Effects and Moderators of Exercise on Sarcopenic Components in Sarcopenic Elderly: A Systematic Review and Meta-Analysis

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**Background:** Sarcopenia is a muscle disease in loss of muscle strength, mass, and function associated with aging. Although protective effects of exercise on muscle mass and function are generally recognized, research findings in sarcopenic adults are inconsistent. It is necessary to conduct a systematic review to determine the effects of exercise on muscle strength, body composition, and physical performance in older adults with sarcopenia, and to examine the potential moderators including sociodemographic characteristics and exercise-related factors.

**Methods:** Six electronic academic databases (Medline, Embase, CINAHL, Scopus, Cochrane Library, and SPORTDiscus) were used to retrieve the eligible studies from inception to May 2020. Two reviewers independently selected and extracted the data from each included study, and effect sizes were calculated by employing random-effect models with 95% confidential interval (CI). The Physiotherapy Evidence Database (PEDro) scale was used to assess study quality.

**Results:** Seventeen studies (985 participants with sarcopenia, aged 67.6–86 years) were included in this review study. The meta-analytic results showed significant improvements in muscle strength [grip strength, SMD = 0.30, 95% CI (0.15, 0.45), \(I^2 = 6\%, p < 0.01\); knee extension, SMD = 0.32, 95% CI (0.15, 0.50), \(I^2 = 0\%, p < 0.01\); and chair and stand, SMD = 0.56, 95% CI (0.30, 0.81), \(I^2 = 36\%, p < 0.01\)], in physical performance [timed up and go, SMD = 0.74, 95% CI (0.48, 1.00), \(I^2 = 0\%, p < 0.01\); and gait speed, SMD = 0.59, 95% CI (0.35, 0.82), \(I^2 = 62\%, p < 0.01\)], and in body composition [skeletal muscle mass index, SMD = 0.37, 95% CI (0.15, 0.58), \(I^2 = 16\%, p < 0.01\); and appendicular skeletal muscle, SMD = 0.31, 95% CI (0.13, 0.49), \(I^2 = 20\%, p < 0.01\)]. However, there were no significant differences in other body composition (SMD = 0.20–0.36). Additionally, meta-regression revealed that the higher percent of female participants was significantly associated with improved gait speed (\(\beta = 0.0096, p = 0.03\)) and decreased skeletal muscle mass index (\(\beta = -0.0092, p = 0.01\)).
Conclusions: The current meta-analysis suggests that exercise is a beneficial therapy, which has protective effects for older adults with sarcopenia. Some beneficial effects may be moderated by gender and exercise intensity.

Keywords: physical exercise, muscle function, physical performance, sarcopenia, meta—analysis

INTRODUCTION

Aging-related health leads to many issues in the 21st century. One of the major public health challenges is to preserve older adults’ physical ability and quality of life, to achieve successful aging in the whole society (1). However, due to internal physiological changes in the human body, gradual declines in skeletal muscle strength, losses of muscle mass, and reductions in physical capacity are inevitable during the aging process. These reductions are commonly known as sarcopenia (2, 3). Despite no consistent diagnostic criteria for sarcopenia, the prevalence and harmfulness of sarcopenia in older adults have been shown to be ubiquitous. For example, a previous review study using the European Working Group on Sarcopenia in Older People (EWGSOP) optional definition found that the prevalence of sarcopenia was between 11 and 20% in old adults (4). Subsequently, a series of adverse health outcomes such as mental illness, physical limitations, fractures, poor therapeutic efficacy, poor quality of life, cancer, and even cachexia in adults, have been shown to be associated with the presence of a high-risk of sarcopenia (5–9). Therefore, to reduce the prevalence of sarcopenia, there is a growing interest in non-pharmacological treatments, such as physical exercise, in which researchers can determine the effects and design optimal interventional strategies.

A wealth of evidence supports that exercise, an important modified lifestyle factor, is feasible and efficacious in improving psychological outcomes (e.g., cognition, mood) in older adults (10–14). Moreover, the literature supports that exercise improves physiology-related muscle strength, muscle strength, and physical performance in older adults, and the associated studies are also growing rapidly (15–17). For example, the randomized study of Liu et al. consisting of older adults, found that physical exercise could elevate physical performance (18). A systematic review study examining the impact of resistance exercise showed that low-load exercise benefited the muscle strength and muscle mass in older adults (19). However, in the literature, health benefits of exercise in sarcopenic adults yields mixed findings. For example, a recently published systematic review including five randomized controlled trials (RCTs) suggested that resistant exercise can improve muscle strength, muscle quality, and muscle function in older adults with sarcopenia or dynapenia compared with the controlled group (20). Similarly, the systematic review of Beckwée et al. concluded that exercise contributed to improving muscle strength, muscle mass and physical performance of sarcopenic adults (21). Conversely, the work of Yoshimura et al. demonstrated that exercise had no significant effects on muscle strength, muscle mass, and physical performance in older adults with sarcopenia (22). A systematic review study including six studies indicated that exercise did not significantly increase muscle strength, muscle mass, and balance ability among sarcopenic adults (23). These discrepant research findings imply that more synthesized studies should confirm the roles of exercise on health outcomes in older adults with sarcopenia. In response to this, a meta-analysis based on multiple studies is necessary to demonstrate the effects of exercise on sarcopenia.

Additionally, it is important for sarcopenic older adults to have optimized exercise programs that can promote their physical health. A previous study has found that the exercise modalities (e.g., duration, intensity, and type) were not met to counteract sarcopenia (24). Denison and colleagues found that demographics (e.g., age and sex) can moderate the effects of exercise in older adults with sarcopenia (25). Considering rapid growth in the research field of exercise and sarcopenia, aggregating sufficient quality studies for meta-analysis cannot only make up the limitations across previous reviews but also comprehensively determine the effects of exercise and then examine the influences of moderating factors.

Therefore, the current study was conducted: 1) to determine the effects of exercise on muscle strength, physical performance, and body composition in older adults with sarcopenia and 2) to investigate whether the potential moderators including sociodemographic characteristics and exercise-related factors that influence the intervention effects, as these moderators have been found affecting the sarcopenia-related health outcomes (25).

METHODS

Search Strategy

This systematic review was prospectively registered at PROSPERO (ID: CRD42020184130; https://www.crd.york.ac.uk/) and performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (26). Articles were retrieved from six databases (Medline, Embase, CINAHL, Scopus, Cochrane Library, and SPORTDiscus) on May 2020. The following keywords were used: 1) “physical activity” OR “physical therapy” OR “aerobic exercise” OR “exercise” OR “resistance training” OR “train”; AND 2) “sarcopenia” OR “sarcopenic” OR “dynapenia” OR “muscular atrophy” OR “muscular weight” OR “grip strength”; AND 3) “older adults” OR “aged” OR “elder”; AND 4) “randomized controlled trials” OR “clinical trial” OR “random allocation.” To retrieve more eligible articles, manual searching was conducted from the bibliographies of the included studies.

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Inclusion and Exclusion Criteria

Articles were included if they met the following criteria: (i) Participants aged over 65 years were diagnosed as sarcopenia based on the definition of EWGSOP, Asia Working Group for Sarcopenia (AWGS) or other clinical diagnosis. (ii) The study was designed as an RCT. (iii) Exercise (e.g., aerobic exercise, resistance training, whole-body variation, or a combination of strength and aerobic exercise program) was used in the intervention group. (iv) No exercise intervention (e.g., usual care or waitlist) was given in the control group. (v) The outcomes were muscle strength, body composition (skeletal muscle mass index, appendicular muscle mass, lean mass, body fat, and fat-free mass), and physical performance (gait speed and timed up and go test). (vi) The study was published in the English language.

Exclusion criteria were: (i) in vitro with an animal trial, (ii) participants with sarcopenia obesity, (iii) insufficient information for calculating the effect size (ES), And (iv) case-study, observational studies, editorials, or review articles.

Data Extraction and Quality Assessment

Detailed information was extracted from each study through a pre-created extraction table by two authors (YZ and LZ). The presenting information included the author and year of publication, study design, participants’ characteristics, interventions, sarcopenia diagnostic criteria, assessment tool for body composition, outcomes, and safety.

Assessment of study quality was conducted using the Physiotherapy Evidence Database (PEDro) scale (27) by two authors (YZ and LZ). This assessment tool consists of 11 items: eligibility criteria, random allocation, concealed allocation, similar measures between groups at baseline, instructor blinding, assessor blinding, participant blinding, more than 85% dropout...
TABLE 1 | Characteristics of randomized controlled trials included in the meta-analysis.

| Study/country | Participants/living status | Sample size | Age (years) | Intervention(s) | Sarcopenia criteria | Assessment tool for body composition | Outcomes | Adverse effect |
|---------------|---------------------------|-------------|-------------|-----------------|---------------------|-------------------------------------|----------|---------------|
| Chen et al. (2018) (31) China | Sarcopenia residents of community dwelling | 33 E = 17, C = 16 (Female 100%) | 67.5 | 2 x 60 min/week, 8 weeks | Waitlist | AWGS | Grip strength, SMI, ASM | No |
| Hassan et al. (2016) (32) Australia | Sarcopenia residents of nursing care facilities | 41 E = 20, C = 21 (Female 71%) | 85.9 | 2 x 60 min/week, 24 weeks | Usual care | EWGSOP | Grip strength, Gait speed, SMI, Lean mass, Body fat | No |
| Iranzo et al. (2018) (40) Spain | Sarcopenia residents in institution | 28 E = 11, C = 17 (Female 75%) | 81.9 | 3 x 30–40 min/week, 12 weeks | Waitlist | EWGSOP | Grip strength, Gait speed, SMI | No |
| Jung et al. (2019) (41) Korea | Sarcopenia residents of community dwelling | 26 E = 13, C = 13 (Female 100%) | 75 | 3 x 25–75 min/week, 12 weeks | Usual care + education | AWGS, DXA | Knee extension strength, SMI, Lean mass, Body fat | No |
| Kim et al. (2012) (42) Japan | Sarcopenia residents of community dwelling | 117 E = 39, C1 = 39, C2 = 39 (Female 100%) | 79 | 2 x 60 min/week, 12 weeks | C1: Nutrition, C2: Health education | AWGS, BA | Knee extension strength, Gait speed, ASM | No |
| Kim et al. (2013) (43) Japan | Sarcopenia residents of community dwelling | 96 E = 32, C1 = 32, C2 = 32 (Female 100%) | 80 | 2 x 60 min/week, 12 weeks | C1: Nutrition, C2: Health education | AWGS, BA | Knee extension strength, Gait speed, TUG, ASM | No |
| Lichtenberg et al. (2019) (44) Germany | Sarcopenia residents of community dwelling | 43 E = 21, C = 22 (Female 0%) | 78.5 | 2 x 50 min/week, 12 weeks | Nutrition | EWGSOP, DXA | Grip strength, Gait speed, SMI | No |
| Mafi et al. (2019) (45) Iran | Sarcopenia residents of community dwelling | 47 E = 14, C1 = 17, C2 = 16 (Female 0%) | 68.5 | 3 x 60 min/week, 8 weeks | C1: Nutrition, C2: Waitlist | EWGSOP, DXA | TUG, ASM | No |
| Makizako et al. 2020 (46) Japan | Sarcopenia residents of community dwelling | 72 E = 36, C = 36 (Female 70.8%) | 75 | 1 x 60 min/week, 12 weeks | C1: Waitlist | AWGS, BA | Grip strength, Chair and stand, Gait speed, TUG | No |

(Continued)
### TABLE 1 | Continued

| Study/country | Participants/living status | Sample size | Age (years) | Intervention(s) | Sarcopenia criteria | Assessment tool for body composition | Outcomes | Adverse effect |
|---------------|-----------------------------|-------------|-------------|----------------|---------------------|--------------------------------------|----------|---------------|
|               |                             |             |             | Experiment group | Control group       |                                      |          |               |
| Maruya et al. (2016) | Sarcopenia residents of community dwelling | 52 females (66%) | 69 | 1 × 90 min/week, 24 weeks. Walking and resistance training | Usual daily activity | AWGS | BIA | Gripping strength, Knee extension strength, Gait speed, SMIs, Body fat | No |
| (47) Japan     |                             |             |             |                |                     |                                      |          |               |
| Pietra et al. (2018) | Sarcopenia residents of community dwelling | 70 females (100%) | 83 | 2 × 60 min/week, 36 weeks. Resistance training | Postural activation | EWGSOP | BIA | Gripping strength, SMIs, Body fat | No |
| (33) Italy     |                             |             |             |                |                     |                                      |          |               |
| Strasser et al. (2018) | Sarcopenia residents of institution | 33 females (91%) | 73 | E1: 2 × 60 min/week, 12 weeks. Resistance training and 3 × 30–35 min/week, walking E2: same E1, home therapeutic exercises | Health education | EWGSOP | BIA | Gripping strength, Knee extension strength, Chair and stand, Gait speed, TUG, SMIs, Lean mass, Fat-free mass | No |
| (34) Austria   |                             |             |             |                |                     |                                      |          |               |
| Tsekovra et al. (2018) | Sarcopenia residents of community dwelling | 70 females (54%) | 70.5 | 3 × 45 min/week, 10 weeks. Resistance training | Waitlist | EWGSOP | DXA | Gripping strength, Knee extension strength, Chair and stand, TUG, SMIs, Lean mass, Fat | No |
| (35) Greece    |                             |             |             |                |                     |                                      |          |               |
| Vikberg et al. (2019) | Sarcopenia residents of community dwelling | 40 females (70%) | 76 | 3 × 24 min/week, 12 weeks. Whole-body vibration training | Waitlist | EWGSOP | BIA | Gripping strength, Knee extension strength, Chair and stand, TUG, SMIs, Lean mass, Fat | No |
| (36) Sweden    |                             |             |             |                |                     |                                      |          |               |
| Wei et al. (2016) | Sarcopenia residents of community dwelling | 84 females (78%) | 84.3 | 2 × 30 min/week, 12 weeks. Resistance exercise | C1: nutrition C2: waitlist | EWGSOP | BIA | Gripping strength, Knee extension strength, Chair and stand, Gait speed, SMIs, Lean mass, Fat | No |
| (37) China     |                             |             |             |                |                     |                                      |          |               |
| Yamada et al. (2019) | Sarcopenia residents of community dwelling | 77 females (75%) | 73 | 2 × 45–60 min/week, 12 weeks. Resistance training and aerobic exercise + 1 time/week, home exercise | Waitlist | EWGSOP | DXA | Gripping strength, Knee extension strength, Chair and stand, Gait speed, SMIs, Lean mass, Fat | No |
| (38) Japan     |                             |             |             |                |                     |                                      |          |               |
| Zhu et al. (2019) | Sarcopenia residents of community dwelling | 77 females (75%) | 73 | 2 × 45–60 min/week, 12 weeks. Resistance training and aerobic exercise + 1 time/week, home exercise | Waitlist | EWGSOP | DXA | Gripping strength, Knee extension strength, Chair and stand, Gait speed, SMIs, Lean mass, Fat | No |
| (39) China     |                             |             |             |                |                     |                                      |          |               |

ASM, appendicular skeletal muscle; AWGS, Asia Working Group for Sarcopenia; EWGSOP, European Working Group on Sarcopenia in Older People; SMI, skeletal muscle mass index; BIA, bioelectrical impedance analysis; DXA, Dual-energy X-ray absorptiometry; TUG, Timed up and go.
rate, intention-to-treat analysis, statistical comparison between groups, and ≥1 key outcome estimated. Each item is scored as 0 (absent) or 1 (present). The total score is in the 0–10 point range after summing scores of all items. The study quality was classified as excellent (9–10 points), good (6–8 points), fair (4–5 points), and poor (<4 points).

**Statistical Analysis**

The Comprehensive Meta-Analysis program (version 2.2) was used for analyzing the extracted data. Since all extracted outcome data were continuous variables with variability between studies, standard mean differences (SMDs) were used for representing the ESs by calculating the mean change from baseline to post-intervention for the intervention and control groups. If there were two exercise groups (or control group) in one study, we halved the number of participants in the control group (or exercise group), while the mean and SD were unchanged. The random effects model, which can avoid the high risk of false-positive results, was used with 95% confidence interval (CI) in overall ESs estimated. According to the Cochrane handbook, the ES was classified as small (<0.2), moderate (0.2–0.49), large (0.50–0.79), and very large (≥0.8) (29). A positive ES value indicated that the results were more favorable to the intervention group, otherwise the control group. Study heterogeneity was evaluated using the $I^2$ test, which was classified as three levels: low, moderate, and high heterogeneity with cutoff points ($I^2 = 25$, $I^2 = 50$, and $I^2 = 75%$). We assessed the publication bias using Egger’s regression test and Funnel plot. The Duval and Tweedie’s trim and fill method was used to assess the potential impact of this publication bias.
FIGURE 2 | Forest plot showing the effects of exercise vs. control on muscle strength: (A) grip strength, (B) knee extension, (C) chair and stand test.
807 of them were excluded because of duplicates, and 107 full-text articles were identified for further confirmation after screening the titles or abstracts. Subsequently, the remaining 107 studies were reviewed for eligibility through reading the full-texts. Finally, 17 studies (31–47) were considered as eligible studies that were included in the meta-analysis.

### Characteristics of Included Studies

The characteristics of the included 17 studies are summarized in Table 1. The included studies were published between 2012 and 2020, located at 12 countries Australia (32), Spain (40), Korea (41), Germany (44), Iran (45), Japan (42, 43, 47), Italy (33), Malaysia (48), Austria (34), Greece (35), Sweden (36), and China (37, 39). A total of 985 participants with sarcopenia were included in the included 17 studies, and the mean age ranged from 67.6 to 86 years. Of note, the diagnostic sarcopenia was based on the two criteria, EWGSOP and AWGS. Eleven studies were published in the included 17 studies, and the mean age ranged from 67.6 to 86 years. Of note, the diagnostic sarcopenia was based on the two criteria, EWGSOP and AWGS. Eleven studies were included in the meta-analysis.

### Synthetic Results

In terms of muscle strength (Figure 2 and Table 3), there were 12 studies, including 15 parallel comparisons on exercise and control conditions (as three studies included two paired trials, respectively), on measuring the grip strength. A pooled comparison revealed that exercise intervention had significant improvement in grip strength (SMD = 0.30, 95% CI [0.15, 0.45], $I^2 = 6\%$, $p < 0.01$). Pooled results from eight trials revealed a significant improvement in chair and stand ($SMD = 0.56, 95\% CI (0.30, 0.81), I^2 = 36\%, p < 0.01$) compared with the control group. Moreover, pooled analysis from 11 parallel trials showed a significant improvement in knee extension in favor of exercise intervention ($SMD = 0.32, 95\% CI (0.15, 0.50), I^2 = 0\%, p < 0.01$) compared with the control group.

In terms of physical performance (Figure 3 and Table 3), the pooled results showed that exercise produced significant improvements in TUG ($SMD = 0.74, 95\% CI (0.48, 1.00), I^2 = 0\%, p < 0.01$), and gait speed ($SMD = 0.59, 95\% CI (0.35, 0.82), I^2 = 62\%, p < 0.01$) compared with the control group.

In terms of body composition (Figure 4 and Table 3), the meta-analysis presented that exercise had significant improvements in SMI ($SMD = 0.37, 95\% CI (0.15, 0.58), I^2 = 16\%, p < 0.01$) and ASM ($SMD = 0.31, 95\% CI (0.13, 0.49), I^2 = 20\%, p < 0.01$) compared with the control group, but there were no significant differences on fat mass ($SMD = 0.20, 95\% CI (−0.07, 0.48), I^2 = 0\%, p = 0.15$), body fat ($SMD = 0.24, 95\% CI (−0.04, 0.53), I^2 = 3\%, p = 0.09$), and fat-free mass ($SMD = 0.36, 95\% CI (−0.10, 0.82), I^2 = 0\%, p = 0.13$) between the exercise group and control group.
Moderator Analysis

To investigate the moderator effects of exercise on interested outcomes, moderator analyses were conducted according to the categorical and continuous variables in Table 4. The effects of exercise on TUG ($Q = 4.45$, $df = 1$, $p = 0.04$) and SMI ($Q = 7.90$, $df = 2$, $p = 0.02$) were significantly moderated by exercise intensity. Moderate–vigorous intensity [SMD = 0.81, 95% CI (0.57, 1.05), $p < 0.01$] of exercise significantly improved TUG compared with the high intensity [SMD = 0.23, 95% CI ($−0.26$, 0.71), $p = 0.37$] of exercise. The high intensity [SMD = 1.39, 95% CI (0.73, 2.06), $p < 0.01$] and moderate intensity [SMD = 0.41, 95% CI (0.10, 0.72), $p < 0.01$] of exercise significantly improved SMI compared with the light-to-moderate intensity [SMD = 0.29, 95% CI ($−0.20$, 0.79), $p = 0.25$] of exercise.

In the meta-regression, the percent of female participants in the original studies was significantly associated with the gait speed ($β = 0.0096$, 95%CI: 0.0006 to 0.0186, $p = 0.03$) (Figure 5 and Table 5) and skeletal muscle index ($β = −0.0092$, 95%CI: $−0.0162$ to $−0.0021$, $p = 0.01$) (Figure 6 and Table 5). In addition, there were no significant moderator effects in age,
Figure 4 | Forest plot showing the effects of exercise vs. control on body composition: (A) skeletal muscle mass index, (B) appendicular muscle mass, (C) lean mass, (D) body fat, (E) fat-free mass.
### TABLE 4 | Moderator analysis for the effects of exercise on measurement outcomes.

| Variables | Muscle Strength | Physical Performance | Body Composition |
|-----------|----------------|----------------------|------------------|
|           | Grip Strength  | Knee Extension       | Chair and Stand  | TUG       | Gait Speed | ASM        | SMI        | Muscle Mass | Lean Mass | BODY FAT |
|           | SMD (95% CI)   | SMD (95% CI)         | SMD (95% CI)     | SMD (95% CI) | SMD (95% CI) | SMD (95% CI) | SMD (95% CI) | SMD (95% CI) | SMD (95% CI) | SMD (95% CI) |
| Criteria  |               |                      |                  |           |           |            |            |            |            |            |
| AWGS      | 0.23 (0.03–0.43) | 0.32 (0.13–0.51)   | 0.55 (0.11–0.88) | 0.69 (0.26–1.13) | 0.55 (0.23–0.88) | 0.25 (0.05–0.44) | 0.18 (0.13 to 0.49) | 0.08 (0.21 to 0.36) | 0.53 (0.25 to 1.31) | 0.36 (0.18 to 0.91) |
| EWGSOP    | 0.41 (0.15–0.67) | 0.34 (0.10–0.78)   | 0.54 (0.22–0.87) | 0.79 (0.43–1.16) | 0.64 (0.28–1.00) | 0.47 (0.00–0.94) | 0.49 (0.18–0.80) | 0.19 (0.20 to 0.57) | 0.16 (0.14–0.45) | 0.16 (0.22 to 0.54) |
| Sex       |               |                      |                  |           |           |            |            |            |            |            |
| Female    | 0.39 (0.03–0.76) | 0.39 (0.12–0.66)   | –                | 0.91 (0.46–1.35) | 0.95 (0.59–1.31) | 0.25 (0.02–0.48) | 0.27 (0.07 to 0.62) | 0.13 (0.11 to 0.37) | 0.28 (0.12–0.68) | 0.55 (0.26 to 1.37) |
| Male      | 0.97 (0.34–1.60) | –                    | –                | 1.08 (0.35–1.81) | 0.39 (0.22 to 0.99) | 0.94 (0.59 to 2.48) | 1.40 (0.73–2.06) | –            | –            | –            |
| Mixed     | 0.21 (0.03–0.39) | 0.28 (0.05–0.51)   | 0.5 (0.30–0.81)  | 0.26 (0.26–0.86) | 0.43 (0.15–0.70) | 0.27 (0.03–0.50) | 0.27 (0.02–0.52) | 0.001 (0.68 to 0.68) | 0.13 (0.25 to 0.52) | 0.13 (0.20 to 0.46) |
| Exercise type |           |                      |                  |           |           |            |            |            |            |            |
| RT        | 0.33 (0.14–0.51) | 0.32 (0.09–0.54)   | 0.31 (0.02–0.61) | 0.80 (0.37–1.23) | 0.50 (0.19–0.81) | 0.33 (0.13–0.52) | 0.54 (0.15–0.74) | 0.11 (0.11 to 0.34) | 0.16 (0.14 to 0.45) | 0.16 (0.17 to 0.49) |
| RT+AE     | 0.24 (0.02 to 0.05) | 0.35 (0.01–0.68)   | 0.71 (0.33–1.08) | 0.59 (0.23–0.96) | 0.92 (0.35–1.50) | 0.19 (0.25 to 0.64) | 0.18 (0.20 to 0.55) | –            | 0.53 (0.25 to 1.31) | 0.50 (0.42 to 1.42) |
| WBV       | –            | 0.34 (0.29 to 0.96) | 0.88 (0.23–1.53) | 0.90 (0.25–1.55) | 0.61 (0.02 to 1.25) | –            | –            | –            | –            | –            |
| Exercise frequency |           |                      |                  |           |           |            |            |            |            |            |
| ≥3 times/week | 0.14 (0.16 to 0.44) | 0.46 (0.07–0.85)   | 0.72 (0.39–1.04) | 0.79 (0.43–1.16) | 0.85 (0.41–1.29) | 0.68 (0.18 to 1.55) | 0.25 (0.02 to 0.53) | 0.24 (0.18 to 0.65) | 0.31 (0.22 to 0.83) |
| <3 times/week | 0.36 (0.16–0.55) | 0.29 (0.10–0.48)   | 0.35 (0.06–0.64) | 0.69 (0.26–1.13) | 0.47 (0.19–0.85) | 0.26 (0.08–0.43) | 0.48 (0.06–0.90) | 0.11 (0.11 to 0.34) | 0.18 (0.19 to 0.55) | 0.23 (0.23 to 0.68) |
| Exercise duration |           |                      |                  |           |           |            |            |            |            |            |
| >12 weeks | 0.39 (0.12–0.65) | 0.33 (0.02–0.65)   | 0.77 (0.11–1.44) | –            | 0.38 (0.02–0.75) | 0.25 (0.04 to 0.54) | 0.28 (0.01 to 0.58) | 0.19 (0.20 to 0.57) | 0.18 (0.19 to 0.55) | 0.18 (0.27 to 0.62) |
| ≤12 weeks | 0.27 (0.06–0.47) | 0.32 (0.11–0.53)   | 0.44 (0.19–0.68) | 0.74 (0.48–1.00) | 0.63 (0.35–0.92) | 0.34 (0.11–0.57) | 0.43 (0.08–0.79) | 0.08 (0.21 to 0.36) | 0.24 (0.18 to 0.65) | 0.34 (0.17 to 0.86) |
| Session time |           |                      |                  |           |           |            |            |            |            |            |
| ≤45min   | 0.14 (–0.09 to 0.37) | 0.31 (–0.07 to 0.68) | 0.44 (0.19–0.68) | 0.66 (0.25–1.06) | 0.55 (0.15–0.96) | 0.35 (0.05–0.64) | 0.29 (0.01 to 0.59) | 0.12 (–0.37 to 0.59) | 0.61 (0.18 to 0.94) | 0.68 (–0.31 to 0.62) |
| >45min   | 0.41 (0.19–0.65) | 0.34 (0.12–0.56)   | 0.77 (0.11–1.44) | 0.82 (0.44–1.19) | 0.62 (0.33–0.92) | 0.30 (0.07–0.53) | 0.42 (0.04–0.79) | 0.11 (–0.11 to 0.34) | 0.24 (0.09 to 0.58) | 0.43 (–0.04 to 0.90) |
| Exercise intensity |           |                      |                  |           |           |            |            |            |            |            |
| Light    | 0.22 (–0.01 to 0.46) | 0.27 (–0.08 to 0.61) | 0.58 (0.03–1.20) | –            | 0.24 (–0.11 to 0.59) | 0.31 (0.02–0.60) | 0.29 (–0.20 to 0.79) | –            | –            | 0.06 (–0.59 to 0.71) |

(Continued)
TABLE 4 | Continued

| Variables                      | Muscle Strength                              | Physical Performance                        | Body Composition                        |
|--------------------------------|---------------------------------------------|---------------------------------------------|-----------------------------------------|
|                                | Grip Strength                               | TUG                                         | BODY FAT                                |
|                                | SMD (95% CI)                                | SMD (95% CI)                                | SMD (95% CI)                            |
| Moderate-vigorous              | 0.36 (0.09–0.61)                            | 0.38 (0.08–0.61)                            | 0.30 (0.06–0.54)                        |
| Vigorous                       | 0.31 (0.01–0.61)                            | 0.30 (0.01–0.61)                            | 0.30 (0.01–0.61)                        |
| Active                         | 0.30 (0.01–0.61)                            | 0.30 (0.01–0.61)                            | 0.30 (0.01–0.61)                        |
| Passive                        | 0.30 (0.01–0.61)                            | 0.30 (0.01–0.61)                            | 0.30 (0.01–0.61)                        |
| Chair and stand                | SMD (95% CI)                                | SMD (95% CI)                                | SMD (95% CI)                            |
|                              | 0.38 (0.13–0.62)                            | 0.38 (0.13–0.62)                            | 0.38 (0.13–0.62)                        |
| Knee extension                 | 0.31 (0.19–0.43)                            | 0.31 (0.19–0.43)                            | 0.31 (0.19–0.43)                        |
| Extension                      | 0.28 (0.13–0.43)                            | 0.28 (0.13–0.43)                            | 0.28 (0.13–0.43)                        |
| ASM                            | SMD (95% CI)                                | SMD (95% CI)                                | SMD (95% CI)                            |
|                              | 0.22 (0.06–0.59)                            | 0.22 (0.06–0.59)                            | 0.22 (0.06–0.59)                        |
| SMI                            | SMD (95% CI)                                | SMD (95% CI)                                | SMD (95% CI)                            |
|                              | 0.22 (0.06–0.59)                            | 0.22 (0.06–0.59)                            | 0.22 (0.06–0.59)                        |
| Gait speed                     | SMD (95% CI)                                | SMD (95% CI)                                | SMD (95% CI)                            |
|                              | 0.28 (0.12–0.42)                            | 0.28 (0.12–0.42)                            | 0.28 (0.12–0.42)                        |
| TUG                           | SMD (95% CI)                                | SMD (95% CI)                                | SMD (95% CI)                            |
|                              | 0.23 (0.09–0.43)                            | 0.23 (0.09–0.43)                            | 0.23 (0.09–0.43)                        |

\[\text{SMD} = \frac{\text{Mean}_{	ext{intervention}} - \text{Mean}_{	ext{control}}}{\text{SE}_{\text{intervention}} + \text{SE}_{\text{control}}}\]

\[\text{ES} = \frac{\text{SMD}}{\text{SD}_{\text{control}}}\]

\[\text{CI} = \text{SMD} \pm 1.96 \times \text{SE}\]

\[\text{p} < 0.05\]

\[\text{AE}, \text{aerobic exercise}; \text{ASM}, \text{appendicular skeletal muscle}; \text{AWGS}, \text{Asia Working Group for Sarcopenia}; \text{EWGSOP}, \text{European Working Group on Sarcopenia in Older People}; \text{RT}, \text{resistance training}; \text{TUG}, \text{timed up and go}; \text{WBV}, \text{whole-body vibration training}.

**Publication Bias**

Publication bias was evaluated using Egger’s test (in Table 3) and Funnel plot (in Supplementary Figures). Of which, although the asymmetrical Funnel plot and Egger’s test (Egger’s regression intercept = 6.1, \(p < 0.05\)), the Duval and Tweedie’s trim and fill showed that five studies were missing on the left side of the mean effect. The adjusted value was SMD = 0.35, 95% CI (0.08, 0.61), which was substantially lower than our estimation (SMD = 0.59). There seems to be evidence for publication bias in this meta-analysis since studies with smaller effect sizes are not provided.

**DISCUSSION**

The present systematic review and meta-analysis consisting of 17 RCTs (985 individual participants, 726 female, with sarcopenia) investigated the effects of exercises on muscle strength, physical performance, and body composition. The main findings of this systematic review with meta-analysis showed that exercises had significant benefits on muscle strength (grip strength, knee extension, and chair-stand), physical performance (timed up and go, and gait speed), and body composition (skeletal muscle mass index and appendicular skeletal muscle) compared with the control group in older adults with sarcopenia. The effects of exercise on gait speed and SMI were moderated by sex in the study and exercise intensity. These results may be important for implementing exercise interventions for sarcopenic older adults in clinic.

Since the differences in diagnostic criteria for sarcopenia, according to different organizations, the EWGSOP updated the definition and diagnostic criteria in 2008. This definition highlights that muscle strength is a principal element in sarcopenia diagnosis and is a useful predictor of adverse outcomes in people with sarcopenia (2). The EWGSOP and AWGS recommend that handgrip strength and chair-stand test are suitable measures of muscle strength. In our study, muscle strength was measured using the handgrip strength, chair stand test, and knee extension strength. The findings from this meta-analysis demonstrated that after exercise, older adults with sarcopenia demonstrated significant improvements in muscle strength. More specifically, exercises had small effects for grip strength (15 trials, ES = 0.31) and knee extension strength (11 trails, ES = 0.36) and moderate effect for chair and stand (eight trials, ES = 0.56) compared with the control groups, respectively. Consistent with previous meta-analysis and systematic reviews (49, 50), exercise has significant effects on muscle strength in older adults. Increased muscle strength may be associated with the neuronal adaptations, such as increases in muscle fiber tissue or synchronization of muscle contractions (51). During exercise training, muscle fiber are re-structured, leading to an increase in neuronal activity that stimulates an increase in muscle strength (52).
In regard to physical performance, the common testing tools include gait speed and TUG. Previous studies have demonstrated that poor physical performance, similar to low muscle strength, is associated with a higher risk of death in older adults [53, 54]. The latest EWGSOP consensus recommends using physical performance to assess the severity of sarcopenia. Herein, gait speed and TUG were used to measure the physical performance in this review study. Our meta-analysis found that exercise's benefit is improving gait speed and TUG, and the positive effects can be supported by a previous review study targeting older adults [55]. These meaningful results are of great importance because there is a close relationship between muscle strength and physical performance [56]. Consistent with another similar study, the study of Capodaglio et al. on older adults over 75 years found that significant improvements in walking ability and TUG were attributed to the improved lower limb strength after exercise training [57]. Thus, our findings reinforce the important role of exercise in physical performance in older adults with sarcopenia.

With reference to the body composition, in particular, the use of DXA or BIA to measure skeletal muscle mass and appendicular skeletal muscle mass has been considered as an important approach to assess the muscle quantity or quality to identify sarcopenia in the latest consensus (2). On this basis, our meta-analysis study indicated that the SMI and ASM have been significantly improved after exercise in sarcopenic older adults, which was inconsistent with previous systematic reviews [22, 58]. The possible reason is that the improved muscle mass indicates an anabolic potential of exercise, inducing muscle hypertrophy via resistance exercise or aerobic exercise such as cycling and walking among all of ages [59]. More importantly, improved skeletal muscle mass might be attributed to the increase in size of slow muscle fibers [60] and the increase in fast-twitch fiber sizes [61]. Moreover, the statistical power in our study was augmented through including more eligible studies than previous meta-analysis studies [22, 58]. Thus, it is believed that older adults with sarcopenic can improve their muscle mass through appropriate exercise.

In addition, the moderator analyses revealed that moderate to vigorous intensity exercise (ES = 0.81) could produce greater effects on TUG than did vigorous intensity exercise (ES = 0.23). This result may be inconclusive due to the small number of included studies investigating vigorous intensity exercise and the different methods on coding intensity exercise in the subgroup. Actually, a recent systematic review study has documented that both moderate and vigorous intensity exercises can improve functional ability in frail older adults [55]. Future research is warranted to determine the effect of exercise at different intensities on physical performance. As for SMI, after practicing exercise at moderate and vigorous intensity, sarcopenic adults had significant improvement in their SMI compared with those practiced exercise at low intensity. This finding is similar to a previous study by Csapo et al., in which they found that high-intensity exercise had more advantage on increasing skeletal muscle mass than low-intensity exercise in older adults [19]. Indeed, moderate to high-intensity exercise enhances the skeletal muscle mass via stimulating protein synthesis [62]. On the
TABLE 5 | Meta-regression for continuous variables to predict exercise effects on measurement outcomes.

| Variables               | Muscle strength | Physical performance | Body composition |
|-------------------------|----------------|----------------------|-----------------|
|                         | Grip strength  | Knee extension       | Chair stand test| TUG $\beta$ (95% CI) | Gait speed $\beta$ (95% CI) | ASM $\beta$ (95% CI) | SMI $\beta$ (95% CI) | Muscle mass $\beta$ (95% CI) | Lean mass $\beta$ (95% CI) | Body fat $\beta$ (95% CI) |
| Age                     | -0.0089        | -0.0110              | -0.0255         | 0.0069               | -0.0252                   | -0.0134               | 0.0117              | -0.0210                   | 0.0007              | 0.0023               |
|                         | (-0.0364 to -0.0186) | (-0.0474 to -0.0254) | (-0.0765 to -0.0255) | (-0.0618 to -0.0259) | (-0.0758 to 0.0254)       | (-0.0443 to 0.0447) | (-0.0249 to 0.0248) | (-0.0736 to 0.0306) | (-0.0438 to 0.0452) | (-0.0100 to 0.0146) |
| Percent of female       | -0.0021        | 0.0025                | 0.0018           | 0.0096               | (0.00006 to 0.0006)       | -0.0051               | -0.0092              | 0.0144                   | 0.0036              | 0.0096               |
|                         | (0.0046)       | (0.0128)              | (0.0438)         | (0.0071)             |                           | (0.0094 to 0.0186)    | (0.0017)           | (0.0144 to 0.0661)       | (0.0949)           | (0.0098 to 0.0240)    |
| participants            |               |                      |                 |                     |                           |                       |                     |                         |                   |                     |
| Exercise time per week  | 0.0021         | 0.0021                | -0.0004          | 0.0016               | 0.0046                    | 0.0024                | -0.0033              | -0.0055                   | -0.0124             | -0.0011              |
| in minutes              | (-0.0014 to -0.0016) | (-0.0018 to -0.0028) | (-0.0038 to -0.0075) | (-0.0041 to -0.0009) | (-0.0039 to 0.0004)       | (-0.0033 to 0.0055)   | (-0.0033 to -0.0012)   | (-0.0144 to -0.0014)      | -0.0011             | -0.0010             |
|                         | 0.0056         | 0.0069                | 0.0075           | 0.0021               | 0.0101                    | 0.0024                | -0.0033              | 0.0055                   | -0.0124             | -0.0011             |
| Exercise duration       | 0.0063         | 0.0069                | -0.0141          | 0.0026               | 0.0172                    | 0.0024                | -0.0033              | 0.0055                   | -0.0124             | -0.0011             |
|                         | (-0.0129 to -0.0125) | (-0.0135 to -0.0257) | (-0.0657 to -0.0378) | (-0.0268 to -0.0705) | (-0.0382 to 0.0705)       | (-0.0255 to 0.0275)   | (-0.0275 to 0.0021)    | (-0.0150 to 0.0297)       | (-0.0255 to 0.0231)   | (-0.0522 to 0.0425)   |
| Dose of exercise        | 0.00000        | 0.00001               | 0.0001           | 0.0004               | 0.0001                    | 0.00000               | -0.00001             | 0.00001                  | -0.00001            | -0.00001            |
| intervention            | (-0.0001 to 0.0001) | (-0.0001 to -0.0001) | (-0.0002 to -0.0003) | (-0.0005 to 0.0002)   | (-0.0003 to 0.0003)       | (-0.00001 to 0.00001) | 0.00002             | 0.00002                  | (-0.00002 to 0.0002)  |                 |

*p < 0.05.

ASM, appendicular skeletal muscle; SMI, skeletal muscle mass index; TUG, timed up and go; --, the continuous variable in each study is equivalent.
contrary, lack of stimulation of the protein synthesis in muscle is related to low-intensity exercise, and it is recommended to increase skeletal muscle mass by compensating for more repetitions and velocity of motion (63). Despite this, it is recommended to explore the underlying mechanism of effects of exercise at different intensities.

Additionally, the meta-regression revealed gender-specific effects on exercise-related changing in gait speed and SMI, implying a tendency that female participants had more improvements in gait speed and SMI than male participants after practicing exercise. The explanations for this findings may be attributed to external confounding (e.g., completed quality and motivation of the participants) that might affect the results (36). Based on this hypothesis, gender-specific effects did contribute to significant differences on other outcomes, such as grip strength, chair and stand, TUG, etc. Further studies are warranted to investigate the gender difference on the effects of exercise on physical performance and skeletal muscle mass.

Our systematic review and meta-analysis have some strengths that should be noted. All studies included in this meta-analysis were RCTs, which provided the empirical data for understanding the evidence of a treatment's efficacy. Furthermore, participants in this present study were only sarcopenic older adults without other physical conditions, like not being obese; so our research findings can be applied to the prevention or treatment in this sarcopenia population. Additionally, other potential confounders were examined to find whether they had any influence on the effects of exercise. This novelty could provide more information for future research to look at the influences of these confounders.

There are, however, several limitations in our study. First, as there were no consistent assessment criteria for sarcopenia, participants who met the initial sarcopenia defined by the EWGSOP and AWGS were included in our study. It may result in publication bias. Herein, according to the latest operational definition of sarcopenia (e.g., EWGSOP, AWGS), uniform cutoff points are expected to diagnose the subject and measure the outcomes in the future study. Second, the included studies used different instruments to measure the interested outcomes such as body composition (e.g., BIA, DEXA), which will contribute to the effect size of outcomes. While both of them used to examine the sarcopenia in clinical research, which is suggested by EWGSOP and AWGS, the multifrequency BIA equivalent to the DEXA measurements could be used in future research so as to ensure the accuracy of the diagnosis. Moreover, confirming the effect of exercise on interested outcomes by analyzing different instruments used to measure muscle mass separately is warranted. Third, studies using a sole exercise intervention to treat sarcopenia were included, excluding studies combing exercise intervention and nutrition. As a source of muscle synthesis, nutrient intake methods are important for the prevention and treatment of sarcopenia. There is a need for further research that examines the effect of combined exercise and nutrition intervention on sarcopenia. Four, the percentage of the female participants (female 74%) was considerably high compared with male participants, and the findings may not generalize all populations. As a result, further study may benefit from investigating the effects of exercise on sarcopenia in males and females separately due to physical difference in gender.
CONCLUSION

These meta-analysis results suggest that exercise interventions have positive effects on muscle strength, physical performance, and skeletal muscle mass for sarcopenic elderly, but no effect is found in body composition (e.g., fat mass, lean mass, and fat-free mass). Further researches need to use the latest consensus criteria proposed by EWGSOP or AWGS to identify the sarcopenia, and a larger number of studies are recommended to confirm our findings. Meanwhile, the effective exercise protocol should be designed as promoting strategies in treating sarcopenia.

DATA AVAILABILITY STATEMENT

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

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AUTHOR CONTRIBUTIONS

YZ and WS conceptualized the study. YZ, LZ, JB, and XL handled the methodology. YZ, S-TC, DK, and XL were in charge of the software. DK, XL, and WS did the validation. YZ, LZ, and S-TC performed the formal analysis. YZ, LZ, S-TC, and JB conducted the investigation. YZ and XL were in charge of the resources. YZ, JB, and XL did the data curation. YZ, LZ, and XL prepared and wrote the original draft. LZ and WS reviewed, edited, and wrote the manuscript. YZ, S-TC, and DK did the visualization. WS was in charge of the supervision and project administration. All authors have read and agreed to the published version of the manuscript.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2021.649748/full#supplementary-material
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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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