Review

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Physical exercise as a treatment for adult and juvenile myositis

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Abstract. Alexanderson H (Karolinska Institutet, Huddinge, Stockholm; and Karolinska University Hospital, Solna, Stockholm, Sweden). Physical exercise as a treatment for adult and juvenile myositis (Review). *J Intern Med* 2016; doi: 10.1111/joim.12481.

There is growing evidence to support the safety and efficacy of exercise in patients with adult and juvenile idiopathic inflammatory myopathies. Five randomized controlled trials including adult patients with polymyositis and dermatomyositis (DM) and additional open studies have demonstrated reduced impairment and activity limitation as well as improved quality of life. In addition, recent studies have shown reduced disease activity assessed by consensus disease activity measures and reduced expression of genes regulating inflammation and fibrosis. Furthermore, exercise could improve muscle aerobic capacity as shown by increased mitochondrial enzyme activity. These data suggest that intensive aerobic exercise and resistance training could reduce disease activity and inflammation and improve muscle metabolism. Encouraging results have been reported from available open studies including patients with inclusion body myositis (IBM) and juvenile DM, indicating reduced impairment, activity limitation and improved quality of life also in these patients. Larger studies are needed to increase understanding of the effects of exercise in patients with active, recent-onset polymyositis and DM as well as in patients with IBM and juvenile DM.

Keywords: aerobic exercise, disease activity, impairment, inflammation, inflammatory myopathies, resistance training.

Introduction

The idiopathic inflammatory myopathies (IIM) are a heterogeneous group of rare diseases that primarily affect skeletal muscles. In adults, IIMs are divided into polymyositis (PM), dermatomyositis (DM) and inclusion body myositis (IBM) [1], while children are mostly affected by juvenile dermatomyositis (JDM) although some are diagnosed with overlap juvenile idiopathic inflammatory myopathy [2]. The common feature of all patients with IIMs is impaired muscle function, however each subgroup presents with characteristic muscle pathology and clinical symptoms such as interstitial lung disease, fatigue and dysphagia. Patients with IBM often have a history of frequent falls [1]. Standard medical treatment for patients with PM, DM or JDM consists of oral corticosteroids in combination with immunosuppressive treatment, although the role of biological agents is growing [3].

The World Health Organization has published the International Classification of Functioning Disability and Health (ICF) as a unified nomenclature and framework to describe health and health-related conditions as well as the impact of a health-related condition on the affected individual [4] (Figure S1). In this review, exercise effects will be described based on the ICF. Herein, structure relates to the structure of all organs in the human body, for example skeletal muscle, whereas body function relates only to the function of muscles. The term impairment will be used to describe pathological processes and reduced function of skeletal muscles. Impairment can often lead to reduced ability to perform daily activities of choice (activity limitation) and to participate in society (participation restriction). The ICF also comprises personal and external factors. Personal factors relate to an individual's thoughts and beliefs or, for example, level of motivation. Environmental factors relate to family and friends as well as the living and working

environment [4]. Quality of life is a multifaceted concept that is covered by ICF domains to a limited extent.

A large body of evidence supports *the notion that* exercise is a safe and beneficial treatment for rheumatoid arthritis (i.e. another inflammatory rheumatic disease) [5]. A Cochrane review in 2013 of five randomized controlled trials (RCTs) of exercise in muscle disease, including one study with patients with PM or DM, demonstrated that the evidence for positive effects of exercise is insufficient due to the small number of trials included and their risk of bias [6]. However, since then the results of three additional RCTs including adult patients with PM or DM have been published; these studies will be further discussed below [7–9]. Habers and Takken concluded that although most exercise studies are small and often without control groups, they all suggest that exercise is safe and probably effective for improving muscle impairment in all subsets of myositis patients [10]. In addition, exercise has emerged as an important part of the treatment for patients with IIMs [9, 10]. During the last 15 years, intensive research activity has resulted in the accumulation of evidence to support the benefit of exercise in patients with both established and newly diagnosed inflammatory active disease.

The aim of this review was to outline the effects of exercise with regard to structure (disease activity, inflammation, metabolic milieu and muscle structure) as well as impairment, activity limitation, participation restriction and quality of life in patients with adult and juvenile IIMs, according to the ICF.

Exercise studies in patients with IIMs

Since the two-first case reports on the effects of exercise in patients with myositis were published in 1993, a total of 32 studies evaluating exercise effects on different aspects of health have been published in adults and children with IIMs; in all these studies outcome variables were considered according to the ICF. A majority of studies included patients with adult PM and DM (n = 22) [7–9, 11–29], while a few focused on IBM (n = 6) [30–35] and JDM (n = 3) [36–38]. A small number of studies have also evaluated the feasibility of a single exercise test or exercise bout in patients with JDM [39–42]. The vast majority of studies have evaluated exercise in patients with noninflammatory active established disease [7, 8, 11, 13–15, 17–23, 25, 27–38], whereas patients with recent-onset, inflammatory active disease were included in only six studies [9, 12, 16, 18, 24, 26]. All studies have investigated exercise durations of 4–12 weeks except one in which exercise effects up to 6 months were studied [14]. Two studies have included an open extension follow-up of between 1 and 2 years [7, 9]. All studies evaluating exercise durations >3 weeks included creatine phosphokinase (CK) levels as a proxy measure of disease activity, all demonstrating unchanged or reduced levels of CK following exercise. Sixteen studies also investigated the effects of exercise on disease activity and muscle inflammation, metabolism and characteristics [7–9, 15, 16, 20–23, 25, 28, 30–32, 35, 42] (Table 1).

Exercise programmes

A variety of exercise programmes have been evaluated in patients with myositis, including resistance training (ranging from easy to intensive), a combination of resistance training and aerobic exercise, and exclusively aerobic exercise (Table 2). Home exercise alone or in combination with exercise in a hospital setting has been used in several studies and some have used supervised hospital-based exercise. Below, some of the exercise programmes, all of which were well-tolerated, are presented more in detail; they are referred to herein with programme numbers (P1–10). All exercise programmes are summarized in Table 2, with the degree of tolerability shown in Table 3.

Exercise programmes evaluated for adult patients with recent-onset or refractory disease

One resistive home exercise programme performed 5 days a week for 12 weeks (P1) is the only programme that has been extensively evaluated for safety analysing CK levels, magnetic resonance imaging and inflammatory infiltrates in muscle biopsy in patients with recent-onset, active PM and DM [9, 16] (Figure S2). The absolute loads were not registered, but patients performed about 10–15 repetitions of each exercise. In an RCT [9], the programme was combined with outdoor aerobic walking for 20 min, 5 days a week, at 50–70% of estimated maximal heart rate (i.e. 220 – age).

Mattar *et al.* [26] were the first to evaluate exercise in refractory PM and DM using an in-hospital resistance training and aerobic exercise programme that was well-defined with regard to

Table 1 *Effects of exercise on disease activity, inflammation, metabolism and muscle characteristics in patients with myositis*

Study/design	Diagnosis/ patients, *n*/disease activity/HCs, *n*	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Disease activity compared to HCs where applicable/ responders, *n*	Inflammation compared to controls where applicable/ responders, *n*	Metabolites compared to HCs where applicable/ responders, *n*	Muscle characteristics/ blood flow
Alemo Munters *et al.* (2013) [7] RCT, 1-year open extension	PM, DM EG $n = 12$ CG $n = 11$, Established HCs $n = 12$	Aerobic, endurance 12 weeks 3 d w^{-1}	70%/VO_2max 1 × 30–40 VRM	*6-item core set* EG: Resp. $n = 7$ CG: Resp. $n = 0$ ($P < 0.01$)	CD3+Tcell 0	NA	NA
Alemo Munters *et al.* (2013) [8] RCT (same exercise protocol as [31])	PM, DM EG $n = 11$, CG $n = 10$ Established HC $n = 12$	Aerobic, endurance 12 weeks 3 d w^{-1}	70%/VO_2max 1 × 30–40 VRM	*6-item core set* EG: Resp. $n = 6$ CG: Resp. $n = 0$	NA	*Lactate* Pre-exercise: Pt-HC: 0 Post exercise: EG:-($P < 0.01$) CG: 0 *Mitochondrial enzymes (EG)* CS + ($P < 0.001$) β-HAD + ($P < 0.05$)	NA
Alexanderson *et al.* (2014) [9] RCT, 2-year open extension	PM, DM EG $n = 10$, CG $n = 9$ Active	Resistance, aerobic 24 weeks 5 d w^{-1}	NR 50–70% of predicted max HR	*CPK* Pre-exercise: 0 24 weeks: 0 52 weeks EG: decreased ($P < 0.05$) 104 weeks: 0	*Biopsy* EG: 0 CG: 0	NA	NA

Table 1 (*Continued*)

Study/design	Diagnosis/ patients, *n*/disease activity/HCs, *n*	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Disease activity compared to HCs where applicable/ responders, *n*	Inflammation compared to controls where applicable/ responders, *n*	Metabolites compared to HCs where applicable/ responders, *n*	Muscle characteristics/ blood flow
Alexanderson *et al.* (2007) [20] Open, repeated measure	PM, DM Established *n* = 8	Resistance training 7 weeks 3 d w^{-1}	70% of 1 VRM	*6-item core set* Resp: *n* = 2 MITAX reduced ($P < 0.05$)	*Gene expression* Inflammation reduced ($P < 0.001$) Fibrosis reduced ($P < 0.001$) Biopsy 0	NA	NA
Alexanderson *et al.* (2000) [16] Open study	PM, DM Active *n* = 11	Resistance, home exercise 12 weeks 5 d w^{-1}	NR	CK 0	Biopsy 0 MRI 0	NA	NA
Alexanderson *et al.* (1999) [15 Open study	PM, DM Established *n* = 10	Resistance, home exercise 12 weeks 5 d w^{-1}	NR	CK 0	Biopsy 0 MRI 0	NA	NA
Arnardottis *et al.* (2003) [31] Open study	IBM *n* = 7	Resistance, home exercise 12 weeks 5 d w^{-1}	NR	CK 0	Biopsy 0	NA	NA
Bertolucci *et al.* (2014) [32] Controlled/open	PM, DM *n* = 20 Established HC *n* = 15 4/20 pts exercised	Aerobic 12 weeks 3 d w^{-1}	60–75% of predicted max HR	CK 0	NA	*Lactate* Pre-exercise: Pts lower vs. HCs ($P < 0.001$) Post-exercise: Pts reduced	NA

Table 1 (*Continued*)

Study/design	Diagnosis/ patients, *n*/disease activity/HCs, *n*	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Disease activity compared to HCs where applicable/ responders, *n*	Inflammation compared to controls where applicable/ responders, *n*	Metabolites compared to HCs where applicable/ responders, *n*	Muscle characteristics/ blood flow
Chung *et al.* (2007) [22] RCT, double-blind	PM, DM Established CrG $n = 19$ PlacG $n = 18$	Resistance, home exercise 20 weeks 5 d w^{-1}	NR	CK 0	NA	*PCr/β-NTP ratio* EG increase vs. CG ($P < 0.05$) CG: 0	NA
Dastmalchi *et al.* (2007) [21] Open study (same protocol as [15])	PM, DM $n = 9$ Established HC $n = 11$	Resistance, home exercise 12 weeks 5 d w^{-1}	NR	NA	NA	NA	*Fibre type* Pre-exercise: Pts fewer type 1 fibres vs. HCs ($P < 0.05$) Post-exercise: Pts more type 1 fibres vs. baseline ($P < 0.05$) *CSA* Pts–HC: 0 Post-exercise: Type 1 increased Type 2 increased ($P < 0.05$)
Dalise *et al.* (2012) [28] Case study	PM Established $n = 1$	Aerobic, treadmill + arm cycle 5 weeks 5 d w^{-1}	65–80% of predicted max HR	CK reduced by 36%	NA	Lactate	

Table 1 (*Continued*)

Study/design	Diagnosis/ patients, *n*/disease activity/HCs, *n*	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Disease activity compared to HCs where applicable/ responders, *n*	Inflammation compared to controls where applicable/ responders, *n*	Metabolites compared to HCs where applicable/ responders, *n*	Muscle characteristics/ blood flow
Gualano *et al.* (2010) [35] Case report	IBM Established *n* = 1	Resistance, vascular occlusion 12 weeks 2 d w^{-1}	30% of max	CK 0	NA	NA	*Biopsy, mRNA expression* MGF (upregulated 3.97 fold) Atrogin-1 (downregulated 0.62 fold) MuRF-1 (upregulated 1.18 fold) mTOR (downregulated 1.28 fold) CSA (+4.7%)
Habers *et al.* (2013) [42] Open, controlled study	JDM *n* = 11 JIA *n* = 10 Established HC *n* = 13	1 CPET (until volitional exertion)	NR	NA	NA	NA	*Δ [O_2Hb]* No difference between groups *Δ [tHb]* JDM pts reduced vs. HCs ($P < 0.01$)

Table 1 (*Continued*)

Study/design	Diagnosis/ patients, *n*/disease activity/HCs, *n*	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Disease activity compared to HCs where applicable/ responders, *n*	Inflammation compared to controls where applicable/ responders, *n*	Metabolites compared to HCs where applicable/ responders, *n*	Muscle characteristics/ blood flow
Mattar *et al.* (2014) [25] Open study	PM, DM Established $n = 13$	Resistance training under blood flow restriction 12 weeks 2 d w^{-1}	5 × 15 sets at 30% of VRM	Phys VAS reduced ($P < 0.05$) Pt VAS reduced ($P < 0.05$) CK, Ald 0	NA	NA	CSA increased ($P < 0.01$)
Omori *et al.* (2012) [37] Open study	JDM Established $n = 10$	Resistance, dynamic + aerobic, treadmill 12 weeks 2 d w^{-1}	8–12 VRM, 70% of HR at VO_{2peak}	DAS-28: 0	NA	NA	NA
Spector *et al.* (1997) [30] Open study	IBM Established $n = 5$	Resistance training 12 weeks 3 d w^{-1}	5 VRM	CK 0	Biopsy 0	NA	CSA 0

Table 1 (*Continued*)

Study/design	Diagnosis/ patients, *n*/disease activity/HCs, *n*	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Disease activity compared to HCs where applicable/ responders, *n*	Inflammation compared to controls where applicable/ responders, *n*	Metabolites compared to HCs where applicable/ responders, *n*	Muscle characteristics/ blood flow
Nader *et al.* (2010) [23] Open study (same protocol as [20])	PM, DM Established *n* = 8	Resistance training 7 weeks 3 d w^{-1}	70% of 1 VRM	NA	*Biopsy, mRNA expression* 34 pro-inflammatory genes downregulated (−1.5 to −3.5 fold)	*Biopsy, mRNA expression* 3 pro-oxidative metabolism genes upregulated (+1.6 to +1.8 fold) 4 pro-lipid synthesis genes downregulated (−1.5 to −2.6 fold)	*Biopsy, mRNA expression* 22 pro-fibrotic genes downregulated (−1.5 to −3.7 fold) 3 anti-fibrotic genes upregulated (+1.5 to +2.7 fold)

PM, polymyositis; DM, dermatomyositis; JDM, juvenile dermatomyositis; JIA, juvenile idiopathic arthritis; EG, exercise group; CG, control group; HC, healthy control; CK, creatine phosphokinase; Ald, Aldolase; 0, no statistically significant difference/change; NA, not assessed NR, not reported; Resp. (*n*) = number of responders i.e. improve >20% compared to baseline; d w^{-1}, days $week^{-1}$; VRM, voluntary repetition maximum (e.g. 1 × 30–40 VRM = 30–40 VRM performed in one set, 3 × 8–12 VRM = 8–12 VRM performed in three sets); VO_2max, maximal oxygen uptake; CS, citrate synthase; β-HAD, β-hydroxyacyl-CoA dehydrogenase; MITAX, Myositis Intention to Treat Index; MRI, magnetic resonance imaging; CrG, creatine group; PlacG, placebo group; PCr/β-NTP, phosphocreatine/β-nucleoside triphosphate; CSA, cross-sectional area; MGF, mechanogrowth factor; mTOR, mammalian target of rapamycin; MuRF-1, muscle RING finger 1; Δ [O_2Hb], change in balance between oxygen delivery and oxygen consumption; Δ [tHb], change in blood volume; CPET, cardiopulmonary exercise test; Phys VAS, physician global visual analogue scale; Pt VAS, patient global visual analogue scale; Das-28; Disease activity score-28; VO_2peak, peak oxygen uptake; IBM, inclusion body myositis; RCT, randomized controlled trial; pt, patient; max, maximum.

Table 2 *Effects of exercise on impairment, activity limitation/participation restriction and quality of life*

Study/design	Diagnosis/patients, *n*/disease activity/HCs, n	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Impairment	Results	Activity limitation/ participation restriction	Results	Quality of life	Results
Resistance training									
Hicks *et al.* (1993) [11] Case report	PM Established *n* = 1	Isometric in right leg, left leg control 6 weeks 3 d w^{-1}	60% of max	Isometric PT	(+%)	NA		NA	
Escalante *et al.* (1993) [12] Open study	PM, DM Active *n* = 5	Dynamic and ROM 8 weeks NR	NR	Isometric PT	+	NA		NA	
Spector *et al.* (1997) [30] Open study	IBM Established *n* = 5	Dynamic 12 weeks 3 d w^{-1}	50–70% of max	Isometric PT 3 VRM MMT FSS	0 + 0 0	Barthel's index	0	NA	
Alexanderson *et al.* (1999) [15] Open study	PM, DM Established *n* = 10	Dynamic, home-based 12 weeks 5 d w^{-1}	NR	FI	+	NA		SF-36	+
Alexanderson *et al.* (2000) [16] Open study	PM, DM Active *n* = 11	Dynamic, home-based 12 weeks 5 d w^{-1}	NR	FI	+	NA		SF-36	+
Heikkilä *et al.* (2001) [17] Open study	PM, DM, IBM Established *n* = 22	Dynamic 3 weeks NR	NR	FI Grip VAS pain	+ 0 0	HAQ	0	NA	
Arnardottis *et al.* (2003) [31] Open study	IBM Established *n* = 7	Dynamic, home-based 12 weeks 5 d w^{-1}	NR	Isometric PT (kin/com) FI	0 0	NA		NA	
Varju *et al.* (2003) [18] Open study	PM, DM Established, active *n* = 19	Dynamic 3 weeks 5 d w^{-1}	NR	Muscle strength (dynamometer) FI FVC VAS fatigue VAS pain	+ + + + 0	NA		NA	
Harris-Love (2005) [19] Case report, controlled	PM Established *n* = 1	Dynamic, eccentric 12 weeks 2 d w^{-1}	70% of max	Isometric PT VAS pain Passive ROM	(+) (0) (0)	NA		NA	

Table 2 (*Continued*)

Study/design	Diagnosis/patients, *n*/disease activity/HCs, n	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Impairment	Results	Activity limitation/ participation restriction	Results	Quality of life	Results
Alexanderson *et al.* (2007) [20] Open, repeated measures	PM, DM Established $n = 8$	Dynamic 7 weeks 3 d w^{-1}	10 VRM (70% of max)	10 VRM FI-2 Grippit (hand)	$+^{a,b,c}$ $+^{a,d}$ 0^{a}	MAP	0^{a}	NA	
Chung *et al.* (2007) [22] RCT, double-blind	PM, DM Established $n = 37$	Dynamic, home-based 20 weeks 5 d w^{-1}	NR	AFPS MMT FI Pain (McGill pain questionnaire)	EG-CG + EG-CG + EG-CG + 0	NA		NHP HADS	0 0
Johnson *et al.* (2007) [33] Open study	IBM Established $n = 7$	Dynamic, home-based 16 weeks Twice a day	NR	Strength (hand held dynamo)	+	30 m walking Stair climbing Sitting-to-standing	+ + 0	NA	
Gualano *et al.* (2010) [35] Case report	IBM Established $n = 1$	Dynamic, vascular occlusion 12 weeks 2 d w^{-1}	30% of max	1 RM leg press	(+15.9%)	TUG HAQ	(+ 60%) 0	SF-36	(+)
Regardt *et al.* (2014) [27] Open study	PM, DM Established $n = 11$	Dynamic, home-based hand exercise 12 weeks 3 d w^{-1}	NR	Strength Grip (Jamar) Pinch grip Grip ability Dexterity	0 + 0 0	DASH	0	NA	
Mattar *et al.* (2014) [25] Open study	PM, DM Established $n = 13$	Dynamic, vascular occlusion 12 weeks 2 d w^{-1}	30% of max	1 RM leg press 1 RM knee extension	+ +	TST TUG HAQ	+ + +	SF-36	+
Aerobic exercise alone or in combination with resistance training									
Wiesinger *et al.* (1998) [13] RCT	PM, DM Established $n = 14$	Aerobic, stationary cycling + step-up class 6 weeks 2–3 d w^{-1}	60% VO_2max	VO_{2peak} Isometric PT	EG-CG: + EG-CG: +	FASQ	EG-CG: +	NA	
Wiesinger *et al.* (1998) [14] CT	PM, DM Established $n = 13$	Aerobic, stationary cycling + step-up class 24 weeks 1–2 d w^{-1}	60% VO_2max	VO_{2peak} Isometric PT	EG +/CG 0 EG +/CG 0	FASQ	EG +/CG 0	NA	

Table 2 (*Continued*)

Study/design	Diagnosis/patients, *n*/disease activity/HCs, n	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Impairment	Results	Activity limitation/ participation restriction	Results	Quality of life	Results
Karper *et al.* (2001) [29] Case study	DM Established $n = 1$	30–40 min walking, resistance training 3 d w^{-1}	NR	Vital capacity PEF Hand grip Muscle endurance Walking ability	(+26%) (+29%) (+200%) (+50%) (+36%)	ADL	Scored autonomy in more of tasks vs. baseline	Quality of Life index	(+8%)
Omori *et al.* (2010) [36] Case report	JDM ($n = 1$, age 7) HC ($n = 1$, twin)	Resistance, dynamic + aerobic, treadmill/ 16 weeks	8–12 VRM, 70% of HR at VO_{2peak}	VO_2peak 1 RM Hand grip MMT CMAS	(+ 6%) (+ 15–30%) (+ 37%) 0 0	TST TUG CHAQ	(+12%) (+30%) 0	NA	
Omori *et al.* (2012) [37] Open study	JDM Established $n = 10$	Resistance, dynamic + aerobic, treadmill 12 weeks 2 d w^{-1}	8–12 VRM, 70% of HR at VO_2peak	VO_{2peak} 1 RM Hand grip MMT CMAS	+ + + 0 +	TST TUG	+ +	Patient/parent PedsQL	+
Hejazi *et al.* (2012) [24] Case report	PM Active $n = 1$	4-week rehabilitation: resistance training, aerobic, stationary cycling, ADL training 5 d w^{-1}	NR	MMT	(+/0) values 0–5	Modified Barthel's index	(+65–2/100)	NA	
Riisager *et al.* (2013) [38] Open study	JDM Established $n = 10$	Aerobic, home-based, stationary cycling 12 weeks 3 d w^{-1}	60% VO_{2max}	VO_{2max} W_{max} MMT-8 CMAS Physical activity level	+ + 0 0 +	6MWT	+	NA	
Johnson *et al.* (2009) [34] Open study	IBM Established $n = 7$	Aerobic, stationary cycling + resistance, home-based 12 weeks 7 d w^{-1}	80% of max HR NR	VO_2peak Strength (myometer)	+ + (4/8 tasks)g	30 m walking Stair climbing	0 0	NA	
Dalise *et al.* (2012) [28] Case study	PM Established $n = 1$	Aerobic, treadmill + arm cycle 5 weeks 5 d w^{-1}	65–80% of predicted max HR	Isometric strength (MVC) Balance (BBS)	(+10% to +155%) (+4%)	10 m walking test TUG 6MWT Barthel's index	(+17%) 0 0 (+11% +13%)	HADS	(+50%)

Table 2 (*Continued*)

Study/design	Diagnosis/patients, *n*/disease activity/HCs, n	Exercise/ duration/ frequency	Load/intensity, % of max/VRM	Impairment	Results	Activity limitation/ participation restriction	Results	Quality of life	Results
Bertolucci *et al.* (2013) [32] Open study	PM, DM Established *n* = 4	Aerobic, treadmill 6 weeks 3 d w^{-1}	60–75% of predicted max HR	NA		6MWT 10 m walking test TUG Barthel's index	(−4% to +18%) (+2% to15%) (+3 to +28%) (+11−45%)	NA	
Alemo Munters *et al.* (2013) [7] RCT, 1-year open extension	PM, DM Established *n* = 23	Aerobic, stationary cycling + resistance, dynamic (home-based and hospital 12 weeks 3 d w^{-1}	70% of VO_2max, 30–40 VRM	VO_2max 5 VRM	EG-CG: + EG-CG: +	Patient preference (MACTAR) MAP Moving around Household Social Leisure	EG: + EG-CG: + EG: + EG: + EG: +	SF-36 PF GH V MH	EG-CG: + EG: + EG-CG: + EG: +
Alemo Munters *et al.* (2013) [8] RCT	PM, DM Established *n* = 21	Same as (7)	Same as (7)	Stationary cycling to exhaustion	EG-CG: +	NA		NA	
Alexanderson *et al.* 2014 (9) RCT, 2-year open extension	PM, DM Active *n* = 19	Resistance, home-based + aerobic, outdoor walking 12 weeks 5 d w^{-1}	NR, 50–70% of predicted max HR	FI Estimated VO_2 by submax Ebberling treadmill test	EG: + CG: + EG: + CG: +	NA		NHP	EG-CG: 0 EG: + Energy CG: + Sleep
Mattar *et al.* (2014) [26] Case report	PM Active *n* = 3	Resistance + aerobic treadmill 12 weeks 2 d w^{-1}	8–12 VRM, HR at VAT − 10% below RCP	VO_2peak 1 RM Grip	(+ 7–91%) (−20% to +55%) (−12% to +33%)	TST TUG HAQ	(+ 0 to +10%) (−6% to +13%) (+7% to +43%)	SF-36 PF SF-36 PSC SF-36 MSC	(+14 to + 100%) (−5 to+ 72%) (+0.3 to + 67%)

PM, polymyositis; DM, dermatomyositis; IBM, inclusion body myositis; JDM, juvenile dermatomyositis; HC, healthy control; +, statistically significant difference within groups; EG-CG +, statistically significant improvement in EG versus CG; (+%), change in percentage without statistical analysis; PT, peak torque; ROM, range of motion; VRM, voluntary repetition maximum; RM, repetition maximum; NR, not reported; NA, not assessed; HR, heart rate; VO_{2max}, maximal oxygen uptake; CT, controlled trial; ADL, Activities of daily living; PEF, peak expiratory flow; CHAQ, Childhood Assessment Questionnaire; MMT, manual muscle test; MMT-8, MMT 8 muscle groups; FSS, fatigue severity scale; SF-36, Short Form 36; SF-36 PF, Physical Function; GH, General Health; V, Vitality; MH, Mental Health; PSC, SF-36 Physical score; MSC, SF-36 Mental score; HAQ, Health Assessment Questionnaire; FI, Functional Index; VAS, visual analogue scale; kin/com, Kinetic Computer system; FVC, forced vital capacity; BBS, Berg Balance Scale; MAP, Myositis Activities Profile; AFPS, aggregate functional performance score; HADS, Hospital Anxiety and Depression Scale, FASQ, Functional Assessment Screening Questionnaire; VAT, ventilator anaerobic threshold; RCP, respiratory compensation point; NHP, Nottingham Health Profile; TST, Timed Stands Test; TUG, Timed Up and Go; DASH, Disability of the Arm, Shoulder and Hand questionnaire; MVC, maximal voluntary contraction; VAT, ventilator anaerobic threshold; HAQ, Health Assessment Questionnaire; CMAS, Childhood Myositis Assessment Scale; Pediatric Quality fo Life Inventory; 6MWT, 6 min walking test; MACTAR, MacMaster Toronto Arthritis Patient Preference Questionnaire; VO_2peak, peak oxygen uptake; d w^{-1}, days $week^{-1}$; RCT, randomized controlled trial; max, maximum.

[a]No significant changes between −4 weeks and baseline in any of the measures.

[b]Significant improvement in deltoids, quadriceps, gastrocnemius, abdominal muscle groups, but not in biceps/latissimus dorsii.

[c]All eight participants improved >20% (defined as clinically relevant change).

[d]Improved significantly in shoulder flexion task, but not in other muscle groups.

Table 3 *Summary of exercise programmes, the diagnosis for which they were evaluated, and their tolerability*

Exercise programme	Diagnosis	Tolerability
Home exercise, resistance training and aerobic walking at 50–70% of estimated maximal heart rate, 5 days a week for 12 weeks (P1) [9]	Recent-onset PM and DM	Well-tolerated by all participants. The programme needed to be divided between morning and afternoon sessions during the first weeks of exercise, due to muscle weakness and fatigue, for two patients
Resistance training (8–12 VRM) and high-intensity aerobic exercise (P2) [26]	Refractory PM and DM	Well-tolerated by all participants
Resistance training at 10 VRM, 3 days a week, for 12 weeks (P3) [20]	Established PM and DM	One patient with arthritis in finger and wrist joints did not quite reach goal intensity for upper extremity tasks
Resistance training at 30% of 1VRM during vascular occlusion, twice a week for 12 weeks (P4) [25]	Established PM and DM	Well-tolerated
Home exercise, resistance training, twice a day for 16 weeks (P5) [33]	IBM	Well-tolerated by all participants
Resistance training at 3–15 VRM, 3 days week $^{-1}$ for 12 weeks (P6) [30]	IBM	Well-tolerated by all participants
Aerobic exercise at 70% of VO_2max and resistance training at 30–40% of VRM, 3 days week $^{-1}$ for 12 weeks (P7) [7]	Established PM and DM	Well-tolerated by all participants
Home-based hand exercise, 3 days week $^{-1}$ for 12 weeks (P8) [27]	Established PM and DM	Well-tolerated by all participants
Resistance training at 8–12 VRM and aerobic exercise at 70% of VO_2peak for 12 weeks (P9) [37]	Established JDM	Well-tolerated by all participants
Home-based aerobic exercise at 65% of VO_2max, every other day for 12 weeks (P10) [38]	Established JDM	Well-tolerated by all participants

PM, polymyositis; DM, dermatomyositis; IBM, inclusion body myositis; JDM, juvenile dermatomyositis; VRM, voluntary repetition maximum; VO_2max, maximal oxygen uptake; VO_2peak, peak oxygen uptake. P1–10, specific exercise programs described in this paper.

load and intensity. Patients exercised twice a week for 12 weeks (P2). Following a 5-min warm up, strength training was performed for 40 min at an intensity of 8–12 repetition maximum [(RM) i.e. the weight that can be lifted a maximum of 8–12 times) in three sets with a 1-min rest between sets. Both upper and lower limbs were exercised, using stationary training equipment, including horizontal leg presses, vertical bench presses, latissimus dorsi pull-downs, leg extensions, seated rowing, squats and abdominal crunches. Then patients performed high-intensity aerobic treadmill walking for 40 min, followed by stretching.

Exercise programmes used in patients with established, low disease activity

An intensive resistance training programme was employed in patients with established, low-disease activity PM and DM (P3) and consisted of a 10-min warm-up on a stationary bike or a treadmill at 50% of individually estimated maximal heart rate (220 – age) followed by 45 min of resistance training at 10 voluntary repetition maximum (VRM) in three sets separated by a 90-s rest (Figure S3) [20]. Patients exercised three times a week on nonconsecutive days for 7 weeks and new sets of 10 VRM were tested every other week and loads were adapted according to progress. Loads were initiated at about 50% of individual 10 VRM and slowly increased during the first 3 weeks of exercise.

In one very recent study, a supervised submaximal twice weekly exercise programme during blood flow restriction for 12 weeks was evaluated in 15 patients with established PM or DM (P4) [25]. An air cuff was placed in the inguinal fold of both thighs and blood flow was restricted by 50% while performing leg-presses and knee extensions at 30% of 1 RM for 15 repetitions in five sets separated by a 1-min rest. Exercise was introduced at lower intensity with four sets at 20% of 1 RM during the first week and four sets at 30% of 1 RM during the following 4 weeks. New sets at 1 RM were assessed every 4th week and exercise loads were adjusted accordingly. This programme was well tolerated. The same research group used a similar protocol in an earlier case study of a 65-year-old man with IBM [35] in whom this exercise protocol also seemed to be well tolerated.

Another home exercise programme was evaluated in patients with IBM (P5) [33]. The programme consisted of whole-body rising from sitting to standing, biceps and deltoid curls, wrist flexor exercises, seated rowing, heel and toe lifts, stretching of the calf muscles, seated dynamic knee-extensor exercise and isometric thigh-adductor contractions. The programme was performed twice from the beginning, but participants were told not to exercise on any given day if experiencing fatigue or pain from the previous days during the first 2 weeks. Following this, participants were instructed to exercise twice daily for the remaining 14 weeks. One of the first exercise studies in IBM evaluated a resistance training programme at loads between 3 and 15 VRM in a small group of patients (P6) [30].

One RCT evaluated an aerobic exercise programme in adult patients with PM or DM including stationary cycling at 70% of maximal oxygen uptake (VO_2max) for 30 min, in combination with quadriceps endurance training at 30–40 VRM, performed on three nonconsecutive days a week for 12 weeks (P7) [7]. Patients initiated the exercise at about 50% of VO_2max and increased intensity during the first 2 weeks. Patients also performed endurance resistance training in the deltoids and trunk muscles at about 30 VRM.

The first hand-exercise programme to be evaluated in patients with PM and DM comprised exercises for pinch gripping, thumb opposition, finger abduction and adduction as well as finger flexion, extension and opposition. Exercise resistance was adapted individually with putties using standardized doughs (P8). During the study, the resistance as well as the number of repetitions could be increased (up to 30 repetitions). Patients considered that the exercise programme was too long and suggested omitting the finger abduction and adduction exercises and performing only 10–20 repetitions 2–4 days a week [27]. Further evaluation of this programme is needed.

Exercise programmes in JDM

Two well-defined exercise programmes have been evaluated in two small open studies in patients with JDM. The first programme (P9) included a warm-up of treadmill walking for 5 min followed by 20 min of resistance training at 8–12 VRM in three sets combined with aerobic treadmill exercise at 70% of peak oxygen consumption (VO_{2peak}) for 30 min and finally stretching. The exercise was initiated with two sets of 15–20 VRM [37]. In the second study, an aerobic home exercise programme was evaluated with stationary cycling

at 65% of VO_2max every other day for 12 weeks (P10) [38]. Pulse rate data were collected throughout the study.

Effects of exercise in adults and children with IIM

Exercise effects on body structure: inflammation, disease activity and muscle metabolism

The results of all published exercise studies have demonstrated that exercise is safe in terms of tolerance and feasibility as well as inflammation and disease activity in adults and children with active, recent-onset or refractory disease and in those with established disease with low disease activity (Table 1).

Many of the earlier studies used only assessments of serum CK levels as a proxy for disease activity and inflammation before and after exercise. However, the introduction of the six-item core set for assessment of disease activity proposed by IMACS [43], as a tool to evaluate the effects of exercise on clinical disease activity, has led to a more clinically relevant assessment of disease activity in patients with IIMs. Criteria in this core set for minimal clinical improvement were defined as improvement by ≥20% in three of the six measures with worsening by >25% in no more than two measures [not including the manual muscle test (MMT)] [44]. A significantly larger number of participants in the exercise group, seven of 11 patients in the exercise group who performed an intensive aerobic and muscle endurance programme (P7) for 12 weeks were responders with reduced disease activity according to the IMACS criteria, compared to no patients in the control group [7]. Two patients responded with reduced disease activity according to these criteria after 7 weeks of intensive resistance training (P3), and disease activity assessed by the myositis intention to treat index was reduced in the entire group after 7 weeks of exercise compared to baseline [20]. After these two exercise programmes (P3 and P7) as well as an easy to moderate 12-week home exercise programme (P1), analysis of CD3+ T cell infiltrates indicated no signs of increased inflammation compared to a control group with established [8] and active disease [9, 16]. Furthermore, levels of inflammatory infiltrates were unchanged following exercise in patients with IBM [30, 31].

Physicians' and patients' global assessments of disease activity were significantly reduced after 12 weeks of resistance training during vascular occlusion (P4) compared to baseline in patients with established PM and DM [25]. The intensive exercise programme tested in three patients with refractory PM and DM (P2) was well-tolerated by all three patients and one showed a 33% reduction in CK levels after 12 weeks compared to baseline [26]. These findings of reduced disease activity and inflammation are supported by an analysis of gene expression using microarray analysis in repeat muscle biopsies. A large number of genes regulating inflammation and fibrosis were downregulated after 7 weeks of intensive resistance training (P3) [23], supporting the hypothesis that intensive exercise could be used as an anti-inflammatory treatment; however, these changes also need to be evaluated at the protein level. One study in JDM patients demonstrated reduced disease activity measured by the Disease Activity 28 score after exercise compared to baseline [37].

Intracellular matrix lactate levels were evaluated by microdialysis in patients and healthy control subjects matched for age, gender and physical activity levels. The same experimental procedure was used in patients with PM or DM at baseline and after 12 weeks of aerobic exercise and endurance resistance training in an RCT including an exercise group and a control group (P7) [8]. The microdialysis membrane was inserted in the vastus lateralis muscle and samples were collected before and after a stationary cycling session at 70% of VO_2max until exhaustion. There was no difference in lactate levels between healthy subjects and patients, although cycling time until exhaustion was significantly shorter in patients. After 12 weeks, the exercise group demonstrated an almost two-fold increase in cycling time until exhaustion with significantly lower lactate levels compared to baseline, while there were no changes in the control group. In addition, analysis of muscle biopsies showed increased mitochondrial enzyme activity (citrate synthase and β-hydroxyacyl-CoA dehydrogenase) [8]. In biopsies from a smaller subset of patients, analysis revealed an increased number of capillaries at 12 weeks in the exercise group compared to baseline [8]. In another study, lactate levels were evaluated in blood before, during and after a submaximal treadmill walking session [32]. Twenty patients with established PM or DM and 15 healthy control subjects were included. It was found that patients had significantly higher lactate levels and reduced walking time compared to the control subjects. Four patients started a 12-week aerobic exercise

programme at an intensity of 70% of VO_2max. Results indicated significantly lower lactate levels compared to baseline [32]. These data suggest that patients with established PM and DM respond to exercise with improved muscle aerobic capacity and capillarization. Phosphocreatine nucleoside triphosphate (PCr NTP) and inorganic phosphate levels were assessed by magnetic resonance spectroscopy after 3 and 5 months of creatine supplements in combination with home exercise (P1) in an RCT [22]. PCr NTP levels were increased significantly in the creatine supplement group compared to the control group [22].

A significant increase in cross-sectional area of the thigh muscles was recorded after resistance training during vascular occlusion (P4) in patients with established PM or DM [25]. Furthermore, a case study indicated a 4.7% increased cross-sectional area in a man with IBM after a similar exercise regimen as well as increased mRNA expression of mechanogrowth factor associated with muscle hypertrophy [35]. Arnardottis *et al.* [31] analysed muscle biopsies from seven patients with IBM following a 12-week home exercise programme and reported no change in capillary diameter, but a significant decrease in capillary density; the authors speculated that this could be due to a trend towards increased cross-sectional area. Habers *et al.* [42] studied the change in balance between oxygen delivery and oxygen consumption as well as blood volume using near-infrared spectroscopy in the vastus medialis and lateralis in children with JDM or juvenile idiopathic arthritis (JIA) and in healthy control subjects before and after an incremental all-out cycle ergometer test [42]. Children with JDM had significantly reduced blood volume in the vastus medialis compared to control subjects, but not compared to children with JIA, while there was no difference in the oxygen delivery/consumption balance between groups [42]. The authors concluded that these results could indicate that children with JDM had impaired blood volume that increased during moderate and strenuous exercise compared to healthy subjects, and that treatment for JDM should focus on improving oxygenation. However, these results need to be confirmed using other imaging techniques. A group of adult patients with established PM and DM were found to have a reduced number of type-1 oxygen-dependent muscle fibres compared to healthy control subjects. Easy-to-moderate home exercise (P1) for 12 weeks resulted in a significant increase in the proportion of type I fibres [21].

Based on these results it seems that resistive and aerobic exercise is not only safe but also can reduce disease activity and inflammation in patients with myositis and that exercise could restore the damaged metabolic milieu in skeletal muscle.

Effects of exercise on body functions: muscle strength and endurance, aerobic capacity, fatigue and pain

All studies conducted in patients with adult PM and DM as well as JDM have indicated reduced muscle impairment whereas the results of studies in IBM patients have been inconclusive (Table 2). In adults with PM and DM, aerobic/endurance exercise had positive effects not only on muscle endurance but also on muscle strength. Wiesinger *et al.* [13] reported improved aerobic capacity and isometric peak torque following a 1-h exercise programme of stationary cycling and step-up exercises in a group of seven patients compared to the control group. The authors of a more recent RCT came to the same conclusion, reporting improved aerobic capacity and muscle endurance after 30 min of intensive stationary cycling and quadriceps endurance training (P7) as well as improved quadriceps strength assessed by five VRM compared to a nonexercising control group. It also seems that low-intensity resistance training during vascular occlusion (P4) could improve muscle strength in adults with PM/DM and IBM [25, 35].

Intensive resistance training at 10 VRM in three sets (P3) resulted in marked improvements in muscle strength in a small group of patients with established PM and DM, with some improvements in muscle endurance assessed by the Functional Index-2 [20].

The feasibility of a home hand-exercise programme (P8) was recently evaluated [27]. At the group level, three-jaw pinch grip improved significantly in the left hand after 12 weeks whereas all other measures of strength and activity limitations were unchanged. Several patients demonstrated a clinically relevant improvement in grip strength limitations defined as >15% improvement according to the IMACS criteria [45].

A few studies have investigated the effects of exercise on impairments in patients with recent-onset

or refractory adult PM and DM [9, 12, 16, 18, 26]. In the only RCT, 10 patients were randomly assigned to a resistive home exercise programme (P1) and nine patients to a range of motion programme about 4 weeks after diagnosis and introduction of high-dose corticosteroids and immunosuppression [9]. After 12 weeks there were no significant differences in muscle endurance or aerobic capacity between the exercise and control groups, implying that early easy-to-moderate intensity exercise does not add any extra value to improve function in the short-term. After the 12 weeks of resistive home exercise, the exercise group was encouraged to start gym training twice a week for the rest of the study duration of 2 years. The results from this programme further supported the safety of exercise in inflammatory, active, recent-onset myositis, but conclusions could not be drawn about the effectiveness of frequent home exercise. A case study including three patients with refractory active PM and DM demonstrated the safety of intensive resistance and aerobic training (P2). Clinically relevant improvements (>20% compared to baseline) in both muscle strength and aerobic capacity were observed [26].

Encouraging results were reported from an open study including seven patients with IBM performing a resistive home exercise programme twice daily [33]. After 16 weeks of home exercise (P5) a significant improvement was observed in all muscle groups, including the knee extensors and finger flexors, assessed by a handheld myometer. The patients also improved in terms of time required to walk 30 m and to climb a flight of stairs. The same research group also investigated aerobic exercise at 80% of maximal heart rate 3 days a week for 12 weeks in combination with the home exercise programme (P5) performed once a day for 4 days a week. Aerobic capacity improved significantly, but muscle strength and other functional measures remained unchanged [34]. The results of an early open exercise study indicated improved muscle strength following intensive resistance training (P6) assessed by three VRM of between 25% and 120% with the largest improvements in the least affected muscle groups [30]. However, there were no changes in muscle strength assessed by the MMT or in fatigue.

Intensive resistance and aerobic exercise (P9 and P10) led to significantly improved aerobic capacity in children with JDM [37, 38]. The combination of resistance and aerobic exercise improved muscle function as assessed by RM and the Childhood Myositis Assessment Scale; however, there were no improvements as assessed by the MMT [37], as the group had already achieved the maximum MMT score at baseline.

Supplementation and exercise

Creatine supplements can further improve the effects of exercise in patients with established PM and DM. One of the largest RCTs in the field of exercise in myositis showed that creatine supplements in combination with resistive moderate-intensity home exercise (P1) 5 days a week for 5 months resulted in significantly improved physical capacity (aggregate functional performance time measure including 50-foot walking time, Timed-up and Go and stair ascent–descend test), muscle function assessed by the MMT and Functional Index compared to the control group (exercise with placebo supplements) [22].

Effects of exercise on activity limitation, participation restriction and quality of life

The majority of studies have evaluated the effects of exercise on activity and participation and/or quality of life using objective performance scores as well as self-reported instruments after both resistance training and aerobic exercise or the two combined (Table 2).

Most studies demonstrated improvements in objectively assessed activity limitation, such as walking ability and the ability to rise from a chair, in patients with active and established PM/DM as well as in those with IBM and JDM. Alemo Munters *et al.* [7] used a patient-preference instrument, the McMaster Toronto Arthritis Patient Preference Disability Questionnaire [46, 47], to assess activity limitations and reported a within-exercise group improvement with no change in the control group following intensive aerobic and resistance exercise (P7). Further, they also showed that the exercise group improved significantly in the disease-specific Myositis Activities Profile [48] subscale Moving Around compared to the control group with additional within-exercise group improvements in subscales/single items Household, Social and Leisure activities [7]. A smaller RCT to evaluate a similar intensive aerobic exercise programme was also able to demonstrate significantly improved activity limitation in the exercise group compared to the control group [13, 14]. Mattar *et al.* reported a

significantly improved Health Assessment Questionnaire score [49] after training during vascular occlusion (P4) [25], but not after a shorter 3-week rehabilitation programme [17]. Earlier open studies indicated that resistive home exercise (P1) could improve SF-36 [50] domains Physical Function in patients with established PM/DM [15] and Physical Function, Bodily Pain and Vitality in patients with active, recent-onset disease [16].

Increased quality of life assessed by patients' and parents' Pediatric Quality of Life Inventory scales [51] was reported after intensive resistance and aerobic exercise in JDM patients (P10) [37]. No other study has evaluated the effects of exercise on activity and participation level or quality of life in patients with JDM.

Long-term effects of exercise

Based on the finding of Alemo Munters *et al.* [7] that only muscle strength assessed by five VRM was improved at the 1-year follow-up compared to baseline, we assumed that regular exercise over long periods of time are necessary to sustain as well as to achieve further improvements. This is supported by the results of a study in patients with active PM/DM in which the exercise and control groups were encouraged to continue to exercise and be physically active during a 2-year follow-up period. Improvements in muscle endurance and aerobic capacity were sustained up to the 1-year follow-up in both groups and up to the 2-year follow-up (intenstion-to-treat analysis) in the exercise group [9].

Discussion

Recent data suggest that intensive aerobic exercise and resistance training can reduce disease activity and inflammation in patients with established PM and DM [7, 16, 23]. Exercise could be an effective anti-inflammatory treatment in patients with rheumatic diseases, however the underlying mechanisms are not fully understood. Strength training or intensive aerobic exercise and resistance training may reduce inflammation by increasing muscle mass/decreasing fat mass, improving cardiovascular and autonomic function and/or reducing levels of pro-inflammatory and increasing levels of anti-inflammatory cytokines [52]. In fact, the notion that exercise could increase inflammation has not been supported by any published evidence. As demonstrated by Mattar *et al.* [26], three patients with refractory PM and DM receiving relatively high doses of glucocorticoids tolerated moderate-to-high intensity resistance training and aerobic exercise, which supports the possibility that patients with recent-onset high disease activity could also exercise using a similar exercise programme. However, it is important to adapt the exercise intensity to an individual's disease activity, oral glucocorticoid dose, fatigue and pain. Furthermore, it is important to initiate exercise at a low load/intensity and adapt activities to each individual patient with myositis, and then slowly increase intensity. It is also recommended that exercise should be started under the supervision of a physical therapist, and patients should be followed up regularly to enable them to exercise at the optimal level.

In several of the studies of exercise in myositis, patients improved with aerobic exercise/endurance training not only in terms of muscle endurance and aerobic capacity but also with regard to isometric or dynamic muscle strength [7, 13, 20]. An exercise load of 40–50% of maximal strength is sufficient to improve muscle strength in healthy sedentary individuals, whereas further high-intensity strength training is required to achieve the same result in more physically active and well-trained individuals [53]. Patients with PM and DM have reduced aerobic capacity and muscle function compared to age-, gender- and physical activity-matched healthy control subjects [7, 54] which probably explains the positive nonspecific exercise response.

Exercise during vascular occlusion is a new approach for patients with myositis. The rationale for this type of exercise is a greater muscle fibre recruitment resulting in a similar degree of hypertrophy following low-intensity exercise during partial blood restriction as would be expected following high-intensity resistance training [55]. Mattar *et al.* considered that patients with myositis might not be able to perform high-intensity resistance training due to poor muscle function. The same group described the feasibility of resistance training during vascular occlusion in a man with IBM showing improved muscle strength and quality of life [35], and this type of exercise is now being studied in an RCT in Denmark. It would also be interesting to test this type of exercise in patients with recent-onset disease and receiving high glucocorticoid doses who might not tolerate high-intensity resistance training.

Results from the case study of exercise during vascular occlusion [35], the resistance training

programme reported by Spector *et al.* [30] and the 16-week home exercise programme performed twice a day [33] are encouraging as there is no effective medical treatment available for patients with IBM. It seems that the most affected muscle groups such as the knee extensors and the finger flexors have the least potential to improve, which supports the hypothesis that exercise should be initiated as soon as possible following a diagnosis of IBM. However, as Johnson *et al.* [33] reported, improvements in strength and function even in patients with severe muscle weakness support the notion that all patients should exercise regularly. It is not known whether the high frequency of twice daily exercise is the effective component of this home exercise programme. Clinical experience from Karolinska University Hospital indicates that patients who can sustain twice daily home exercise show improvements in the most important activities such as walking and the ability to rise from a chair. This and other exercise programmes in IBM patients need to be evaluated in larger controlled trials.

Recent studies also increase understanding of the effects of exercise in patients with JDM. Not only is maximal aerobic capacity testing safe and feasible, but children with low disease activity tolerate long-term resistance and aerobic exercise. The results of one study even suggested that disease activity was reduced following exercise [37]. Habers *et al.* [42] reported that children with JDM have a reduced ability to increase blood flow during a high-intensity exercise bout, indicating that treatment should be focused on improving circulation at rest and during exercise. Endurance and aerobic exercise over months could provide such a treatment. Further studies are needed to evaluate the safety and feasibility of exercise in patients with active JDM and also to establish the effects of exercise in all patients with JDM. There is also an urgent need to further investigate the effects of hand exercise in all patients with myositis. Patients with established PM and DM have significantly reduced grip strength compared to normal values [27]. This finding highlights the importance of assessing grip strength and hand function to further reduce impairments and activity limitations. In addition, there have been no studies to explore the effects of hand exercise in patients with IBM.

At present, there is not enough evidence to support specific guidelines for exercise for adults with PM or DM, and even less evidence for patients with IBM and JDM. However, based on the available data, it seems that recommendations for patients with myositis do not differ considerably from those for healthy adults (Table 4). Higher levels of muscle and cardiorespiratory fitness are strongly associated with better health outcome. Furthermore, exercise according to recommendations can reduce the risk of cardiovascular and metabolic diseases and osteoporosis in healthy populations [56].

Summary

Current evidence supports the safety and efficacy of exercise to reduce impairments and activity limitations and to improve quality of life in patients with IIMs; indeed, intensive exercise could even be considered an anti-inflammatory treatment in adult patients with PM and DM. Recent studies have demonstrated encouraging results for exercise, showing safety and improved function and quality of life also in patients with IBM and JDM. Exercise should be introduced for all patients with IIM individually adapted to disease activity, glucocorticoid dose and the level of pain and fatigue. Exercise should be introduced at low loads and

Table 4 *Recommendations for health-enhancing physical activity and exercise for healthy individuals*

	Duration of exercise bouts, min	Intensity, percentage of VRM	Intensity, percentage of age predicted maximal heart rate	Frequency, times week $^{-1}$
Increase muscle strength	2–3	–	60–80	–
Increase muscle endurance	2–3	–	30–40	–
Increase aerobic capacity	3	30–60		60–85
Improve/maintain health	4–7	30	–	50–70

VRM, voluntary repetition maximum. Ewing Garber *et al.* [56].

intensity under the supervision of a trained physical therapist, and effects should be monitored by validated objective and patient-reported outcome measures. Further studies are needed to establish the optimal type of exercise regimen in different disease phases and different subgroups of IIMs with respect to both clinical outcome measures and inflammation. The optimal physical activity level in patients with myositis is another area that needs to be studied.

Conflict of interest statement

No conflicts of interest were declared.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Domains of the international classifications of functioning, disability and health [4].

Figure S2. Easy to moderate home exercise program for patients with recent onset, active PM and DM. Numbers of repetitions and extra loads need to be adapted to individual muscle performance. The programme can be combined with 15-20 minute walk on 50–70% of predicted maximal heart rate (220-age).

Figure S3. 10 VRM resistance training that can be employed in patients with established PM and DM. A) Biceps and Latissimus dorsii, B) lower extremities, C) Deltoids, D) Quadriceps. Perform each exercise in 3 sets with a 90-sec rest in-between. Initiate the exercise on lower loads and progress slowly to goal intensity.

