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REVIEW

Effects of non-pharmacological therapies on hand function and the ability to perform daily activities in people with systemic sclerosis: A systematic review and meta-analysis of randomized control trials

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Abstract

Background: Systemic sclerosis (SSc) is an autoimmune rheumatic disease. Individuals with a diagnosis of SSc describe repercussions on their activities of daily living and instrumental activities of daily living that affect their everyday functional capacity. The objective of this systematic review was to explore the effectiveness of non-pharmacological interventions to improve hand function and the ability to perform activities of daily living.

Methods: A systematic review was conducted on the Cochrane Library, Medline/PubMed, OTseeker, PEDro, Scopus, Web of Science up to September 10, 2022. Inclusion criteria were defined following PICOS recommendations (Populations, Intervention, Comparison and Outcome measures). Methodological quality was assessed with the Downs and Black Scale and risk of bias was assessed using version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2). A meta-analysis of each outcome was performed.

Results: A total of 8 studies met the inclusion criteria, providing data on 487 individuals with SSc. The non-pharmacological intervention applied the most was exercise. The effects of non-pharmacological interventions were better than those of the waiting list or no treatment control conditions in both outcomes – hand function (mean difference [MD] = −6.98; 95% CI [−11.45, − 2.50], $P = 0.002$, $I^2 = 0\%$) and performance of daily activities (MD = −0.19; 95% CI [−0.33, − 0.04], $P = 0.01$, $I^2 = 0\%$). Moderate risk of bias was found in the majority of the studies included.

Conclusion: There is emerging evidence that non-pharmacological interventions can improve hand function and performance of daily activities in individuals with a diagnosis of SSc. Given the moderate risk of bias found in the studies included, the results should be considered with caution.

KEYWORDS
activity, function, hand, scleroderma, systemic sclerosis

1 | INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune rheumatic disease characterized by microvascular damage and generalized fibrosis in the skin and visceral organs such as the gastrointestinal tract, heart, lungs, and kidneys.[1–4] SSc can be divided into 2 basic categories based on the extent of pathological changes: limited and diffuse cutaneous SSc,[5] which provides a clinically useful profile of individuals who have various rates of progression of skin thickening and survival,[6–8] and diffuse cutaneous SSc, characterized by generalized hardening that affects a large area of the skin,[9,10] with large joint contractures and disease involvement in many internal organs with lung fibrosis, myocardial lesions and kidney failure.[11] The disease affects women more frequently than men, and the overall prevalence is approximately 7.2–33.9 cases per 100 000 individuals in Europe and 13.5–44.3 in North America.[12] As there is no cure for SSc and few effective disease-modifying agents, SSc is linked to significant morbidity and mortality and reduced health-related quality of life. Furthermore, SSc is associated with a large healthcare cost, with a high annual health service utilization cost per individual.[13,14]

The consequences of SSc on activities of daily living change with disease state and time.[2,15] Individual descriptions of living with the disease range from bothersome to impossible to live with.[16] Patients also describe repercussions on their activities of daily living and instrumental activities of daily living affecting everyday functional capacity.[17,18] SSc, in functional terms, affects body care and dressing, household chores, medical care, leisure activities (eg, shopping, sport, cultural and religious activities), mobility, parenting, professional activities, and sexuality.[16,18,19] Because of the limitations mentioned above, individuals report renouncing their "previous life" and the need for both pharmacological and non-pharmacological interventions to alleviate the consequences of SSc.[20–22] Non-pharmacological interventions can provide complementary therapy, offering versatile approaches to improve outcomes like hand function in addition to a decrease in pain, depression, and fatigue as well as to improve or sustain quality of life and performance of daily activities.

A non-pharmacological intervention can be defined as a treatment not involving a registered medication and can be used alone or in combination with other treatments. A non-pharmacological intervention requires a combined expertise of different health professionals to guarantee adequate disease control and prevent organ complications. Multidisciplinary teams (MDTs) are composed of health professionals such as nurses, occupational therapists, physical therapists and rheumatologists. Members of MDTs can effectively deal with several aspects of the disease that impact the prognosis and quality of life of individuals with SSc, improving communication and empowering them. In this regard, a previous systematic review of the effectiveness of non-pharmacological interventions in SSc identified a total of 23 articles published between 1990 and 2014, of which 9 were randomized controlled trials (RCTs).[23] Researchers assessed various oral health interventions, MDT care and diverse therapeutic approaches. In addition to this review, 3 more recent systematic reviews have been published[20,24,25] exploring the effects of non-pharmacological interventions on SSc individuals. One of them evaluated the effectiveness of exercise therapies such as aerobic exercise, muscle strengthening or orofacial exercises in individuals with SSc. It concluded that the evidence on the effect and safety of exercise therapy in SSc is not enough and more studies are necessary.[24] The other review evaluated the effectiveness of dietary interventions for gastrointestinal symptoms in SSc, concluding that the evidence supporting dietary modification for gastrointestinal involvement in SSc is currently too limited to generate robust recommendations.[20] The latter review synthesized rehabilitation interventions to improve different outcomes in individuals with SSc. Yet, only good or excellent quality studies were reported in its results, and it did not identify all available evidence on this topic.[25] This affected its conclusions, since they were biased by the selection of evidence and only included positive results. All 3 reviews had certain limitations: a small number of participants included in each study, generally high risk of bias across studies, and the use of alternative synthesis methods despite having data susceptible to meta-analysis. These limitations made it difficult to draw conclusions.

Research on non-pharmacological interventions to improve hand function and the performance of activities of daily living in SSc has grown in recent years, probably due to advances in science and the relevance for both individuals with SSc and health professionals. These articles on non-pharmacological therapies included different therapeutic approaches such as exercise therapies,

Key Messages

- Non-pharmacological interventions improve hand function in patients with SSc.
- Non-pharmacological interventions improve the ability to perform daily activities in patients with SSc.
- Current evidence supports personalized and supervised hand exercise training as one of the best non-pharmacological therapeutic approaches.

self-management programs, and educational and/or home interventions. The objective of this systematic review was to explore the effectiveness of non-pharmacological interventions to improve hand function and the ability to perform activities of daily living in individuals with SSc.

2 | METHODS

2.1 | Protocol and registration

This systematic review and meta-analysis was undertaken in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis)[26] and PRISMA-S (PRISMA-S extension for searching)[27] statements. Its registration number in PROSPERO is CRD42021262884.

2.2 | Search strategy

The following electronic databases were searched: Cochrane Library, MEDLINE (via PubMed), PEDro, OTseeker, Scopus, and Web of Science (including the KCI Korean Journal Database, MEDLINE, Russian Science Citation Index, and SciELO Citation Index) from their inception to September 10, 2022 using a search strategy. The strategies were peer reviewed by an information specialist prior to their implementation using the Peer Review of Electronic Search Strategies (PRESS) Checklist.[28] The full search strategy is available in Appendix S1. Terms were obtained using 2 thesauri (DeCS and MeSH) and by consulting the keywords used in literature on a similar topic. The search was carried out using the thesauri and reviewing the title/abstract/keywords when it was possible. When searched databases allowed limits, searches were restricted to human beings, RCTs, and English, French, Italian and Spanish languages. Reference lists of included articles were manually screened to identify additional studies.

2.3 | Selection criteria

We established our research question following PICOS recommendations[29] (Populations, Intervention, Comparison and Outcome measures) as follows. What is the effect of non-pharmacological interventions on hand function (main outcome) and the ability to perform activities of daily living (secondary outcome) compared to a passive control group, a waiting list group, a usual care group and pharmacological intervention in individuals with SSc?

2.4 | Types of participants

The population included individuals with a diagnosis of SSc.

2.5 | Types of interventions

The intervention could be any non-pharmacological intervention. There were no restrictions on the types, format, duration or frequency of the intervention.

2.6 | Types of comparators

The comparator group could be a passive control group, a waiting list group, a usual care group or a pharmacological intervention group.

2.7 | Types of outcome measures

The outcome measures were hand function (main outcome) and the ability to perform activities of daily living (secondary outcome), for which the scores were measured using a valid and reliable scale. If multiple scales were used to assess the same outcome within the same study, the main measurement of the outcomes was adopted for this systematic review. If the main outcome measure was not specified, the measurement obtained via the most commonly used scale was included.

2.8 | Types of studies

This systematic review included RCTs only as their information was more likely to be unbiased compared to other study designs. Studies written in English, French, Italian or Spanish were included. No limitations on dates were established.

2.9 | Excluded studies

Studies that exclusively evaluated the comparative effectiveness of different non-pharmacological interventions, animal studies, systematic reviews, meta-analyses, descriptive studies, books, editorials, letters, conference papers and doctoral theses were excluded.

2.10 | Study selection

Two independent reviewers (ANO and AOR) completed the data collection process following the steps established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[26] and PRISMA-S[27] (literate search extension) recommendations. Reviewers independently screened the title and abstracts to ascertain relevancy to the topic. The full text of all potentially relevant articles was read. When necessary, another reviewer (MCV) helped reach a consensus about whether to include the article in the study.

TABLE 1 Characteristics of included studies in the qualitative synthesis.

First author, y (country)	Aim	Participants, (men), age (mean ± standard deviation)	Intervention	Session duration/ frequency/program duration	Outcome		Findings
					Hand function	Performance of daily activities	
Filippetti (Italy)[33]	To evaluate the effect of a home-based exercise program on functional capacity, HRQoL, and disability, in patients with SSc	*n*: 44 (9), 56.85 ± NR IG: 22 (4), 63.60 ± 10.40 CG: 22 (5), 61.80 ± 14.40	IG: home-based exercise minimally supervised (stationary cycle, strengthening and stretching) CG: usual care	30-40 min/3 sessions per wk/24 wks	HAMIS	sHAQ	IG improved the performance of activities of daily living, HRQoL, and disability in comparison with CG
Gokcen 2022 (Turkey)[34]	To investigate the efficacy of a hand exercise program and to demonstrate its effect on hand function, HRQoL, anxiety, and depression in patients with SSc	*n*: 62 (0), 55.25 ± 37.07 IG: 32 (0), 54.5 ± 10.40 CG: 30 (0), 56.0 ± 14.40	IG: hand exercise Training (isometric hand exercise and stretching) + self-administered home exercise (ball squeeze and stretching) CG: passive group	1 hand exercise training conducted by a physiatrist and self-administered home exercise 10 times/2 sets per d/8 wks	HAMIS	HAQ-DI	IG provided a significant improvement in hand function, general health, HRQoL, and psychological status in comparison with CG
Maddali 2009 (Italy)[35]	To evaluate the efficacy of a district specific and global rehabilitation program tailored for SSc patients	*n*: 20 (7), 57.1 ± 15.0 IG: 10 (4), 58.0 ± 15.1 CG: 10 (3), 55.7 ± 14.9	IG: multimodal program (hand and face connective tissue massage, hand manual lymph drainage, respiratory exercise) CG: passive intervention (medical information)	60–120 min/1–2 sessions per wk/9 wks	HAMIS, COCHIN	sHAQ	IG improved disability, HRQoL, hand and face disability and functionality
Maddali 2011 (Italy)[36]	To evaluate the efficacy of MLD in reducing edema and in improving functionality of the hands and perceived HRQoL in SSc patients	*n*: 35 (0), 50.17 ± 15.69 IG: 20 (0), 57.2 ± 10.23 CG: 15 (0), 57.35 ± 12.6	IG: MLD CG: waiting list	60 min/1 session per wk/5 wks	HAMIS	sHAQ	IG reduced hand volume, edema, and pain. IG improved hand function and HRQoL in comparison with CG
Rannou 2017 (France)[37]	To compare a physical therapy program to usual care of SSc patients on disability	*n*: 218 NR IG: 110 (15), 52.7 ± 14.8 CG: 108 (22), 53.1 ± 14.4	IG: exercise supervised program by an occupational therapist (range of motion, stretching, and muscle strength). CG: usual care	180 min/3 sessions per wk/4 wks	COCHIN	HAQ-DI, sHAQ	A personalized physical therapy program did not reduce disability at 12 mo but had short- term benefits for IG participants
Santos 2022 (Brazil)[38]	To investigate the effectiveness of Maitland's joint mobilization and therapeutic exercises on the functionality of the hands in patients with SSc	*n*: 24 (2), 47.42 ± 11.14 IG: 12 (0), 44.08 ± 10.6 CG: 12 (2), 50.75 ± 11.08	IG: physical therapy (joint mobilization and supervised exercise by a physical therapist) CG: passive intervention (information about disease)	60 min/2 session per wk/12 wks	COCHIN	sHAQ	IG improved the functionality of the hands, reduced pain in the hands and wrists, increased range of motion, and improved HRQoL, in comparison with CG
Schouffoer 2011 (Netherlands)[39]	To compare the effectiveness of a multidisciplinary team care program with usual outpatient care in patients with SSc	*n*: 53 (NR), 52.8 ± 10.8 IG: 28 (9), 53.9 ± 10.8 CG: 25 (4), 51.7 ± 10.8	IG: multidisciplinary program (supervised exercises and educational sessions) CG: usual care	NR min/1 session per wk/12 wks	HAMIS	sHAQ	IG improved significantly 6MWD, grip strength, maximal mouth opening, health assessment questionnaire, but not for VO2max, hand mobility in SSc, checklist individual strength 20, SF-36, and VAS for pain in comparison with CG

TABLE 1 (Continued)

First author, y (country)	Aim	Participants, (men), age (mean ± standard deviation)	Intervention	Session duration/frequency/program duration	Outcome: Hand function	Outcome: Performance of daily activities	Findings
Stefanantoni 2016 (Italy)[40]	To evaluate the effect of occupational therapy intervention, integrated with a self-administered stretching program on the hands of patients with SSc, after 1 and 3 mo of treatment	N: 31 (1) 60.95 ± NR IG:15 61.4 ± NR CG:16 (1) 60.5 ± NR	IG: exercise supervised program by an occupational therapist (stretching and educational sessions) CG: passive intervention (information about disease)	NR min/NR session per wk/demonstrative and supervised hand exercises and weekly call/12 wks	COCHIN	HAQ-DI	A rehabilitation program including occupational therapy and self-administered stretching exercises may be effective to improve and maintain hand function in patients with SSc

Abbreviations: ACE, arm crank ergometer; CE, cycle ergometer; CG, control group; COCHIN, Cochin Hand Functional Scale; HAMIS, Hand Mobility in Scleroderma; HAQ-DI, Health Assessment Questionnaire-Disability Index; HIIT, high intensity interval training; HRQoL, health-related quality of life; IG, intervention group; MACTAR, McMaster Toronto Arthritis Patient Preference Disability Questionnaire; MCID, minimal clinically important difference; min, minutes; MLD, manual lymph drainage; 6MWD, 6-minute walk distance; *n*, number of participants per study; NR, non-reported; PASS, Patient Acceptable Symptom State; SF-12, Medical Outcomes Study 12-Item Short Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey; sHAQ, Scleroderma Health Assessment Questionnaire; SSc, systemic sclerosis; VAS, visual analog scale; VO2max, maximum volume of oxygen use in exercise.

2.11 | Data extraction

Data extraction followed the PICOS recommendations[29] to synthesize the information. Two reviewers independently extracted data from the studies included. Information about the objectives, number and age of participants, population group, intervention (ie, intensity, duration, and frequency), and outcomes was obtained. Data were collected using a standardized data extraction sheet. Disagreements between the 2 reviewers were resolved by discussion with MCV. If the required data were not published, they were obtained from the study authors whenever possible.

2.12 | Methodological quality assessment

Two independent reviewers (ANO and AOR) performed a methodological quality assessment using the Downs and Black Scale.[30] The scale consists of 27 questions relating to quality of reporting (10 questions), external validity (3 questions), internal validity (bias and confounding) (13 questions), and statistical power (1 question). The original scale provides a total score out of 32 points, with 1 question in the reporting section carrying a possible 2 points, and the statistical power question carrying a possible 5 points. Previous studies have frequently used a modified version by simplifying the power question and awarding a single point if a study had sufficient power to detect a clinically important effect, where the probability values for a difference due to chance are <5%. Therefore, the modified version has a maximum score of 28 points. We used the modified version in this study. Each paper was assigned a grade of "excellent" (24–28 points), "good" (19–23 points), "fair" (14–18 points), or "poor" (<14 points).

2.13 | Methodological assessment of risk of bias

Risk of bias was assessed using version 2 of the Cochrane risk-of-bias tool for RCTs (RoB 2).[31,32] The revised tool is structured into 5 domains of bias, according to the stages of a trial in which problems may arise: (1) the randomization process; (2) deviations from intended intervention; (3) missing outcome data; (4) measurement of the outcome; and (5) selection of the reported result. The judgment for each domain is "low risk of bias", "some concerns", or "high risk of bias". In addition, the same 3 judgment options are available for overall risk of bias. The assessments apply to a specific result of the trial rather than to the study as a whole.

2.14 | Data analysis

Where appropriate, study results were pooled and a meta-analysis was undertaken using Review Manager software (RevMan version 5.3, updated March 2011). For continuous data, the standardized mean difference (SMD), defined as the absolute mean difference divided by the standard deviation (SD) or the mean difference (MD),

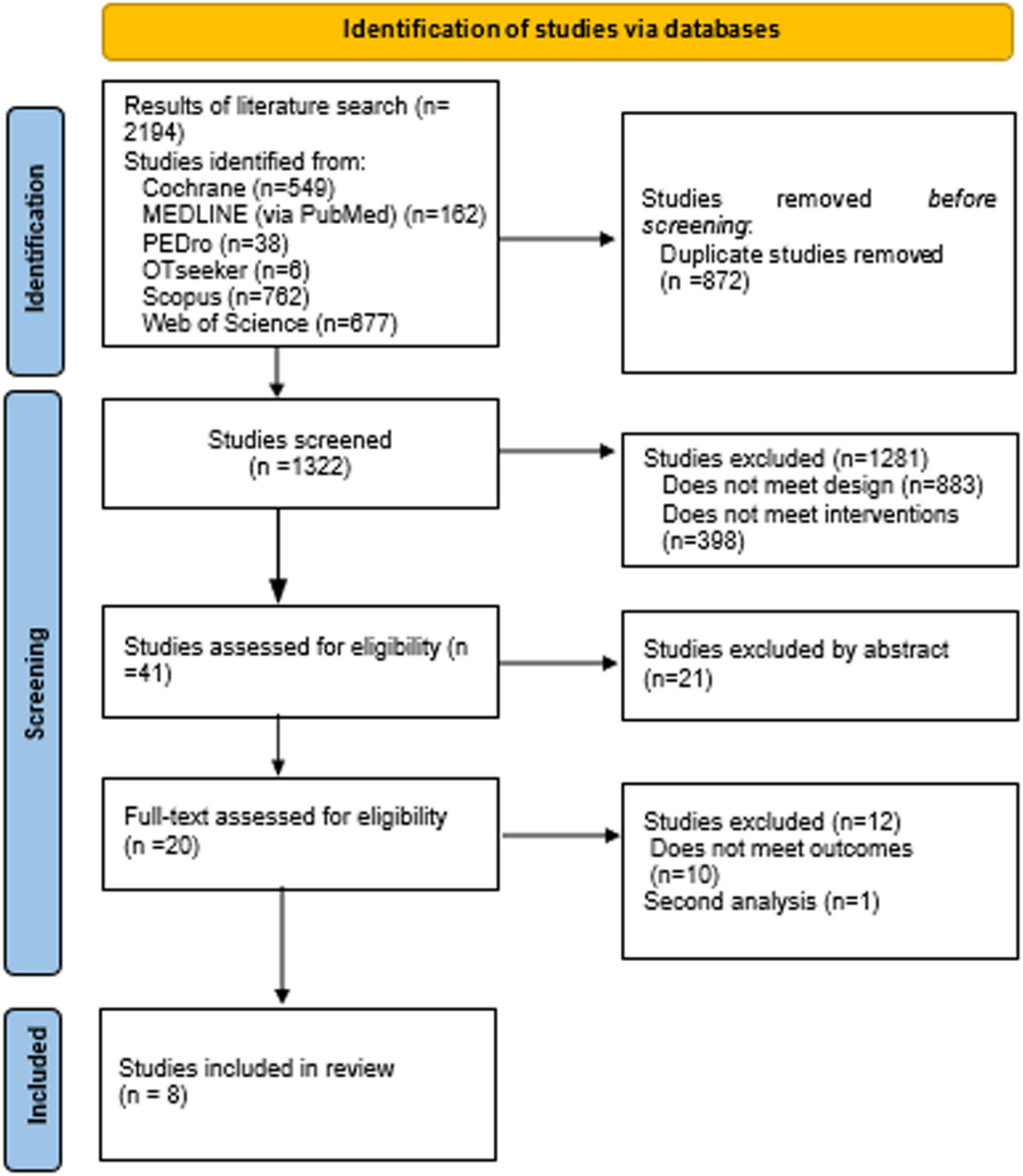

FIGURE 1 Flow diagram showing the selection of trials.

was estimated along with the corresponding 95% confidence interval (CI). The magnitude of heterogeneity of the studies was assessed using the Q and I^2 statistics. Random effect models were used, as the estimated effects in the included studies were not identical. I^2 values of 25%, 50% and 75% indicated low, moderate and high heterogeneity, respectively. Forest plots were generated to illustrate the overall effect of interventions.

3 | RESULTS

According to the method of literature retrieval, 2194 articles were obtained through the different databases. After inputting them into a reference manager software, 872 repetitive articles were excluded through the software's system check function and 1322 articles were left. By reading the titles and abstracts

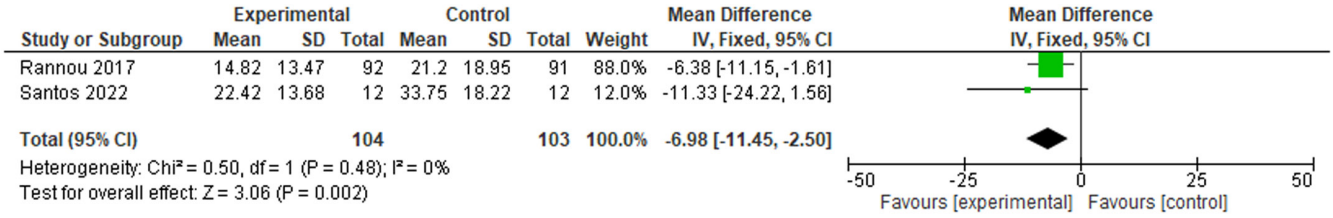

FIGURE 2 Forest plot of the results of the meta-analyses of those studies evaluating the effect of non-pharmacological intervention compared to the control group in relation to hand function.

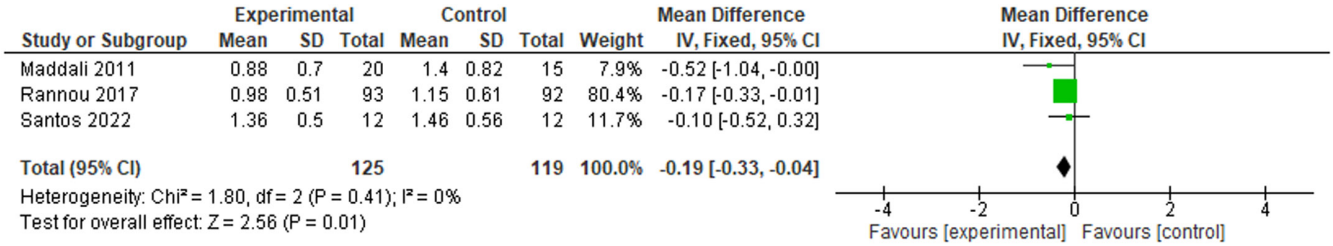

FIGURE 3 Forest plot of the results of the meta-analyses of those studies evaluating the effect of non-pharmacological intervention compared to the control group in relation to the performance of activities of daily living.

TABLE 2 Results of quality assessment using Downs and Black checklist.

First author, year (country)	Study quality (11)[a]	External validity (3)[a]	Internal validity - bias (7)[a]	Internal validity - confounding (6)[a]	Power (1)[a]	Total score (28)	Grade
Filippetti 2020 (Italy)[33]	9	1	4	3	0	17	Fair
Gokcen 2022 (Turkey)[34]	9	1	6	4	1	21	Good
Maddali 2009 (Italy)[35]	8	1	4	3	0	16	Fair
Maddali 2011 (Italy)[36]	8	1	4	3	0	16	Fair
Rannou 2017 (France)[37]	11	1	6	6	1	25	Excellent
Santos 2022 (Brazil)[38]	11	1	6	6	0	24	Excellent
Schouffoer 2011 (Netherlands)[39]	10	0	6	6	1	23	Good
Stefanantoni 2016 (Italy)[40]	8	2	6	4	0	20	Good

[a]Maximum score in each subscale.

of the literature, 883 articles did not meet the design criteria and 398 did not include non-pharmacological interventions. A total of 1281 articles were excluded and the remaining 41 were left. By reading the abstract in the remaining documents, 21 studies were excluded, leaving 20 articles. After thorough reading of the documents, 12 articles were excluded. Finally, a total of 8 RCTs[33–40] involving 487 participants were included – 249 in the experimental group and 238 in the control group (see Table 1). A more detailed description of this process can be found in the PRISMA flow diagram (Figure 1).

Four studies had been conducted in Italy,[33,35,36,40] 1 in France,[38] 1 in Brazil,[37] 1 in the Netherlands[39] and 1 in Turkey.[34] The included studies evaluated different non-pharmacological interventions for individuals with a diagnosis of SSc. All the individuals were adults, mostly women, ranging from a mean age of 47.42 years to 66.5 years, although the ranges (when reported) consisted of adults aged 40 to older than 65 years. Non-pharmacological interventions explored in the trials included different modalities of exercises, self-management and manual therapy or a combination of those.

A total of 3 studies explored the effects of exercises, 1 study trained an intervention group with 1 month of physical therapy followed by home sessions,[37] other studies used a home-based exercise program focus to improve performance of activities of daily living,[33] 1 used exercises and mobilization in the intervention,[36] and 1 explored the efficacy of a hand exercise program.[34] Only 1 study used an occupational therapy intervention including a self-administered stretching program on the hands[40] while another study described

FIGURE 4 Risk of bias summary: review of authors' judgments about each risk of bias item for each included study. (+) Low risk of bias. (?) Unclear risk of bias. (−) High risk of bias.

a multidisciplinary program including a standard group session and individual sessions.[39] The rest of the studies ($n=2$) were conducted by Maddali Bongi et al.[35,36] In 1 of them, the authors used a district specific and tailored global rehabilitation program,[35] while in the other study the authors explored the effects of manual lymphatic drainage.[36] Interventions varied in duration from 4 to 24 weeks with sessions ranging from 1 to 3 times per week and durations from 30 to 180 minutes. None of the studies reported adverse events.

All studies evaluated hand function. Four of them used the Hand Mobility in Scleroderma (HAMIS) test,[33,34,36,38] while the remainder used the Cochin Hand Function Scale (CHFS).[37,38,40]

Only 1 study used both instruments to assess hand function.[37] However, only 3 studies reported enough data to run a meta-analysis. Figure 2 shows the forest plot used to evaluate the effectiveness of the non-pharmacological interventions to improve hand function. Significant differences were found in favor of the experimental group (MD = −6.98; 95% CI [−11.45, − 2.50], $P=0.002$, $I^2=0\%$).

Seven studies measured the ability to perform activities of daily living with different instruments. Five studies used a specific tool to evaluate the ability to perform activities of daily living with a specific instrument for SSc, the Scleroderma Health Assessment Questionnaire (sHAQ).[33,35,36,38,39] Two studies used the generic instrument for rheumatic disease: the Health Assessment Questionnaire-Disability Index (HAQ-DI).[34,40] Finally, 1 study registered the ability to perform daily activities with more than 1 instrument, using sHAQ and HAQ-DI.[37] A meta-analysis was run with a total of 3 studies. Significant differences were found in favor of the experimental group (MD = −0.19; 95% CI [−0.33, −0.04], $P=0.01$, $I^2=0\%$; Figure 3).

3.1 | Methodological quality and risk of bias assessment

After evaluating the methodological quality of the studies selected using the Downs and Black Scale, the scores ranged from 16 to 25 points. According to the classification proposed, 2 studies had "excellent" quality,[37,38] 3 studies had "good" quality,[35,39,40] and the remaining studies had "poor" quality.[33,35,36] No studies had excellent methodological quality. The most common limitations were related to power and external validity. A total of 5 studies did not include a power analysis. Table 2 shows the methodological quality of the selected studies using the Downs and Black Scale.[28] The results of the risk of bias assessment using the RoB 2[31] are shown in Figures 4 and 5.

4 | DISCUSSION

To the best of our knowledge, the present review provides the first comprehensive revision of the effectiveness of non-pharmacological interventions for hand function and the ability to perform daily activities in individuals with SSc. The results of the included studies revealed that non-pharmacological interventions improved hand function and the ability to perform activities of daily living in individuals with SSc. The meta-analysis showed significant statistical results in favor of the experimental group for both outcomes studied: hand function and the ability to perform activities of daily living. When exploring the risk of bias using the RoB 2, the risk of performance bias was unclear in the majority of the items for each study. An important aspect associated with this evidence is that the results

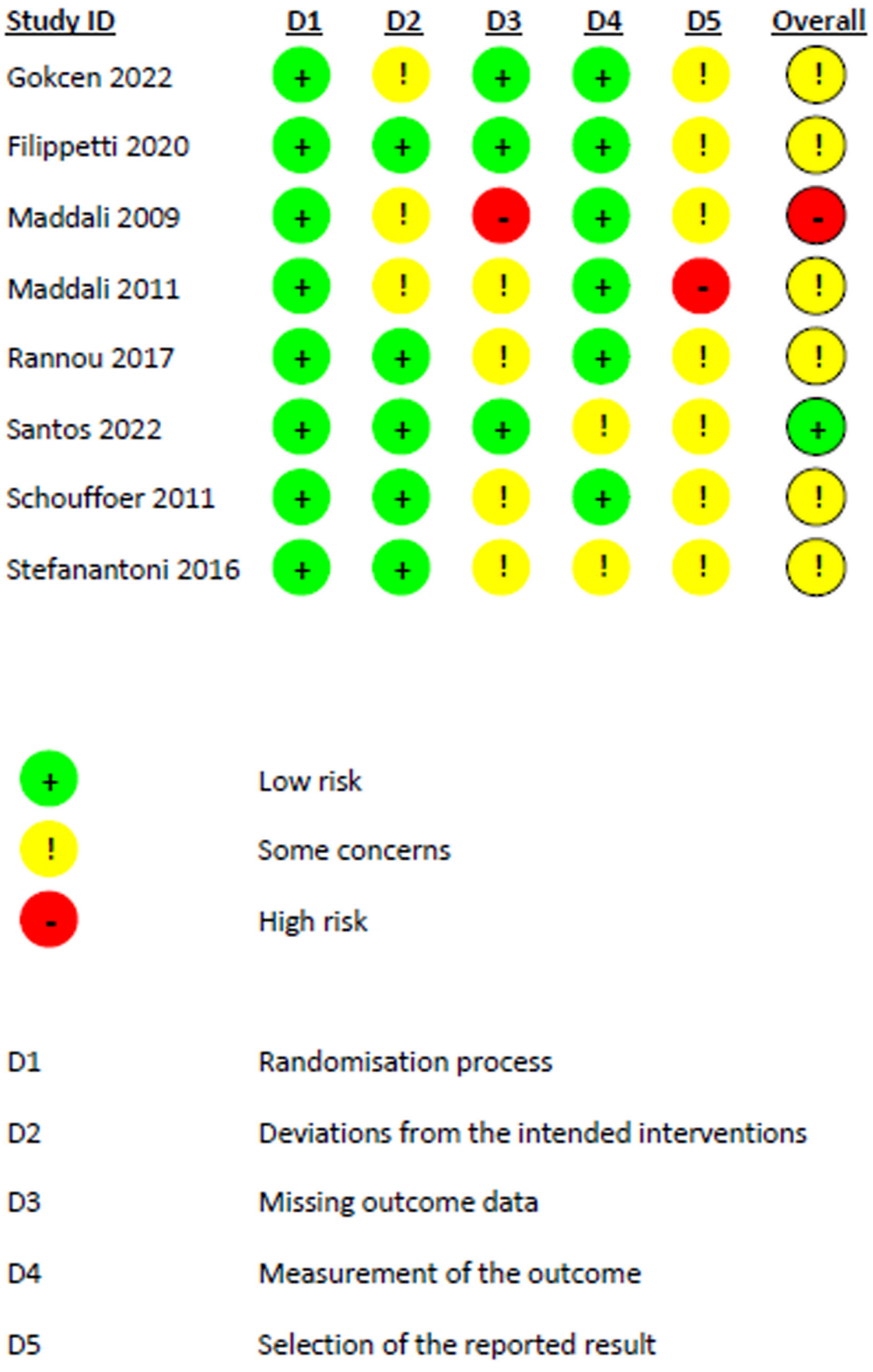

FIGURE 5 Risk of bias graph: review of authors' judgments about each risk of bias item for each included study. (+) Low risk of bias. (!) Unclear risk of bias. (–) High risk of bias.

obtained by the methodological quality assessment using the Down and Black Scale[30] ranged from 16 to 25 points, with the most common score being 16 points. For this reason, the results obtained in this systematic review and meta-analysis must be interpreted with caution. Larger and more rigorously designed non-pharmacological studies such as blind RCTs are necessary in this population.

As there is a high prevalence of pathological changes in the musculoskeletal system in individuals with SSc,[41] there is an urgent concern about the efficacy of all potential non-pharmacological interventions. Pain and edema in the hand joints, deformity, finger contractions, phalangeal ulcers, swelling and limitation of the range of motion of joints usually translates into functional disturbances of the hand, which significantly limits an individual's dexterity and the ability to perform daily activities.[42] The treatment of SSc focuses primarily on pharmacological approaches and the literature has scarcely summarized the evidence that has been published exploring the effect of non-pharmacological interventions.[43,44] One of the most important issues in the rehabilitation of individuals with SSc should be the maintenance of upper limb function. Although perceived symptoms and difficulties in activities of daily living among patients with SSc may vary greatly,[17] our study has shown the importance and effectiveness of non-pharmacological interventions. Research in the area of physical intervention is virtually absent in SSc, even though the efficacy of these interventions has been established in other similar pathologies. As a result, conducting studies similar to ours is essential for the advancement of knowledge in the treatment of this disease.

This review explored 8 RCTs with different interventions to improve hand function and the ability to perform daily activities that were hard to classify into specific categories.[33–40] Although interventions were different, most therapeutic approaches included hand exercises as a basic part of the intervention. However, interventions varied in content, delivery, length, dose and outcome measures collected, which made it difficult to synthesize the results. Interventions varied in duration from 4 to 24 weeks with sessions ranging from 1 to 3 times per week and different durations ranging from 30 to 180 minutes. However, given the high variability and the fact that some studies showed that possible effects and adherence might wane after stopping the program, it is important to evaluate the specific preferences and needs of individuals. An additional complication is that the studies reviewed were conducted in many countries with different healthcare systems and reimbursement structures. These differences have implications for how interventions could be translated into clinical practice outside of the study's country of origin.

5 | LIMITATIONS

The main limitations found when this study was carried out were the scarcity of studies and their moderate methodological quality. Another limitation of our study is related to the possible exclusion of some non-pharmacological interventions due to their languages. Furthermore, we included only 8 studies with small study populations, which makes it hard to draw firm conclusions. Another limitation of this systematic review and meta-analysis is that we extracted data only on outcomes directly related to hand function and the performance of activities of daily living and did not consider other outcomes such quality of life or emotional status.

6 | CONCLUSION

The results obtained from this systematic review and meta-analysis have several implications for future research and clinical practice in the rehabilitation area and for understanding the effective evidence-based non-pharmacological interventions available for enhancing the hand function and performance of daily activities in patients with SSc. The majority of studies included hand exercise as part of their intervention protocol. Therefore, further research is necessary on the use of hand exercises in SSc individuals, considering the different types of exercise that exist. It is also important to improve the methodological quality of the studies. For example, personnel blinding would be relatively easy to implement.

AUTHOR CONTRIBUTIONS

Conceptualization: ANO, MCV and AOR. Methodology: ANO, SGC, AOR and MCV. Formal analysis: AHC, ACM, JMN and ANO. Investigation: SGC, JMN and MCV. Data curation: JMN, ANO, MCV, AOR. Writing—Original draft preparation: ANO, SGC, JMN, AHC, ACM, AOR, MCV. Writing—Review and Editing: ANO, SGC, JMN, AHC, ACM, AOR, MCV. All authors have read and agreed to the version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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