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REVIEW ARTICLE

Physical therapy in adult inflammatory myopathy patients: a systematic review

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Abstract

The safety and effect of physical therapy in adult patients with idiopathic inflammatory myopathies (IIMs) are currently unclear. Considering the muscle weakness resulting from disease activity as well as from the administered drugs, these patients could benefit from an evidence-based physical therapy program. To perform a systematic review to assess safety and effects of physical therapy on the functional outcome of patients with idiopathic inflammatory myopathies in both active and quiescent disease: Pubmed, Embase, and Cochrane. Patients with one of the following idiopathic inflammatory myopathies: polymyositis, dermatomyositis, immune-mediated necrotizing myopathy, and/or overlap myositis. The intervention included several types of rehabilitation programs, from strength and resistance training to endurance training, with a minimal duration of 1 month. Studies reporting intervention-related adverse events, disease activity, and functional outcomes were eligible. The risk of bias was assessed using the Cochrane guidelines. We included five randomized controlled and seven open-label non-randomized non-controlled trials. Data on statistical significance were extracted for all the trials. Included trials were of medium-quality evidence given the low number of patients and some risk of bias factors. Physical therapy does not have a negative effect on the disease activity of idiopathic inflammatory myopathies in quiescent disease and could improve functional outcome. The physical therapy program should minimally include endurance training. A combination with resistance training might be beneficial.

Keywords Dermatomyositis · Exercise therapy · Inflammatory myopathy · Physical therapy · Polymyositis · Rehabilitation

Introduction

Idiopathic inflammatory myopathies (IIMs) can be divided into five major subtypes: dermatomyositis (DM), inclusion-body myositis (IBM), immune-mediated necrotizing myopathy (IMNM), overlap myositis, and polymyositis (PM) [1–8]. They are rare entities with incidence rates estimated between 4.27 and 7.89 per 100,000 person years and prevalence rates from 9.54 to 32.74 cases per 100,000 individuals [9, 10]. IIMs are characterized by muscle inflammation, which is the result of an important interplay between adaptive, innate immune, and non-immune mechanisms [11–14]. Clinical characteristics include muscle weakness (in proximal upper and lower limb, neck extensor, pharyngeal and respiratory muscles), muscle atrophy in severe cases, and extramuscular manifestations such as fever, weight loss, rash, cardiac arrhythmias or ventricular

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dysfunction, and pulmonary complications [1, 15]. The diagnosis is based on the combination of clinical history, tempo of disease progression, pattern of muscle involvement, muscle enzyme levels, electromyographic findings, muscle biopsy analysis, and an ever-increasing diagnostic role of myositis-specific antibodies [1, 16]. Treatment consists of glucocorticoids and/or immunosuppressive therapy such as methotrexate, azathioprine, mycophenolate mofetil and in selected cases, biologicals such as rituximab [1, 17–20]. Despite these treatment options, the disease course may be fatal, and many patients have sustained disability and poor quality of life [21–25].

Physical therapy may be an additional treatment method to improve functional outcome. Many cases have been described in which physical exercise positively affected several outcome parameters [26–28]. Exercise could improve muscle strength and performance, functional and aerobic capacity, and clinical disease activity in patients with IIMs [29–35]. The molecular mechanisms that lead to these effects are not fully understood but could partly be explained by downregulation of genes associated with inflammation and fibrosis and upregulation of genes associated with aerobic metabolism in muscle tissue [36].

The aim of this systematic review is to evaluate the safety and the effects of physical therapy on the functional outcome of patients with IIMs. We included randomized controlled trials (RCTs) and in extension also open-label non-randomized non-controlled trials. Additionally, we aim to evaluate the optimal type and timing of the training intervention(s).

Materials and methods

Eligibility criteria

We included RCTs and non-randomized non-controlled trials studying patients diagnosed with IIMs (PM, DM, IMNM and/or overlap myositis) according to the Bohan and Peter criteria [37, 38] or the International Myositis Assessment and Clinical Studies Group (IMACS) criteria [3]. Trials including patients with juvenile DM and/or IBM were excluded. The intervention could be several types of rehabilitation programs, from strength and resistance training to endurance training. The rehabilitation program had to have a minimal duration of 1 month, thus excluding trials investigating a single exercise in order to examine long-term effects. To assess possible risk of increasing disease activity by physical therapy, one of the following disease activity measures was required: levels of C-reactive protein (CRP), creatine phosphokinase (CPK) and aldolase, erythrocyte sedimentation rate (ESR), patient's and physician's global disease activity on a visual analogue scale (PGA and PhGA), assessment of extraskeletal muscle disease activity in six organ systems using the Myositis Intent-to-Treat Activity Index (MITAX), 0 to 100 visual analogue scales (VAS) for assessing pain, and fatigue and the Borg CR-10 Scale [39]. Intervention-related adverse events were also eligible as safety measures but could not be found as outcome measures in the different trials. We accepted a broad range of functional outcome measures [40]: the Health Assessment Questionnaire Disability Index (HAQ-DI) [22, 24], the Myositis Activities Profile (MAP) [41], the Modified Functional Assessment Screening Questionnaire (MFASQ) [42, 43], the McMaster Toronto Arthritis Patient Preference Disability Questionnaire (MACTAR) [44], the Functional Independence Measure (FIM) [45], the Medical Outcomes Study 36-Item Short-Form Health Survey questionnaire (SF-36) [46], the Swedish version of the Nottingham Health Profile (NHP) [47], and the Kendall Manual Muscle Test (MMT); isometric/isokinetic assessments of muscle strength (peak isometric/isokinetic torque or PIT) [48–50]; the disease-specific functional index (FI) [51]; the distance covered in a 6- or 7-min walk test (6- or 7-min WT) [52]; 1, 5, 10 or 15 voluntary repetition maximum (VRM) measures of muscle strength; timed-stands test (TST) [53]; timed-up-and-go test (TUGT) [54]; quadriceps cross-sectional area (QCSA); grip strength (GS) [55]; and aerobic capacity (VO_2 max and time to exhaustion). Only trials written in English were included.

Information sources

We searched the following databases: *Pubmed*, *Embase*, and *Cochrane*. The search was carried out between February 2018 and February 2019. Review articles were hand-searched for relevant references.

Search strategy

Based on the PICO search model (patients defined as patients diagnosed with IIMs, intervention being any form of physical therapy, comparison being conventional treatment and outcomes being disease activity measures, intervention-related adverse events and functional outcomes). We searched three databases (*Pubmed*, *Embase*, and *Cochrane*) for two of the four concepts, namely patients and intervention. We searched *Pubmed* using MeSH-terms (Medical Subject Headings) and terms in title and abstract to find articles that have been indexed during the last 6 months ([tiab]). We searched articles in *Embase* using Emtree-terms (Embase Subject Headings) and also terms in title and abstract (:ti,ab). In *Cochrane*, we used MeSH terms and terms in title and abstract (:ti,ab). For the full search, see S1.

Study selection

Studies were selected based on title, abstract, and/or full text. We used our eligibility criteria to rule out irrelevant articles. There were no limits for publication date.

Data collection process

The journal citation report with all the appraised articles was constructed in Word by one of the authors.

Data items

The data items are listed in Table S2.

Risk of bias in individual studies

The risk of bias was assessed for the six RCTs using the Cochrane guidelines. Every domain (selection bias, performance bias, detection bias, attrition bias, and reporting bias) was judged as having a low, high, or unclear risk of bias, and this judgment was further clarified and justified. For this purpose, we used Review Manager 5.3 (*Review Manager* (*RevMan*) [*Computer program*]. *Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014*).

Additional analyses

No additional analyses were performed.

Results

Study selection

We identified 1349 articles: 476 articles in *Pubmed*, 779 articles in *Embase*, and 94 articles in *Cochrane*. No additional articles were found by hand searching review articles for relevant references. We excluded 419 *Pubmed* articles, 740 *Embase* articles, and 90 *Cochrane* articles based on patient population and/or study question, retaining a total of 100 articles. Removal of duplicates resulted in 74 retained articles that were screened based on abstract and/or full text. This resulted in the exclusion of 57 articles based on study design, outcome measure(s), or patient population (juvenile DM and/or IBM). Four conference abstracts were retrieved in *Embase*. Two were excluded because they were duplicates of published full articles. The remaining two were excluded because they did not contain sufficient methodologic information. Our study selection resulted in five RCTs [56–60] with one open-label extension [61] and seven non-randomized non-controlled trials [62–68]. The flow diagram of the study selection process is depicted in Fig. 1.

Study characteristics

Characteristics of the 12 individual studies are presented in Tables 1 and 2. Data on study size, study design, year of publication, inclusion criteria, exclusion criteria, intervention, comparison, and primary and secondary outcome measures and follow-up were extracted.

Risk of bias within studies

The evaluated risk of bias of the five RCTs is presented in Table S3–7 with a judgment of low, high, or unclear risk of bias and the support for this judgment. These results are depicted as a risk of bias graph in Fig. 2 and a risk of bias summary in Fig. 3. Overall, there is a high risk of performance bias and detection bias for patient-reported outcome measures since it was impossible to blind patients for the intervention (given that it is a rehabilitation program). The risk for attrition and reporting bias is unclear. Since all included RCTs used adequate randomization methods, the risk of selection bias was interpreted as low.

Results of individual studies

The aim of this systematic review was to assess safety and effect of physical therapy on the functional outcome of patients with IIMs. In addition, we assessed the optimal training timing and intervention type.

We divided outcome measures used in the clinical trials in seven groups: activities of daily living, quality of life, muscle function, aerobic capacity, disease activity, pain, and fatigue. Safety could only be assessed by the evolution in disease activity measures since intervention-related adverse events were not reported as outcome measures in any of the trials. When drawing our conclusions, we put more emphasis on the results of the RCTs because of the higher level of evidence.

The results of the 12 trials and the open-label extension are presented in Table 3 as significant effect, non-significant effect, or no data provided. The table clearly visualizes the heterogeneity of outcome measures. For full data, see Table S8–13.

Safety

Physical therapy does not have a negative effect on the disease activity. In all appraised studies, disease activity measures remained stable or improved. As such, we conclude that physical therapy does not lead to disease flares.

Complications of the intervention (for example cardiovascular or musculoskeletal) were not specifically addressed as outcome measures. None of the trials mentioned any adverse event linked to the intervention. Nevertheless, the reasons for dropout were not always mentioned so it is not clear if it was intervention-related or not (see Table S3–7). Most of the trials included a statement that the program was well tolerated by all the patients.

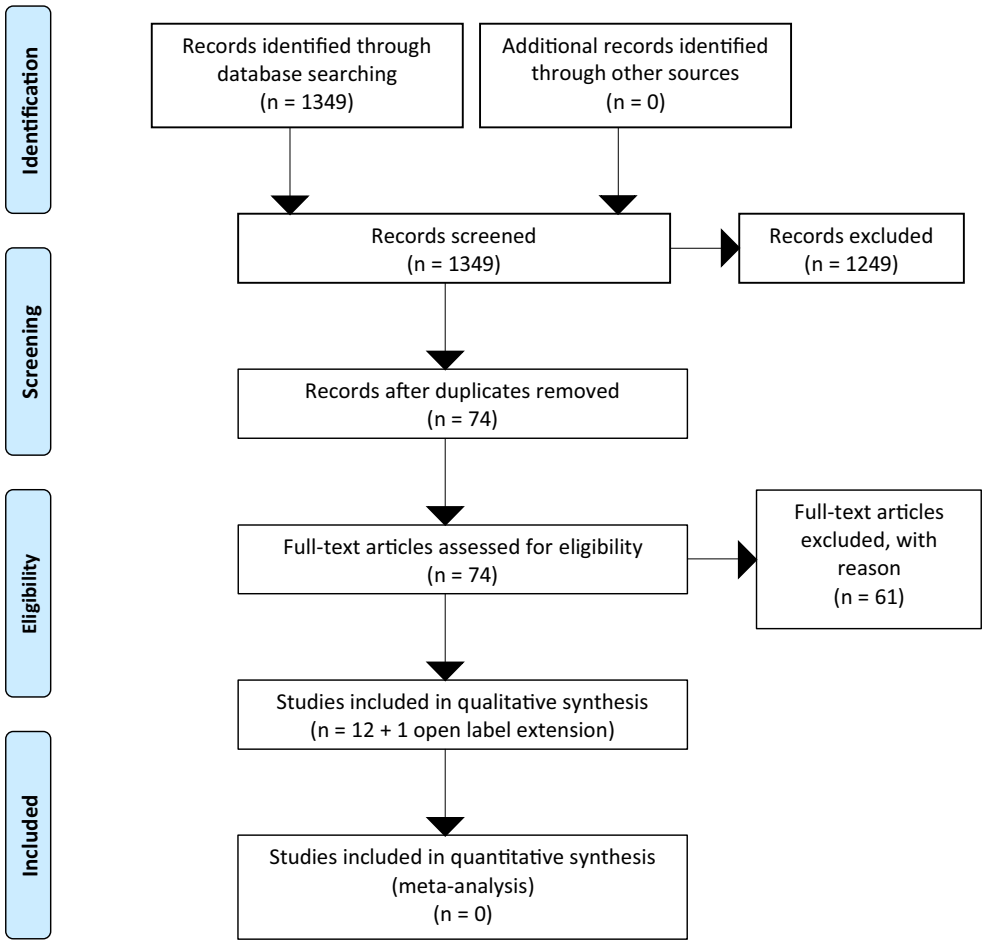

Fig. 1 Representation of the study selection process by the PRISMA flowchart. The second and third rows have been interchanged as removal of the duplicates was performed after the first screening

Effect on functional outcome

A clinically significant improvement in the activities of daily living was seen in two trials [56, 60], measured by the HAQ-DI and the MFASQ, respectively. In one trial, pain significantly improved whereas fatigue did not [56]. The scales used to address quality of life (SF-36 and NHP) are divided into different subscales. None of the RCTs demonstrated significant improvement in all of the subscales and, when comparing the different RCTs, no single subscale improved consistently across all studies. Therefore, no uniform conclusions can be drawn about the effect on quality of life.

We considered muscle function and aerobic capacity to be important outcome measures to determine the effect on functional outcome. One group noted a significant improvement in muscle function, measured by the PIT [60], whereas another did not [56]. Furthermore, there was no consistent improvement in the MMT in this last trial [56]. In one trial, significance results were not provided for the MMT [58]. Five voluntary repetition maximum measures of muscle strength were only significant for the left side in another trial [59]. Regarding aerobic capacity, an improvement was found in VO_2 max in three RCTs [58–60] and in time to exhaustion in one RCT [58]. One group did not find a significant improvement in aerobic capacity and FI, another outcome measure related to muscle function [57].

Components of the training program

The investigated rehabilitation programs consisted of endurance training, resistance training, or a combination of both. As written above, a clear improvement in muscle function and aerobic capacity was seen in three RCTs [58–60]. All three RCTs investigated an endurance training program which suggests that this is the most optimal training intervention. These findings are also in line with the open-label extension [61], which is an extension of the previous RCT [60]. These endurance programs had a frequency of two or three times a week, lasted approximately 1 h and covered a period between 6 and 12 weeks. They consisted of a period of warm-up (for example cycling at 50% of VO_2max), more intense cycling with a gradual increase in intensity (for example aiming at 70% of VO_2max), muscular endurance exercise, step aerobics, and/or a period of cool-down and stretching.

Table 1 Study characteristics of the five RCTs

	Tiffreau V, Rannou F, Kopciuch F et al. [56]	Alexanderson H, Munters LA, Dastmalchi M et al. [57]	Munters LA, Dastmalchi M, Katz A et al. [58]	Munters LA, Dastmalchi M, Andgren V et al. [59]	Wiesinger GF, Quittan M, Aringer M et al. [60]
Study size (n)	$n = 21$	$n = 19$	$n = 23$ ($n = 15$ in randomized controlled part of the trial)	$n = 23$	$n = 14$
Year of publication	2017	2014	2013	2013	1998
Inclusion criteria	(1) PM or DM (IMACS criteria) (2) Age > 18 years (3) HAQ-DI ≥ 0.5 (4) Recent, ongoing relapse (5) Decrease in muscle strength of ≥ 20% on a scale of 0 to 100 (6) Muscle pain VAS ≥ 30/100	(1) PM or DM (Bohan and Peter criteria) (2) Age 18–70 y ears (3) Disease duration < 3 months (4) Clinical signs of improvement with conventional immunosuppressive treatment (5) Able to exercise	(1) PM or DM (2) Age ≥ 18 years (3) Disease duration > 6 months (4) Stable medication ≥ 1 months (5) Exercising ≤ 1/week	(1) PM or DM (2) Age > 18 years (3) Disease duration > 6 months (4) Stable medication ≥ 1 months (5) Exercising ≤ 1/week	(1) PM or DM (2) Disease duration > 6 months (3) Stable medication ≥ 3 months (4) Clinical activity (presence of proximal muscle weakness and/or elevation of serum muscle enzyme values)
Exclusion criteria	(1) Another chronic disorder (2) Malignancy (3) No recent relapse (4) Cognitive disorders or lack of fluency in French (5) Inability to give informed consent (6) Participation in a standardized rehabilitation program in the 6 m before inclusion (7) Ongoing or recent participation in another therapeutic trial	(1) Severe heart conditions (2) Malignancy (3) Severe osteoporosis	(1) Severe heart or lung conditions (2) Severe osteoporosis (3) Not being able to exercise	(1) Severe heart or lung conditions (2) Severe osteoporosis (3) Not being able to exercise	(1) Severe heart or lung conditions (2) Malignancy (3) Not being able to exercise (4) IBM (5) Fever (6) Increase in muscle destruction during the past 3 m
Intervention	Personalized rehabilitation program (4 weeks) + subsequent home-based, self-managed rehabilitation program (44 weeks)	Resistive home exercise program and brisk walking (12 weeks) + subsequent 2/week home/gym exercise (12 weeks)	1 h exercise program 3/week (12 weeks)	1 h exercise program 3/week (12 weeks)	6-week training program: stationary cycling and step aerobics
Comparison	Standard care + 30 min sessions with a private practice physiotherapist 3/w	15 min ROM exercise program 5/week + ADL and ordinary walks (24 weeks)	No change in physical activity level	No change in physical activity level	No training
Primary outcome measures	HAQ-DI	FI	(1) HAQ-DI (2) MMT (3) VO_2 max (4) Time to exhaustion (5) CPK levels (6) PGA (7) PhGA (8) MITAX (9) Lactate levels (10) Muscle biopsies (11) Activity of citrate synthase (12) Activity of *β-hydroxyacyl-C-oA dehydrogenase*	(1) HAQ-DI (2) MAP (3) MACTAR (4) SF-36 (5) MMT (6) 5 VRM measures of muscle strength (knee extensors) (7) VO_2 max (8) CRP levels (9) CPK levels (10) ESR (11) PGA (12) PhGA (13) MITAX	(1) MFASQ (2) PIT (hip flexors and knee extensors) (3) VO_2 max (4) CPK levels (5) Aldolase levels

Table 1 (continued)

	Tiffreau V, Rannou F, Kopciuch F et al. [56]	Alexanderson H, Munters LA, Dastmalchi M et al. [57]	Munters LA, Dastmalchi M, Katz A et al. [58]	Munters LA, Dastmalchi M, Andgren V et al. [59]	Wiesinger GF, Quittan M, Aringer M et al. [60]
			(13) Myositis disease Damage Index	(14) Global damage tool	
Secondary outcome measures	(1) SF-36 (2) MMT (3) PIT (knee flexor and extensor muscles) (4) 6-min WT (5) CRP levels (6) CPK levels (7) Pain (VAS) (8) Fatigue (VAS) (9) Motor function measure	(1) NHP (2) Aerobic capacity (3) CPK levels (4) Muscle biopsies			
Follow-up	(1) 4 weeks after inclusion (2) 24 weeks after inclusion (3) 48 weeks after inclusion	(1) 24 weeks after inclusion (2) 52 weeks after inclusion (3) 78 weeks after inclusion (4) 104 weeks after inclusion	12 weeks after inclusion	(1) 12 weeks after inclusion (2) 52 weeks after inclusion	6 weeks after inclusion

PM polymyositis, *DM* dermatomyositis, *IMACS* International Myositis Assessment and Clinical Studies group, *HAQ-DI* Health Assessment Questionnaire Disability Index, *VAS* visual analogue scale, *IBM* inclusion-body myositis, *ROM* range of motion, *ADL* activities of daily living, *SF-36* Medical Outcomes Study 36-Item Short-Form Health Survey questionnaire, *MMT* Kendall Manual Muscle Test, *PIT* peak isometric/isokinetic torque, *WT* walk test, *CRP* C-reactive protein, *CPK* creatine phosphokinase, *FI* functional index, *NHP* Nottingham Health Profile, *PGA* patient's global disease activity, *PhGA* physician's global disease activity, *MITAX* Myositis Intent-to-Treat Activity Index, *MAP* Myositis Activities Profile, *MACTAR* McMaster Toronto Arthritis Patient Preference Disability Questionnaire, *VRM* voluntary repetition maximum, *ESR* erythrocyte sedimentation rate, *MFASQ* Modified Functional Assessment Screening Questionnaire, *h* hours, *min* minutes

On the other hand, there could also be some beneficial effect of a combination of endurance and resistance training given the fact that there was a significant improvement in the HAQ-DI in one trial [56] even though there was no improvement in muscle function. This implies that adding resistance training improves self-perceived functionality or improves disabilities encountered by patients.

Six out of seven non-randomized non-controlled trials investigated a resistance training program [62, 64–68]. Although five trials reported significant improvements in some muscle function measures, we cannot generalize results due to low methodological study design and conduct, namely no control arm and few study participants.

Timing

All RCTs were performed in the stable stage of the disease [56–60]. Three of the seven non-randomized non-controlled trials were carried out during the active stage of the disease or following acute exacerbation [63, 65, 66]. There were no drop outs in these trials. The first trial consisted of only three patients and as such could not provide any data on statistical significance [63]. The second trial only showed a significant improvement in muscle strength in a part of the muscle groups [65]. The last trial showed significant improvements in the FI score, but the relative impacts of the exercise program and the medical treatment could not be separated [66]. This would probably be inherent to any physical therapy intervention in an active phase of the disease where patients need regular pharmacological treatment adaptations and ongoing disease activity is still affecting functional evolution.

Additional analysis

No additional analyses were performed.

Discussion

In conclusion, physical therapy does not lead to disease flares, at least in patients medically treated and with stable disease course. However, the lack of elaboration on the reasons for dropouts does not allow firm conclusions as potential intervention-related adverse events could have been missed. There is also a possibility of inclusion bias to consider because if muscle damage and trainability is too low, inclusion in these trials is probably not always possible.

Table 2 Study characteristics of the seven non-randomized non-controlled trials

	Mattar MA, Gualano B, Perandinini LA et al. [62]	Mattar MA, Gualano B, Roschel H et al. [63]	Alexanderson H, Dastmalchi M, Esbjörnsson-Liljedahl M et al. [64]	Varju C, Pethö E, Kutas R et al. [65]	Alexanderson H, Stenstrom CH, Jenner G et al. [66]	Alexanderson H, Stendstrom CH, Lundberg I et al. [67]	Escalante A, Miller L et Beardmore TD [68]
Study size (*n*)	*n* = 13	*n* = 3	*n* = 9	*n* = 21	*n* = 11	*n* = 10	*n* = 5
Year of publication	2014	2014	2007	2003	2000	1999	1993
Inclusion criteria	PM or DM (Bohan and Peter criteria)	(1) PM (Bohan and Peter criteria) (2) Corticosteroids and/or immuno-suppressants ≥ 6 months (3) Stable medication ≥ 3 months (4) Clinical and laboratory evidence of disease activity	(1) PM or DM (Bohan and Peter criteria) (2) Disease duration > 12 m (3) Stable medication and disease ≥ 3 months	PM or DM (Bohan and Peter criteria)	(1) PM or DM (2) Age 15–80 years (3) Able to exercise (4) Corticosteroid treatment <3 months (5) Self-reported reduction of muscle function and as assessed by FI in myositis	Diagnosis verified by inflammatory infiltrates in a muscle biopsy or by pathological EMG	(1) PM or DM (Bohan and Peter criteria) (2) Disease duration < 1 year
Exclusion criteria	(1) Another chronic disorder (2) Not able to exercise (3) Acute or chronic infection (4) Active disease	(1) Involvement of liver, kidney, and heart (2) Acute or chronic infection	(1) Malignancy (2) Severe osteoporosis (3) Comorbidities contraindicating exercise (4) Exercising > 1/week (5) IBM	–	(1) Comorbidities contraindicating exercise (2) Exercising > 1/week	IBM	–
Intervention	2/week blood flow restriction training program (12 weeks)	2/week exercise training program (aerobic and strength exercises) (12 weeks)	3/w exercising on loads allowing 10 VRM (7 weeks)	Bending and stretching exercises + isotonic muscle training + respiratory training	Resistive 15 min home exercise program (exercises against gravity or added weights) + 15 min walk 5/week (12 weeks)	15-min home exercise program +15-min walk 5/week (12 weeks)	Rehabilitation program (functional training and resistive and non-resistive exercise)
Comparison	No comparison	No comparison	No comparison	No comparison	No comparison	No comparison	No comparison
Primary/secondary outcome measures	(1) HAQ-DI (2) SF-36 (3) 1 RM (leg press and knee extension) (4) TST (5) TUGT (6) QCSA (7) CPK levels	(1) HAQ-DI (2) SF-36 (3) Muscle function - Leg press - Bench press - Handgrip - TST - TUGT (4) Aerobic capacity - Time to exhaustion	(1) HAQ-DI (2) MAP (3) MMT (4) FI-2 (5) 10–15 VRM (5 muscle groups) (6) GS (7) CPK levels (8) PGA (9) PhGA	(1) HAQ-DI (2) FIM (3) CRP levels (4) CPK levels (5) ESR (6) VAS (pain and fatigue) (7) Overall clinical evaluation (8) Muscle strength	(1) SF-36 (2) FI (3) CRP levels (4) CPK levels (5) ESR (6) Muscle biopsies (7) MRI scan of the thighs (8) Subjective global disease impact (SGDI)	(1) SF-36 (2) FI (3) Walking distance (4) CRP levels (5) CPK levels (6) ESR (7) VAS (pain and fatigue) (8) Muscle biopsies	(1) MMT (2) PIT (3) CPK levels (4) ADL

Table 2 (continued)

	Mattar MA, Gualano B, Perandinini LA et al. [62]	Mattar MA, Gualano B, Roschel H et al. [63]	Alexanderson H, Dastmalchi M, Esbjörnsson-Liljedahl M et al. [64]	Varju C, Pethö E, Kutas R et al. [65]	Alexanderson H, Stenstrom CH, Jenner G et al. [66]	Alexanderson H, Stendstrom CH, Lundberg I et al. [67]	Escalante A, Miller L et Beardmore TD [68]
	(8) Aldolase levels (9) PGA (10) PhGA (11) Adverse events (12) Potential disease-flare episodes (13) Clinical examination	- Time to achieve VAT - Time to achieve RCP - VO_{2peak} - CR - ΔHRR1 - ΔHRR2 (5) CPK levels (6) Aldolase levels	(10) MITAX (11) Borg CR-10 scale (pain) (12) Patients' global assessment of the overall impact of disease on well-being (VAS) (13) Muscle biopsy samples from the vastus lateralis	(9) Changes in respiratory function - Forced vital capacity (FVC) - Forced expiratory flow $FEF_{(25–75\%)}$ - Forced expiratory volume 1 s to FVC (FEV1/FVC) ratio		(9) MRI of the thigh muscles	
Follow-up	After 12 weeks of exercise	After 12 weeks of exercise	(1) 4w prior to baseline (2) At baseline (3) After 7w of exercise	After 3 weeks of exercise	(1) After 6 weeks of exercise (2) After 12 weeks of exercise	After 12 weeks of exercise	Until discharge from the hospital

PM polymyositis, *DM* dermatomyositis, *FI* functional index, *EMG* electromyography, *IBM* inclusion-body myositis, *VRM* voluntary repetition maximum, *HAQ-DI* Health Assessment Questionnaire Disability Index, *SF-36* Medical Outcomes Study 36-Item Short-Form Health Survey questionnaire, *RM* repetition maximum, *TST* timed-stands test, *TUGT* timed-up-and-go test, *QCSA* quadriceps cross-sectional area, *CPK* creatine phosphokinase, *PGA* patient's global disease activity, *PhGA* physician's global disease activity, *VAT* ventilatory anaerobic threshold, *RCP* respiratory compensation point, *CR* chronotropic reserve, *ΔHRR1* heart rhythm at the first minute after the test, *ΔHRR2* heart rhythm at the second minute after the test, *MAP* Myositis Activities Profile, *MMT* Kendall Manual Muscle Test, *GS* grip strength, *MITAX* Myositis Intent-to-Treat Activity Index, *CR* category ratio, *VAS* visual analogue scale, *FIM* functional independence measure, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate, *FVC* forced vital capacity, $FEF_{(25-75\%)}$ forced expiratory flow, *FEV1/FVC* forced expiratory volume 1 s to forced vital capacity ratio, *MRI* magnetic resonance imaging, *SGDI* subjective global disease impact, *PIT* peak isometric/isokinetic torque, *ADL* activities of daily living, *min* minutes

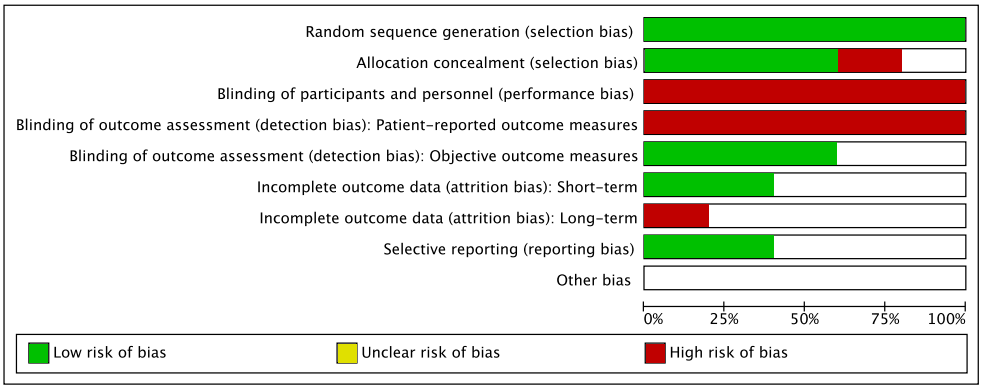

Fig. 2 Risk of bias graph

Current evidence supports the use of endurance training while the benefit of resistance training or combination of both remains unclear. Our results apply only to patients with a diagnosis of PM or DM. However, many patients now

Fig. 3 Risk of bias summary

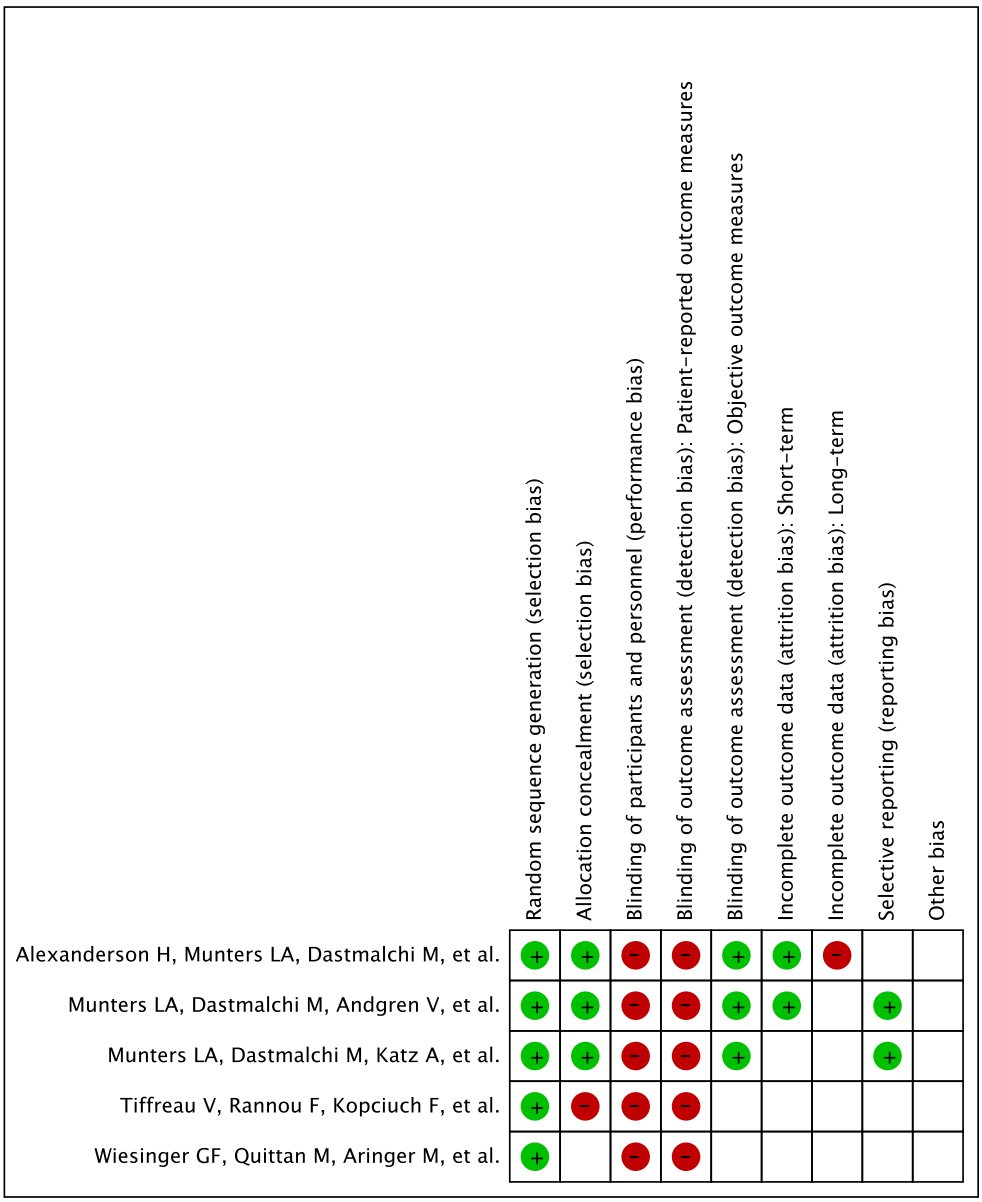

Table 3 Results of individual studies; + = significant effect, 0 = non-significant effect, NDP = no data provided, +/0 = a part of the data is significant, and a part is non-significant, +/NDP = a part of the data is significant, and a part is not provided, gray = outcome measure not used

	Activities of daily living					Quality of life		Muscle function								Aerobic capacity		Disease activity							Pain	Fatigue
	HAQ-DI	MAP	MFASQ	MACTAR	FIM	SF-36	NHP	MMT	PIT	FI	6- or 7-min WT	1, 5, 10 or 15 VRM	TST	TUGT	QCSA	GS	VO2max	Time to exhaustion	CRP	CPK	Aldolase	ESR	PGA	PhGA	MITAX	Pain	Fatigue
Tiffreau et al. [56]	+					+/0		+/0	0		0								NDP	NDP						+	NDP
Alexanderson et al. [57]							+/NDP			NDP							NDP			NDP							
Munters et al. [58]	NDP							NDP									+	+									
Munters et al. [59]	NDP	+/0		0		+/0		NDP				+/0					+		NDP	NDP		NDP	NDP	+	NDP		
Wiesinger et al. [60]			+						+								+			NDP	NDP						
Wiesinger et al. [61]			+						+								+			0							
Mattar et al. [62]	+					+						+	+	+	+					0	0		+	+			
Mattar et al. [63]	NDP					NDP			NDP			NDP	NDP	NDP			NDP	NDP		NDP	NDP						
Alexanderson et al. [64]	NDP	0						NDP			+/0	+/0				0				NDP			NDP	NDP	NDP	0	
Varju C et al. [65]	+				0				+/0										NDP	NDP		NDP				0	+
Alexanderson et al. [66]						+/0				+									0	0		0					

recognized as IMNM or overlap myositis were previously classified as PM, currently a diagnosis of exclusion [7].

Regarding the timing of intervention, evidence supports that physical therapy has a beneficial effect during the stable stage of the disease. We cannot draw clear conclusions about a beneficial effect during the active stage.

There are a number of limitations that we have to consider

First of all, an important limiting factor is that IIMs are rare diseases and it is difficult to find an adequate number of patients to include in clinical trials. As a consequence, many trials have a lack of power, recruitment targets were not always achieved, and baseline characteristics were not always completely comparable due to random chance mechanisms.

Secondly, there are some risk of bias factors (see Table S3–7). One of the main problems is that patients were not blinded because the intervention consisted of a rehabilitation program. Therefore, performance bias could not be excluded. This problem could be solved by comparing a light rehabilitation program (instead of placebo) with an active rehabilitation program. Patients were also not blinded when they had to complete patient-reported outcome measures (such as filling in a questionnaire) which could introduce a form of detection bias. On the other hand, independent assessors who had to assess objective outcome measures were blinded in most studies, which reduces the magnitude of detection bias. The randomization methods in the six RCTs were carried out thoroughly, which makes selection bias unlikely. Due to missing data and the fact that not all data were always reported, there is an unclear risk of attrition and reporting bias.

Finally, comparison between trials was frequently not possible due to the heterogeneity of outcome measures. These issues precluded a meta-analysis.

Conclusions

Physical therapy does not have a negative effect on the disease activity of patients with IIMs, and it could improve the functional outcome of these patients. We recommend physical therapy in the form of endurance training such as cycling or step aerobics at a frequency of three times a week. Addition of resistance training is safe, though no clear conclusion on effect could be drawn. Physical therapy seems to be safe during the stable stage of disease and possibly also in the active stage, though at the moment, only a favorable effect in the stable stage can be supported by evidence from multiple randomized clinical trials.

Future research should focus on the effects of physical therapy during the active stage of the disease, the added value of resistance training alongside endurance training, and the possible differences in rehabilitation programs for the different subtypes of IIMs. Trials investigating effects during the active stage of the disease pose specific methodological

challenges in terms of efficacy evaluation given the concurrent effect of the natural evolution of the disease and pharmacological treatment. To take care of this, larger sample sizes will be needed and pharmacological treatment will have to be standardized as much as possible, while medication and evolution of disease activity will have to be included as confounders during statistical evaluation.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical standards Not applicable.

GLOSSARY OF ABBREVIATIONS AND ACRONYMS

ADL	Activities of daily living
CPK	Creatine phosphokinase
CR	Category ratio/chronotropic reserve
CRP	C-reactive protein
DM	Dermatomyositis
EMG	Electromyography
Emtree	Embase subject headings
ESM	Erythrocyte sedimentation rate
$FEF_{(25-75\%)}$	Forced expiratory flow
FEV1/FVC	Forced expiratory volume one second to forced vital capacity ratio
FI	Functional index
FIM	Functional independence measure
FVC	Forced vital capacity
GS	Grip strength
HAQ-DI	Health assessment questionnaire disability index
IBM	Inclusion-body myositis
IIM	Idiopathic inflammatory myopathy
IMACS	International myositis assessment and clinical studies group
IMNM	Immune-mediated necrotizing myopathy
MACTAR	McMaster Toronto arthritis patient preference disability questionnaire
MAP	Myositis activities profile
MeSH	Medical subject headings
MFASQ	Modified functional assessment screening questionnaire
MITAX	Myositis intent-to-treat activity index
MMT	Manual muscle test
MRI	Magnetic resonance imaging
NHP	Nottingham health profile
PGA	Patient's global disease activity
PhGA	Physician's global disease activity
PICO	Patient intervention comparison outcome
PIT	Peak isometric/isokinetic torque
PM	Polymyositis
QCSA	Quadriceps cross-sectional area
RCP	Respiratory compensation point
RCT	Randomized controlled trial
RM	Repetition maximum
ROM	Range of motion
SDGI	Subjective global disease impact
SF-36	Medical outcomes study 36-item short-form health survey questionnaire
TST	Timed-stands test
TUGT	Timed-up-and-go test
VAS	Visual analogue scale
VAT	Ventilatory anaerobic threshold
VRM	Voluntary repetition maximum
WT	Walk test
ΔHRR1	Heart rhythm at the first minute after the test
ΔHRR2	Heart rhythm at the second minute after the test

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