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Review Article

Efficacy and Safety of Electrical Myostimulation for Sedentary Elderly People at Risk of Primary Sarcopenia: A Systematic Review and Meta-Analysis

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SUMMARY

This systematic review aimed to produce a meta-analysis summarizing the efficacy and safety of electrical myostimulation (EMS) for sedentary elderly people at risk of primary sarcopenia.
PubMed (OVID), EMBASE (OVID) and Cochrane Central Register for Randomized Controlled Trials (CENTRAL) were searched for randomized controlled trials (RCTs) from the inception of the databases to March 2019 to identify applicable studies that involved sedentary elderly people and compared EMS as a sole or adjunct intervention with no treatment, a placebo, or an active control. Two researchers reviewed the literature independently for eligibility and methodological quality and extracted outcome data for the meta-analysis.
Nine studies involving a total of 508 elderly participants met the inclusion criteria. Analysis showed that, compared to the control group, EMS groups showed significant improvements in muscle strength (MD 1.68, 95% CI 0.66 to 2.69), and only marginal improvements in appendicular skeletal muscle mass (ASMM) (SMD 0.24, 95% CI -0.11 to 0.59), lean body mass (LBM) (SMD 0.11, 95% CI -0.29 to 0.50), the Timed Up and Go Test (TUGT) (MD 0.13, 95% CI -1.18 to 1.43) and the cross-sectional area (CSA) of the rectus femoris (MD 0.47 95% CI -0.11 to 1.05).
The results suggest that EMS may be an effective treatment for the elderly population to prevent the loss of muscle mass and function. However, definite conclusions cannot be drawn based on the available evidence due to a limited amount of pooled data and heterogeneity across studies.

1. Introduction

Aging is a global phenomenon currently attracting much concern worldwide, skeletal muscle degeneration is one of the major medical issues among elderly people. It has been almost 30 years since Irwin Rosenberg proposed the term “sarcopenia” to describe the progressive decline of skeletal muscle.[1] However, the parameters cut-off value for sarcopenia diagnosis might vary in different populations.[2] Based on the existing literature, the prevalence of sarcopenia is 5–13% in 60- to 70-year-old people, and 11–50% in people over 80 years old.[3] Sarcopenia may lead to several adverse prognoses, such as falls, disabilities, and poor quality of life, and may also increase mortality rates.[4] Francesco even demonstrates that disability, more than multimorbidity, may predict mortality in elderly people over 80 years old.[5]

Many studies have focused on strategies, medicines, and devices that might be useful in maintaining muscle mass or function. The primary intervention strategy includes protein supplementation and physical exercise. Although both are effective in preventing and treating the sarcopenia, some older adults may benefit less due to anabolic resistance or immobility. Furthermore, there are no investigational drugs with promising effectiveness and safety. Thus, researchers are eagerly looking for new therapies to prevent and treat age-related muscle weakness.

Electrical myostimulation (EMS) may be an alternative method for improving skeletal muscle mass and function. EMS may produce a comfortable and controlled contraction of a skeletal muscle,[6] which is equivalent to 20% to 40% of a maximum voluntary muscle contraction.[7] Prior studies have demonstrated that electrical stimulation promotes the protein anabolic metabolism of skeletal muscle.[8] In addition, EMS is a time-efficient, joint-friendly and highly customizable exercise technology that is suitable for the aging population.

Despite all these findings, the overall estimated effect of EMS on elderly people with primary skeletal muscle decline still lacks power and precision. Therefore, a systematic review and meta-analysis are necessary for improving a comprehensive synthesis regarding the efficacy and safety of EMS for degenerative muscle changes in the elderly population.

2. Methods

This meta-analysis follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[9] Randomized controlled trials (RCTs) were included in the review, regardless of whether the intervention was blinded to patients, physicians, or other researchers. Review articles, case reports, animal

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trials, editorials, conference abstracts, letters and observational studies were excluded.

2.1. Participants

Trials were included in this meta-analysis if the following criteria were met. First, the studies focused on the elderly population; therefore, studies that recruited participants with an average age of ≤ 60 years were excluded. Second, the studies mainly focused on degenerative muscle change; therefore, we excluded those studies that involved participants with muscle atrophy related diseases such as cancer, HIV/AIDS, chronic obstructive pulmonary disease (COPD), a special medical history (glucocorticoids) or denervated muscle atrophy. Lastly, the studies that recruited participants with sedentary lifestyles were included and studies with athletes or subjects undergoing long-term physical training programs were excluded.

2.2. Intervention

EMS can be offered to participants as a sole intervention or as an adjunct to nutritional supplements or some kind of exercise. EMS was mainly applied to the lower extremities but was not limited to the lower extremities. The studies in which EMS was applied to the whole body were also included. However, the studies in which EMS was only applied to local areas such as the abdomen or trunk were excluded. No limitations were introduced regarding the program duration, intervention frequency, session length, or characteristics of the applied pulse. The studies that evaluated the short-term effects (less than one week) of an EMS intervention were excluded. The control groups could be either an active control group or an inactive control group.

2.3. Outcomes measures

Muscle strength was considered the primary outcome of the prior studies analyzed in our review. Handgrip strength can be used conveniently as a screening tool for sarcopenia, which is strongly related to lower limb muscle power, knee extension torque and calf cross-sectional area (CSA).[10] The maximum isometric strength of the leg or trunk extensor is also widely used to evaluate the power of skeletal muscles.

Additionally, we examined three secondary outcomes. The first was “muscle mass”: dual-energy X-ray absorptiometry (DXA), bioelectrical impedance analysis (BIA), and computed tomography (CT)/magnetic resonance imaging (MRI) can be used to assess muscle mass; appendicular skeletal muscle mass (ASMM), lean body mass (LBM) and the skeletal muscle mass index (SMI) are commonly used parameters. The second was “physical performance” which can be measured by the Short Physical Performance Battery (SPPB), preferred gait speed, the Timed Up and GoTest (TUGT) and the 6-Min Walk Test (6MWT). Third, we examined the cross-sectional area (CSA) of specific muscle groups reported in the studies, as this can directly reflect muscle atrophy.

2.4. Search strategy

The following electronic databases were comprehensively searched from the inception to March 2019: PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL). The language of eligible literature was limited to English. Search terms were “sarcopenia”, “muscle mass”, “muscle strength”, “muscle function”, “muscle atrophy”, “physical performance”, “muscle wasting”, “lean body mass”, “whole-body electromyostimulation”, “electrical stimulation”, “neuromuscular electrical stimulation”, and “electromyostimulation”. A sample of the search strategy used for MEDLINE is provided in the appendix for reference.

2.5. Data extraction

Two reviewers (HNJ, YY) assessed the titles and abstracts of studies independently after removing duplicates. The full texts of the potentially eligible studies were retrieved and evaluated to identify studies that completely fulfilled the inclusion criteria. Reviewers resolved potential discrepancies by discussion, and a customized extraction form was designed and utilized to record the details of each study.

2.6. Quality assessment

All included articles were independently assessed for risk of bias by two raters (HZ and WWL) using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*. The criteria helped to evaluate the methodological quality of the included studies. In any case where a discrepancy existed between two raters, a third assessor was included in the discussion and final decisions were based on consensus.

2.7. Statistical analysis

Data were analyzed using RevMan 5.3 software, and a comparison of effectiveness was conducted between the EMS and the control interventions. Inverse variance weighting was adopted as a statistical method. Calculations were based on mean, standard deviations, p-values, and sample sizes of the groups, according to data reported in the primary studies. A chi-squared test was used to assess the heterogeneity of the trials. When the p-value was less than 0.10 ($I^2 \geq 50\%$), a significant degree of heterogeneity existed. If significant heterogeneity existed, a random-effects model was selected for data pooling; otherwise, a fixed-effects model was selected. For continuous data, the mean difference (MD) was calculated with a 95% confidence interval (CI). However, the standardized mean difference (SMD) was used when the original studies had used differing measurement scales. Sensitivity analysis was performed to find the specific trial that caused the heterogeneity. When a meta-analysis was inappropriate for some outcomes, only a narrative was presented. Publication bias was examined using a funnel plot.

3. Results

3.1. Search results

Among the 2307 articles identified, only 29 eligible articles were retrieved for full-text review. Among these articles, 20 articles were excluded for the following reasons: the study was not a randomized controlled trial (n 7), EMS was not applied to lower limb skeletal muscle groups (n 4), the study evaluated the short-term effects of EMS (n 2), and the study was a duplicate (n 7). Finally, nine studies[11–19] met the eligibility criteria. Figure 1 shows the details of the screening process. All groups with EMS interventions were involved in the meta-analysis.

3.2. Participants

A total of 9 studies including a total of 508 participants were

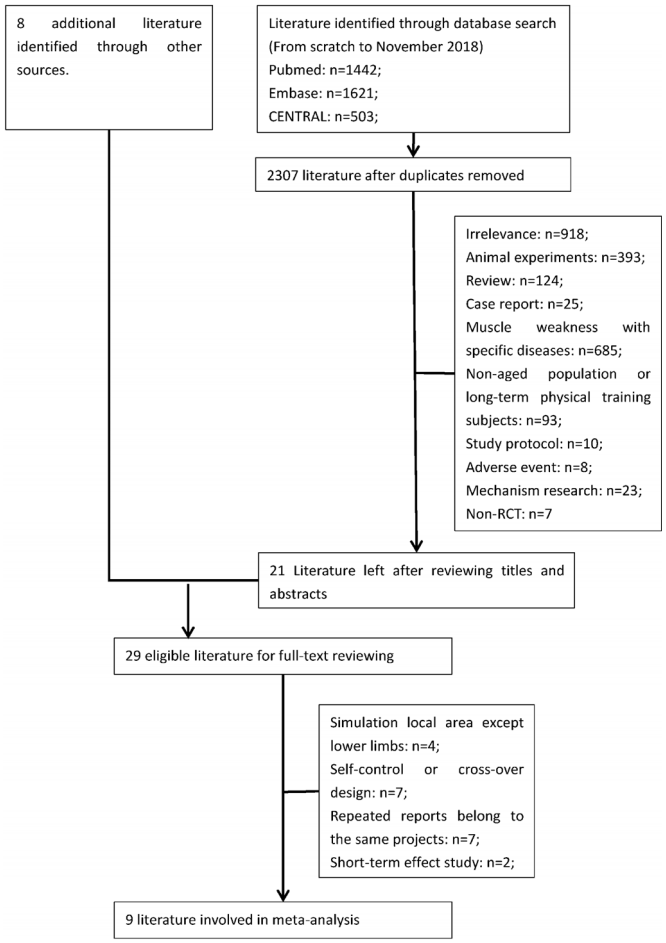

Figure 1. Study flow diagram.

included in the meta-analysis. The mean age of the participants ranged from 67.8 to 82 years. All the studies enrolled elderly subjects who lived a sedentary lifestyle in the community or healthcare institutions. Only two studies[11,12] defined sarcopenia with precise cut-off points, while other studies only stated age and lifestyle in the inclusion criteria. Table 1 shows the characteristics of the included studies.

3.3. Interventions and controls

To allow close supervision, EMS was offered to participants in institutions in all of the included studies, except for one[13] in which the intervention was offered at home. All programs targeted skeletal muscle groups in the lower limbs, including the quadriceps muscle, hamstring muscle and tibialis anterior, but three programs[11,12,16] applied EMS to the whole body in addition to the lower extremities. Four studies[11,13,17,18] used EMS alone as therapy in one of their intervention groups, while other studies combined EMS with amino acid/protein supplementation,[11,12] calcium/vitamin D supplementation[16] or a specific kind of physical exercise.[14,15,17–19] Details about the program characteristics and stimulation parameters are presented in Table 2.

3.4. Outcomes measures

For muscle mass measurement, DXA was used in three studies[11,16,18] while BIA was used in one study[12] and three other studies[11,12,16] used LBM. One study[18] used fat-free mass (FFM) to determine muscle mass. Only two studies[12,16] used ASMM, and three studies[11,12,16] used SMI. However, the SMI equations differed as, ASMM/(body height)^2 (kg/m^2) was used in two of those studies[11,16] and, ASMM/BMI in the other.[12]

Handgrip strength and maximal isometric strength are widely used parameters to evaluate muscle strength. Four studies assessed handgrip strength; among these studies, three studies used a hand dynamometer,[11,12,16] and one study did not mention related equipment.[17] Four studies assessed maximal isometric strength, in which an isometric tester,[16] an ergometer[18] and a Biodex system[15,19] were used, respectively.

Walking speed or walking distance within a specified duration of time, TUGT and SPPB are widely used assessments of physical performance. Four studies assessed habitual walking speed within a 10-m-distance,[11–13,16] two studies assessed participants' walking distance within 6 min at their maximal speed,[17,18] and one study measured participants' maximum gait speed within 10 m.[19] Four studies used the TUGT.[13,14,17,19] Only one study used the SPPB.[13]

Other parameters used in assessing skeletal muscle condition, included the sarcopenia Z-score, CSA of specific lower limb muscles and the Berg Balance Scale (BBS). The sarcopenia Z-score suggested by Johnson[20] summarizes three sarcopenia criteria, —gait speed, grip strength, and SMI— into one single index. Two studies[11,12] used the Z-score to comprehensively assess muscle condition. Two studies[15,17] measured the CSA of the rectus femoris. Two studies[14,17] used the BBS to evaluate a participant's ability to maintain balance.

3.5. Quality assessment

All nine studies performed a randomization procedure to minimize selection bias. Sequence generation was described adequately in six studies,[11,12,15,17–19] which used computers to generate random numbers or draw lots. Therefore, we considered these studies to have a low risk of bias in this domain. Sequence generation was not mentioned in the remaining three studies, which are considered to have an unclear risk of bias.

Three studies[11,12,17] described details about allocation concealment with opaque plastic shells; therefore, the risk of bias is low in this domain. Allocation concealment was not mentioned in the remaining six studies, which are considered to have an unclear risk of bias.

Designing placebo controls for this kind of intervention can be challenging. Only one study[16] mentioned and adequately described blinding of the participants to the testing conditions, so we considered it to have a low risk of performance bias. The remaining eight studies did not design a blinding procedure, considered to have a high risk of bias in this domain.

Six studies[11,12,15,17–19] that mentioned blinding of the outcome assessors were considered to have a low risk of detection bias. The remaining three studies did not mention blinding of the outcome assessors, considered to have an unclear risk of bias in this domain.

Over 20% of the participants did not have complete follow-up data in two studies,[14,16] and finisher analysis was performed accordingly. We considered these studies to have a high risk of attrition bias. All subjects finished the program with complete data available in three studies.[15,17,19] A small portion of the participants withdrew from the program, but the intention-to-treat analysis was performed in two studies.[11,12] We considered both conditions to have a low risk of bias in this domain. The remaining two studies[13,18] did not provide adequate information regarding the loss of data in the follow-ups or adverse events, therefore, they were considered to have an unclear risk of bias.

Table 1
Characteristics of included studies.

Author	Publication (year, country)	Study design	Sample size (male/ female)	Participants status (Inclusion criteria)	Age (MV ± SD or range)	Control	Description of Intervention
Wolfgang Kemmler	2016; Germany	RCT	75(0/75)	Community-dwelling women more than 70 years with sarcopenic obesity Inclusion criteria: (a) Sarcopenia (SMI < 5.75 kg/m^2); (b) Obesity (> 35 % body fat)	WB-EMS group: 77.3 ± 4.9; WB-EMS&P group: 76.4 ± 2.9; Control: 77.4 ± 4.9	(1) WB-EMS&P group (n = 25): WB-EMS and protein supplementation (150 kcal/day, 56% protein); (2) Non-training control group (n = 25): maintain their habitual life style.	WB-EMS group (n = 25): Consisted of one weekly session of 20 min (bipolar electric current, 85 Hz, 350 us, 4 s of strain-4 s of rest) performed with moderate to high intensity for 26 weeks.
Wolfgang Kemmler	2013; Germany	RCT	76(0/76)	Lean, non-sportive, osteopenic women 70 years and older that focused on sarcopenia and osteoporosis	75 ± 4	Semi-active control group (n = 38): Subjects intermittently exercised for 10 weeks (1 session/ week with 60 min) with 10 weeks of rest. Two 10-week blocks were realized during the 54-week interventional period.	WB-EMS group(n = 38): 18 min of WB-EMS (bipolar, 85 Hz, impulse breadth of 350 us intermittently with 6 s of EMS simulation using a direct impulse boost to perform the movement and 4 s of rest using WB-EMS devices) 3 sessions in 14 days (1.5 sessions/week) for 54 weeks.
Wolfgang Kemmler	2017; Germany	RCT	100(100/0)	Community-dwelling northern Bavarian men aged 70 years with sarcopenia and obesity Inclusion: skeletal muscle mass index (SMI) < 0.789 suggested by the FNIH for sarcopenia and body fat > 27% for obesity recommended by Baumgartner for obesity	WB-EMS&P group: 77.1 ± 4.43; Protein group: 78.1 ± 5.1; Control group: 76.9 ± 5.1	1) Protein group (n = 33): Isolated protein supplementation (1.7–1.8 g/kg/body mass per day); 2) Nonintervention control group (n = 34).	WB-EMS&P group (n = 33): WB-EMS (1.5 × 20 min, bipolar electric current, 85 Hz, 350 us, 4 s of strain to 4 s of rest) applied with moderate-to-high intensity while moving) and protein supplementation (1.7–1.8 g/kg/body mass per day) for 16 weeks.
Sandra Zampieri	2015; Italy	RCT	25(?)	70 year old sedentary seniors	?	LP group (n = 9): leg press as voluntary exercise (consisted of three training sessions a week for nine weeks)	ES group (n = 16): Electrical stimulation as passive exercise (consisted of three training sessions a week, for a period of nine weeks).
V. Benavent-Caballer	2014; Spain	RCT	89(?)	Inclusion participants had to be aged 75 or older, able to ambulate independently, able to communicate, and willing to stay in the same geriatric nursing home for the next 6 months.	NMES group: 82.9 ± 4.3; NMES+ group: 83.6 ± 3.6; VC group: 85.5 ± 4.7; Control group: 83.6 ± 5.6	1) NMES+ group (n = 22): NMES superimposed onto voluntary contractions; 2) VC group (n = 22): Volitional contraction; 3) Control group (n = 23).	NMES group (n = 22): three weekly non-consecutive exercise sessions for 16 weeks. Each session lasted 30 to 35 min.
Martina Anna Maggioni	2012; Italy	RCT	40(0/40)	Hospitalized elderly women inclusion criteria: 1) age ≥ 75 years; 2) hospitalization period longer than 1 month; 3) autonomous ambulation; 4) absence of severe cognitive impairment assessed by a preliminary Mini Mental State Examination (MMSE) score > 24/30 and by a Barthel Index > 70/100, according to Mahoney and Barthel and Folstein.	82 ± 7	1) KT group (n = 10): kinesitherapy; 2) KT + ES group (n = 10): KT combined with ES; 3) Control group (n = 10).	ES group (n = 10): 3 day/week for 6 weeks 18 electrical stimulation sessions of the quadriceps muscle on both legs. Bi-phasic squarewaves delivered by an electrical stimulator on vastus lateralis, vastus medialis and rectus femoris muscles. Stimulation frequency increased from 35 Hz in first 6 sessions, to 75 Hz in the following 6 sessions (7th–12th) and to 85 Hz in the last 6 sessions (13th–18th), in accordance to the manufacturer's instructions.
Yoshio Takano	2010; Japan	RCT	20(6/14)	Community-dwelling elderly people having no medical problems	67.8 ± 4.8	The WMT group (n = 10): the weight machine equipment for knee flexion and extension was used in the study. One training session required 19 minutes to complete. The training intensity was changed from flexion to extension.	The HYBT group: (n = 10): All the subjects performed knee flexion and extension for 19 min per session, twice a week for 12 weeks. Electrical stimulation parameters were based on a standard Russian waveform in which a 5,000 Hz carrier frequency was modulated at 40 Hz to deliver a rectangular voltage biphasic pulse.
Kerem Alptekin	2016; Turkey	RCT	67 (?)	Patiens aged 60 years and over with balance disorder diagnosed using the Timed Up and Go (TUG) test	69.56 ± 6.55	1) Balance exercise + static posturography group (n = 23): The patients participated in a 15-minute exercise with TetraxR which consisted of 15 minutes exercise session 3 times weekly for 4 weeks; 2) Balance exercise group (Control group) (n = 20): Patients did 6-week balance exercises which were performed by other groups as well.	Balance exercise + electrostimulation to postural muscles group (n = 24): The patients received an electrostimulation program (30 Hz, 300 us) of postural muscles of 40 minutes per session 3 times weekly for 4 weeks, besides balance exercise.
Yoshio Takano	2016; Japan	RCT	16(6/10)	Community dwellings in Okawa City	71.8 ± 3.9 (66–77 years)	CTR group (n = 8): The squat and single leg lift training only.	The CTR with HTS training group (n = 8): Some electrical stimulation was applied to the quadriceps and hamstring muscles in the HTS group. The subjects performed training for 25 min per session 3 times a week for 12 weeks. The training consisted of squats (10 minutes) and single leg lifts using HTS (15 minutes). The stimulation waveform used in this study consisted of a 5,000 Hz carrier frequency with a pulse width of 200us modulated at 40Hz to deliver a rectangular biphasic pulse.

RCT: randomized controlled trial; SMI: skeletal muscle mass index; WB-EMS: whole body-electrical myostimulation; LP: leg press; ES: electrical stimulation; NMES: neuromuscular electrical stimulation; VC: volitional contraction; KT: kinesitherapy; WMT: weight machine training; HYBT: hybrid training; CTR: control; HTS: hybrid training system.

Table 2
Programme characteristics and stimulation parameters.

Study ID	Location	Muscle groups	Combined/alone	Stimulation parameters								
				Programme duration	Session Frequency	Session interval	Session length	Impulse width	Pulse frequency	Current intensity	Pulse interval	Pulse shape
Wolfgang 2016	Institution	Whole body	Two intervention groups: one is EMS alone; another is combined with protein supplementation (150 kcal/day, 56% protein)	26 weeks	1/week	NA	20 min	350 us	85 Hz	Moderate to high intensity	4-6 s stimulation; 4 s rest	Bipolar electric current
Wolfgang 2013	Institution	Whole body	Combined with basic movements and calcium (1200 mg/d)/ cholecalciferol (800IE/d) supplementation	54 weeks	1.5/week	NA	18 min	350 us	85 Hz	NA	6 s stimulation; 4 s rest	Bipolar electric current
Wolfgang 2017	Institution	Whole body	Combined with protein supplementation (1.7–1.8 g/kg/ body mass per day)	16 weeks	1.5/week	NA	14 to 20 min	350 us	85 Hz	Moderate to high intensity	4 s stimulation; 4 s rest	Bipolar electric current
Sandra 2015	Home-based	Quadriceps muscle	EMS alone	9 weeks	3/week	NA	NA	NA	NA	NA	NA	NA
Benavent 2014	Institution	Anterior thigh	Two intervention groups: one is EMS alone; another is combined with voluntary contractions	16 weeks	3/week	NA	30 to 35 min	400 us	50 Hz	40% of one-repetition maximum	6 s stimulation; 2 s rest	Biphasic symmetrical square wave form
Martina 2012	Institution	Quadriceps muscle	Two intervention groups: one is EMS alone; another is combined with kinesitherapy	6 weeks	3/week	24 hours	45 min	NA	35 Hz~85 Hz	NA	NA	Compensated biphasic square waves
Yoshio 2010	University laboratory	Quadriceps femoris; hamstring muscles	Combined with knee flexion and extension exercises	12 weeks	2/week	48 hours	19 min	NA	40 Hz	29.5 $\pm$ 6.5 V for the quadriceps femoris and 31.4 $\pm$ 6.7V for hamstring muscles	2.4 ms on; 22.6 ms off	Rectangular voltage biphasic pulse
Kerem 2016	Institution	Quadriceps; tibialis anterior	Combined with balanced exercises	4 weeks	3/week	NA	40 min	300 us	30 Hz	NA	NA	NA
Yoshio 2016	University laboratory	Hamstrings; quadriceps	Combined with squats and single leg lifts	12 weeks	3/week	48 hours	25 min	200 us	40 Hz	23 mArms; under 80 V	2.4 ms on; 22.6 ms off	Rectangular biphasic

One study[18] did not fully report all the major outcomes stated in the protocol, which is considered to have a high risk of selective reporting bias. The remaining eight studies were considered to have a low risk of reporting bias.

Due to the small sample sizes, all nine studies that had fewer than 50 participants per study arm were considered to have a high risk of bias.

3.6. Primary outcome

3.6.1. Muscle strength

Seven studies (416 participants) evaluated muscle strength with a hand dynamometer or an isometric tester. For handgrip strength measured by a hand dynamometer, there was no significant heterogeneity among the studies (I^2 = 0%), and a fixed-effects model was used in the pooled analysis. Compared to the control groups, the EMS groups significantly improved grip strength (MD 1.68, 95% CI 0.66 to 2.69), which can be considered a large effect size (Figure 2).

For lower limb muscle strength, different studies used various parameters. Thus, data pooling was inappropriate, and only a narrative statement was made instead. In one study,[16] the intergroup difference between the EMS and control groups in the maximum isometric strength of the leg extensors was significant (9.8 ± 12.9% vs. 0.2 ± 10.4%; p = 0.003). In both of Takano's studies,[15,19] comparisons were made between hybrid training and a positive control group. Knee extension torque was significantly higher in the control group than in the EMS group in one study[15] (39% in the EMS group vs. 42% in the control group, p < 0.05) but not in another.[19] In the study by Maritinain 2012, the maximal voluntary static contraction (MVC) of the leg extensor muscles normalized by body mass (N/kg) significantly increased after the EMS intervention from 5.1 ± 3.3 N/kg to 5.6 ± 1.2 N/kg.

3.7. Secondary outcomes

3.7.1. Muscle mass

Four studies (291 participants) measured muscle mass with DXA[11,16,18] or BIA.[12] However, different studies used various parameters to assess muscle mass. The use of various parameters is not conducive for data pooling; thus, we conducted a meta-analysis separately. A fixed-effects model (I^2 = 0%) was used in the pooled analysis for both ASMM and LBM. Compared to the control groups, the EMS groups did not show significant improvements in ASMM (SMD 0.24, 95% CI -0.11 to 0.59) or LBM (SMD 0.11, 95% CI -0.29 to 0.50) (Figure 3). Due to the limited number of studies involved in data pooling, subgroup analysis was not necessary. For SMI, two studies[11,12] used different equations that are unsuitable for data pooling. However, both studies reported significant improvements in SMI after the EMS intervention.

3.7.2. Physical performance

For gait speed, a fixed-effects model (I^2 = 41%) was used in the pooled analysis. Compared to the control group, the EMS group did

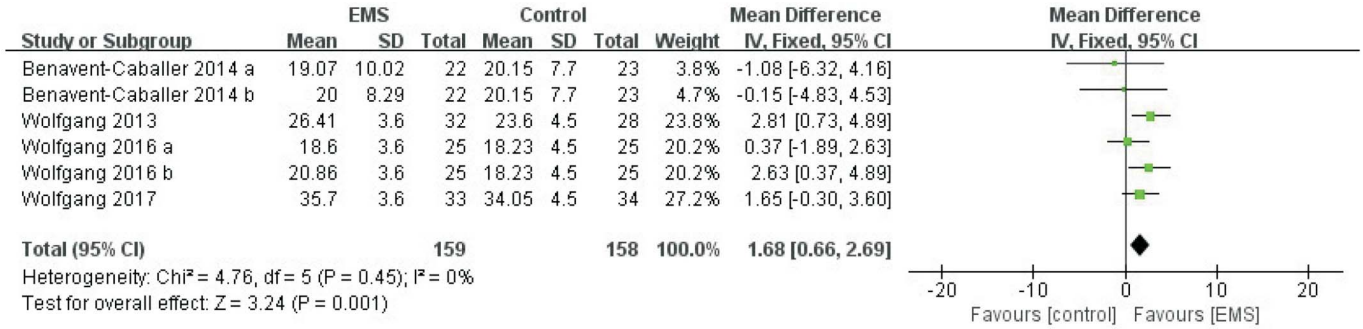

Figure 2. Forest plot of grip strength for EMS versus control. Benavent-Caballer 2014a, neuromuscular electrical stimulation alone; Benavent-Caballer 2014b, neuromuscular electrical stimulation superimposed onto voluntary contractions. Wolfgang 2016a, whole-body electrical myostimulation alone; Wolfgang 2016b, whole-body electrical myostimulation with dietary supplementation.

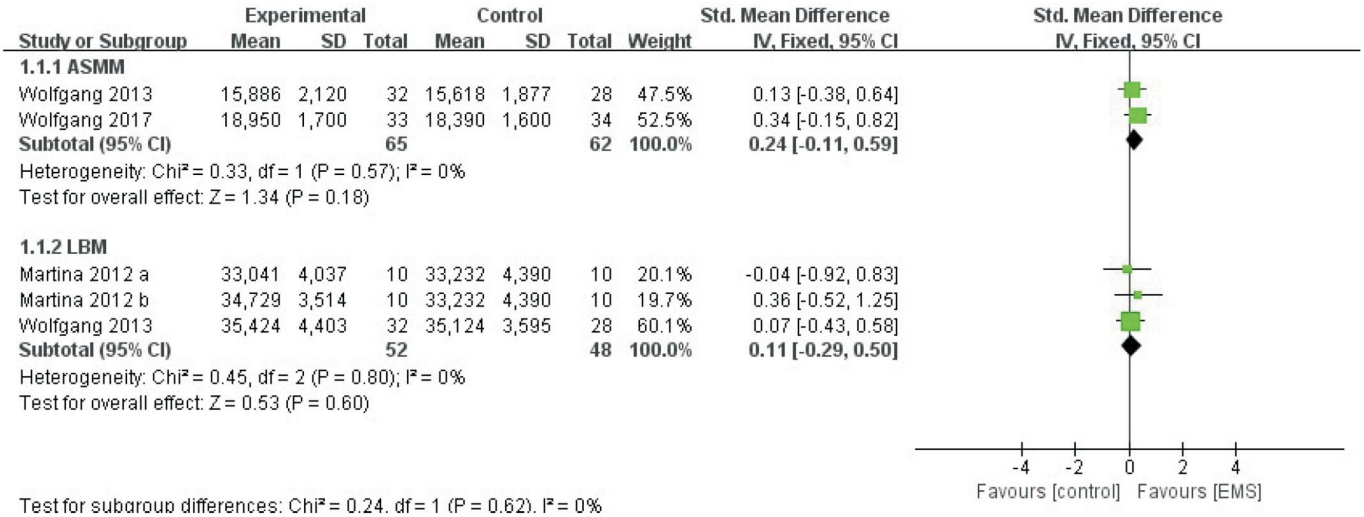

Figure 3. Forest plot of muscle mass for EMS versus control. Martina 2012a, electrical myostimulation alone; Martina 2012b, electrical myostimulation with kinesitherapy.

not show statistically significant improvements in gait speed (MD -0.00, 95% CI -0.06 to 0.05) (Figure 4).

For the TUGT, a random-effects model (I^2 = 53%) was used in the pooled analysis. Compared to the control group, the EMS group improved TUGT without statistical significance (MD 0.13, 95% CI -1.18 to 1.43)) (Figure 5).

For the 6MWT, only two studies[17,18] conducted this test. However, Martina did not provide outcome data for the control group, whose original data cannot be retrieved. Benavent-Caballer reported no significant effects on the 6MWT results after the EMS intervention. However, Martina reported the distance covered by the 6MWT significantly increased from 247 ± 79 to 271 ± 81 m ($p < 0.01$) after the rehabilitation program.

3.7.3. Other parameters

Two studies evaluated the CSA of the rectus femoris using MRI[15] or a portable ultrasound unit.[17] A fixed-effects model (I^2 = 0%) was used in the pooled analysis. Compared to the control group, the EMS group show only marginal improvements in the CSA of the rectus femoris without statistical significance (MD0.47, 95% CI -0.11 to 1.05) (Figure 6).

3.8. Adherence to the program

In five studies,[13,15,17–19] all the participants finished the prescribed program. There were several individuals that left the program in the remaining studies. The rates of adherence with the recommended program ranged from 71.64% to 100%, with an average adherence rate of 90%. The most common reasons for leaving the program were: disease or hospitalization unrelated to the program, removal from the program, a loss in interest, death, absence at a follow-up assessment, and discomfort with the intervention.

3.9. Occurrence of adverse events

None of the studies reported serious adverse events (AE). Two studies[12,16] reported discomfort with EMS application. Four studies[11,15,17,19] declared no AE occurred throughout the study period. The remaining three studies[13,14,18] did not mention AE; thus, we considered their quality of evidence to be low in this domain.

4. Discussion

An EMS program might be acceptable and safe for sedentary elderly people at risk of developing primary sarcopenia. Compared to the control groups, the EMS groups showed statistically significant improvements in handgrip strength (MD 1.68, 95% CI 0.66 to 2.69). Preserving muscle strength is important for elderly people in maintaining independence and preventing disability. Although we did not perform a pooled analysis for lower limb muscle strength due to considerable heterogeneity among the studies, handgrip strength is an alternative metric that is recognized as a typical indicator for skeletal muscle strength.

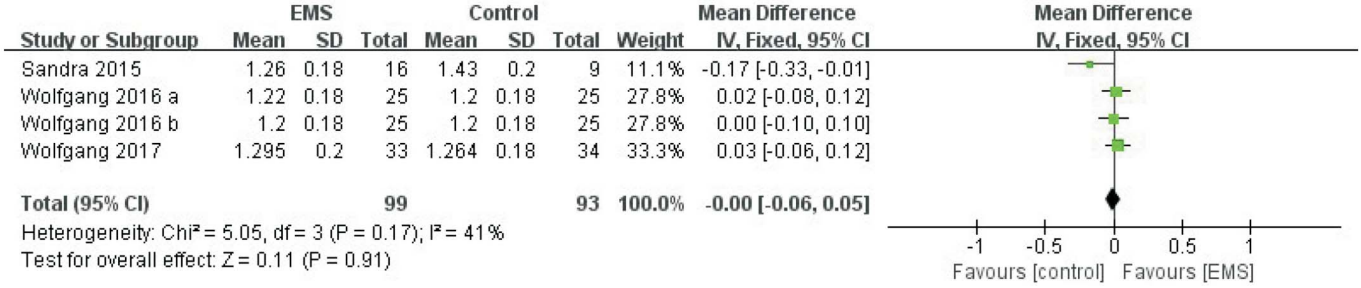

Figure 4. Forest plot of gait speed for EMS versus control. Wolfgang 2016a, whole-body electrical myostimulation alone; Wolfgang 2016b, whole-body electrical myostimulation with dietary supplementation.

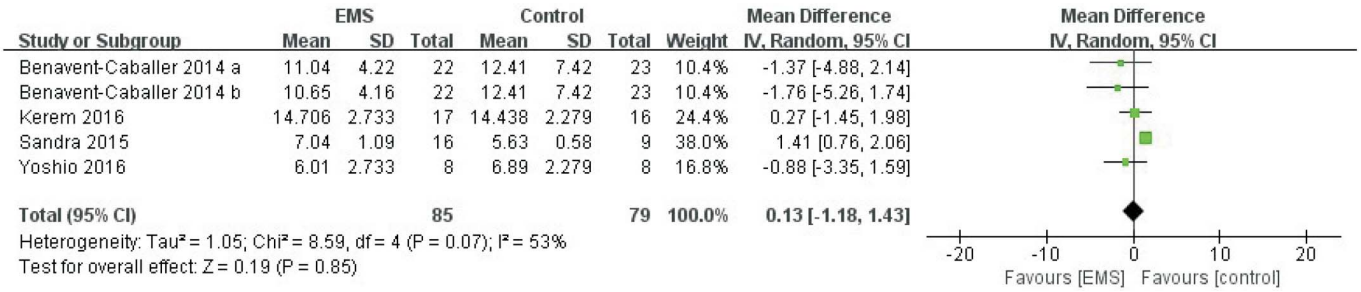

Figure 5. Forest plot of TUGT for EMS versus control. Benavent-Caballer 2014a, neuromuscular electrical stimulation alone; Benavent-Caballer 2014b, neuromuscular electrical stimulation superimposed onto voluntary contractions.

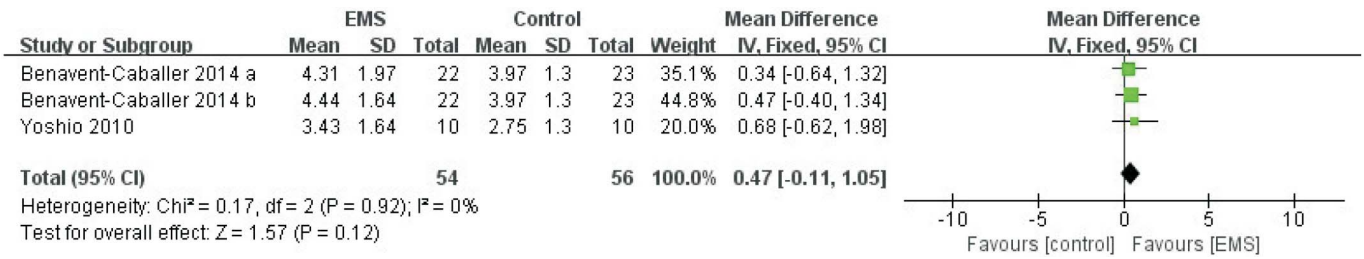

Figure 6. Forest plot of Rectus femoris CSA for EMS versus control. Benavent-Caballer 2014a, neuromuscular electrical stimulation alone; Benavent-Caballer 2014b, neuromuscular electrical stimulation superimposed onto voluntary contractions.

The meta-analysis did not indicate any other positive statistically significant results. EMS only marginally improved ASMM (SMD 0.24, 95% CI -0.11 to 0.59) and LBM (SMD 0.11, 95% CI -0.29 to 0.50). Thus, the evidence suggesting the efficacy of EMS in improving the muscle mass of sedentary elderly people was inadequate. Regarding physical performance, the performance of the EMS groups did not exceed that of the control groups in gait speed (MD -0.00, 95% CI -0.06 to 0.05). But the EMS groups showed marginal improvements in the TUGT results (MD 0.13, 95% CI -1.18 to 1.43). Therefore, we could not draw a definite conclusion about the effects of EMS on physical performance based on the existing evidence. There were also marginal improvements in the CSA of the rectus femoris (MD 0.47, 95% CI -0.11 to 1.05). The limited amount of high-quality evidence prevented the analysis of other muscle function-related outcomes.

Methodological quality differed across the studies. The randomization process was adequately described in most studies. However, the allocation concealment process was only clearly stated in three out of the nine studies. Thus, we considered the risk of selection bias to be moderate. The majority of studies did not implement blinding for participants, which induced a high risk of performance bias. However, blinding of the outcome assessors was clearly reported in six out of nine studies, which indicated a low risk of detection bias. Attrition bias was moderate since half of the involved studies had potential or apparent incomplete outcome data. All but one study fully reported the outcome parameters according to the protocol; thus, we considered the risk of reporting bias to be low. Since a small number of participants were enrolled in each study, small sample size bias should be considered when interpreting the data. Publication bias was observed using a funnel plot (Figure 7). Unpublished negative results are the underlying cause.

Elderly people with sedentary lifestyles are vulnerable to muscle weakness, which may decrease quality of life and increase mortality rates. Sarcopenia is a geriatric syndrome characterized by the loss of muscle mass and function. Although sarcopenia has been studied for more than a decade, diagnostic criteria are not unified due to different assessment technologies and ethnicities. Thus, the parameters used to assess muscle weakness vary, which leads to heterogeneity among studies. Furthermore, subgroup analysis is inappropriate due to the small number of studies; therefore, studies cannot be classified by various control methods and analyzed. Third, most studies were small in size had different levels of methodology quality. Lastly, previous studies showed that EMS application less than 3 times/week may be inadequate. However, the studies by Wolfgang had larger sample sizes but less intensity of muscle stimulation (1–1.5/week). Sub-group analysis based on intensity heterogeneity was not performed in this study, due to the small number of study participants involved. These issues are the main drawbacks of the meta-analysis.

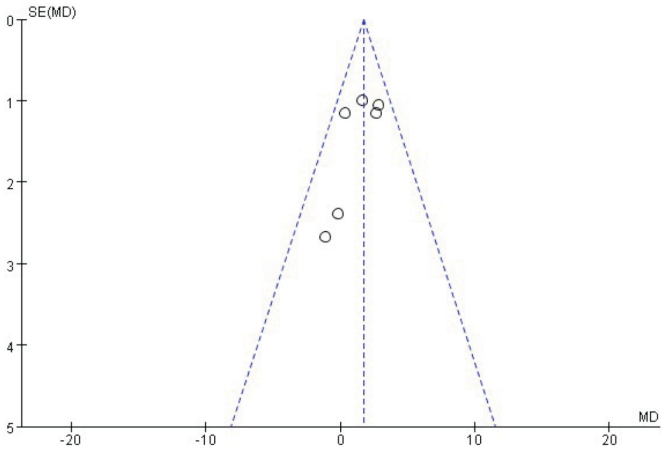

Figure 7. Funnel plot for primary outcome grip strength.

This meta-analysis is the first study on EMS interventions in sedentary elderly people. Multiple causes may lead to muscle atrophy, including AIDS, COPD, and denervated conditions. There have been a large number of studies on muscle weakness with a certain etiology, whereas there have been few studies on degenerative muscle changes associated with the aging process. Thus, having only limited available research prevents researchers from comprehensively analyzing the studies and performing meta-analyses. Previously, one review[21] stated that most studies confirmed a positive effect of EMS on muscle strength and physical performance in an older aged population but not on muscle mass. Our findings are similar to that previous review in terms of findings in regard to muscle strength improvements but not in terms of muscle mass or physical performance.

5. Conclusion

Available data were insufficient to draw definite conclusions as to the effects of EMS, either alone or as part of hybrid therapies, on degenerative muscle weakness. The results indicate that EMS can improve muscle strength significantly, but may only marginally improve muscle mass and physical performance. There were no serious safety concerns with the EMS interventions. More evidence is required to indicate the efficacy and safety of EMS. In the future, well-designed randomized controlled trials with large sample sizes are needed to provide solid evidence regarding the effectiveness of EMS on degenerative muscle weakness.

Author disclosure statement

No potential conflicts of interest were disclosed.

Acknowledgement

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Appendix 1: A sample search strategy for Medline

(1) Search Sarcopenia[Title/Abstract]
(2) Search Muscle mass[Title/Abstract]
(3) Search Muscle strength[Title/Abstract]
(4) Search Muscle function[Title/Abstract]
(5) Search Muscle atrophy[Title/Abstract]
(6) Search Physical performance[Title/Abstract]
(7) Search Muscle wasting[Title/Abstract]
(8) Search Lean body mass[Title/Abstract]
(9) Search sarcopenia[MeSH Terms]
(10) Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
(11) Search Whole-Body Electromyostimulation[Title/Abstract]
(12) Search Electrical stimulation[Title/Abstract]
(13) Search Neuromuscular electrical stimulation[Title/Abstract]
(14) Search Electromyostimulation[Title/Abstract]
(15) Search electrical stimulation[MeSH Terms]
(16) Search #11 OR #12 OR #13 OR #14 OR #15
(17) Search #10 AND #16