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Systematic review

Effect of exercise interventions in the early phase to improve physical function after hip fracture – A systematic review and meta-analysis

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Abstract

Background The efficacy of exercise interventions in the early recovery phase, i.e. started within the first three months after hip fracture, has been poorly studied compared to prolonged exercise interventions.
Objective To examine the effect of exercise interventions to improve physical function in the early phase after hip fracture.
Data sources Seven databases including MEDLINE via Ovid, The Cochrane Library, Embase, Cinahl, Pedro, AMED and Web of Science were comprehensively searched till December 2019.
Eligibility criteria Randomised controlled trials (RCTs) of exercise interventions initiated within the first three months after hip fracture to improve physical function, were eligible for inclusion. Primary outcome was physical function assessed using walking ability, walking speed, balance, muscle strength, mobility, and endurance.
Data extraction and data synthesis We conducted subgroup analyses specifically to investigate outcomes of these individual measurements. A meta-analysis was conducted to examine the overall effect of early exercise interventions. A meta-regression was conducted to examine the impact of study characteristic on exercise interventions. We used the PEDro score to determine quality of the included studies.
Results Nine studies (669 patients) were included. Despite high statistical heterogeneity, there was high to moderate quality evidence that exercise provided benefit in improving physical function (standardised mean difference (SMD) 1.07; 95% CI: 0.44 to 1.70; $p < 0.001$). There was no statistically significant difference in outcome, when measured by the individual physical function outcome ($p > 0.05$). Meta-regression demonstrated no statistically significant association between study characteristics and exercise interventions ($p > 0.05$).
Conclusion Exercise in the early phase of hip fracture rehabilitation can improve physical function. It remains unclear what type of exercise is superior in the early phase after hip fracture.
Limitations This conclusion should be interpreted with caution given the high statistical heterogeneity reported and non-significant subgroup analyses of specific physical function measures, which were underpowered.

Protocol Registration (PROSPERO): CRD42018091135.

Keywords: Hip fracture; Exercise; Physical function; Early phase; Review; Meta-analysis

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Key messages:

- Exercise has the potential to improve the patients' physical function in the early phase after hip fracture.
- It remains unclear what type of exercise is superior for this population in this phase.
- More research is warranted to elaborate on these conclusions.

Introduction

Hip fracture is the most serious fall-related fracture with a mortality rate of 5–10% during the first month and 20–30% during the first year postfracture [1]. In 2000 there was reported 1.6 million hip fractures worldwide, accounting for approximately 20% of all fractures in people aged 50 years and older [2]. Age-adjusted rates of hip fractures are highest in Scandinavian and North-American populations and lower in Southern Europe [3].

Hip fracture frequently leads to reduced physical function [4]. Physical function is the capacity of an individual to perform their physical activities of daily living. It reflects motor function and control, physical fitness, and habitual physical activity [5], and it is a strong measure of biological age and a biomarker for health and quality of life in older people [6–9]. Physical function as an assessment domain is measured through various approaches including: mobility, endurance, muscle strength, and balance [10]. Physical performance assessments as outcome measures are vital when the effect of interventions of physical function are examined [11].

Patients who experience a hip fracture are often vulnerable and fragile [12]. In the early phase after hip fracture, reduced mobility and hospitalisation may cause severe decline in a patient's muscle mass, muscle strength, and consequently, their physical function [13]. This can lead to reduced independence with increased need of assistance in daily tasks [14]. Furthermore, these patients are at high risk of increased fear of falling, muscle weakness, and postoperative pain through reduced mobility and loss of independence [12].

Exercise interventions after hip fracture aim to improve physical function and prevent or reverse physical deconditioning [15]. However, a Cochrane systematic review and meta-analysis on hip fracture recovery reported inconsistent effects of exercise interventions on mobility [16]. A recent meta-analysis reported a small improvement in overall mobility following a structured exercise intervention [4]. These meta-analyses included studies with exercise interventions up to one year after the fracture [4,16]. The efficacy of exercise interventions in the early recovery phase, i.e. started within the first three months after hip fracture, has been poorly studied [17].

The aim of this systematic review and meta-analysis is to determine the effectiveness of exercise interventions on physical function in the early phase after hip fracture.

Methods

Data sources and search strategy for identification of studies

This review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The following electronic databases were searched in May 2018 (updated December 2019): The Cochrane Database of Systematic Reviews, Medline, Embase, Cinahl, PEDro, and AMED. Search strategies are shown in *Supplementary File 1*.

Eligibility criteria

Studies were included based on the following eligibility criteria: all randomised controlled trials (RCTs) assessing the efficacy or effectiveness of exercise interventions commenced within the first three months posthip fracture surgery, for patients aged 65 years and older. We define exercise interventions as interventions that include physical activity to improve or maintain one or more components of physical function. Included studies reported at least one performance based outcome measure of physical function, such as walking ability, walking speed, strength, balance, mobility, and endurance. Studies investigating muscle stimulation, passive management strategies, self-training interventions, and welfare technology studies were excluded. We excluded studies that did not have a PEDro score of level 1 evidence (6–10 points).

Article screening and selection

Titles and abstracts from all individual citations were screened by one reviewer (MB) with duplicates removed. One reviewer (MB) read all the included full-text articles and three reviewers (KEH, VB-O, AB) read each a third of the selected full-text articles. Any disagreements between the reviewers were addressed through discussion until consensus was met.

Data extraction

For each included study, we extracted data using a specifically developed data extraction form (*Supplementary File 2*). One reviewer extracted all data (MB). The extraction was verified by one of the three other reviewers (KEH, VB-O, AB). Data extracted included: study origin, interventions (exercise components, duration, frequency, and intensity), outcome measures, and results. When differences in opinion occurred between the reviewers, consensus was met through discussion.

Quality assessment

The PEDro score was used as each included study's methodological quality [19,20]. A study with a PEDro score of ≥6 was considered Level 1 evidence (6–8: good, 9–10: excellent) and included in the review [21]. One reviewer independently assessed the quality of the included studies (MB). This was verified by one of three reviewers (KEH, VB-O, AB).

Statistical analysis

Study heterogeneity was assessed by examining the data extraction tables. The reviewers determined that the trial designs, population characteristics, and interventions were satisfactorily homogeneous to permit a meta-analysis. Based on this, a random-effect model meta-analysis was deemed appropriate. We calculated standardised mean differences (SMD) with 95% confidence intervals (CIs) to assess pooled physical function outcomes. The interpretations of the SMD as an effect size were based on Cohen's *d* (0.2 is small, 0.5–0.6 is moderate, and 0.8–1.0 is large) [22]. I^2 statistics, *p*-values, *Q* statistics, and degree of freedom were used to assess statistical heterogeneity [23,24].

The primary analysis was the overall effect of exercise interventions on physical function. When more than one physical function outcome was reported in a study, the outcome measure considered most related to the intervention was selected, according to the principle of specificity [25]. The estimates of SMD for the first postintervention time point were extracted for meta-analysis. Subgroup analyses were undertaken to assess the specific outcomes within the domain of physical function i.e. walking speed, mobility, balance, and endurance.

We assessed for any association between study characteristics (study year, hospital or community setting, days since surgery, sample size, mean age of participants, Pedro score of the study, intensity of intervention, and follow-up weeks) and exercise intervention (strength training versus non-strength training) through a meta-regression. Stata version 15 (Stata Corp, Texas, USA) was used with the meta-analysis metan [26], metafunnel [27] and meta-regression [28] packages.

Results

Description of included studies

The results of the search strategy are presented in Fig. 1. In total, 2225 studies were identified after duplicates were removed. From the 26 potentially eligible studies, nine met the eligibility criteria and were included in the review. The characteristics of the included studies are reported in Table 1. In total 669 participants with a mean age of 81 years (mean age range: 77–84 years) were included. Included studies were published from 2002 to 2018. The sample sizes for the individual studies varied from 20 to 160 participants. Three studies were undertaken in Australia, whereas single studies originated from Italy, United States of America, Canada, Denmark, Netherlands, and Germany.

The included studies examined combinations of exercise interventions (Table 1). Five studies examined the effect of high-intensity exercise. Of these, two studies investigated the effect of high-intensity physiotherapy [29,30], three studies investigated the effect of high-intensity progressive resistance training [31–33], two studies examined endurance training [34,35], one study examined weight-bearing exercise [36], and one study examined balance task-specific training [37]. Control groups for each study are presented in Table 1. Across the studies, the number of sessions varied from 10 to 36 sessions. The overall duration of interventions in the included studies varied from 1 to 12 weeks. In three studies, the interventions were delivered to participants during their hospital stay [29,32,36] with intervention start at mean nine days postoperatively (range 5–19 days after surgery). In three studies, the exercises were delivered in a community setting [34,35,37] with intervention start at mean ten days postoperative (range 5–14 days since surgery). Three studies delivered exercise interventions across both hospital and community settings [30,31,33], commencing at a mean 45 days postoperatively (range 14–90 days since surgery).

Principal analysis

We pooled data from four different measures of physical function (mobility, walking speed, endurance, and balance). There was high to moderate quality evidence that exercise provided benefit in improved physical function at three to six months postoperatively (SMD: 1.07; 95% CI: 0.44 to 1.70; $p < 0.001$. $I^2 = 92\%$, $Q = 103.66$) (Fig. 2). Because of the very large effect in one study [37], we additionally performed a sensitivity meta-analysis excluding this study. The meta-analysis still reported a statistically significant overall improvement in favour of exercise (SMD: 0.36; 95% CI: 0.05 to 0.67; $p < 0.024$).

Subgroup analyses

Mobility as assessed with the Timed Up and Go (TUG) test was reported in five high-quality studies ($n = 296$) [29,31,32,34,35]. The studies were of high quality according to the PEDro score (Table 1). There was no statistically significant difference in TUG results between the exercise and comparison groups (SMD: 0.48; 95% CI: −0.14 to 1.10; $p = 0.126$; $I^2 = 82\%$, $Q = 21.76$) (Fig. 3).

Walking speed was assessed using the 6-m and 10-m walk test in four high-quality studies ($n = 334$) [30,31,35,36]. There was no statistically significant difference in walk test results between the exercise and comparison groups (SMD: 0.35; 95% CI: −0.04 to 0.73; $p = 0.078$; $I^2 = 57\%$, $Q = 7.01$) (Fig. 3).

Table 1
Characteristics of included trials.

	Setting	Start of inter-vention/Days since surgery	Sample size	Mean age (years)	Pedro score	Outcome	Characteristics of intervention	Comparator	Number of sessions	Duration of intervention (weeks)
Binder *et al.* (2004) [33]	Hospital & Community	90	90	81	7	(S) Walking endurance m/min (S) Bergs balance scale	High intensive progressive resistance training of lower limb	Low intensity non-progressive strength training of lower limb	36 sessions	12
Hauer *et al.* (2002) [31]	Hospital & Community	42–56	24	81	7	(S) Timed Up & Go (S) Max walking speed m/s	High intensity progressive resistance training of lower limb	Placebo motor activities such as callisthenics, games and memory tasks whilst seated	36 sessions	12
Kimmel *et al.* (2016) [29]	Hospital	5	92	81	8	(S) Timed Up & Go	Intensive physiotherapy consisting of strength exercises and gait re-training three times daily	Physiotherapy consisting of strength exercises and gait re-training one time daily	21 sessions	1
Kronborg *et al*. (2017) [32]	Hospital	3	90	79	8	(S) Timed Up & Go	Progressive knee-extension strength training in addition to basic mobility and exercise therapy aimed at lower extremities	Basic mobility and exercise therapy aimed at lower extremities	14 sessions	2
Mendelsohn *et al*. (2008) [34]	Community	5	20	81	7	(S) Timed Up & Go (S) Walking endurance m/min (S) Bergs balance scale	Endurance training by using an arm crank ergometer in addition to physical and occupational therapy 5 times a week	Physical and occupational therapy consisting of balance, strength, gait, flexibility and ADLs 5 times a week	12 sessions	4
Monticone *et al*. (2018) [37]	Community	10	52	77	8	(S) Bergs balance scale	Balance task-specific training	General physiotherapy including open kinetic chain exercises and walking	15 sessions	3
Moseley *et al.* (2009) [30]	Hospital & Community	14	160	84	8	(P) Walking speed m/s	Weight bearing exercises twice daily for a total of 60 minutes per day	Exercises sitting or lying in addition to a small amount of walking for a total of 30 minutes per day	28 sessions	4
Sherrington *et al*. (2003) [36]	Hospital	19	80	81	7	(S) Walking speed m/s	Weight bearing exercises in addition to usual physiotherapy such as walking, bed mobility sit to stand and stair climbing	Non-weight bearing exercises in addition to usual physiotherapy such as walking, bed mobility sit to stand and stair climbing	10 sessions	2
Van Oijen *et al*. (2016) [35]	Community	14	70	83	7	(P) Timed Up & Go (S) Walking speed m/s	Endurance training, adaptability treadmill training	Conventional treadmill training	30 sessions	6

(P) = primary, (S) = secondary.

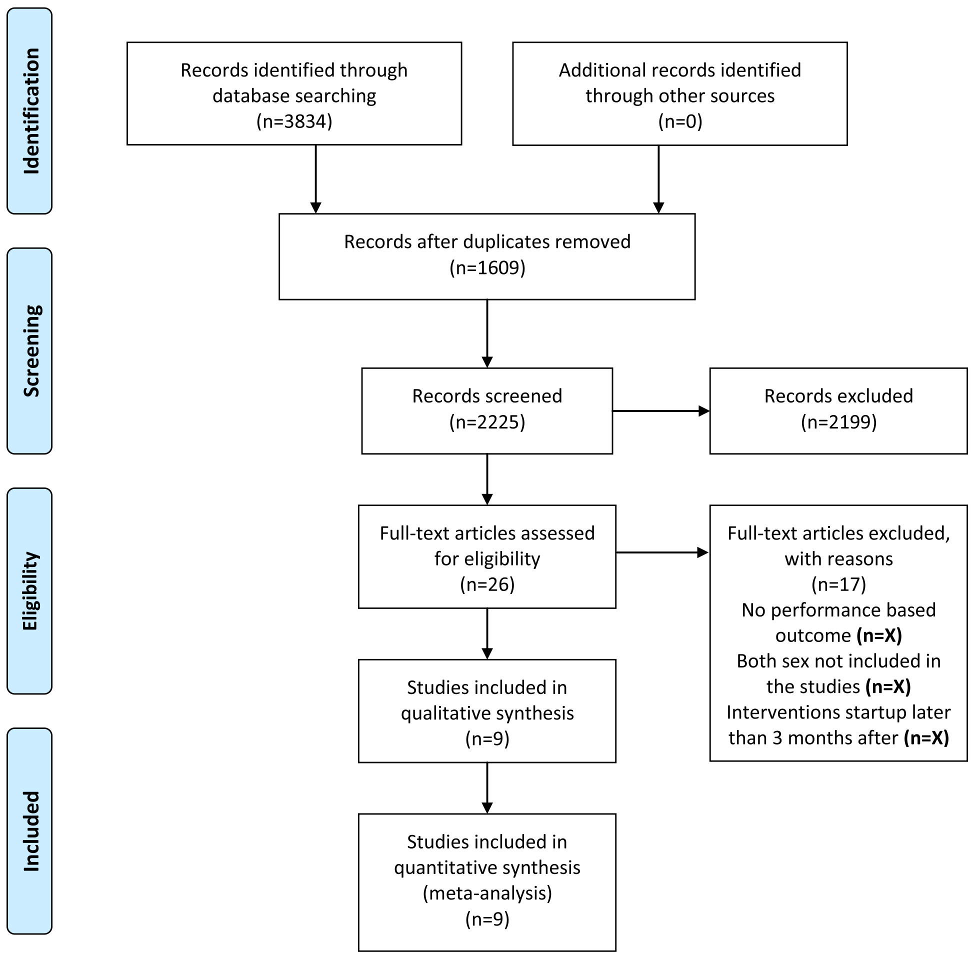

Fig. 1. Flow chart o f the screening and selection process.

Endurance was measured using number of metres per minute, such as 2-minute walking test, in two high-quality studies ($n = 110$) [33,34]. There was no statistically significant difference between the exercise and comparison groups (SMD: 1.52, 95% CI: −0.75 to 3.79; $p = 0.189$; $I^2 = 92\%$, $Q = 11.80$) (Fig. 3).

Balance measured using Berg Balance scale was reported in three high-quality studies ($n = 162$) [33,34,37]. There was no statistically significant difference in balance function between the exercise and comparison groups (SMD: 2.84, 95% CI: −0.25 to 5.93; $p = 0.071$; $I^2 = 97\%$, $Q = 69.09$) (Fig. 3).

Meta-regression

The meta-regression indicated no statistically significant association between study intervention characteristics and exercise interventions ($p > 0.05$).

Discussion

The overall results suggest that exercise interventions prescribed in the early phase of recovery after hip fracture, improve physical function. However, within the subgroup analyses of mobility, walking speed, endurance, and balance no effects were demonstrated, compared to control groups. The meta-analyses presented high statistical heterogeneity and should therefore be interpreted with caution. The meta-regression could not identify an exercise intervention that was superior in association with physical function.

To our knowledge, this is the first systematic review and meta-analysis to examine the effectiveness of exercise interventions in the early phase after hip fracture. The overall improvement in physical function compared to the lack of improvement in the subgroup analyses may be explained through various reasons. Firstly, the sub-group analyses were underpowered. The non-statistical difference may therefore reflect a type-2 statistical error. With an assumed clinically significant effect of 0.5 SMD, high heterogeneity between studies and an average study size of 50 participants in each group, we estimated that five to six studies would be needed to obtain around 80% statistical power [38]. This may have been magnified by a potential reduced between-group difference in physical function since both experimental and control interventions offered an exercise intervention. As the evidence-base developed, further exploration of the specific

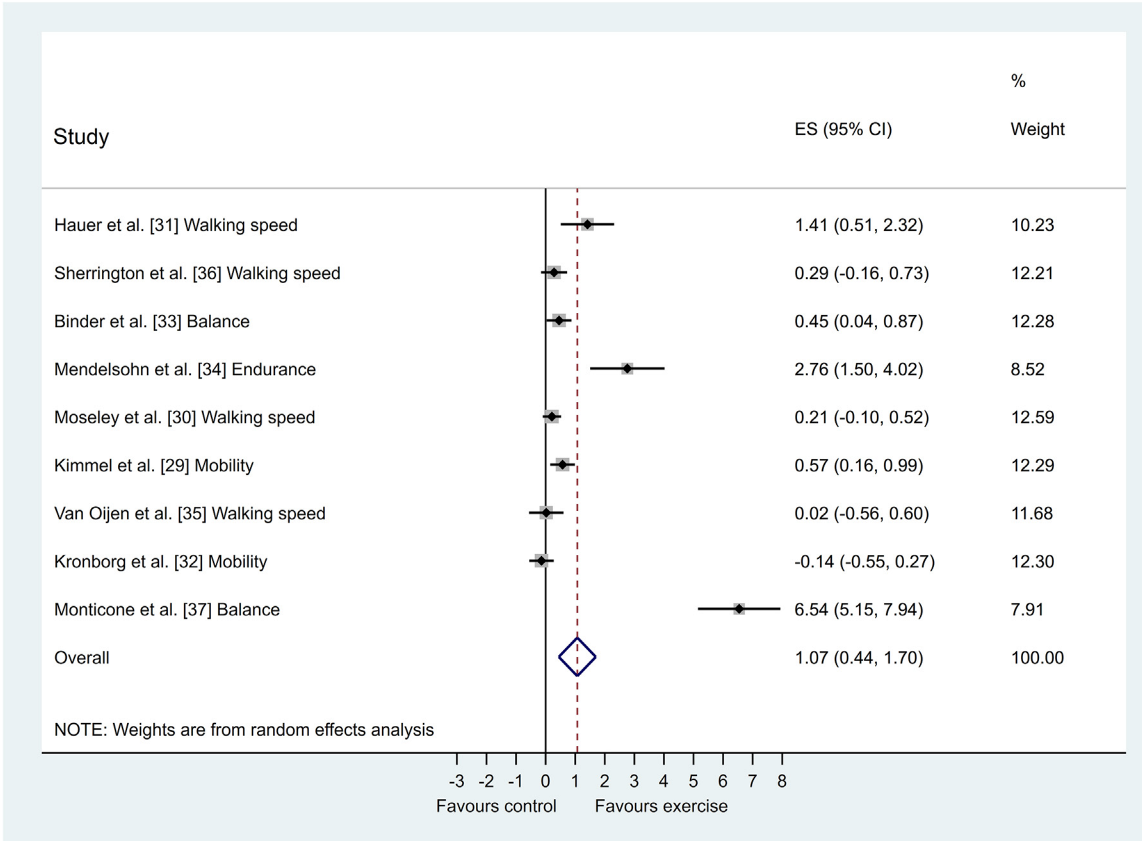

Fig. 2. Forest plot of the overall effect of exercise interventions on physical function after hip fracture, by random effect model.

instruments used to assess physical function is desirable, to better interpret the results reported in this analysis.

The results of this review are in agreement with a recent meta-analysis reporting outcomes at a later-stage in hip fracture recovery [39]. The meta-analysis reported that balance training from early to the chronic phase after hip fracture improved overall physical function, such as balance, walking, lower limb strength, ADLs, performance task score, and health related quality of life scores [39]. The authors highlight that balance exercises were particularly effective at this later-stage, but it was not possible to ascertain whether a specific exercise programme offered superior outcomes over another [39]. However, we can surmise that exercise in this phase of recovery is beneficial. Further research to reveal whether there are differences in outcome by specific exercise interventions are warranted.

Timing may be a confounding factor on the effect of exercise interventions after hip fracture. Binder *et al*. (2004) and Hauer *et al*. (2002) showed that progressive resistance exercise was an effective intervention for improving physical function after hip fracture [31,33]. In the study by Binder *et al*. (2004) the intervention started at mean 90 days after the hip fracture surgery [33]. Hauer *et al*. (2002) started their intervention 6–8 weeks after hip fracture surgery. Physiological timing may be assumed to be a potential confounding factor where pain and healing after surgery may impact on the patient's ability to engage with exercise and therefore outcomes.

A systematic review by Cadore *et al*. (2013) reported that a multicomponent exercise programme consisting of strength training, endurance, and balance appeared to be the best strategy to improve physical function and maintain functional capacity in older adults [40]. Given the results from Cadore *et al*. and the summary of results above, one may argue that a wide scope of exercise can be beneficial for these elderly patients with hip fracture. The limited association reported in our review may have been attributed to type-2 errors. Further research should be undertaken to better reveal the potential impact of timing of different exercise interventions and whether they influence outcomes in the early phase following hip fracture.

Limitations

This systematic review and meta-analysis is presented with some limitations that should be considered. Firstly, only a single assessor (MB) screened all citations. Therefore it may be a higher risk that the single assessor, instead of three assessors, missed out of relevant studies. Secondly, given the low number of studies identified, it was not possible to assess

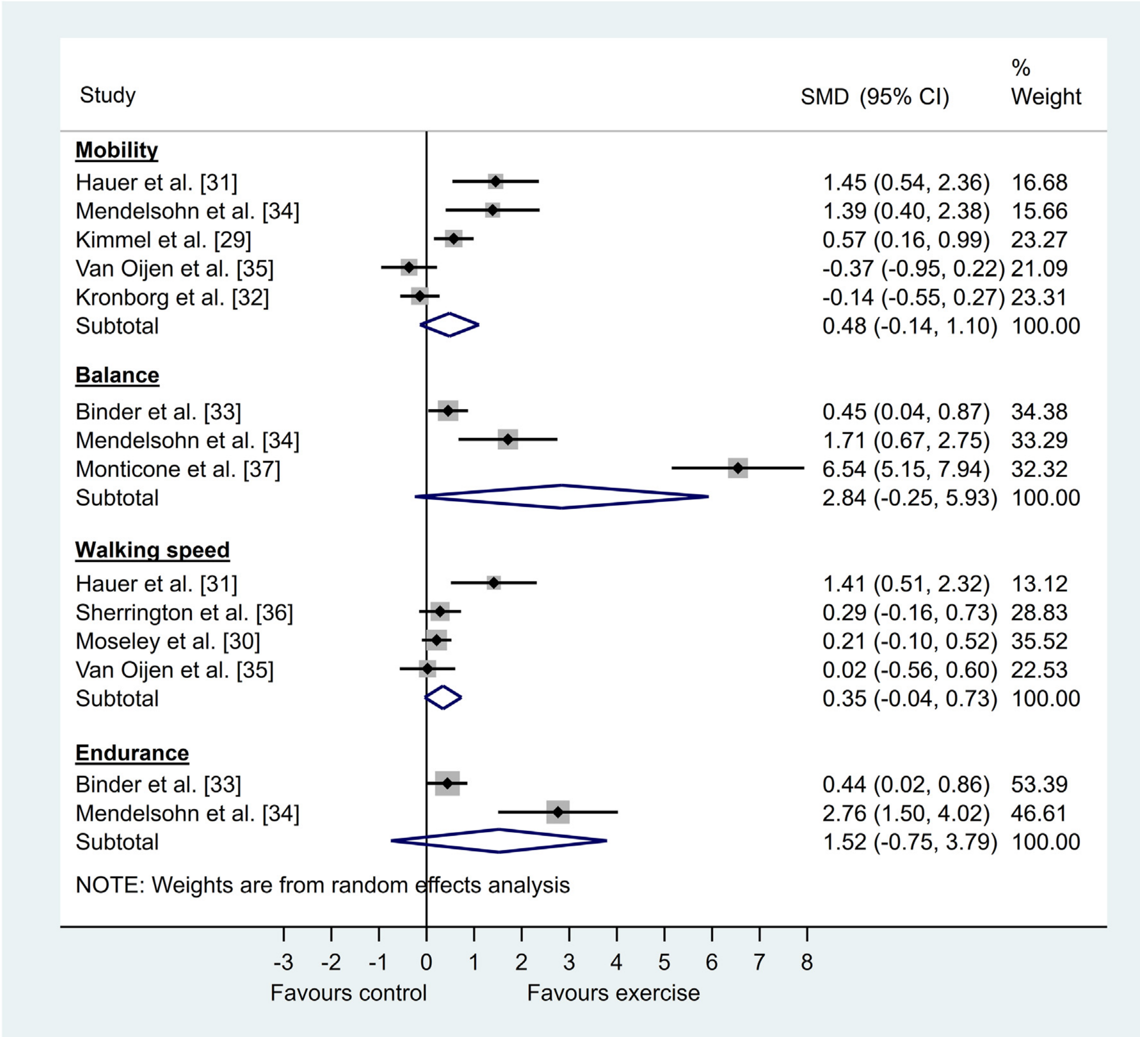

Fig. 3. Forest plot of sub group analyses of mobility, walking speed, endurance and balance after hip fracture, by random effect model.

for the risk of publication bias through a funnel plot or statistical means. Thirdly, there was sufficient homogeneity to pool the data in a meta-analysis. However, we acknowledge high statistical heterogeneity across the meta-analyses indicating unknown between-trial variability. The results of the meta-analysis should therefore be viewed with caution.

Conclusion

In this systematic review and meta-analysis evidence from early phase exercise after hip fracture was evaluated. Based on moderate to high-quality evidence, exercise interventions could have the potential to improve the patients' physical function after hip fracture. The results should be interpreted with caution due to high statistical heterogeneity and under-powered subgroup analyses. The clinical implications from our results suggested that different types of exercise could be beneficial in the early phase after hip fracture.

Conflict of interest: There are no conflicts of interest.

Ethical Approval: There are no ethical considerations.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.physio.2020.04.009.

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