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REHABILITATION SCIENCES AND THE RHEUMATIC DISEASES

Rehabilitation Interventions in Systemic Sclerosis: A Systematic Review and Future Directions

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Objective. To systematically review evidence of rehabilitation interventions for improving outcomes in systemic sclerosis (SSc) and to evaluate evidence quality.

Methods. Several electronic databases were searched to identify studies in which rehabilitation professionals delivered, supervised, or participated in interventions for individuals with SSc. Randomized controlled trials (RCTs) or non-randomized trials, one-arm trials, and prospective quasi-experimental studies with interventions were included if they had ≥10 participants. Quality appraisal was conducted by 2 independent raters using the Physiotherapy Evidence Database (PEDro) Scale.

Results. A total of 16 good or excellent quality studies (15 RCTs, 1 prospective quasi-experimental study) were included. Most rehabilitation interventions focused on hands/upper extremities, followed by multicomponent, orofacial, and directed self-management. Sample sizes varied between 20–267 participants (median 38). In 50% of studies, participants in intervention groups significantly improved compared to controls. Most studies demonstrated within-group improvements in intervention groups. Interventions varied in content, delivery, length, and dose and outcome measures collected.

Conclusion. Existing evidence provides some support for rehabilitation in SSc, such as interventions that focus on hand and upper extremity outcomes or are multicomponent, although there is high study heterogeneity. The evidence base would benefit from interventions testing similar replicable components, use of common outcome measures, and incorporation of delivery modes that enable larger sample sizes. There are challenges in recruiting participants due to the rarity of SSc and high disease burden, as participants' involvement in rehabilitation studies requires active participation over time. Intervention studies designed to reduce participation barriers may facilitate translation of effective interventions into practice.

INTRODUCTION

Systemic sclerosis (SSc; scleroderma) is a rare, chronic, and progressive autoimmune disease characterized by skin fibrosis, vasculopathy, and visceral damage (1). SSc is often classified into 2 subtypes, including limited and diffuse cutaneous SSc, which provides a clinically useful profile of people who have different progression of skin thickening and survival rates (2). People with both limited or diffuse subtypes of SSc commonly experience Raynaud's phenomenon, pain, fatigue, decreased flexibility, reduced strength, and visceral involvement. People with diffuse cutaneous SSc are more likely to have significant skin disease burden with large joint contractures and to have severe disease involvement in internal organs with lung fibrosis and renal crisis, whereas those with limited cutaneous SSc are likely to have associated pulmonary arterial hypertension. Organ involvement, which can be life threatening, is a focus of clinical care in SSc, while less attention is paid to resultant disability and quality-of-life issues such as hand involvement, appearance changes, and fatigue (3–5). Yet, these symptoms are of significant concern to people with SSc (5). Regardless of subtype, there is high symptom burden

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SIGNIFICANCE & INNOVATIONS

- To the best of our knowledge, this is the first systematic review of rehabilitation literature in systemic sclerosis (SSc).
- Rehabilitation interventions demonstrate improvements in hand/upper extremity function, and health-related quality of life; however, the studies mainly involve small samples and vary in intervention content and dose.
- Multicomponent interventions and those that focus specifically on hands and upper extremities showed the most improvements in outcomes.
- Evidence-building in SSc will require attention to enhancing comparability across studies such as by testing similar interventions, using the same outcome measures, and reporting findings appropriately.

and disability that have significant effects on work and participation in life roles (6,7). There have been treatment advances, but no approved disease-modifying antirheumatic drugs for SSc. Without a cure, strategies that help individuals with SSc with chronic disease management are needed.

Rehabilitation is an important tool to help individuals manage SSc and potentially slow its disabling effects; however, there are difficulties in translating evidence-based rehabilitation strategies into practice. Less than 1 in 4 people with SSc across several countries reported using rehabilitation services (physical or occupational therapy) (8) and there are low referral rates to rehabilitation (9). Additionally, most rehabilitation professionals do not have clinical experience with SSc due to its rarity, and there is little clinical guidance available for rehabilitation professionals when encountering these patients.

There have been articles that have discussed the effectiveness of rehabilitation treatments in SSc; however, the literature has not been systematically reviewed for interventions specifically performed or supervised by rehabilitation professionals. Since 2001, and the updated definition of diffuse and limited cutaneous subtypes (10), there have only been 2 narrative reviews that have examined rehabilitation treatments, which were either limited to musculoskeletal impairments (11) or to describing local and generalized rehabilitation treatments (12); and neither review examined evidence based on study quality. Systematic reviews done in SSc encompass some rehabilitation studies but also included other nonpharmacologic treatments, such as nutrition and dental treatments (13), or examine effects of exercise but include studies that were not conducted as part of rehabilitation (14). A systematic review of rehabilitation treatments is still needed to provide a current understanding of the quality of this literature and provide the foundation to future directions to build evidence in this area. The objective of this systematic review was to examine the evidence for rehabilitation interventions in SSc. Therefore, the following was our primary research question: What is the effectiveness of rehabilitation interventions on clinical outcomes in individuals with SSc? Our secondary question was: What is the overall quality of the body of evidence in SSc rehabilitation literature?

MATERIALS AND METHODS

Search strategy. The following databases were selected for the literature search: Medline through Ovid, Scopus, Embase, Cumulative Index to Nursing and Allied Health Literature, the Cochrane Central Register of Controlled Trials, OTseeker, and Physiotherapy Evidence Database (PEDro). These databases were selected in conjunction with our university library informationist along with guidance from the rehabilitation literature (15). In addition to searching these databases, we examined publication reference lists and other reviews for studies that would potentially meet study criteria. The informationist performed a literature search in these databases from the year 2001 and later because the diagnostic classifications of SSc (diffuse and limited cutaneous) were updated that year (10) and we wanted to ensure that we were including comparable patient samples. Searches involved subject headings unique to each database but similar to the Medline medical subject headings. The complete search strategy with terms used are provided (see Supplementary Appendix A, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24737/abstract). The protocol for this systematic review is published in an online registry (16) and was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Inclusion and exclusion criteria. Because our intent was to select publications that examined rehabilitation practices, intervention studies were eligible for inclusion if the interventions included a rehabilitation professional (physical therapist/physiotherapist, occupational therapist, ergotherapist, rehabilitation specialist, or speech pathologist) for delivery or supervision. Interventions that were multidisciplinary and included rehabilitation were also considered within scope. Interventions were excluded if they were conducted by related but different disciplines (e.g., respiratory therapy, nursing, or dentistry) or if they were complementary and alternative treatments not conducted by rehabilitation (e.g., acupuncture or spa treatments). Interventions performed for the primary purpose of examining effects on a biomarker or physiologic outcome in a research environment and not a clinical treatment were also excluded. Publications that involved adult samples (ages ≥18 years) who had a diagnosis of SSc (limited or diffuse according to 1988 classification criteria and updated in 2001) (10) were included. Studies also needed to include samples that had ≥10 participants, which, similar to another review (13), excluded studies with a very low sample size given the heterogeneity of SSc. Given the state of the evidence, we felt it was important to consider all intervention studies with

designs in which participants were either randomized or not, including pre-post, single-arm studies and prospective studies that involved interventions. We also included published abstracts for the purpose of identifying additional research studies based on work reported in the abstracts. Because some team members were fluent in languages other than English, we also considered articles written in French or Chinese.

Article selection. Citations generated from the search were imported into Covidence systematic review software for title and abstract screening. A pair of reviewers (SLM, JLP, YTC, and AL) independently screened all titles and abstracts to determine if the articles met inclusion criteria. Conflicts were resolved by a third reviewer, who was a coauthor of the study. A full-text review of each eligible article was then conducted by the same pair of reviewers. These reviewers independently coded each full text for the inclusion criteria. Disagreements in the full-text evaluation were resolved through discussion, and misunderstandings were corrected to ensure consistency for the remainder of the article evaluation. After full-text evaluation, there were 33 articles to include in quality assessment and data extraction.

Assessment of methodologic quality. Quality appraisal was used to answer the secondary research question (regarding the quality of the body of evidence in the literature). The PEDro scale was used to assess article quality (17); it was developed for rehabilitation literature quality appraisal and has been shown to be a more comprehensive measure for rehabilitation evidence than the commonly used Jadad scale (18). The PEDro scale has a possible score of 10, in which 1 point is given for each quality metric that is met. Quality classifications are <4 = poor, 4–5 = fair, 6–8 = good, and 9–10 = excellent (19). Two independent raters, consisting of coauthors (SLM, JLP, YTC, and AL), trained in use of the PEDro scale independently rated each included article for quality. Any article for evaluation that was written by members of the study team did not include that member as a rater. We calculated interrater agreement of methodologic quality for 18% of the articles (i.e., 6 articles) using Cohen's kappa. After all raters reached a high level of agreement of articles by quality category (0.80 or above) (20), they completed evaluation of the remaining articles. Discrepancies on remaining articles were resolved through discussion.

Data extraction. We extracted data from articles that met a quality classification of ≥6 on the PEDro scale (good to excellent quality) (19). Data extraction was verified for 20% of articles. Data was independently extracted by a rater pair and then checked for consistency by a third rater. Only 1 discrepancy was found and resolved. Tasks for data extraction and verification were divided among coauthors Murphy, Poole, Chen, and Lescoat. One coauthor then extracted data from the remaining articles with data verification by a different coauthor.

Evidence synthesis. Studies were summarized by aspects of the intervention, such as intervention content, setting in which it was delivered (clinic, home, telehealth, or some combination), length, and dose. After a review of intervention content of included studies, interventions were categorized as hand/upper extremities (UE), orofacial, multicomponent, or directed self-management. Hand/UE included any treatments for hand or UE symptom reduction or increased mobility (like thermal treatments, manual therapy, or exercises). Orofacial included an exercise intervention addressing mouth opening. Multicomponent rehabilitation interventions involved >1 treatment for a specific body part such as hand or face, but also more generalized whole-body treatments, such as aerobic or water-based exercises. Directed self-management included a rehabilitation-involved, self-paced, symptom self-management program.

Sample characteristics were summarized by age, sex, ethnicity/race, subtype of SSc, and disease duration. Other elements of the synthesis included study design, timing of outcomes collection, assessment measures used, and whether study authors designated a primary outcome. Due to variability in outcome assessments, outcome domains were created to summarize findings.

RESULTS

Search results. The systematic literature search yielded 3,478 publications in which titles and abstracts were screened by rater pairs. There was disagreement regarding eligibility among pairs in 79 (2%) of 3,478 cases, which was resolved by a third rater. The most common reason for exclusion was due to being an abstract with insufficient data on the involvement of a rehabilitation professional in the intervention (72% of those excluded). Ninety full texts were evaluated and 33 were selected for quality appraisal (Figure 1). There were 16 articles included in this review.

Characteristics of studies. The characteristics and main findings of each study are shown in Table 1. Of the 16 articles, 15 were randomized controlled trials (RCTs) and 1 used a prospective quasi-experimental study design (21). The sample sizes ranged from 20 to 267 people (median sample size 38). Thirty-eight percent of the articles (6 of 16) came from Italy (3 of which were by the same author), 3 were from the US, and remaining articles came from other countries. Most studies involved a high proportion of female to male participants (the lowest percentage of female participants was 47%, 15 of 16 studies ranged 65–100% female participants). In the US, the study by Yuen et al (22) had the highest proportion of minorities (52% African American participants, followed by Murphy et al [23] with 22%). The average age of participants across studies ranged from 50 to 65 years. Only 3 studies involved patients early in their disease process (average of 1–3 years since diagnosis [23,24], or median of 4 years since diagnosis [25]). The average disease duration of participants in

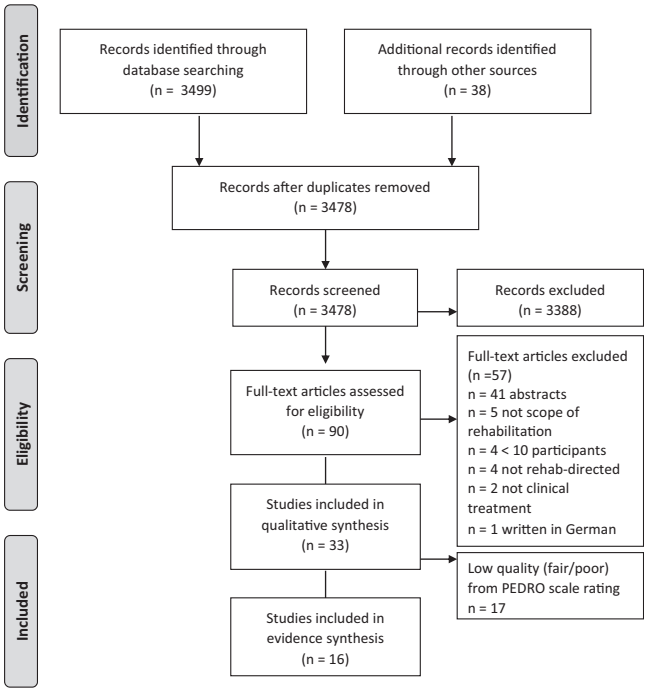

Figure 1. Flow diagram of studies of rehabilitation in systemic sclerosis. PEDro = Physiotherapy Evidence Database scale.

the remainder of articles was ≥6 years. With regard to disease subtype, 19% of articles did not specify a subtype. In terms of primary outcome, 6 (38%) of 16 articles did not specify a primary outcome.

Quality. Of potentially eligible articles reviewed, only 48% were considered of good quality or better on the PEDro scale and were included. Of these 16 articles, the mean ± SD PEDro score was 7.0 ± 0.97. Articles rated by each quality metric are demonstrated (see Supplementary Table 1, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24737/abstract). Only 1 article was rated as excellent (26). The number of included articles by quality criteria on the PEDro scale are shown in Figure 2. The aspect of quality that was met by the fewest studies was blinding. More than half of articles (56%) used blinded outcome assessors, only 2 had participants that were blinded, and no articles had therapists who were blinded.

Intervention delivery and content. Of the interventions, which we classified by categories, including hand/UE, orofacial, multicomponent, and directed self-management (Table 1), hand/UE was the focus for more than half of the studies (9 of 16), followed by multicomponent interventions (5 of 16). All multicomponent interventions included treatments targeted to hands/UE, but other aspects such as orofacial exercises, general aerobic or resistance exercise, or supervision or check-in calls from therapists were also included. There was 1 intervention that focused only on orofacial exercises (22) and another that involved a rehabilitation-directed self-management program that had moderated online discussion boards with participants involving a rehabilitation professional (27). Intervention length ranged from 2 weeks to 12 months. Delivery mode was most often done in clinic either with a home component, such as an exercise program (n = 4), without a home component (n = 4), or with a telehealth component, which was an app-delivered exercise program with education (n = 1) (23). The remaining 7 studies were designed as home interventions with two having a telehealth component (27,28).

Investigators in almost all studies, regardless of intervention content, evaluated quality of life (Table 2). The most commonly used measures were the Health Assessment Questionnaire (HAQ and HAQ disability index [HAQ DI]) (n = 9) and the Short Form 36 health survey (SF-36; n = 11), which are reliable and valid outcomes in persons with SSc. Furthermore, since the majority of the studies were categorized as hand/UE or multicomponent, the other most frequent outcome measure was the Hand Mobility in Scleroderma test (n = 9), also validated for people with SSc. Other outcomes, grouped in domains, such as skin, pulmonary, and cardiac, were used less frequently and were specific to intervention content (Table 2).

Table 2 shows findings for articles based on between-group differences in outcomes measured (for more details, see Supplementary Table 1, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.24737/abstract). Most effects from SSc interventions were in hand/UE function and health-related quality-of-life domains, followed by orofacial function. Interventions with the most effects had a hand exercise component or were multicomponent. In the hand/UE intervention category, findings varied as did interventions. The 2 studies that examined the effect of heat (warm water, paraffin) reported no significant difference between intervention and control groups (29,30), as did 2 studies that focused on hand exercises or massage with or without glove wearing (24,28). The exceptions were studies that incorporated manual lymph drainage (32) or negative pressure and stretching (23) reported significant between-group differences for some hand/UE outcomes. The only study that compared modality use (biofeedback, deep oscillation) to a control condition, found a significant improvement in biofeedback compared to the control group, while the oscillation group revealed a trend in improvement (25). Furthermore, within hand/UE interventions, in the intervention group, significant improvements were reported in 7 (78%) of 9 studies for hand/UE function outcomes and in 5 (71%) of 7 studies that had quality-of-life outcomes.

More positive group differences were reported in the multicomponent studies especially ones in which the interventions took place over a longer time period (33–35). In these studies, significant differences were reported between intervention and

Table 1. Characteristics of rehabilitation studies included in evidence synthesis (n = 16)*

Author, year, country (ref.)	Sample, total no. (IG/CG)	Participants	Intervention duration/dose	Control/comparator description	Delivery mode	Intervention content
Hand/UE function studies						
Gregory et al, 2019, UK (29)	36 (17/19)	Female: IG = 76%, CG = 63%; % diffuse SSc: IG = 41%, CG = 42%	9 weeks: paraffin wax baths, no less than 4 times/week; hand stretch exercises, 3–10 times/day	Hand stretch exercise only	Home	Paraffin wax baths
Kristensen et al, 2019, Denmark (30)	86 (43/43)	Female: IG = 84%, CG = 63%; % diffuse SSc: IG = 60%, CG = 37%	6 months: 30-minute sessions, 2 times/day	Lukewarm water hand immersion prior to hand exercises	Home	Paraffin wax baths
Maddali Bongi et al, 2009, Italy (31)	40 (20/20)	Female: IG = 80%, CG = 70%; subtype NS	9 weeks: massage and manipulation, 1-hour session 2 times/week; home exercise, 20-minute session daily	Home hand exercise program	Clinic/home	Hand massage, joint manipulation
Maddali Bongi et al, 2011, Italy (32)	35 (20/15)	Female = 100%; subtype NS	5 weeks: 1-hour session/week	Waitlist	Clinic	Manual lymph drainage (UE focus)
Murphy et al, 2021, US (24)	32 (16/16)	Female = 72%; % diffuse SSc = 100%	18 weeks: OT sessions, 1-hour session 1 time/week for 8 weeks; app-delivered hand exercises, daily	App hand exercises only	Clinic/telehealth	Thermal treatments (UE), negative pressure treatment, ROM, Home hand ROM exercises tailored by OT
Piga et al, 2014, Italy (28)	20 (10/10)	Female = 100%; % diffuse SSc = 40%	12 weeks: maximum of 50-minute sessions, 5 days/week	Home program of hand strength and mobility exercises using common objects	Telehealth	Hand exercises
Sporbeck et al, 2012, Germany (24)	28 (10 [BF]/8 [DO]/10 [CG])†	Female (range across 3 groups) = 80–90%; % diffuse SSc (range across 3 groups) = 10–50%	4 weeks: 3 times/week	Waitlist	Clinic	Biofeedback or deep oscillation to UE
Stephanantoni et al, 2016, Italy (25)	31 (15/16)	Female: IG = 100%, CG = 94%; % diffuse SSc: IG = 47%, CG = 31%	3 months: daily home exercise; weekly check-in calls between first and second assessments	General hand exercise	Clinic/home	Hand exercises tailored by OT
Vannajak et al, 2014, Thailand (23)	28 (14/14)	Female: IG = 64%, CG = 25%; % diffuse SSc = 100%	2 weeks: superficial heat 20- minute sessions daily; TTM 30-minute sessions daily; hand stretches 30-second sessions, each hand, daily; wearing gloves 6-hour sessions daily	Same daily home program as IG without gloves	Home	Traditional Thai massage to UE, joint manipulation, home hand ROM exercises, insulation gloves
Orofacial						
Yuen et al, 2012, US (22)	48 (26/22)	Female: IG = 81%, CG = 77%; % diffuse SSc = 44%	6 months: 6-minute sessions, 2 times/day	Usual dental care	Home	Manual mouth-stretching and oral augmentation exercises with a wooden stick

(Continued)

Table 1. (*Cont'd*)

Author, year, country (ref.)	Sample, total no. (IG/CG)	Participants	Intervention duration/dose	Control/comparator description	Delivery mode	Intervention content
Multicomponent						
Filippetti et al, 2020, Italy (33)	44 (22/22)	Female: IG = 80%, CG = 79%; % diffuse SSc = IG = 44%, CG = 25%	6 months: 3 times/week	Usual care with general recommendation to increase physical activity	Home	Aerobic exercise (bike), UE resistance exercise, hand stretching, PT calls
Horvath et al, 2017, Hungary (21)	53 (31/22)	Female: IG = 93%, CG = 91%; % diffuse SSc = IG = 58%, CG = 50%	3 weeks: 5 days/week for all therapies except for UE, mud baths every other day, and thermal baths daily	Mud baths, thermal baths, exercise for large joints, without treating hands	Clinic	Thermal treatments to UE, hand stretching, massage to trunk/UE, stretching and exercise to lower extremities
Maddali Bongi et al, 2009, Italy (50)	20 (10/10)	Female = 65%; subtype NS	9 weeks: hands, 1-hour session 2 times/week; face, 1-hour session, 2 times/week; global, 1-hour session/week	Educational advice and medical information about SSc	Clinic	Connective tissue massage, Kabat's technique, kinesitherapy, and a home exercise program
Rannou et al, 2017, France (34)	220 (112/108)‡	Female: IG = 86%, CG = 80%; % diffuse SSc: IG = 47%, CG = 50%	12 months: PT/OT, 3 weekly, 3-hour sessions; splinting, 2-hour sessions daily; resting splints, nightly; home exercise daily	Usual care by physician with no restrictions on PT	Clinic/home	Multidisciplinary intervention (PT/OT) aerobic and resistance exercise, ROM for mouth, face, UE/LE and splinting
Schouffoer et al, 2011, Netherlands (35)	53 (28/25)	Female: IG = 68%, CG = 84%; % diffuse SSc: IG = 54%, CG = 60%	12 weeks: multidisciplinary weekly program; PT weekly; home exercise, 6 days/week	Usual care by physician with no restrictions on PT	Clinic/home	General exercise, hand/mouth exercises, education, PT supervised home exercise
Directed self-management						
Khanna et al, 2019, US (27)	267 (134/133)	Female: IG = 92%, CG = 90%; % diffuse SSc: IG = 43%, CG = 44%	16 weeks: self-paced with weekly moderated discussion board	Received a copy of popular scleroderma resource	Telehealth	Self-paced web-based self-management program with rehab-directed discussion board

* All study designs were randomized controlled trials except Horvath et al (21), which used a prospective quasi-experimental design. CG = control group; DASH = Disabilities of the Arm, Shoulder and Hand questionnaire; FIHOA = Functional Index for Hand Osteoarthritis; HAMIS = Hand Mobility in Scleroderma test; HAQ DI = Health Assessment Questionnaire disability index; IG = intervention group; LE = lower extremity; NS = not specified; PROMIS = Patient-Reported Outcomes Measurement Information System; PT = physical therapy; OT = occupational therapy; Ref. = reference; ROM = range of motion; SSc = systemic sclerosis; TTM = traditional Thai massage; UE = upper extremity; VAS = visual analog scale.
† The study by Sporbeck et al (24) consisted of 3 groups: biofeedback (BF), deep oscillation (DO), or waitlist control group (CG).
‡ A total of 218 participants were assessed in this study.

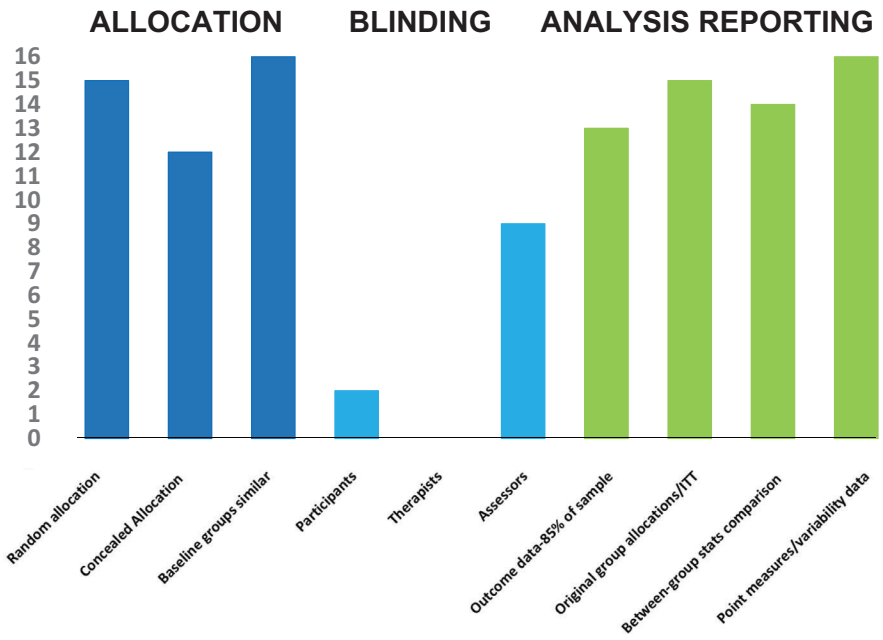

Figure 2. Articles rated by quality criteria on the Physiotherapy Evidence Database (PEDro) scale. ITT = intent-to-treat.

control groups for hand/UE function, orofacial, and quality of life (33–35). Specifically, 4 (80%) of 5 studies in the multicomponent category reported within-group improvements in the intervention group in hand/UE function outcomes and quality-of-life outcomes. In the 1 orofacial intervention, there were significant improvements in oral aperture (face/mouth function) in the intervention group, which were significantly different than the control group (22). The 1 directed self-management study did not report significant group differences (27). In general, many studies did report significant improvements in outcome measures within the intervention groups, but the improvements were not significantly different from changes observed in the control groups.

DISCUSSION

We systematically reviewed the literature in SSc to examine the effectiveness of rehabilitation interventions. From the 33 studies identified, just less than half (48%) met the quality standard for inclusion. Sixteen studies that represented rehabilitation interventions focused on hand/UE or orofacial, were multicomponent, or involved rehabilitation-directed self-management were rated as good to excellent quality. Half of these studies showed between-group differences in which the intervention group had a statistically significant improvement compared to the control outcome (22,23,25,26,32–35). Most studies in this review had relatively small sample sizes, which may have resulted in lack of power to detect between-group interventions in studies with active comparator groups. However, the heterogeneity in studies and interventions make it difficult to synthesize the literature. These findings can be framed around the following 2 main challenges that have implications for translation of research into practice: evidence-building of rehabilitation research and conducting rehabilitation studies in the SSc population.

The complexity and patient-centered nature of rehabilitation contribute to the challenges of evidence-building and synthesizing results across rehabilitation trials. One problem is inconsistency in trial reporting, such as the lack of a predefined primary outcome measure, even among good-quality studies. There is a lack of consensus in reporting in rehabilitation RCTs in many areas, such as participant characteristics (36), randomization procedures, statistical analyses and power (37), and intervention description (38). Tools under development, such as checklists to extend the Consolidated Standards of Reporting Trials (CONSORT) group statement for rehabilitation trial reporting (39) should help increase study quality and the ability to synthesize findings. Many studies in this review had variable reporting of patient characteristics, intervention description, and comparator/control groups, and lacked power analyses. Blinding was not done frequently and is challenging in a real-world environment with therapists, outcome assessors, and participants. Despite challenges, some recommendations have been discussed to help ensure study rigor, such as blinding assessors and using active comparator groups where participants can be blinded to which intervention is hypothesized to be better (40).

Interventions tested in this review were difficult to synthesize even within a specific category. Hands and UE were most commonly addressed in interventions, but intervention content and dose were highly variable. Description of treatment rationale,

Table 2. Between-group differences by outcome in rehabilitation studies in systemic sclerosis (n = 16)*

Outcome measure	No. of studies evaluating the outcome	Study (ref. number) with significant difference between intervention and control groups ($P < 0.05$)
Skin		
MRSS, hand MRSS	2	–
Hand/UE function		
HAMIS	9	32, 35
Durouz Hand Index/Cochin Hand Function test	6	34
QuickDASH or DASH	2	–
FIHOA	1	–
Kapandji index	1	34
Mobility (hand opening, hand abduction, fist closing, fingertips to palmer crease, total active motion, HAI)	5	–
Hand volume	2	32
VAS hand pain, interference	2	32
VAS hand edema, VAS interference edema	1	32
Pinch strength	3	23
Grip strength	6	33, 35
Biceps strength	1	33
Raynaud's phenomenon		
Raynaud's phenomenon symptoms VAS	2	25
Digital ulcers		
VAS digital ulcers	1	–
Orofacial		
Oral aperture or mouth opening, MMO, microstomia, face involvement	4	22, 34, 35
Cardiac		
6MW	2	33, 35
Vo2 peak/max, aerobic capacity	3	–
Pulmonary		
VAS shortness of breath	1	–
Gastrointestinal		
VAS gastrointestinal symptoms	1	–
Musculoskeletal		
Quadriceps strength	1	33
Global health		
Global health VAS or questionnaire, general VAS	3	–
VAS overall disease severity	1	–
Health-related quality of life		
PROMIS physical function	1	–
PROMIS-29	1	–
Patient activation measure	1	–
Pain VAS	2	34
PROMIS self-efficacy for managing symptoms	1	–
Checklist individual strength	1	–
HAQ DI or HAQ, SHAQ	9	32–35
MACTAR	1	34
SF-36	11	32, 33
VAS satisfaction with health	1	–
COPM	1	26
EQ-5D, QALYs, SWAP	1	–

* 6MW = six-minute walk test; CHFT = Cochin Hand Function Test; COPM = Canadian Occupational Performance Measure; DASH = Disabilities of the Arm, Shoulder and Hand questionnaire; EQ-5D = EuroQol-5-domain questionnaire; FIHOA = Functional Index for Hand Osteoarthritis; HAI = Hand Anatomical Index; HAMIS = Hand Mobility in Scleroderma; HAQ = Health Assessment Questionnaire; HAQ DI = Health Assessment Questionnaire Disability Index; MACTAR = McMaster Toronto Arthritis Patient Preference Disability Questionnaire; MMO = maximum mouth opening; MRSS = Modified Rodnan Skin Thickness Score; PROMIS = Patient Reported Outcome Measure Information System; QALYs = quality-adjusted life-years; RP = Raynaud's phenomenon; SF-36 = Short Form 36 health survey; SHAQ = Scleroderma Health Assessment Questionnaire; SWAP = Brief Satisfaction with Appearance Scale; UE = upper extremity; VAS = visual analog scale.

goals and expected benefits, and underlying theory of interventions are recommended for reporting (41), and consistent information across studies could help build evidence and reduce variability. In addition, thought about the mechanism of action is critical. While SSc rehabilitation treatments incorporate specific elements, such as thermal modalities, massage, and stretching, few studies discuss why these components are essential or investigate how they work. For example, to examine if negative

pressure treatment affects skin thickness in SSc, Murphy and colleagues developed a protocol to use musculoskeletal ultrasound to examine changes in skin thickness after an occupational therapist–delivered treatment (42). Testing mechanism of action in rehabilitation treatments will help design and better target interventions in the future.

Most studies in the present review required participants to come to clinics to receive all or some of the intervention. Even for interventions designed to be done at home, participants had to travel to receive a device (wax or exercise machine) and/or instruction. Only 1 intervention was done completely via telehealth (27). Participation in interventions requiring in-person attendance may be prohibitive for those who do not live in urban areas or near scleroderma centers, or have transportation. Telehealth is an emerging mode of intervention delivery within rehabilitation. The recent global pandemic has led to massive changes in how health care and interventions are delivered. People have been forced to be more tech savvy and virtual interventions are becoming more accessible. The increased opportunity for virtual interventions helps to respond to the unmet need identified by people with SSc who want information delivered via the internet (43). Yet, virtual telehealth intervention delivery presents challenges to those with limited internet access, no video capabilities on their phones, and/or in areas with unstable connections. Further, telehealth is limited in its ability to provide hands-on treatment, like massage or stretching, by a rehabilitation professional that may reap greater benefits at least in the short term or be preferred by patients.

A further complication is that the reviewed studies were conducted in many countries with different health care 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. Becetti and colleagues (8) reported that use of rehabilitation was higher in Canada and France compared to the US and speculated that referral could be related to access to rehabilitation and health care costs. Other studies that surveyed providers reported referrals driven by costs (44) and a lack of understanding of the role of rehabilitation in management of SSc (45,46).

In the US, Black individuals have a higher prevalence of diffuse cutaneous SSc and more severe disease (47). However, the number of Black participants in research studies of SSc remains low. Although the 3 US studies reported on race and/or ethnic characteristics of samples, inclusion of diverse samples will be needed to better understand differences by race and ethnicity in the future.

For many studies in this review, outcome measures used have psychometric support for SSc. Stronger support exists for the HAQ DI, The Cochin Hand Function Test, and SF-36 than for the other outcomes (48). While these outcomes are largely self-reported and considered patient-centered, they do not measure what is important to patients or patients' goals. Only the COPM or MACTAR used in 2 studies (26,34) were truly patient-centered, and in one study, goals identified on the COPM guided the intervention (26). Engaging patient stakeholders as members of research teams may also help initiate use of goal identification as outcomes and to guide interventions thus improving adherence.

The design of future SSc rehabilitation trials may benefit from lessons inherited from recent RCTs evaluating pharmacologic treatments in SSc. Taking into account different subsets of the disease and impact of the natural history of SSc may help to include more homogeneous and comparable patient populations. Maddali Bongi and Del Rosso have recommended that rehabilitation treatments be tailored to individuals based on phase of disease (49), because individuals with early disease tend to have a higher symptom burden. Another strategy is to focus on just 1 SSc cutaneous subtype, such as diffuse (23,24). Specifying a clinically meaningful primary outcome measure that is tailored for a targeted disease subset (such as people in the edematous phase [32]) may help to improve statistical power of future RCTs. The coordination of centers of excellence with a multidisciplinary approach may also help expedite recruitment and ensure consistency of outcome measures. The use of web-based approaches for intervention delivery is a promising option to implement rehabilitation for daily SSc management as it may reduce some barriers to access, more readily allow for longer follow-up periods, and facilitate treatment adherence. The long-term impact of these techniques will also need to be demonstrated in RCTs as SSc remains a chronic disorder without available disease-modifying pharmacologic agents and without demonstration of improved quality of life with current medications. Rehabilitation may thus play an important role to improve such patient- reported outcomes with impact more of a holistic approach, including rehabilitation, on SSc patients' mental and social health as well as physical functioning.

The findings reported are limited by studies that are somewhat heterogeneous and consist of small sample sizes that may be underpowered to detect effects, even in this group of studies considered to be of good to excellent quality. However, understanding weaknesses in study design and reporting can help to build the evidence by increasing potency of interventions and consideration of how to best tailor them. Importantly, interventions were of low risk to participants and had effects on both physical and quality-of-life outcomes, supporting the need for inclusion as part of clinical care.

In conclusion, rehabilitation interventions have been recommended for people with SSc to address the musculoskeletal and systemic involvement leading to significant disability and reduction in meaningful activities (50). This comprehensive review of rehabilitation literature supports short-term efficacy of rehabilitation interventions and provides several future directions to further build the evidence and develop interventions that can reduce access barriers.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Murphy had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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