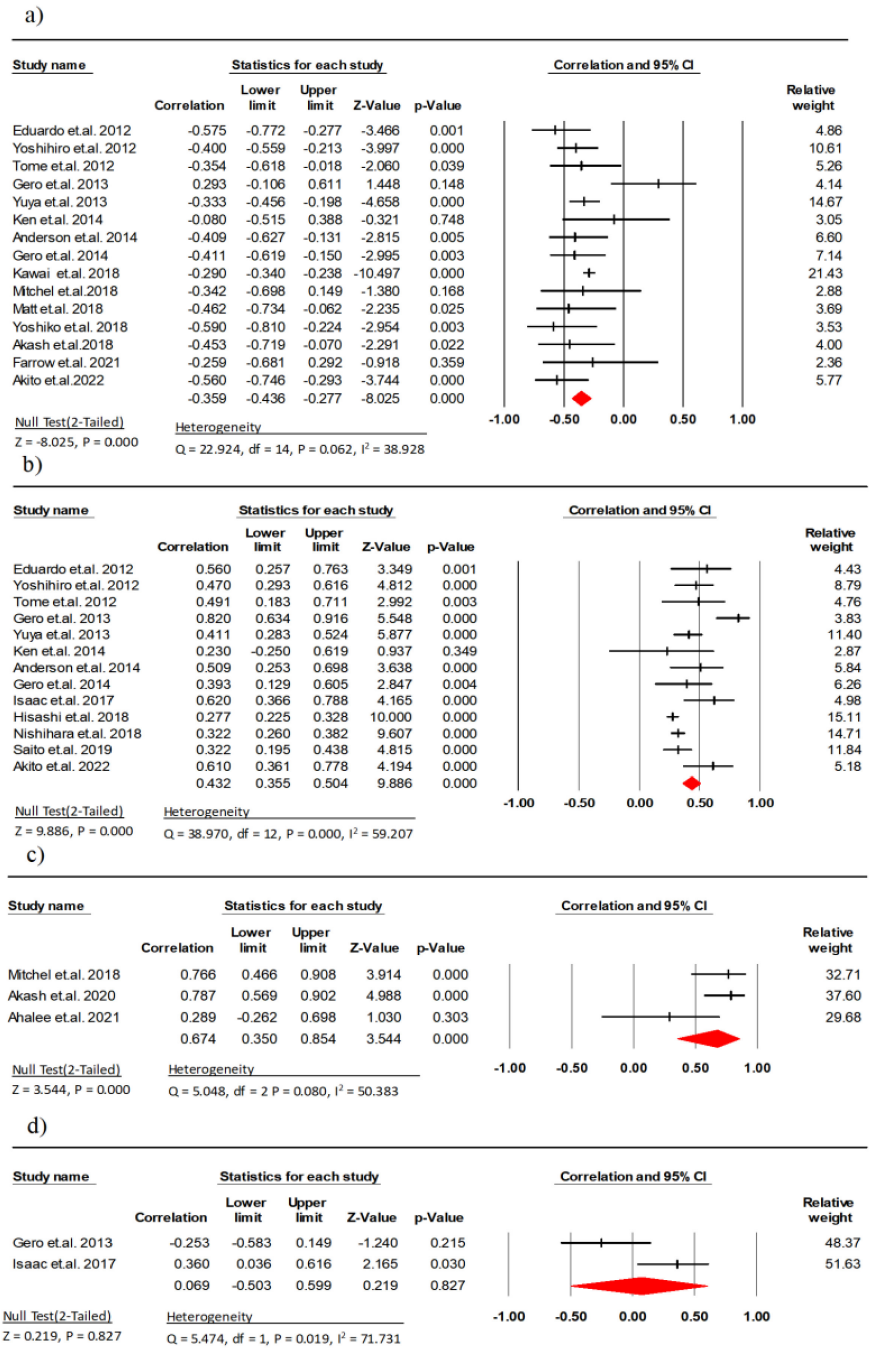

FIGURE 2
Associations (r_z values) between maximal strength and **(a)** echo intensity, **(b)** muscle thickness, **(c)** cross-sectional area, **(d)** pennation angle. CI, confidence interval; df, degrees of freedom.

3.2.2 Explosive power

Two studies (involving 245 participant) analyzed the association between EI and explosive power in healthy older persons (9, 34) and a significant moderate negative correlation was detected between EI and explosive power ($r = -0.47$, 95% CI: -0.88 to 0.35, $P = 0.256$, $I^2 = 86.68$).

Two research studies (comprising 245 participants) examined the link between MT and explosive power (9, 34). The results indicated a strong correlation between MT and explosive power ($r = 0.53$, 95% CI: -0.16 to 0.87, $P = 0.129$, $I^2 = 85.51$) (Figure 3).

3.2.3 Handgrip strength

Three research studies (comprising 199 participants) examined the link between EI and handgrip strength (11, 29, 35). The results indicated a moderate negative correlation between EI and handgrip strength ($r = -0.32$, 95% CI: -0.44 to -0.19, $P < 0.001$, $I^2 = 0.000$). There was no indication of publication bias ($t = 2.98$, $p = 0.20$; Supplementary Figure 2A).

Three research studies (comprising 1,071 participants) examined the link between MT and explosive power (11, 34, 36). The results indicated a weak correlation between MT and explosive

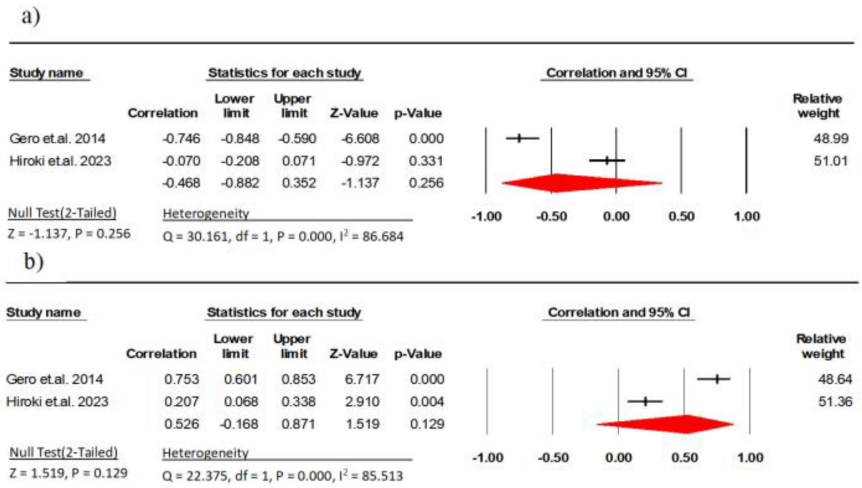

FIGURE 3
Associations (r_z values) between explosive power and **(a)** echo intensity, **(b)** muscle thickness. CI, confidence interval; df, degrees of freedom.

power (r = 0.25, 95% CI: 0.11 to 0.39, P = 0.001, I^2 = 67.31) (Figure 4). There was no indication of publication bias (t = 0.80, p = 0.56; Supplementary Figure 2B).

3.3 Association between US parameters and physical function

3.3.1 Gait speed

Nine studies (involving 614 participants) investigated the association between EI and gait speed (9–11, 29, 30, 32–34, 37). The combined effect size for EI and gait speed was r = −0.01 (95% CI: −0.07 to −0.06, P = 0.67, I^2 = 58.00), indicating no linear correlation between the two with moderate heterogeneity. Subgroup analysis showed a weak negative correlation between usual gait speed (UGS) and EI (r = −0.17, 95% CI: −0.27 to −0.07, P < 0.001, I^2 = 0.000), while there was a weak positive correlation between maximal gait speed (MGS) and EI (r = 0.10, 95% CI: 0.01 to 0.18, P = 0.018, I^2 = 55.82) (Figure 5). There was no indication of publication bias (t = 0.70, p = 0.49; Supplementary Figure 3A).

Ten studies (involving 1,523 participants) investigated the association between MT and gait speed (9, 11, 23, 26, 28, 30, 34, 35, 38, 39). The combined effect size for MT and gait speed was r = −0.08 (95% CI: −0.12 to −0.04, P = 0.78, I^2 = 69.01), indicating no linear correlation between the two with moderate heterogeneity. Subgroup analysis showed a weak negative correlation between UGS and MGS with MT (r = −0.09, 95% CI: −0.15 to −0.03, P = 0.002, I^2 = 0.000) (r = −0.08, 95% CI: −0.13 to −0.02, P < 0.001, I^2 = 0.000) (Figure 3). Due to indication of publication bias (t = 2.01, p = 0.03; Supplementary Figure 3B), the Trim and Fill procedure was applied, adjusting the mean effect size to 0.79 (95% CI = −0.11 to 3.33).

Five studies (involving 222 participants) investigated the association between FL and gait speed (23, 26, 30, 32, 38). The combined effect size for FL and gait speed was r = −0.03 (95% CI: −0.15 to 0.09, P = 0.602, I^2 = 0.000), indicating no linear correlation between the two. Subgroup analysis showed a weak negative correlation between UGS and MGS with FL (r = −0.06, 95% CI: −0.27 to 0.14, P = 0.528, I^2 = 37.31) (r = −0.01, 95% CI: −0.16 to 0.14, P = 0.855, I^2 = 0.000) (Figure 5). Moreover, there was no indication of publication bias (t = 0.36, p = 0.72; Supplementary Figure 3C).

Four studies (involving 123 participants) investigated the association between PA and gait speed (23, 26, 30, 38). The combined effect size for PA and gait speed was r = 0.11 (95% CI: −0.05 to 0.27, P = 0.94, I^2 = 0.000), indicating weak linear correlation between the two. Subgroup analysis showed a weak correlation between UGS and PA (r = 0.24, 95% CI: 0.02 to 0.43, P = 0.031, I^2 = 0.000), while there was a weak negative correlation between MGS and PA (r = −0.05, 95% CI: −0.29 to 0.19, P = 0.674, I^2 = 0.000) (Figure 5). Across studies, no indication of publication bias (t = 0.19, p = 0.85; Supplementary Figure 3D) was observed.

3.3.2 Chair stand test

Eleven studies (involving 931 participants) investigated the association between EI and the chair stand test (9–12, 32–34, 37, 39–41). The combined effect size of EI and chair stand test was r = 0.10 (95% CI: −0.04 to 0.24, P = 0.15, I^2 = 75.68), with a weak statistical correlation and considerable heterogeneity. Subgroup analyses showed a weak negative correlation between EI and the 5TSTS and the 30SS (r = −0.26, 95% CI: −0.06 to 0.53, P = 0.11, I^2 = 69.17; r = −0.26, 95% CI: −0.54 to 0.07, P = 0.12, I^2 = 7.84, respectively). There was a weak correlation between EI and the TUG (r = 0.15, 95% CI: −0.02 to 0.32, P = 0.08, I^2 = 55.39) (Figure 6). The Begg and Mazumdar rank correlation (t = 0.51, p = 0.61) and the symmetrical funnel plot (Supplementary Figure 4A) suggest publication bias was absent.

Twelve studies (involving 1,605 participants) investigated the association between MT and the chair stand test (11–14, 25, 30, 33, 34, 36, 39, 41, 42). The combined effect size of MT and chair stand test was r = −0.15 (95% CI: −0.23 to −0.07, P < 0.001, I^2 = 67.55), with a weak statistical correlation and moderate heterogeneity. Subgroup analyses showed a moderate negative weak between MT and the 5TSTS and the TUG (r = −0.24, 95% CI: −0.35 to −0.12,

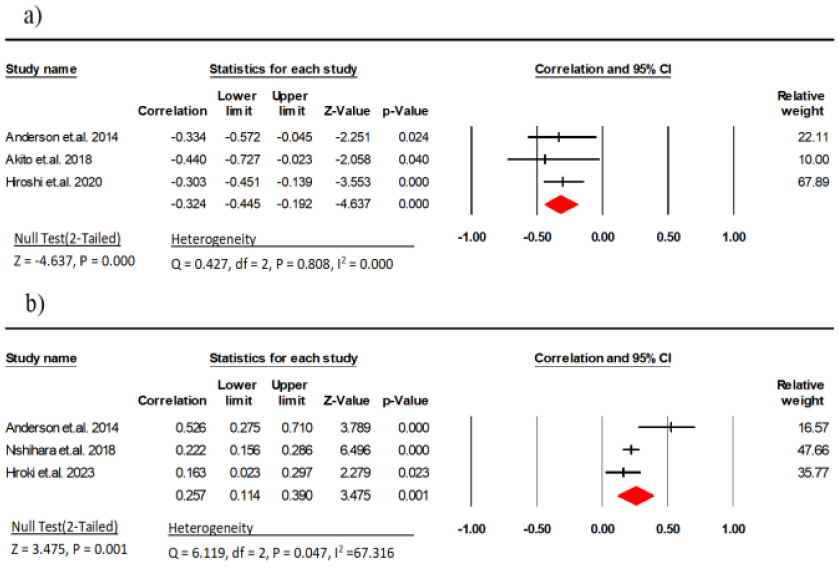

FIGURE 4
Associations (r_z values) between handgrip strength and **(a)** echo intensity, **(b)** Muscle thickness. CI, confidence interval; df, degrees of freedom.

$P < 0.001$, $I^2 = 15.85$; $r = -0.16$, 95% CI: −0.28 to −0.05, $P = 0.006$, $I^2 = 55.75$, respectively). There was a weak correlation between MT and the 30SS ($r = 0.26$, 95% CI: 0.01 to 0.47, $P = 0.03$, $I^2 = 60.27$) (Figure 6). There was no indication of publication bias ($t = 0.22$, $p = 0.82$; Supplementary Figure 4B).

Tour studies (involving 237 participants) investigated the association between FL and the chair stand test (12, 26, 32, 38). The combined effect size of FL and chair stand test was $r = 0.12$ (95% CI: −0.01 to 0.24, $P = 0.06$, $I^2 = 54.50$), with a weak statistical correlation and moderate heterogeneity. Subgroup analysis showed a moderate correlation between FL and the 30SS ($r = 0.40$, 95% CI: −0.14 to 0.61, $P = 0.003$, $I^2 = 0.000$), and a weak correlation with the 5TSTS ($r = 0.09$, 95% CI: −0.10 to 0.28, $P = 0.356$, $I^2 = 0.000$). There was a weak correlation between FL and the TUG ($r = -0.01$, 95% CI: −0.22 to 0.19, $P = 0.02$, $I^2 = 47.49$) (Figure 6). There was also no indication of publication bias ($t = 0.20$, $p = 0.85$; Supplementary Figure 4C).

Two studies (involving 88 participants) investigated the association between PA and the TUG (26, 38). The combined effect size of EI and chair stand test was $r = -0.17$ (95% CI: −0.37 to 0.04, $P = 0.11$, $I^2 = 0.000$), with a weak statistical correlation (Figure 6).

4 Discussion

The objective of this meta-analysis was to comprehensively examine the association between US parameters, muscle strength, and sarcopenia-related exercise performance in healthy older adults. The results of the meta-analysis indicate moderate to strong correlations between EI and MT with maximal strength, explosive power, and handgrip strength in the context of muscle strength. Additionally, CSA shows a strong correlation with maximal strength. However, regarding sarcopenia-related exercise performance, no significant correlations emerged between US parameters and gait speed. The strength of association with sit-to-stand tests varied based on the specific test type, with EI and MT demonstrating only weak correlations in these tests. Furthermore, none of the US parameters demonstrated a significant correlation with TUG test.

4.1 Correlation between US parameters and muscle strength

According to our study findings, among older individuals, EI, MT, and CSA appear to be robust indicators for detecting maximal muscle strength. We observed a moderate negative correlation ($r = -0.56$) between EI and maximal muscle strength, consistent with previous studies (24). This suggests that as individuals age, non-muscular components such as fat and connective tissue gradually increase in the muscle, leading to higher EI in US images. Supporting this, existing literature recognizes EI as an effective indicator reflecting the content of non-muscular components in muscle tissue (43). Additionally, a moderate to strong positive correlation was noted between MT ($r = 0.43$) and CSA ($r = 0.67$) with maximal muscle strength. Older adults commonly undergo a decline in muscle quality and size, possibly attributable to a reduction in the number and diameter of muscle fibers (44). This is consistent with the decrease in MT and CSA, affecting overall muscle strength. However, the correlation with PA and muscle strength did not reach significance. This lack of significance may be attributed to the relatively minor impact of PA in older individuals, exhibiting greater variability compared to other muscle parameters. Additionally, technical factors, including US image resolution and sampling position, might influence the measurement of PA, introducing some uncertainty. Past research on the relationship between PA and muscle strength has produced inconsistent results, potentially influenced by individual differences, measurement methods, and study designs (45, 46).

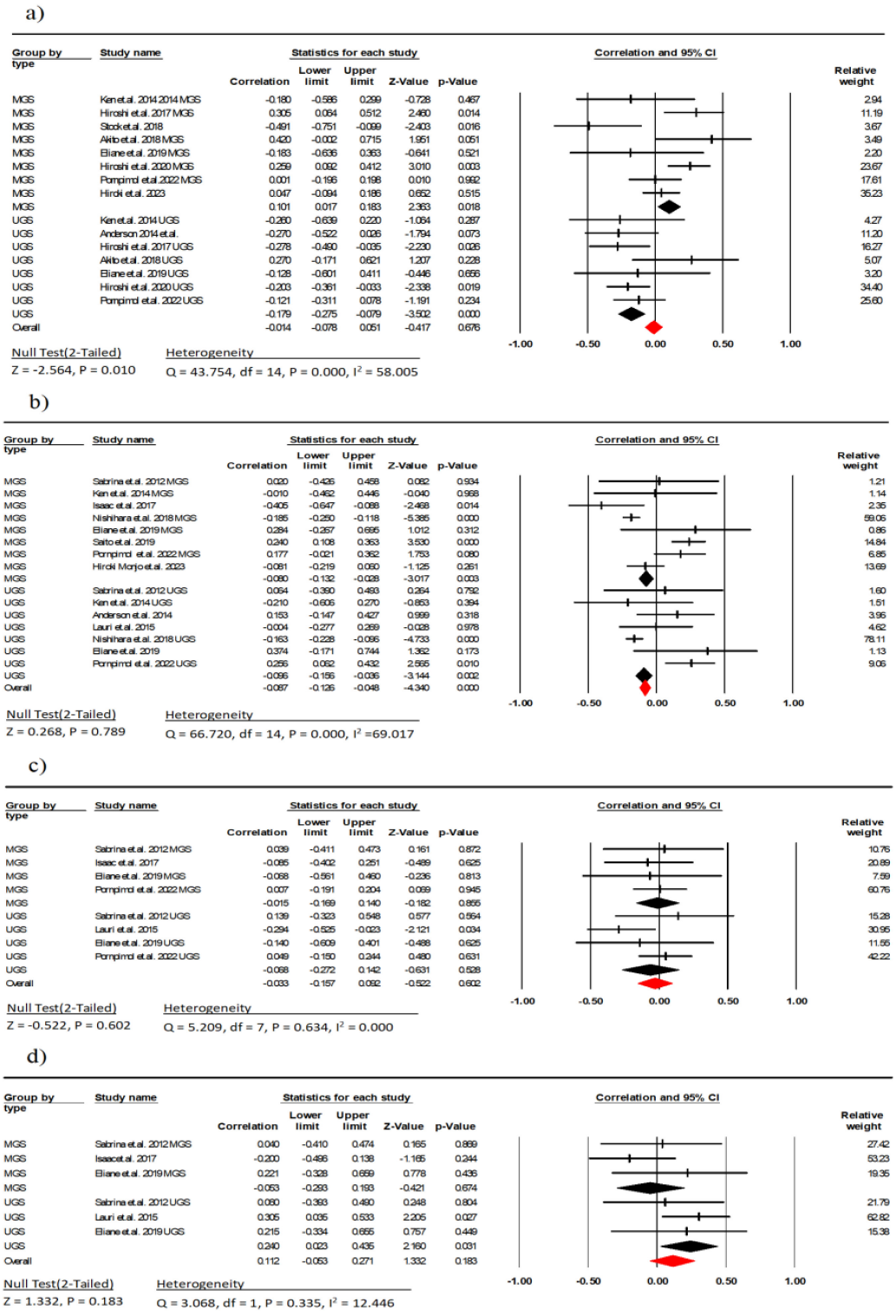

FIGURE 5
Associations (r_z values) between Gait speed and **(a)** echo intensity, **(b)** Muscle thickness; **(c)** cross-sectional area, **(d)** pennation angle. MGS, maximal gait speed; UGS, usual gait speed; CI, confidence interval; df, degrees of freedom.

Our research findings highlight that only two US parameters, specifically EI and MT, demonstrate significant correlations with explosive force and handgrip strength. Notably, we identified a substantial negative correlation between EI and explosive force ($r = -0.47$). Increased EI is commonly associated with a heightened presence of non-muscular components, such as fat and connective tissue, within the muscle (43). These non-muscular components may adversely impact muscle elasticity and power transmission, leading to a reduction in explosive force. Consequently, the rise in US EI could be attributed to various factors linked to

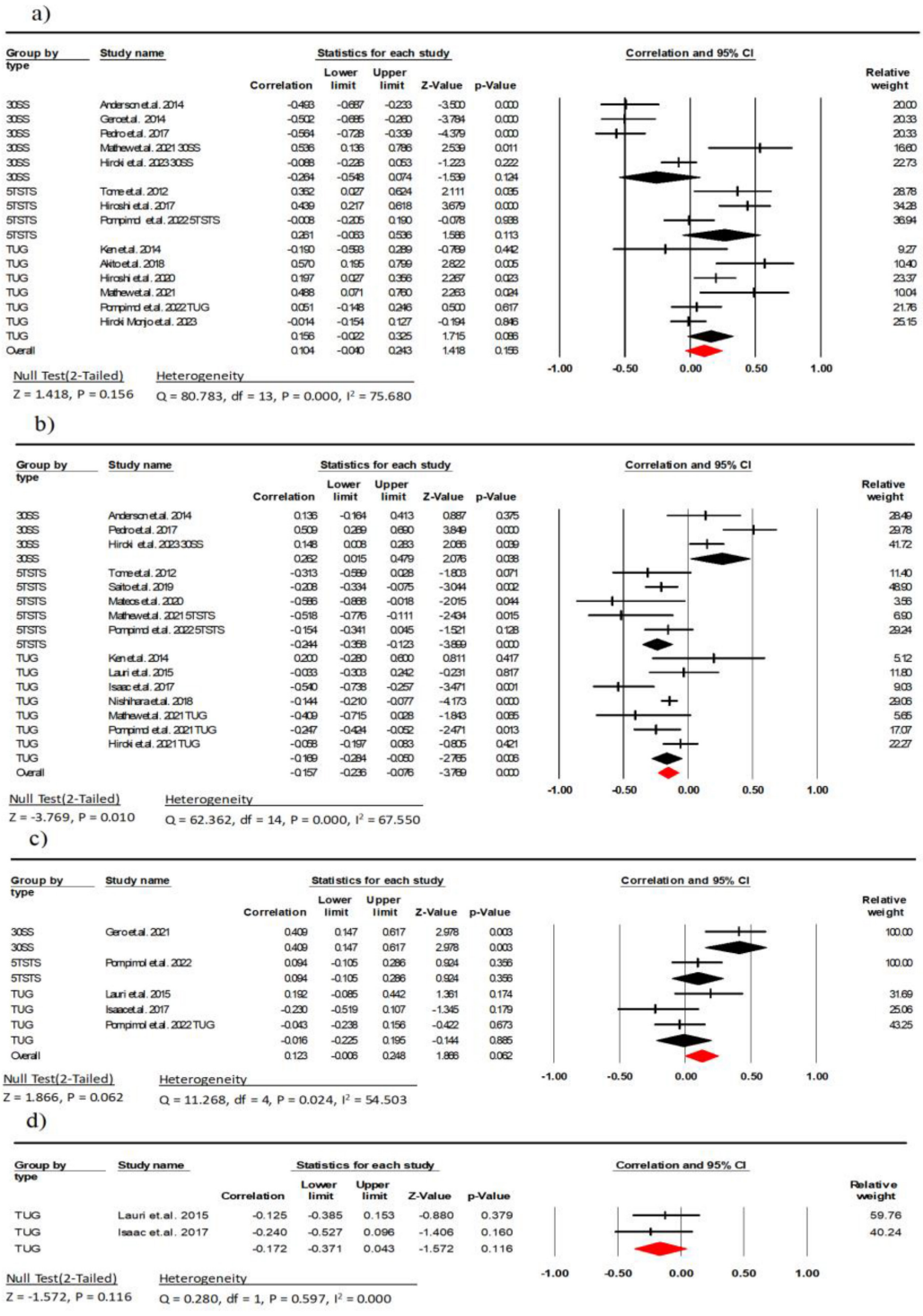

FIGURE 6
Associations (r_z values) between chair stand test and **(a)** echo intensity, **(b)** muscle thickness **(c)** fascicle length, **(d)** pennation angle. 30SS, 30-s Sit-to-Stand; 5TSTS, 5-time Sit-To-Stand; TUG, Timed Up-and-Go; CI, confidence interval; df, degrees of freedom.

intramuscular fat infiltration, encompassing a decline in single fiber contraction speed, decreased power output, modifications in muscle mechanical characteristics, heightened muscle stiffness, and alterations in fiber shortening and expansion (47, 48). In contrast, MT exhibits a substantial positive correlation with explosive force ($r = 0.53$). This discovery aligns with prior research supporting the notion that greater MT corresponds to increased muscle strength (49). Larger MT typically signifies a higher number of muscle fibers, contributing to enhanced explosive force. This association can be explained by the fact that MT directly reflects the augmentation in muscle quality available for power generation (50).

Our research results emphasize the significance of EI and MT as US parameters for assessing handgrip strength. The specific data reveals that the correlation coefficients observed ($r = -0.32$ and $r = 0.26$, respectively) are statistically significant ($p < 0.05$). This serves to underscore the negative correlation between EI and handgrip strength, as well as the positive correlation between MT and handgrip strength. These findings are in accordance with prior research, which recognizes handheld dynamometry as a reliable indicator of muscle strength (51). They contribute to a more profound comprehension of the relationship between muscle structure and function, providing practical implications for the clinical evaluation of handgrip strength.

4.2 Correlation between US parameters and sarcopenia-related exercise performance

US parameters have been a subject of considerable attention in gait speed research. However, our data reveals a notably weak correlation, approaching nonexistence, between these US parameters and both UGS and MGS ($r = -0.01$ to $r = 0.11$, respectively). Consistent with a previous study involving a cohort of healthy adults, US parameters showed no significant association with gait speed ($r = -0.02$ to $r = 0.14$) (40). The main contributing factor for this disparity could be the restricted age range of the participants. The study by Mangine et al. (52) emphasized that within the younger demographic, specific US parameters may demonstrate some correlation with gait speed. However, this correlation is unstable and marked by notable individual variations. Furthermore, the study indicates that following the correction for subcutaneous fat, US parameters show a notably enhanced correlation with gait speed in older adults (53). Hence, consideration of age range and conducting subcutaneous fat correction are crucial factors for a thorough comprehension of the association between US parameters and gait speed.

We conducted a study on the relationship between US parameters and chair stand tests, finding a weak correlation and significant heterogeneity among the parameters. Subgroup analysis revealed correlations between EI, MT, and FL with the 30SS ($r = -0.26$, $r = 0.26$, and $r = 0.41$, respectively). Notably, the association between FL and leg flexibility was more pronounced, which is unsurprising considering that the chair stand test occurs within a typical range of motion and is relatively straightforward. Our findings align with prior reports, (54) suggesting that releasing the fascia of leg muscles contributes to enhanced mobility by expanding the range of motion in the hip and knee joints. However, we observed no significant correlation between the TUG test and the various parameters. Given our emphasis on thigh muscles and the absence of observed correlations between the parameters and TUG, in contrast to previous findings on the contribution of the gastrocnemius and soleus muscles to TUG (34), we assert that further in-depth research is needed to ascertain the value of muscle US parameters in predicting functional physical fitness in older adults. The TUG test encompasses diverse rapid movements, including walking and turning, implying that its complexity may warrant a more comprehensive examination.

Through the synthesis of findings from two studies, it has been established that parameters derived from non-invasive and radiation-free US can serve as predictive indicators for muscle strength and physical function in older adults. This comprehensive understanding encompasses multiple facets of US application in assessing the muscle health of older individuals, covering structural parameters such as MT and CSA, in addition to EI. However, it is imperative to acknowledge that obtaining dependable data from US measurements necessitates precise methodologies. Variables including the patient's positioning, muscle contraction during measurement, and the angle of the sensor relative to the skin surface all have the potential to influence muscle US measurements.

This study has several limitations. Firstly, the meta-analysis was constrained to cross-sectional design studies, limiting the exploration to associations and precluding the establishment of causal relationships. Secondly, insufficient data for the calf impede a comprehensive understanding of lower limb walking and gait-related aspects. Secondly, due to a lack of sufficient data for the calf, our understanding of lower limb walking and gait-related aspects is not comprehensive. Additionally, some included studies lacked effective control for confounding variables. The focus on outcomes in older adults did not involve a separate investigation of gender, introducing uncertainties about potential gender differences. Finally, the presence of heterogeneity in chair test evaluations stems from the utilization of diverse methodologies, underscoring the importance of meticulously selecting suitable approaches to mitigate pertinent limitations when investigating the correlation with chair stand test performance.

To address the aforementioned limitations and advance future research in this field, combining ultrasound with complementary techniques such as bioimpedance analysis (BIA) and functional near-infrared spectroscopy (fNIRS) could provide a more comprehensive evaluation of muscle health in older adults. BIA offers non-invasive assessment of body composition, including muscle mass and fat distribution, (55) which could provide additional insights into the relationship between muscle quality and overall body composition when used alongside ultrasound. Similarly, fNIRS methodology allows for real-time monitoring of muscle oxygenation and hemodynamics during exercise, (56) potentially bridging the gap between structural measurements and functional outcomes, particularly in areas where our analysis showed weak correlations, such as gait speed and TUG tests. This multi-modal approach could lead to improved strategies for early detection and monitoring of sarcopenia and more targeted interventions, ultimately enhancing our understanding of muscle function and quality of life in aging populations.

5 Conclusion

This meta-analysis reveals significant correlations between ultrasound parameters (echo intensity and muscle thickness) and muscle function in healthy older adults. These findings underscore the potential of ultrasound as a diagnostic tool for assessing muscle characteristics in this population. However, the observed heterogeneity across studies highlights the need for further research. Future investigations should focus on standardizing measurement techniques, establishing age- and

sex-specific reference values, and conducting longitudinal studies with larger sample sizes. Such efforts could enhance the clinical applicability of ultrasound in assessing and monitoring muscle health in older adults, potentially improving early detection and intervention strategies for age-related muscle changes.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

HY: Writing – review & editing, Writing – original draft. M-KK: Writing – review & editing, Writing – original draft, Supervision, Conceptualization.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2024.1429530/full#supplementary-material

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Reproducibility and concordance of functional autonomy tests in older adult women: a comparative study of face-to-face and virtual assessments

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Introduction: The literature does not explore functional assessments carried out remotely and in older women in virtual environments.

Objective: This study analyzed the reproducibility and agreement in applying functional autonomy tests face to face (FF) and virtually (V).

Methods: A single evaluator carried out two evaluations. The following tests were performed: walking 10 m, rising from the sitting position (RSP), rising from the ventral decubitus position (RVDP), and sitting and rising from a chair and walking around the house (SRCW).

Results: No significant changes were identified between V and FF ($p > 0.05$ for all). No significant changes were identified between tests considering FF and V conditions ($p > 0.05$ for all). The highest value for the intraclass correlation coefficient was <0.0001 for the SRCW (CL, $r = 0.98$ CI95%: 0.969–0.990 and ICC, $r = 0.99$ CI95%: 0.984–0.995), and the lowest was <0.0001 for the RSP (CL, $r = 0.91$ CI95%: 0.853–0.954 and ICC, $r = 0.95$ CI95%: 0.921–0.976). Regarding agreement between tests, a variation was found between the lowest value of 0.07 ± 0.74 BIAS for the RVDP and the highest value of 0.32 ± 1.89 BIAS for the SRCW.

Conclusion: The tests used in the present study showed good reproducibility and agreement in older people when carried out face to face and virtually.

KEYWORDS

aged, older people, longevity, daily living activity, older adults

Introduction

The demographic profile of the older adult population has undergone significant changes in recent years related to increased life expectancy, with an increasing number of people aged 60 or over. In 2019, older people numbered more than 1 billion worldwide, with projections for 2030 being 1.4 billion and for 2050, 2.1 billion. There are more older people than children under five, demonstrating an inversion in the age pyramid, which also presents a decrease in birth rates, especially in developing countries (1).

Inevitably, the aging process is associated with physiological changes and musculoskeletal changes that cause progressive declines in the function of biological systems (2, 3) as well as the presence of chronic or locomotor conditions, which, in addition to the risk to life, represent a potential threat to the independence and autonomy of movement of older adults. Therefore, to age healthily, it is necessary to focus on maintaining and/or improving multiple health variables such as range of movement, muscular strength, balance, cardiorespiratory endurance, joint mobility, and agility, among others (4–6).

Both physical activity and physical exercise are effective non-pharmacological methods for reducing physical disability, in addition to helping to reduce the risk of various chronic diseases (7–11) recognized as disabling in advanced clinical stages (9, 12–14).

Given this context, the wellbeing, health maintenance, and quality of life of the older adult population are of fundamental importance in global public health. In this regard, considering the importance of functional autonomy in aging well, tests have been developed and validated to analyze functional autonomy. These tests help establish an accurate diagnosis and help support recommendations (whether physical, mental, or social) that contribute to the overall ability of an older person to function effectively in daily life.

With the advent of the COVID-19 pandemic, which was recognized by the World Health Organization (WHO) on 11 March 2020, several guidelines were established for developing occupational activities in the context of the home environment (15, 16). Social restriction was the most widely implemented measure by authorities, resulting in significant changes in citizens' lifestyles and mental health (17). These social restrictions were associated with reductions in physical activity levels and increases in sedentary behavior (18–21). In parallel with social restrictions, there was a considerable increase in physical activity programs delivered remotely using technology, a strategy that has continued to be employed for providing care to individuals with numerous conditions. The unprecedented aspects of the present study are framed within two contexts: first, the continuity of physical exercise practice regardless of social isolation, and second, the need for diagnostic evaluation to support such practices. These aspects highlight the relevance of the present study. To ensure a healthy exercise prescription, continuous evaluation and monitoring of key parameters are essential.

However, the actual effectiveness, reliability, and reproducibility of functional assessments carried out remotely in a virtual environment remain unclear in the literature. Given that physical exercise is an essential tool for reducing the harmful effects of confinement and increasing immunity in older adults, it became necessary to adapt diagnostic assessment instruments for use in the virtual environment. However, the literature presents gaps related to the efficiency of these assessments. To verify the efficiency of applying tests virtually, the objective of the present study was to analyze the reproducibility and agreement in applying functional autonomy tests face to face and virtually for older people. This study anticipates reproducibility and agreement in virtual tests of functional autonomy in older women.

Materials and methods

After approval by the Ethics and Research Committee of the Federal University of Espirito Santo (n° 5.029.735/2022), older women were invited to participate in the study. The invitation was circulated in community centers, squares, parks, and gyms through posters and leaflets, as well as through social networks.

Participants

The inclusion criteria were being 60 or older, physically active, and independent in daily activities. As a non-inclusion criterion, any veto was adopted from clinical examinations or pre-participatory assessments carried out by health professionals. The exclusion was applied to acute or chronic conditions that could compromise or become an impediment to carrying out the tests, such as recent hospitalization, symptomatic cardiorespiratory disease, uncontrolled hypertension or metabolic syndrome, severe kidney or liver disease, cognitive impairment or progressive and debilitating conditions, severe obesity with inability to perform physical activity and recent bone fractures. Older people who did not perform all tests in virtual and face-to-face conditions were excluded from the sample. Initially, 60 older women came forward to participate in the tests. However, after applying the non-inclusion and exclusion criteria, 44 older women were considered eligible to participate.

Test protocols

The applications of functional autonomy tests, virtually and face to face, were randomly distributed using a randomization program with 48-h intervals between them. After familarization, with both tests, two assessments were conducted to analyze the test and retest. Four evaluations were similarly carried out by a single evaluator with experience in the procedures applied. The face-to-face and virtual assessments were carried out in the same environment between both conditions. A conventional microcomputer with Internet access and high resolution was used to carry out the virtual assessment. Figure 1 presents a summary of the study design.

Parameters evaluated

Anthropometric data

To measure body mass and height, the participant was required to be barefoot and wearing physical activity clothing (light clothes, shorts, and a shirt). They stood on the central part of the platform of the Filizola® mechanical scale (Brazil) with INMETRO seal, having an accuracy of 100 g. Weight was measured in kilograms.

The standard previously mentioned was used to measure height with a Cardiomed® WCS model stadiometer, with an accuracy of 1 mm. The

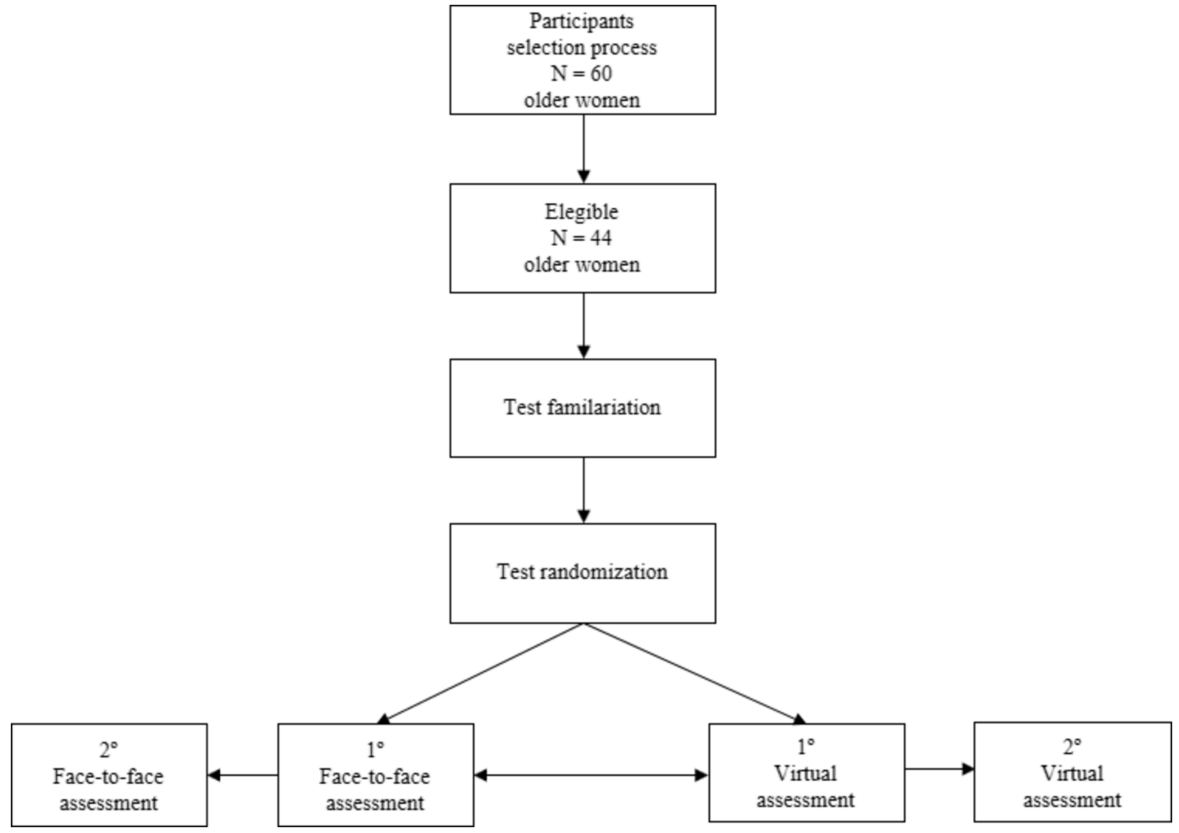

FIGURE 1
Flowchart of experimental design.

participant was instructed to stand upright, with their arms extended along their body and feet together, holding their breath in inspiratory apnea. The head was oriented according to the Frankfurt plane, ensuring the measurement was taken in centimeters. Body mass index (BMI, kg/m ^{2}) was calculated according to the formula: weight/height^2.

Functional autonomy tests

The Latin American Development Group for Maturity (GDLAM) protocol aims to evaluate the functional autonomy of older adults and can be used by professionals in specific areas of health for diagnosis and control of autonomy. It is widely used by researchers from all parts of the world (22).

The following tests assessed functional autonomy: walking 10 m (W10m), which assesses speed, where the individual needs to walk as quickly as possible within 10 m. The objective is to assess gait speed. The participant standing next to the start demarcation, at the command of "Now," walks as quickly as possible within 10 m, and only stops walking when they pass the indicated demarcation. The test area consists of a marking of 10 m (test space) and one of 15 m (5 m of space for deceleration). The test was carried out on flat, ventilated, and illuminated ground to ensure the participant's safety (23).

Rising from a sitting position (RSP). The objective is to assess the functional capacity of the lower limbs. The test begins with the participant sitting in a chair, with arms crossed in front of the chest (so that there is no help from the hands). At the command of "Now," the participant needs to sit down and stand up correctly five times as fast as they can. The test ends with the participant seated in a chair with a back but no arms, with the seat height measuring 46–48 cm from the ground (24). Rising from *de ventral decubitus* position (RVDP). The objective is to assess the participant's ability to get up from the floor as quickly as possible. The test starts with the participant lying face down in the prone position, arms extended alongside the body and supported by the mat, with palms facing upward. Upon hearing the command "Now," the participant rises from the floor as quickly as possible and stands up. The test also involves sitting and standing from a chair and walking around the house (SRCW) (25), aiming to evaluate agility, dynamic balance, and balance recovery. The test begins with the participant sitting with their feet suspended. At the command of "Now," they get up from the chair, move to one of the cones, circle it, return toward the chair and sit down (always taking their feet off the floor when sitting), get up, and repeat the process for the other side, and do this once again for both sides, that is, the process repeats itself twice. The test ends with the participant seated (26). All tests are measured in seconds, and the results are used to calculate the general functional autonomy index (GI). All tests were performed in the order described above, on a single day, using a 3-min interval between them to allow good recovery between tests (22).

Statistical analysis

The Shapiro–Wilk test was used to check data normality. Student's *t*-test was used to verify the differences in the means of the

functional aptitude tests between the first and second assessments. The typical absolute and relative measurement errors of all parameters were calculated following the model proposed by Perini et al. (27). Agreement between measurements was analyzed using linear correlation, with weak (< 0.4), moderate (> 0.4 and < 0.5), and strong (≥ 0.5) correlations as interpretations. Reproducibility was determined by the two-way intraclass correlation coefficient being interpreted as little correlation (<0.25), low correlation (> 0.26 to <0.49), moderate (> 0.50 to <0.69), high (> 0.7 to <0.89), and very high (> 0.9 to <1.0). The reliability between the measures was analyzed using the Bland and Altman graphical arrangement. The effect size was calculated using Hedges' g, with values between 0.2 and 0.5 being interpreted as small, 0.5 and 0.8 as moderate, and values above 0.8 as significant. All statistical analyses were performed using the GraphPad Prism software (version 4.0, San Diego, CA, United States) with a significance level of $p < 0.05$, with data presented as mean ± standard deviation, coefficient of variation, and differences between means and 95% confidence interval.

Results

The older women were 67 ± 5 years old, 1.57 ± 0.5 m in height, and had a body mass index of 28 ± 3 kg/m^2. The results of the test and retest assessments of the older women's functional autonomy parameters are described in Table 1.

No significant changes were identified between the functional autonomy tests considering the first and second assessments in virtual and face-to-face conditions. The values of typical absolute measurement errors varied between the lowest value of 0.01 in the virtual condition and 0.02 in the face-to-face condition for the RSP test. The highest values of typical absolute measurement errors were 0.14 for the SRCW test in the virtual condition and 0.06 for the RVDP test in the face-to-face condition.

The values of typical relative measurement errors varied between the lowest value of 0.15% in the virtual condition for the RSP test and 0.10% in the face-to-face condition for the SRCW test. The highest values of typical absolute measurement errors were 0.58% in the virtual condition and 1.17 for the RVDP test. Table 2 presents the comparative values between the face-to-face and virtual conditions.

No significant changes were identified between the functional autonomy tests considering the face-to-face and virtual conditions. The values of typical absolute and relative measurement errors ranged from the lowest value of 0.04 for the RVDP tests and 0.27% for the SRCW test. The most significant typical absolute and relative measurement errors ranged between 0.08 for the SRCW and 0.84% for the RVDP tests. The analysis of linear correlations and intraclass correlation coefficients is presented in Table 3.

Considering the data relating to linear correlation, the highest value was found (r: 0.98; $p < 0.0001$) for the SRCW test, and the lowest value (r: 0.91; $p < 0.0002$) for the test RSP. Considering the intraclass correlation coefficient, the highest value was found. Figure 2 presents the reproducibility between measures of functional autonomy tests.

Observing the data presented, the reproducibility and agreement between the functional autonomy tests varied between the lowest value of 0.07 ± 0.74 BIAS (−1.38–1.54) for the RVDP test (Figure 2C) and the highest value of 0.32 ± 1.89 BIAS (−3.38–4.04) for the SRCW test (Figure 2D).

Discussion

The objective of the present study was to analyze the reproducibility and agreement in applying four functional autonomy tests face-to-face and virtually for older women. This study found favorable agreement between the information collected in both assessments. There was a high rate of agreement between the application of the tests in the face-to-face and virtual conditions applied by the same evaluator, which makes this diagnostic assessment a reliable alternative for evaluating the functional autonomy of the older person in a virtual environment.

Functional autonomy is a health variable that is primarily strengthened throughout life by moving daily, which is considered a form of physical activity. By carrying out the tasks of daily life, the body shifts from a resting state and generates caloric expenditure (22).

With the advent of the SARS-CoV-2 pandemic, the decrease in these activities was linked to health problems and neurological, physiological, and functional declines inherent to aging and confinement, bringing about a need for virtual connections and online data collection (28).

TABLE 1 Test and retest analyses of the functional assessment parameters of older people in a face-to-face and virtual environment (n = 44).

Tests	Condition	1st Assessment	2nd Assessment	MD	95% CI	TE	t	P	Absolute ETM	Relative ETM
W10m	Face to face	7.06 ± 2.37 (33.62%)	7.02 ± 2.25 (32.13%)	0.04	−0.137–0.046	0.30	1,000	0.322	0.04	0.56%
	Virtual	7.20 ± 2.13 (29.57%)	7.11 ± 2.03 (28.64%)	0.09	−0.249–0.067	0.52	1,159	0.252	0.04	0.57%
RSP	Face to face	8.22 ± 2.67 (32.52%)	8.25 ± 2.60 (31.60%)	0.02	−0.179–0.224	0.67	0.226	0.821	0.02	0.27%
	Virtual	8.36 ± 2.66 (31.91%)	8.36 ± 2.62 (31.38%)	0.00	−0.146–0.146	0.48	0.000	0.999	0.01	0.15%
RVDP	Face to face	4.88 ± 2.99 (61.35%)	5.04 ± 3.04 (60.29%)	0.16	−0.047–0.365	0.68	1,552	0.128	0.06	1.17%
	Virtual	4.97 ± 2.81 (56.58%)	5.02 ± 2.60 (51.79%)	0.04	−0.150–0.241	0.65	0.467	0.642	0.03	0.58%
SRCW	Face to face	30.98 ± 10.57 (34.11%)	31.00 ± 10.14 (32.70%)	0.02	−0.150–0.241	1.05	0.144	0.886	0.03	0.10%
	Virtual	30.89 ± 10.20 (33.03%)	31.73 ± 9.72 (30.66%)	0.84	−0.021–1.703	2.86	1,967	0.057	0.14	0.44%

Values expressed as mean ± standard deviation and coefficient of variation (CV), mean difference (MD), confidence interval (CI), effect size (TE), t-test (t), typical measurement error (ETM) of the walking 10 m (W10m), rising from a sitting position (RSP), rising from de ventral decubitus position (RVDP), sitting and rising from a chair and walking around the house (SRCW) tests.

TABLE 2 Analysis of functional assessment parameters of older people in a face-to-face and virtual environment (n = 44).

Tests	Face to face	Virtual	MD	95% CI	TE	t	P	Absolute ETM	Relative ETM
W10m	6.97 ± 2.30 (33.02%)	7.13 ± 2.09 (29.35%)	0.15	−0.103–0.412	0.85	1,209	0.233	0.06	0.79%
RSP	8.23 ± 2.72 (33.09%)	8.37 ± 2.68 (32.02%)	0.14	−0.181–0.475	1.10	0.858	0.395	0.06	0.67%
RVDP	4.91 ± 3.05 (62.16%)	4.99 ± 2.72 (54.53%)	0.07	−0.148–0.307	0.75	0.704	0.484	0.04	0.84%
SRCW	30.95 ± 10.28 (33.22%)	31.28 ± 9.84 (31.48%)	0.32	−0.249–0.903	1.91	1,145	0.258	0.08	0.27%

Values expressed as mean ± standard deviation and coefficient of variation (CV), mean difference (MD), confidence interval (CI), effect size (TE), t-test (t), typical measurement error (ETM) of the walking 10 m (W10m), rising from a sitting position (RSP), rising from de ventral decubitus position (RVDP), and sitting and rising from a chair and walking around the house (SRCW) tests.

TABLE 3 Linear correlations and intraclass correlation coefficient of functional aptitude tests for older people (n=44).

Parameters	LC			ICC		
	r	95% CI	P	r	95% CI	P
W10m	0.93	0.874–0.961	< 0.0001	0.96	0.929–0.979	< 0.0001
RSP	0.91	0.853–0.954	< 0.0001	0.95	0.921–0.976	< 0.0001
RVDP	0.97	0.950–0.985	< 0.0001	0.98	0.969–0.991	< 0.0001
SRCW	0.98	0.969–0.990	< 0.0001	0.99	0.984–0.995	< 0.0001

Expressed values of the confidence interval (CI) of the linear correlations (LC) and the intraclass correlation coefficient (ICC) of the walking 10 m (W10m), rising from a sitting position (RSP), rising from de ventral decubitus position (RVDP), and sitting and rising from a chair and walking around the house (SRCW) tests between the face-to-face and virtual conditions.

Precautionary measures and social isolation imposed limitations on face-to-face activities, making it challenging to collect data through field trips, resulting in the need to think about alternative methods to the face-to-face ones, thus reaching the virtual environment (29), recommended by American College Sports Medicine [ACSM, 2002] (30), which sought to help and provide tools for people to practice their physical activities at home, using virtual technologies, which are not new, but still promising and with a wide range of applications (31, 32).

Due to its nature as a sustainable and easily accessible test, the virtual intervention model is widespread among older people, especially those with progressive diseases, presenting good results in effectiveness, adherence, easy applicability, feasibility, and autonomy (33–35).

Many studies report on the practice of physical exercise programs at home; however, the literature is scarce regarding the use of diagnostic assessments to support the prescription and supervision of training programs. These assessments are essential for ensuring the success of the results, which, according to Lacroix et al. (34) are superior when the programs are supervised, particularly in outcomes related to balance, strength, and muscular power.

Kis et al. (35), in a systematic review with meta-analysis, observed that supervised home training increased the adoption of exercise programs. The justification for these results is that even under minimal supervision, older people perform exercises with better quality, more attention, at a greater volume, and with more intensity. These characteristics improve cognition, improving the executive function of the physical movements (34).

Corroborating the statements mentioned above, the physical function of older people must be assessed using quantitative measures (36–38), which can be carried out in different settings, such as health promotion centers, clinics, public parks, or at home through digital health intervention, conceptualized by World Health Organization (39) as the use of digital, mobile, and wireless technologies to support the achievement of health objectives.

Since diagnostic assessment is essential for identifying the parameters of the variables involved in functional fitness, for the correct and accurate prescription of the training program (6), and following satisfactory reproducibility and agreement indices, as presented in the results of this study, the application of the evaluation of the functional autonomy tests W10M, RSP, SRCW, and RVDP, enables and reassures the application of these in the older adult population, in a precise, fast, safe and low-cost way. It is also worth noting that performing exercises in the home environment can favor older people's adherence since, in this context, overcoming barriers such as fear of falling and fear of privacy is minimized (40).

When observing the consistency of values between the first and second evaluation of the functional autonomy tests used, the rising from sitting position (RSP) test, which aims to evaluate the functional capacity of the lower limbs (41), showed greater accuracy in face-to-face and virtual assessments, which can be attributed to activities carried out in daily life resulting from the movement of squatting and walking (42–45).

The data relating to the linear correlation and the intraclass correlation coefficient from the SRCW test, which assesses agility, dynamic, and recovered balance (26), showed a higher correlation between the others. Sitting and standing are considered one of the most important measures of physical capacity and one of the most demanding functional tasks from a biomechanical point of view (46, 47). However, the tests carried out by the older adults group are similar to activities of daily living, facilitating the assimilation of the evaluators' verbal commands in the virtual scenario, thus allowing the use of the proposed evaluation carried out remotely, online, and supervised.

The analysis by Bland and Altmann (48) showed agreement between the assessments carried out face to face and virtually since most of the intersections between the bias and the average values were within the limits of agreement. The reproducibility and reliability analysis presented coefficients of variation with values

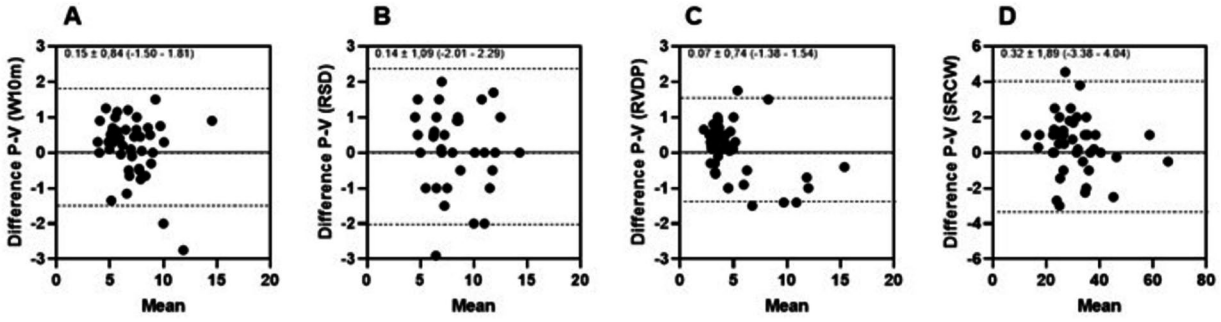

FIGURE 2
Reproducibility between measures of functional autonomy tests by Bland–Altman plot of face-to-face (P) and virtual (V) assessments of the walking 10 m (W10m) **(A)**, rising from a sitting position (RSP) **(B)**, rising from the ventral decubitus position (RVDP) **(C)**, and sitting and rising from a chair and walking around the house (SRCW) **(D)** tests.

varying between the lowest value of 0.07 ± 0.74 BIAS (−1.38–1.54) for the RVDP test and the highest value of 0.32 ± 1, 89 BIAS (−3.38–4.04) for the SRCW test. According to Morrow et al. (49), the lower the coefficient of variation, the greater the reproducibility of the protocol. Considering this aspect, it is believed that the variability of the time to complete the SRCW test, which evaluates the participant's agility and balance can be attributed to the characteristics of the test itself, as it is the longest to perform among all the tests. The other tests, being shorter, allow for greater variability in the results (50), additionally, the participants presenting different levels of physical fitness may have been another contributing factor to this variation.

Alves et al. (51) mentioned that physical fitness and functional capacity are interconnected with advancing age, as they reflect the ability of older people to carry out activities of daily living within their environment, with autonomy. Given that the SRCW test involves movements related to these skills, the observed variability in test execution time among study participants can be justified.

We believe that the results of the present study provide good perspectives for physical and functional assessments of older people. The reproducibility of virtually performed tests facilitates the work of private clinics and public health workers, increasing the possibility of measuring functional health data for older people at a low cost.

The present study presents as a relevant point the originality of applying the functional autonomy test in virtual mode and its reproducibility and reliability. As the study participants were female, with no male participants, and only one evaluator applied the functional autonomy test to older women, we consider this fact a limitation of the study. Therefore, it is recommended that new evaluations be carried out using older men and that more than one evaluator be applied to the test.

Conclusion

According to the results presented, there were no significant changes between V and FF and no significant changes between tests considering FF and V conditions. Additionally, we identified a significant intraclass correlation coefficient for the SRCW and RSP. The tests used in the present study showed good reproducibility and agreement in older people when carried out face to face and virtually. However, more studies are needed to investigate the reproducibility and effectiveness of the applicability of diagnostic assessments of the multiple variables that involve training programs. Furthermore, it is recommended that this study be replicated with different evaluators, male participants, and age groups.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors under reasonable request.

Ethics statement

The studies involving humans were approved by Ethics and Research Committee of the Federal University of Espirito Santo (n° 5.029.735/2022). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

TS: Conceptualization, Investigation, Writing – original draft. RP: Methodology, Supervision, Writing – original draft. AM: Methodology, Project administration, Writing – original draft. FS: Data curation, Visualization, Writing – review & editing. RR: Formal analysis, Project administration, Writing – review & editing. FP: Writing - review & editing. VB: Data curation, Visualization, Writing – review & editing. SG: Conceptualization, Formal analysis, Writing – review & editing. MB: Conceptualization, Formal analysis, Writing – review & editing. DB: Conceptualization, Data curation, Formal analysis, Methodology, Software, Supervision, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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