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Interventions to improve locomotive syndrome: a systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Locomotive syndrome is a musculoskeletal disease of individuals who are highly likely to require nursing care. There is no systematic review that systematically evaluates and consolidates the findings of randomized controlled trials, although the number of randomized controlled trials considering the intervention effect on locomotive syndrome has been increasing with the spread of the concept. Therefore, this systematic review of randomized controlled trials is aimed at consolidating evidence regarding effective interventions to improve locomotive syndrome. We searched seven databases electronically. Studies were included in this systematic review if the following were met: (1) the articles were randomized controlled trials written in English or Japanese in a peer-reviewed journal, and (2) the clinical evaluation of the locomotive syndrome should include at least one of the following: the stand-up test, two-step test, and 25-question Geriatric Locomotive Function Scale. This systematic review included 10 studies. Several individual papers showed that the intervention group significantly improved the outcome measure for the diagnosis of locomotive syndrome compared with the control group. Only oral glucosamine intake provided sufficient information to conduct a meta-analysis, but the results were not statistically significant. This systematic review and meta-analysis did not provide strong evidence for specific interventions in improving locomotive syndrome, although individual randomized controlled trials have shown that oral intake of glucosamine, electrical stimulation, and exercise could improve locomotive syndrome. We hope that more high-quality randomized controlled exercise intervention trials aimed at improving locomotive syndrome, which is a musculoskeletal dysfunction, will be carried out in the future.

Keywords: locomotive syndrome, randomize controlled trial, systematic review, meta-analysis

Abbreviations:
JOA: The Japanese Orthopaedic Association
RCT: randomized controlled trial
GLFS-25: 25-question Geriatric Locomotive Function Scale
EMS: electrical muscle stimulation

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INTRODUCTION

Locomotive syndrome is a common concept proposed by the Japanese Orthopaedic Association (JOA). It is a musculoskeletal disease that will highly likely require nursing care.[1] The intent behind this proposed concept is to promote locomotive system (bones, muscles, joints, and peripheral nerves) health awareness for elderly people in Japan to prevent nursing care and bed rest. Frailty and sarcopenia are similar concepts that describe a declining condition in elderly people similar to locomotive syndrome. Locomotive syndrome is used especially to identify physical frailty with musculoskeletal disorders without social and cognitive frailty, although frailty is a state in which older adults are at high risk of death, disability, and institutionalization.[2] Sarcopenia is muscle degeneration with aging and a component of locomotive syndrome.[2] Therefore, we believe that this is an adaptable concept to not only older adults but also all age groups to prevent musculoskeletal disorders and the unfavorable conditions of locomotive syndrome in the future. In recent years, it has been used as an indicator to evaluate the decline in motor function not only in Japan but also in other countries.[3-6]

There have been many intervention studies for frailty and sarcopenia, including systematic reviews and meta-analyses of several randomized controlled trials (RCTs), which have shown that interventions with exercise, nutrition, and drugs are effective.[7-10] The guidelines for frailty or sarcopenia have already been reported as a result and have been applied in various clinical and community settings to standardize prevention, diagnosis, and treatment.[11,12] JOA proposed sets of exercises for locomotive syndrome called locomotion training to strengthen lower extremity muscle power and improve balance.[13] Aoki et al investigated the effects of the exercise included in locomotion training (single-leg standing with the eyes open and squatting) and vitamin D supplementation on physical function and locomotor dysfunction in community-dwelling elderly individuals.[14] They found that the two-step test results of all participants in the exercise only, vitamin D only, and exercise and vitamin D groups were improved, but it was still unclear which was the most effective intervention because there was no significant difference between the groups and the degree of change.

The recent publication of guidelines for locomotive syndrome edited by JOA and the Japanese Society for Musculoskeletal Medicine has enormous significance. It indicates recommendations and standardized prevention, assessment, and treatment.[15] Substantive evidence from high-quality RCT is needed from the evidence-level perspective. However, there are currently a few recommendations based on high-quality RCTs. There is no review that systematically evaluates and consolidates the findings of RCTs, although the number of RCTs considering the intervention effect on locomotive syndrome has been increasing with the concept's spread. Therefore, this systematic review of RCTs aims to consolidate evidence regarding effective interventions to improve locomotive syndrome. Furthermore, we believe in its importance in maintaining musculoskeletal health to widely promote this concept, which is not yet widely recognized internationally.

MATERIALS AND METHODS

A systematic review of the literature was performed using the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocol (PRISMA-P).[16] This review was registered in PROSPERO (ID: CRD42021266176).

Selection criteria

Studies were included in this systematic review if the following were met: (1) the articles

were RCTs written in English or Japanese in a peer-reviewed journal; (2) the clinical evaluation of the locomotive syndrome should include at least one of the following: stand-up test, two-step test, and 25-question Geriatric Locomotive Function Scale (GLFS-25); and (3) subjects should be to 20 years of age and older.[14] Studies were excluded if the following were met: (1) the study was a review article, and (2) insufficient information was needed to synthesize the results.

Search strategy and study selection

We searched Medline, Cochrane Central Register of Controlled Trials, Physiotherapy Evidence Database (PEDro), Scopus, Web of Science, Ichushi Web (in Japanese), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases electronically. A highly sensitive search strategy to identify RCTs was combined with the word "locomotive syndrome" and tailored to each of the seven databases searched. There were no limits on dates. We did an electronic database search on July 13, 2021. The full search strategies for all databases are shown in supplementary Appendix 1.

The search results from each database were aggregated into a spreadsheet using the software Microsoft Excel 2019. The titles and abstracts were independently selected by two reviewers (YI and TI) from studies that met the predesigned inclusion criteria after deleting duplicate papers. The full text was obtained for the selected papers after that, and content was examined and reviewed again independently based on the inclusion criteria by the two reviewers (YI and TI). A discussion was held, and the final decision was made by a third reviewer (RT) in case of a disagreement between the two reviewers.

Data extraction

We extracted the data of the participants, interventions, and outcome using a spreadsheet with a pre-prepared Microsoft Excel 2019. First, a reviewer (YI) extracted the data, and then, another reviewer (TI) cross-checked the data. Only the stand-up test, two-step test, and GLFS-25 among the items in the outcome, which are diagnostic criteria for locomotive syndrome, were extracted.[14]

The meta-analysis in this review employed the stand-up test, two-step test, and GLFS-25 as the outcome measures, which are criteria for locomotive syndrome.

Risk of bias assessment in individual studies

Two reviewers (YI and TI) independently assessed the risk of bias using the Cochrane risk of bias assessment tool, random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias.[17] The articles were evaluated based on predetermined criteria. A third reviewer (RT) was proposed if consensus was not reached.

Certainty of evidence

The Grading of Recommendations Assessment, Development and Evaluation system was used to assess the quality of the evidence.[18] The Grading of Recommendations Assessment, Development and Evaluation system was performed when there were at least two applicable outcomes. The quality of the evidence was classified as "very low," "low," "moderate," or "high" based on criteria. Factors that reduce quality (risk of bias, inconsistently, indirectness, impression, and publication bias) and factors that increase quality (large effect, plausible confounding, and dose-response) were evaluated.[19]

Statistical analyses

All statistical analysis procedures were performed using Review Manager 5.4. This review examined the effects of various interventions on the locomotive syndrome. Therefore, for the meta-analysis, two or more RCTs with the same intervention method and evaluation conducted at the same time were employed. The value of the change from the baseline was used if actual measurements were not given in the results section. We referred to the Cochrane Handbook for Systematic Reviews of Interventions (Version 6.3, 2022), the random-effect model was used as the integration method, and the mean and standard deviation were employed.[20] The statistically significant level was set at 0.05.

RESULTS

Search results

We found 424 papers (Figure 1) after searching the database. Approximately 222 duplicate papers were excluded, and 202 papers were reviewed on the titles and abstracts. After that, 19 papers (1 paper added by hand search) were reviewed from the full text. Finally, 10 papers were selected for this review because they met the inclusion criteria (Figure 1). The characteristics of the subjects, intervention method, and results are summarized in Table 1. The subjects were over 40 years of age. The average age of each group ranged from 51.0 to 75.6 years. There was a proportion of women overall, and the article by Nishikawa et al only included women.[21] Subjects with knee symptoms were involved in four of the papers, such as osteoarthritis, rather than healthy subjects.[22-25] No RCTs examined the main effect of exercise on locomotive syndrome as an intervention method, and eight articles examined the effect of oral supplements.[14,23-29] In the papers examining the effects of oral intake, three papers examined glucosamine, two papers examined SM-10, and one paper each examined vitamin D, collagen, and C. tubulosa. Simoura et al and Nishikawa et al investigated the effects of electrical stimulation on locomotive syndrome, but their objectives were different: Simoura et al aimed to eliminate pain, whereas Nishikawa et al aimed to increase muscle strength.[21,22] Locomotive syndrome significantly improved with intervention compared to the control group, which was seen in four RCTs.[21,26-28]

Summary of selected papers

Nishikawa et al found that electrical muscle stimulation (EMS) of the quadriceps muscle for 8 weeks improved the two-step test and GLFS-25.[21] They simultaneously measured knee extension torque, muscle thickness, and muscle activity patterns and showed changes after 8 weeks of intervention.[21] Simoura et al found significant improvement in distance and pain in the 6-min walk test with transcutaneous electrical nerve stimulation, but no improvement in the stand-up test or two-step test.[22]

A meta-analysis of the oral glucosamine intervention was performed, and the results are described as follows: Hattori et al performed an additional analysis for those with above-average weight and the same population with a JKOM score of 30 or higher.[26,28] There was no significant difference between groups according to whether the JKOM score was 30 or higher.[26] Conversely, subjects with a JKOM score of 30 or higher and above-average weight showed significant differences in the stand-up test and two-step test, respectively, with the intervention group showing significant improvement.[28]

Other oral interventions included SM-10, vitamin D, collagen, and C. tubulosa, none of which showed significant intervention effects between groups.[14,23-25,29]

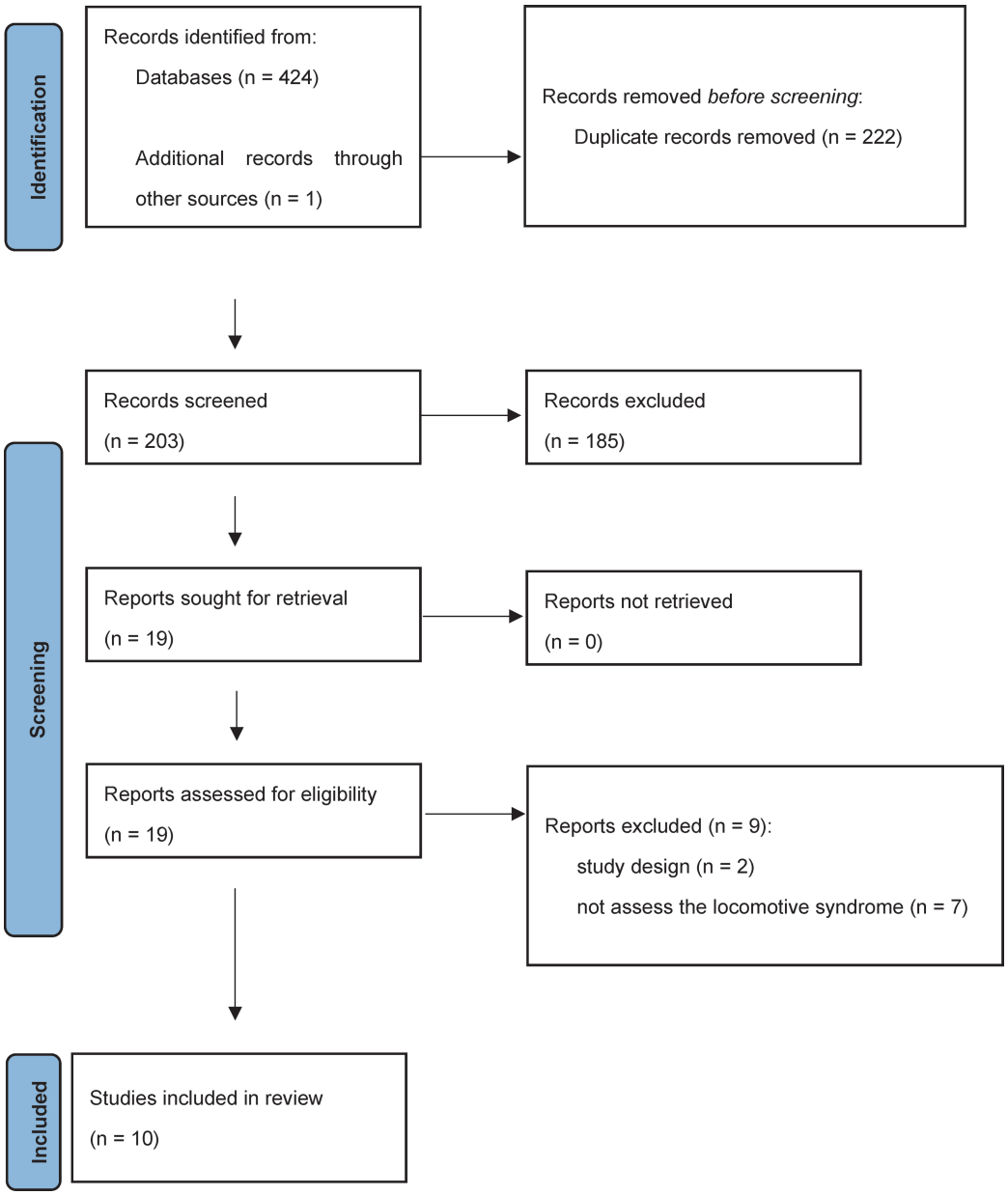

Fig. 1 Flow diagram of the study selection process

Quality assessments

The results of the risk of bias assessment conducted using the Cochrane Risk of Bias assessment are summarized in Table 2. A low risk of bias in all items was judged in six papers. Evidence equality was assessed using the Grading of Recommendations Assessment, Development and Evaluation system. Owing to the small number of RCTs included, we referred to previous studies and the Cochrane Handbook for Systematic Reviews of Interventions (Version 6.3, 2022),

Table 1 Summary of included studies

Study	Participants	Intervention	Control	Follow-up	Main findings
Electrical stimulation					
Shimoura et al[22] *Arch Phys Med Rehab* 2019	50 participants with knee pain (IG=25, CG=25) Mean age (IG=59.1, CG=57.9) Male/Female (IG=6/19, CG=9/16)	transcutaneous electrical nerve stimulation (TENS)	sham-TENS	immediately effect	no difference by intervention or between groups in 2-step test, stand-up test
Nishikawa et al[21] *J Electromyogr Kinesiol* 2019	19 participants (IG=10, CG=9) Mean age (IG=75.6, CG=77.3) Male/Female (IG=0/10, CG=0/9)	electrical muscle stimulation of the quadriceps muscle of both limbs for 8 weeks	N.A.	8, 12 weeks	in Δ two-step test and GLFS-25, IG showed significant improvement compared with CG at 8 weeks
Dietary supplement intake					
Hattori et al[26] *Jpn Pharmacol Ther* 2016	57 without knee OA (IG=28, CG=29) Mean age (IG=54.4, CG=53.4) Male/Female (IG=12/16, CG=12/17)	8 tablets containing Glucosamine, chondroitin sulfate et al every day for 12 weeks	placebo	4, 8, 12 weeks	Δ stand-up test CG showed significant improvement compared with IG at 4, 8, 12 weeks, in two-step test IG showed significant improvement compared with CG at 8 weeks
Tomonaga et al[23] *Jpn Pharmacol Ther* 2017	57 participants with knee symptoms (IG=28, CG=29) Mean age (IG=51.5, CG=53.0) Male/Female (IG=9/19, CG=6/23)	4 tablets (Yeast SM-10; 600mg) a day for 12 weeks	placebo	6, 12 weeks	no group differences
Najima et al[27] *Jpn Pharmacol Ther* 2017	39 healthy participants (IG=20, CG=19) Mean age (IG=57.0, CG=54.5) Male/Female (IG=9/11, CG=9/10)	3 tablets containing Glucosamine, chondroitin sulfate, and hyaluronic acid every day for 16 weeks	placebo	4, 8, 12, 16 weeks	in GLFS-25 IG showed the improvement in 5 out of 25 items, in the two-step test IG showed significant improvement at 8 weeks
Aoki et al[14] *J Orthop Sci* 2018	130 community-dwelling adults (G1=45, G2=42, G3=43) Mean age (G1=71.2, G2=71.3, G3=68.8) Male/Female (G1=11/34, G2=6/36, G3=11/32)	G1=Ex. G1=VitD G3=Ex.+VitD	N.A.	24 weeks	in the two-step test, all groups showed improvement after the interventions no group difference
Yamamoto et al[24] *Jpn Pharmacol Ther* 2018	26 participants with knee symptoms (IG=12, CG=14) Mean age (IG=52.9, CG=52.6) Male/Female (IG=5/7, CG=7/7)	collagen drink 125ml every day for 12 weeks	placebo	6, 12 weeks	in GLFS-25 both groups showed significant improvement at 12 weeks, in two-step test CG showed significant improvement at 12 weeks, no group difference
Nagaoka et al[25] *Funct Food Res* 2018	55 subjects with knee joint pain without the diagnosis of OA Mean age (IG=51.5, CG=53.0) Male/Female (IG=9/19, 6/23)	4 tablets (Yeast SM-10; 600mg) a day for 12 weeks	placebo	6, 12 weeks	no group differences
Hattori et al[28] *Jpn Pharmacol Ther* 2019	16 without knee OA (IG=9, CG=7) Mean age (IG=51.0, CG=59.1) Male/Female (IG=2/7, CG=3/4)	8 tablets containing Glucosamine, chondroitin sulfate et al every day for 12 weeks	placebo	6, 12 weeks	N.A.
Inada et al[29] *Nutrients* 2021	26 healthy participants (IG=15, CG=11) Mean age (IG=69.2, CG=61.3) Male/Female (IG=5/10, CG=2/9)	one stick (C.tubulosa) daily for 12 weeks	placebo	12 weeks	no intervention and group difference

IG: intervention group
CG: control group
GLFS-25: 25-question geriatric locomotive function scale
TENS: transcutaneous electrical nerve stimulation
OA: osteoarthritis
Ex.: exercise
VitD: Vitamin D
N.A.: not applicable

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Table 2 Results of Cochrane Risk of Bias assessment

Study	1	2	3	4	5	6	7
Shimoura et al,[22] 2019	?	?	+	−	−	+	+
Nishikawa et al,[21] 2019	+	?	−	−	+	+	+
Hattori et al,[26] 2016	+	+	+	+	+	+	+
Tomonaga et al,[23] 2017	+	+	+	+	+	+	+
Najima et al,[27] 2017	+	+	+	+	+	+	+
Aoki et al,[14] 2018	+	+	?	?	+	+	+
Yamamoto et al,[24] 2018	+	+	+	+	+	+	+
Nagaoka et al,[25] 2018	?	+	+	?	?	+	?
Hattori et al,[28] 2019	+	+	+	+	+	+	+
Inada et al,[29] 2021	+	+	+	+	+	+	+

1: Random sequence generation (selection bias)
2: Allocation concealment (selection bias)
3: Blinding of participants and personnel (performance bias)
4: Blinding of outcome assessment (detection bias)
5: Incomplete outcome data (attrition bias)
6: Selective reporting (reporting bias)
7: Other bias
+: Low risk of bias
−: High risk of bias
?: Unclear risk of bias

and we did not examine publication bias by funnel plot asymmetry or other statistical methods.[20,30] All parameters were judged to be low to moderate, with inconsistency and impression being the factors that reduced quality (Table 3).

Meta-analysis results

Two studies including 96 participants were used in a meta-analysis to examine the effect of oral glucosamine intake on GLFS-25, with no statistically significant differences at 4 weeks (MD: 1.01; 95%CI: −0.74 to 2.76; Figure 2a), 8 weeks (MD: 0.40; 95%CI: −1.63 to 2.44; Figure 2b), or 12 weeks (MD: 0.72; 95%CI: −0.99 to 2.44; Figure 2c).

Two studies including 96 participants were used in a meta-analysis to examine the effect of oral glucosamine intake on the two-step test, with no statistically significant differences at 8 weeks (MD: −0.00; 95%CI: −0.17 to 0.17; Figure 2d).

We attempted to determine the effect of oral yeast SM-10 intake on each outcome measure used as diagnostic criteria for locomotive syndrome by meta-analysis, but Nagaoka et al did not

Table 3 Grade summary of findings

Outcome		Certainty assessment							No. of patients		Certainty	Importance
		No. of studies	Study design	Risk of bias	Inconsistency (estimates)	Indirectness	Imprecision	Other considerations	Intervention group	Control group		
GLFS-25	4 weeks	2	RCT	Not serious	Not serious (I^2 = 0%)	Not serious	Serious[a]	None	49	47	⨁⨁⨁◯ Moderate	Important
	8 weeks	2	RCT	Not serious	Not serious (I^2 = 0%)	Not serious	Serious[a]	None	49	47	⨁⨁⨁◯ Moderate	Important
	12 weeks	2	RCT	Not serious	Not serious (I^2 = 0%)	Not serious	Serious[a]	None	49	47	⨁⨁⨁◯ Moderate	Important
2-step test	8 weeks	2	RCT	Not serious	Serious (I^2 = 89%)	Not serious	Serious[a]	None	49	47	⨁⨁◯◯ Low	Important

GLFS-25: 25-question geriatric locomotive function scale
RCT: randomized controlled trial
a: wide 95% confidence interval

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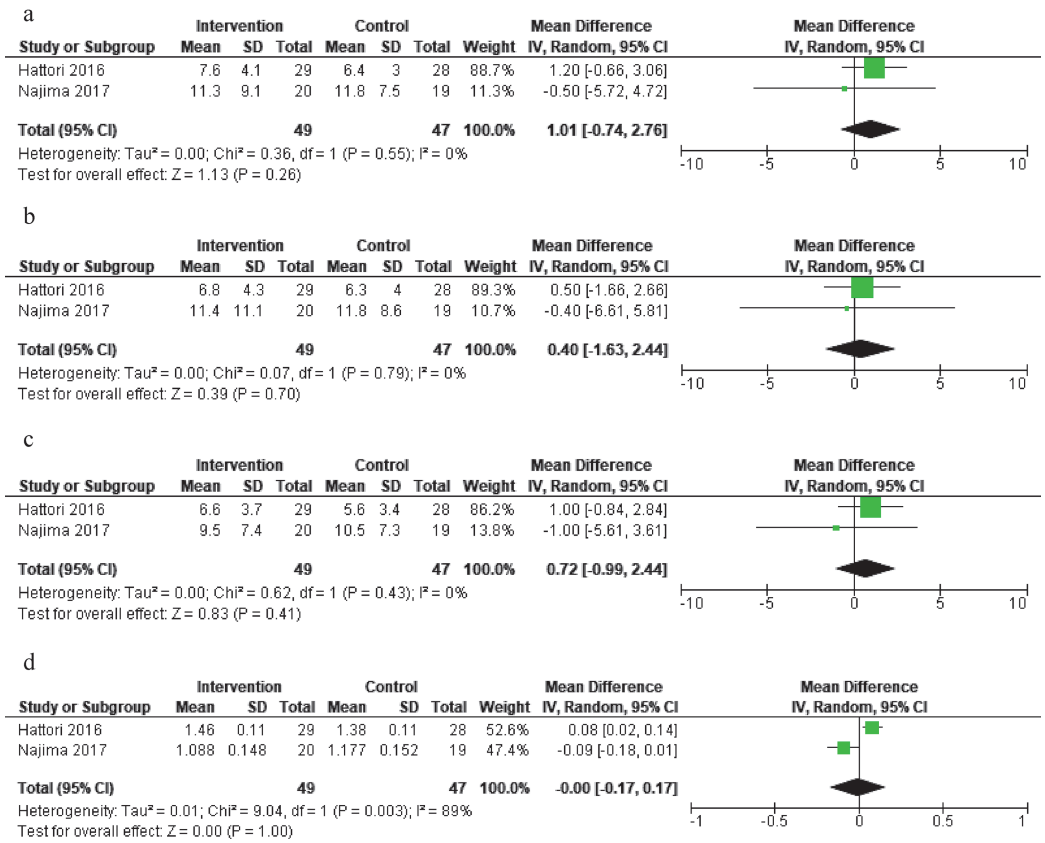

Fig. 2 Forrest plot displaying the mean differences between the intervention and control groups
Fig. 2a: 25-question Geriatric Locomotive Function Scale (GLFS-25) at 4 weeks
Fig. 2b: GLFS-25 at 8 weeks
Fig. 2c: GLFS-25 at 12 weeks
Fig. 2d: two-step test at 8 weeks

provide figures for the results, so we could not perform the analysis.[25]

DISCUSSION

The purpose of this systematic review is to consolidate evidence on effective interventions that improve locomotive syndrome. Several individual papers showed that the intervention group had significantly improved the outcome measure for the diagnosis of locomotive syndrome compared with the control group. However, only the oral intake of glucosamine provided sufficient information to conduct a meta-analysis, and the results were not statistically significant. Therefore, the overall, evidence for locomotive syndrome improvement by intervention is still insufficient. Conversely, this systematic review and meta-analysis is the first paper that examined interventions that improve locomotive syndrome, which is a novel approach to identify the level of evidence of each intervention effect.

Each paper showed the effect of oral glucosamine intake compared to the placebo group,[26-28]

but the meta-analysis did not show a significant difference between the groups. Hattori et al suggested that the reason that the oral intake of glucosamine improves locomotive syndrome is that glucosamine protects knee joint cartilage by inhibiting the degradation of type 2 cartilage collagen, and has anti-inflammatory and chondrogenic effects.[26,28,31-33] These effects of glucosamine on knee cartilage protection and inflammation are thought to have increased knee range of motion and have improved bending and stretching of the knee, thereby improving the locomotive syndrome. Hattori et al conducted a subgroup analysis of those with a JKOM score of 30 or higher,[26] as well as those with a score of 30 or higher, weight that was above the mean for men and women of their age group,[28] and showed greater improvement. The dietary supplement also contained small amounts of chondroitin in all studies, which has been shown to have anti-inflammatory effects.[34] On the basis of these findings, the choice of oral glucosamine may be more beneficial for subjects with knee joint discomfort.

Nishikawa et al showed that an 8-week EMS intervention on the quadriceps muscle improved locomotive syndrome.[21] They showed that isokinetic muscle strength and muscle thickness increased at the same time.[21] It was reported that EMS improves muscle performance such as muscle strength and thickness,[35,36] but it has also been shown to increase the amount of activity in daily life. In their RCT, EMS was implemented only in the intervention group and none in the control group. They additionary suggested that the effects of EMS on muscles other than the quadriceps should be examined because various muscles in the lower extremities work together to perform activities of daily living such as walking.

Other oral interventions were considered, but these did not significantly improve locomotive syndrome compared to the placebo group; these include the yeast SM-10,[23,25] collagen,[24] C.tubulosa,[29] and vitamin D.[14] Aoki et al's RCT was the only one to use exercise as an intervention method.[14] There was no control group to consider the effect of the exercise-only intervention in that report, and although all intervention groups showed improvement in locomotive syndrome, there was no significant difference between the groups. They performed one-legged stance and squatting movements as exercises with the guidance of a physical therapist for the first time in their RCT. There is a possibility that adherence and effectiveness may be reduced in the case of unsupervised self-exercise. We expect that a physiotherapist-supervised exercise, follow-up by videophone, and group exercise will have a greater effect on locomotive syndrome improvement.

This systematic review and meta-analysis is the first report to examine effective interventions based on the findings from RCTs for improving locomotive syndrome. It would also provide useful information for board members when developing or updating guidelines, as well as for clinicians when making choices and decisions regarding locomotive syndrome prevention or treatment. Interventions were orally consumed foods that could be obtained without a physician's prescription in more than half of the RCTs. The locomotive syndrome is a concept proposed by JOA and is a musculoskeletal system problem. The effects of combined nutrition and exercise and the effects of medications have been investigated in systematic reviews of frailty and sarcopenia, which have similar locomotive syndrome concepts.[7-10] Locomotive syndrome is a problematic condition caused by locomotive system problems,[1] and exercise therapy is important for improvement. It is hoped that further RCTs will be widely conducted to investigate the effects of interventions with physician-prescribed drugs and exercise.

There are some limitations to this review. First, there may be a conflict of interest from the viewpoint of scientific objectivity concerning company-sponsored research. The possibility of conflict of interest is explicitly stated in the individual studies and we did not treat it as a risk-reducing factor because the experiments are conducted by a third-party organization. As such, these study results may need to be interpreted conservatively. Second, we did not assess publication bias, which means that effect estimates may be optimistic because of unpublished

negative data. Third, we only included papers that evaluated locomotive syndrome. Previous systematic reviews of RCTs on frailty and sarcopenia might include subjects with locomotive syndrome who have not been specifically evaluated. The results of those studies might apply to those with locomotive syndrome. However, because locomotive syndrome indicates a decline in mobility and it has been reported that the decline in physical function begins with a decline in mobility,[37] we believe that the results of this study will provide findings independent of previous systematic reviews. Fourth, the small number of RCTs and participants included in the study may lead to biased interventions and subject characteristics. This may prevent results generalization. We determined that the number of RCTs was small because the locomotive syndrome is a concept proposed by JOA, but it is not widespread worldwide unlike frailty and sarcopenia. However, we believe that it is an important concept for all generations in maintaining locomotive system health, and we hope that it will be further promoted.

Electrical stimulation and exercise could improve locomotive syndrome, although individual RCTs have shown that oral intake of glucosamine in this systematic review and meta-analysis did not provide strong evidence for specific intervention to improve locomotive syndrome. RCT findings suggest that the current interventions for locomotive syndrome are limited to oral supplements, and we hope to carry out more high-quality RCTs of exercise interventions aimed at improving the locomotive syndrome, which is a musculoskeletal dysfunction. In addition, we hope that this concept will be widely recognized as beneficial for locomotive system health.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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Appendix 1

Search strategy

【Medline】
#1 locomotive syndrome[Title/Abstract]
#2 (((((randomized[Title/Abstract]) OR (placebo[Title/Abstract])) OR (drug therapy[Title/Abstract])) OR (randomly[Title/Abstract])) OR (trial[Title/Abstract])) OR (groups[Title/Abstract])
#3 #1 AND #2

【Cochrane Central Register of Controlled Trial】
#1 (locomotive syndrome):ti,ab,kw
#2 (randomized):ti,ab,kw OR (placebo):ti,ab,kw OR (drug therapy):ti,ab,kw OR (randomly):ti,ab,kw OR (trial):ti,ab,kw OR (groups):ti,ab,kw
#3 #1 AND #2

【Physiotherapy Evidence Database (PEDro)】
“locomotive syndrome”

【Scopus】
TITLE-ABS-KEY (“locomotive syndrome”) AND (TITLE-ABS-KEY (randomized) OR TITLE-ABS-KEY (placebo) OR TITLE-ABS-KEY (“drug therapy”) OR TITLE-ABS-KEY (randomly) OR TITLE-ABS-KEY (trial) OR TITLE-ABS-KEY (groups))

【Web of Science】
#1 ALL=(“locomotive syndrome”)
#2 (((((ALL=(randomized)) OR ALL=(placebo)) OR ALL=(“drug therapy”)) OR ALL=(randomly)) OR ALL=(trial)) OR ALL=(groups)
#3 (#1) AND (#2)

【Ichushi Web [in Japanese]】
(ロコモティブシンドローム/TH or ロコモティブシンドローム/AL) and (RD=ランダム化比較試験)

【Cumulative Index to Nursing and Allied Health Literature】
“locomotive syndrome” AND (randomized OR placebo OR “drug therapy” OR randomly OR trial OR groups)