Exercise recommendations for patients with myositis: a narrative review of safety and efficacy

N. Varone[1], J. Hinojosa[2], D. Nandakumar[3], N. Modi[4], A.R. Bhashyam[5], S.F. Bhai[2,6,7]

[1]School of Health Promotion and Kinesiology, Texas Woman's University, Denton, TX;
[2]Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital, Dallas, TX;
[3]Department of Physical Medicine and Rehabilitation, UT Southwestern, Dallas, TX;
[4]College of Natural Sciences, University of Texas, Austin, TX;
[5]Department of Orthopaedics, Massachusetts General Hospital, Boston, MA;
[6]Department of Neurology, UT Southwestern, Dallas, TX;
[7]Brain Institute, UT Southwestern Medical Center, Dallas, TX, USA.

Nicole Varone, MSc
Jose Hinojosa, MSc
Dhruv Nandakumar
Naysa Modi
Abhiram R. Bhashyam, MD, PhD
Salman F. Bhai, MD

Please address correspondence to:
Nicole Varone
Texas Woman's University,
304 Admission Drive,
76204 Denton, TX, USA.
E-mail: nvarone@twu.edu

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ABSTRACT

Idiopathic inflammatory myopathies (IIM) are marked by progressive muscle weakness and lasting disability. Therapies targeting patient well-being include the use of prescription drugs as well as exercise. Maintaining or increasing muscular strength and endurance as well as cardiorespiratory fitness (CRF) improves quality of life (QoL) as well as functional status in IIM patients. This narrative review highlights exercise interventions in patients of different IIM subtypes with the intent to provide a summary table with exercise recommendations that will safely and effectively improve QoL in myositis patients.

Introduction

The idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of disorders in which patients experience skeletal muscle weakness and inflammation (1), though other organs are also commonly involved, including skin (2, 3) and lungs (4). Common treatment for IIM patients includes immunomodulatory agents (*e.g.* corticosteroids, immunoglobulins, antimetabolites) (3, 5). Exercise as therapy may also provide benefits for IIM patients such as improved physical function (6), gene expression associated with reduced inflammation (7, 8), and reduced lipid infiltration of the muscle (9). Exercise is beneficial for this population, but engagement in physical activity in IIM patients is lower than expected (10). This may be because the benefits of exercise are not widely known or easily implemented. Therefore, the purpose of this review is to provide a summary of exercise interventions for dermatomyositis (DM), polymyositis (PM), sporadic inclusion body myositis (IBM), immune-mediated necrotising myositis (IMNM), and antisynthetase syndrome (ASSD). Each subset of myositis will be briefly described for readers of non-clinical background (5). Likewise, exercise intervention, recommendations, and adherence strategies will be discussed for those of non-exercise background.

The importance of cardiorespiratory and muscular fitness

All-cause mortality is directly related to cardiorespiratory fitness (CRF); therefore, exercise is often prescribed as therapy in many disease populations to decrease mortality risk (11). CRF is measured via submaximal or maximal estimations of oxygen consumption (Vo2) during exercise and is termed $Vo2_{max}$ (12). $Vo2_{max}$ is an indication of the body's ability to deliver and utilise oxygen at the working muscle tissue, or aerobic power (12). It is adaptable and can be increased with regular exercise (13), thereby decreasing all-cause mortality risk (14, 15). Conversely, sedentarism, whether volitional or due to disease, decreases $Vo2_{max}$ (16). $Vo2_{max}$ is reported relative to body mass (ml/kg/min) or in absolute values (L/min). A healthy sedentary adult of an assumed 70kg body mass can be expected to have a $Vo2_{max}$ of 32 to 40 ml/kg/min (17, 18).

The $Vo2_{max}$ of IIM patients is lower than age-matched control and often beneath the reported threshold for maintaining independence. A $Vo2_{max}$ less than 18 ml/kg/min in older men 15 ml/kg/min in older women leads to loss of independence due to an inability to carry out activities of daily living (ADLs) (19). Oxygen demand required for ADLs varies. Metabolic equivalent (METs) is a way to quantify the oxygen demand of various activities. At rest, 1 MET is expended and is equivalent

to a Vo2 of 3.5 ml O_2/kg/min. ADLs such as light housework can require 2 to 5 METs, or 7 to 17.5 ml O_2/kg/min. Heavy housework, such as grocery shopping, can demand up to 7 METs, or 24.5 ml O_2/kg/min. Walking for exercise can range from 1.8 to 5.3 METs (6.3 to 18.6 ml O_2/kg/min) and walking upstairs can demand 4.7 METs (16.5 ml O_2/kg/min) (20). These equivalents and the threshold for independence are of interest when comparing the $Vo2_{max}$ of IIM patients, many of whom have a reported $Vo2_{max}$ less than 18 ml/kg/min in several studies (21-23).

Exercise interventions are often conducted in a controlled research environment to observe the effects of exercise on specific factors in individuals of various fitness levels or disease states. $Vo2_{max}$ can be increased by 4.9 ml/kg/min with consistent endurance training and by 5.5 ml/kg/min with high intensity interval training (13). Intervention studies on disease populations often aim to significantly increase CRF due to the direct relationship between CRF and mortality (24) and have improved QoL in several populations in addition to IIMs, such as myotonic dystrophy and mitochondrial myopathy with minimal reported adverse events (25).

Common strategies to maintain or increase CRF include walking, biking, running, or swimming. The American College of Sport Medicine (ACSM) recommendations for aerobic activity in adults involves three to five days per week or more moderate (46-63% $Vo2_{max}$, or 64-76% maximal heart rate) intensity for at least 30 minutes or two to three days per week for at least 20 minutes at vigorous (64-90% $Vo2_{max}$, or 77-95% maximal heart rate) intensity (24). Target $Vo2_{max}$ intensities can be implemented during exercise bouts by documenting patient heart rate corresponding to desired Vo2 intensity during testing and prescribing intensity via heart rate.

A common outcome measure in several studies of this narrative is the difference in $Vo2_{max}$ pre- and post-exercise intervention. Changes in aerobic stamina can be measured via submaximal intensity work (70-80% $Vo2_{max}$) to exhaustion on a cycle ergometer or treadmill. Aerobic and muscular endurance can be modified with sustained bouts of submaximal physical activity (26). Several studies in this narrative report time to exhaustion to reflect changes in endurance (27-29).

In addition to CRF training, muscular strength and endurance exercise may have substantial metabolic effects that are beneficial to IIM patients (7, 8, 27, 28, 30). Muscular strength is measured via the maximal amount of weight moved once, or one repetition maximum (1RM) (24). Physiologic benefits of endurance and resistance exercise on muscle tissue include angiogenesis and increased mitochondrial biogenesis (31). Performing two to four sets of multi-joint movements such as squats under a load ranging from body mass to 100% of 1RM elicits maintenance or improvements in muscular strength and endurance (32). ACSM recommends two days per week of resistance training on all major muscle groups at 40-50% 1RM progressing to 60-80% 1RM (24). Often, ACSM aerobic and resistance recommendations form the basis of exercise interventions.

Search strategy and selection criteria

This narrative review focuses on peer-reviewed original experimental studies on participants diagnosed with DM, PM, IMNM, ASSD, and IBM. Searches were conducted through Pubmed and MEDLINE with key words "exercise" and "dermatomyositis", "polymyositis", "antisynthetase syndrome", "inclusion body myositis", "immune-mediated necrotizing myositis", "myositis", and "idiopathic inflammatory myopathy". Inclusion criteria were the use of exercise interventions lasting four weeks or more and studies in which five or more total adult (18 years and older) participants completed exercise intervention. Excluded from this narrative were case studies, pilot studies (apart from those used to characterise patients in more than one subsequent study), and interventions targeting juvenile dermatomyositis. Quality of evidence examination was not performed on any of the interventions in this narrative review.

Exercise studies in dermatomyositis and polymyositis

Dermatomyositis background

DM patients often experience symmetrical and proximal muscle weakness along with dermatological symptoms. Histological samples of muscle tissue commonly reveal perifascicular atrophy with inflammatory infiltrates and capillary damage caused by complement deposition (5). Characteristic skin abnormalities such as a "shawl" rash on the back and shoulders or Gottron papules on the metacarpophalangeal and interphalangeal joints are common accompaniments to proximal symmetrical muscle weakness (3). Onset of symptoms is indiscriminate of age (2, 3). Subgroups of dermatomyositis include specific antibody subtypes as well as diagnoses of juvenile dermatomyositis and amyopathic dermatomyositis (3). This segment of the review includes studies with adult DM who engaged in exercise interventions.

Polymyositis background

PM is characterised by progressive, symmetrical muscle weakness of proximal muscle groups. Patients with PM meet diagnostic IIM criteria but lack the skin features hallmark to DM (33, 34). PM is more commonly present in women than men (35, 36) and includes the diagnostic criteria that onset of symptoms occurs after the age of 18 (3). Recently, criteria for classification reveal that many patients previously classified as PM likely would fall into a separate category such as IMNM (37). With a greater pathophysiological understanding of IIMs, PM is becoming a smaller subset of myositis (38) and are a source of misdiagnosis (39). For this narrative, studies identifying patients as PM were included.

Fitness profile in PM and DM

Fitness levels in PM and DM patients were borderline to the level required for independence in performing ADLs. $Vo2_{max}$ was recorded as 15.3 ml/kg/min in PM/DM in a study comparing patients to healthy age-matched controls, who had a reported $Vo2_{max}$ of 28.7 ml/kg/min (21). PM and DM patients have a significantly shorter time to exhaustion

Table I. Effects of exercise intervention in patients with dermatomyositis and polymyositis.

Author/Study design	IIM	Exercise type	Intensity	Treatment	Primary outcome measures	Results	Adverse events
Alexanderson *et al*. (41) 2007/RCT	DM = 5 PM = 3	RT 7 weeks 3 days/week	3 sets w/90s rest beginning @50% of 10VRM and gradually increasing to 100% of 10VRM	N/A	MITAX 10-15 VRM muscle strength Muscle endurance Grip strength Muscular pain VL muscle biopsy: markers of inflammation	MITAX score improved (p<0.05) Resistance: 10-15 VRM: Increase in bilateral repetitions in deltoids, quadriceps, gastrocnemius, abdominals (p<0.05) No change in latissimus dorsi/biceps. Endurance: Increase in bilateral shoulder flexion repetitions. (p<0.05) No change in shoulder abduction, head lift, hip flexion step test, heel lift, toe lift. No change in grip strength No change in muscular pain Reduced inflammation in biopsy sample	1 patient experienced joint swelling and was unable to perform latissimus dorsi/ biceps ex during final 2 weeks.
Nader *et al*. (7) 2010/RCT	DM=5 PM=3	RT 7 weeks/3 days/ week	3 sets of 15 reps 10VRM	Glucocorticoids and Other Immune Based Therapies for 12 months prior and during studies	$Vo2_{max}$ MITAX, Muscular strength Serum C1q VL muscle biopsy: RNA profiling, Muscle Fibrosis	$Vo2_{max}$ increased (p<0.001) MITAX, Muscle Strength changes in above row Median C1q levels decreased (p=0.01) 265 transcripts modulated (41 inflammatory (34 downregulated), 25 pro-fibrotic (22 downregulated, 7 with metabolic regulation) Lower degree of inflammation with scattered T-cells and macrophages found but no statistically significant change after exercise	N/A
Alemo Munters *et al*. (27) 2013/RCT	DM=12 PM=11 CON=12	Combined aerobic/RT 12 weeks/3 days/week	30 min cycling @70%Vo2max RT upper and lower limbs 30-40%1RM	Stable medication for at least 1 month and during the intervention	$Vo2_{max}$, maximal power (W) Cycling time to exhaustion IMACS VL muscle biopsy: mitochondrial enzyme activity (in 3 ex group)	$Vo2_{max}$ and power output increased (p<0.01), decreased Vo2max/unchanged power output in CON Increased cycling time to exhaustion (p<0.01) Improvement in IMACS from exercise intervention in 6/9 EG patients *vs*. 1/9 control group Citrate synthase and β-hydroxyacyl-CoA-dehydrogenase activity increased (p=<0.001 and p=<0.05)	N/A
Alemo Munters *et al*. (61) 2013/RCT	Exercise (DM=6, PM=5) Control (6 DM, 5 PM)	Combined aerobic/RT 12 weeks/3 days/week	30 min Cycling @70% Vo2max 20 min 30-40% VRM knee extensor[a]	Stable medication for at least 1 month	$Vo2_{max}$ SF-36 Strength (5VRM)	$Vo2_{max}$ increased (p=0.010) SF-36 physical function and vitality scores increased (p<0.010 and 0.046) Strength increased: 5 VRM (p=0.026)	N/A
Alexanderson *et al*. (6) 2014/RCT	DM n=9 PM n=10	RT 12 weeks, 5 days/week under Supervision 12 weeks unsupervised	10 reps <20% FI 15-minute walk@ 50-70% Vo2max	Glucocorticoids introduced 2 months prior to intervention	$Vo2_{max}$ Compliance to home exercise regimen and 80-week follow-up Functional Index (FI) score of muscle performance	$Vo2_{max}$ increased (p<0.01), and up to 104 weeks post-intervention (p<0.05) Compliance to home ex 79± 22% and to brisk walks 81± 31 FI score improved after the 12-week intervention (p<0.01), and up to 104 weeks post-intervention (p<0.05)	Low initial tolerance in 2 patients. Regimen divided into 2 segments to accommodate
Mattar *et al*. (66) 2014/QE	DM=9 PM=4	BFR low intensity resistance @70% occlusion 12 week/3 days/week	4 sets of 15 reps @30%1RM until week 4 5 sets of 15 reps @30%1RM after week 5 Adjusted every 4 weeks based on 1RM	N/A	1RM: leg press, knee extension TUG TST CSA quadriceps SF-36 QoL	Leg press and knee extension 1RM increased (p<0.001, p<0.001) TUG improved (p=0.002) TST improved (p<0.001) CSA increase (p<0.01) SF-36 all component improvement (p<0.05)	N/A

Author/Study design	IIM	Exercise type	Intensity	Treatment	Primary outcome measures	Results	Adverse events
Alemo Munters *et al*. (28) 2016/RCT	DM/PM=7 CON=8	Endurance training 12 weeks/3 days/week	30 min Cycling @70% Vo2max 20 min 30-40% VRM knee extensor[a]	Stable dose for at least one month	$Vo2_{max}$ Cycling time to exhaustion VL muscle biopsy: lactate concentration, mRNA profiling, protein, IHC for capillaries	$Vo2_{max}$ increase (p<0.05) Increased cycling time to exhaustion (p<0.01) Decreased disease activity (p<0.05) Decreased lactate levels at exhaustion (p<0.05) Higher number of capillaries per mm^2 (p<0.05) and gene mRNA related to angiogenesis (p<0.01)	N/A
Boehler *et al*. (8) 2017/RCT	Exercise n=11 CON n=12	Combined aerobic/RT 12 weeks/1 day/week	30 min Cycling @70% Vo2max 20 min 30-40% VRM knee extensor[a]	Continue prescribed	Biopsy: microRNA expression, protein levels	Increase in microRNAs involved in decreasing immune response proteins (AK3, HIBADH) in proteins (AK3, HIBADH) in exercised patients	N/A
De Oliviera *et al*. (29) 2019/QE pilot	DM=6 PM=1 ASSD=2 Healthy CON=10	Combined Aerobic/RT 12 weeks/ 2 days/week	8-12RM 30-50 min treadmill mod intensity[b]	Continue prescribed	$Vo2_{max}$ Time to exhaustion Muscle strength 1RM OGTT & β-cell function	$Vo2_{max}$ increase without significance (p=0.068, p=0.052) Time to exhaustion increased (p<0.001) 1RM bench press and leg press increased (p=0.002, p=0.013). Hand grip strength did not (p=0.253) Insulin and β-cell function improvement without significance	N/A

RCT: randomised control trial; QE: quasi-experimental; PM: polymyositis; DM: dermatomyositis; ASSD: anti-synthetase syndrome; ex: exercising group; CON: healthy controls; VRM: voluntary repetition maximum; reps: repetition; 1RM: 1 repetition maximum; $Vo2_{max}$: maximal or peak volume of oxygen consumed; RT: resistance training; SF-36: quality of life questionnaire containing multiple parameters; TUG: timed up and go test; TST: timed stand test; CK: creatine kinase; C1q: serum complement 1q; W: wattage on cycle ergometer; FI: functional index, score 0 (lowest functioning) to 64 (highest functioning) (Josefson, 1996); VL: vastus lateralis; CPK: creatine phosphokinase; CSA: cross-sectional area; MITAX: myositis intention-to-treat activity index; MAP: myositis activities profile; OGTT: oral glucose tolerance test.
[a]Exercise intervention described by Alemo Munters *et al*. (27).
[b]Moderate intensity training defined as heart rate corresponding with the interval between ventilatory anaerobic threshold (VAT) and respiratory compensation point (RCP) (29).

during endurance cycling than healthy individuals (27). In DM patients, there is a higher incidence of fat content infiltration of skeletal muscle than in healthy controls (9), exacerbating muscle weakness and delaying recovery (40). Interventions reporting outcomes on DM and PM participants are presented in Table I.

Summary

Combined aerobic and resistance exercises improve CRF and muscular strength while decreasing pro-inflammatory gene expression and increasing anti-inflammatory gene expression (7, 41). Endurance aerobic exercise improves mitochondrial biogenesis and increases expression of microRNAs responsible for decreasing immune response in patients with DM and PM as well as increasing $Vo2_{max}$ (8). Patients should be encouraged to engage in at least three days per week of combined aerobic and resistance training. Aerobic training lasting 30 minutes on three days per week elicits significant CRF increases. A 15-minute brisk walk on five days per week at an intensity in which heart rate is equivalent to the beats per minute that coincides with 70% of patient $Vo2_{max}$ during fitness testing will also increase CRF. Intensities should be introduced slowly, such as walking at 50% $Vo2_{max}$ (6).

Resistance exercise is an effective therapy that may diminish the negative effects of inflammation on muscle strength without worsening disease progression (7). Three sets of resistance training of upper and lower body major muscle groups with 8-12 repetitions maximum per set and one minute rest between sets may significantly improve muscular strength (7, 29, 41). There were no adverse events reported.

Immune-mediated necrotising myopathy background

IMNM is a group of necrotic myopathies, including presentations of IMNM due to adverse medication side effect, anti-signal recognition protein (SRP), and antibody negative forms (5, 42). For instance, 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) plays a key role in cholesterol synthesis and is the target of statin drugs designed to lower cholesterol (43). Adverse effects of these drugs are a documented cause of IMNM, giving rise to the anti-HMGCR myopathy subgroup of IMNM (44). Antibody status and necrotic and regenerating myofibres on muscle pathology are the main identifiers in patients with IMNM. There is a clear lack of lymphocyte infiltrates, though macrophages are present (45, 46). Proximal and symmetrical muscle weakness affects IMNM patients as is typical in other forms of IIMs (47).

Fitness profile in IMNM

IMNM patients have a fitness level that is borderline for the level required for ADL independence. $Vo2_{max}$ was 18.8 ml/kg/min compared to healthy controls with a $Vo2_{max}$ of 26.1 ml/kg/min. Fat content of skeletal muscle is higher in IMNM patients than healthy controls (9). Interventions reporting outcomes on IMNM participants are presented in Table II.

Table II. Effects of exercise on patients with IMNM.

Author/study design	IIM	Exercise type	Intensity	Treatment	Outcome measures	Results	Adverse events
Borges *et al*. (30) 2021/QE	IMNM=6 (HMGCR=3) DM=7 Healthy CON=10	Combined aerobic/RT 12 weeks/ 2 days/week	30-50 min treadmill mod intensity[b,c] 8-12RM	Continue prescribed	$Vo2_{max}$ VL muscle biopsy: Gene expression relevant to autophagy and UPS pathways	$Vo2_{max}$ increase (p=0.397) Increase in genes related to autophagy (p<0.05) Reduction in genes associated with UPS (SKM atrophy) (p<0.05 in some, but not all genes)	N/A
De Oliviera *et al*. (9) 2023/QE	IMNM=6 DM=7 Healthy CON=10	Combined Aerobic/RT 12 weeks/ 2 days/week∞	30-50 min treadmill mod intensity[b,c] 8-12RM	Continue prescribed	VL muscle biopsy: SKM fat content lipid oxidation and insulin pathway gene expression	SKM fat content decreased in type 1 and 2 fibres (p=0.038, p=0.032) Upregulation in genes related to lipid oxidation and insulin (p<0.05).	N/A

QE: quasi-experimental; IMNM: immune-mediated necrotising myopathy; DM: dermatomyositis; ex: exercising group; CON: healthy controls; reps: repetition; 1RM: 1 repetition maximum; RT: resistance training; $Vo2_{max}$: maximal or peak volume of oxygen consumed; SKM: skeletal muscle; VL: vastus lateralis; UPS: ubiquitin-proteosome system (skeletal muscle atrophy).
[b]Moderate intensity training defined as heart rate corresponding with the interval between ventilatory anaerobic threshold (VAT) and respiratory compensation point (RCP) (9).
[c]Exercise intervention described by De Oliveira *et al*. (9).

Table III. Effects of exercise on patients with anti-synthetase syndrome.

Author/study design	IIM	Exercise type	Intensity	Treatment	Outcome measures	Results	Adverse events
De Oliviera *et al*. (9) 2019/QE pilot	ASSD=2 DM=6 PM=1	Combined aerobic/RT 12 weeks/2 days/week∞	8-12RM 30-50 min treadmill mod intensity[b,c] function	Continue prescribed	$Vo2_{max}$ Time to exhaustion Muscle strength 1RM OGTT & β-cell	$Vo2_{max}$ increase without significance (p=0.068, p=0.052) Time to exhaustion increased (p<0.001) 1RM bench press and leg press increased (p=0.002, p=0.013). Hand grip strength did not (p=0.253) Insulin and β-cell function improvement without significance	N/A

QE: quasi-experimental; PM: polymyositis; DM: dermatomyositis; ASSD: anti-synthetase syndrome; 1RM: 1 repetition maximum; $Vo2_{max}$: maximal or peak volume of oxygen consumed; RT: resistance training; OGTT: oral glucose tolerance test.
[b]Moderate intensity training defined as heart rate corresponding with the interval between ventilatory anaerobic threshold (VAT) and respiratory compensation point (RCP) (9).
[c]Exercise intervention described by De Oliveira *et al*. (9).

Summary

Aerobic activity two days per week improved CRF, but not significantly. Muscle strength improvements were observed in bench press and not leg press (9, 30). Two days per week combined aerobic and resistance training protocols upregulated autophagy, which assists in skeletal muscle repair, and downregulated genes associated with skeletal muscle atrophy (30). This population should be encouraged to engage in aerobic activity more than two days per week. Resistance training two days per week at 8-12 repetitions maximum attenuates muscle atrophy and intramuscular lipid deposit (9, 30). There were no adverse events reported.

Antisynthetase syndrome background

ASSD patients may share myopathy qualities with myositis patients, with the additional prominence of interstitial lung disease (ILD), rashes, and arthritis (4). Clinical diagnosis in these patients is assisted by evaluating antibodies called anti-aminoacyl-tRNA (anti-ARS) synthetase antibodies (48). Muscle biopsy typically shows greater perifascicular necrotic findings than in DM (5). ASSD affects women more commonly than men and onset is predominantly in adulthood, post 40 years of age (4, 49).

Fitness profile in ASSD

Fitness levels are borderline to the requirement for ADL independence, with a $Vo2_{max}$ of 16.5 ml/kg/min in ASSD patients compared to 22.4 ml/kg/min in controls. Anaerobic capacity is lower than in DM comparison group (22). Regarding exercise, much is to be characterised as this subset is increasingly recognised and outcome measures are being reported separately from other groups. This group of patients currently lack rigorous studies. Interventions reporting outcomes on ASSD participants are presented in Table III.

Summary

ASSD patients demonstrate an ability to increase muscular strength, $Vo2_{max}$, and functionality comparable to DM and PM patients (29). Individual disease characteristics present challenges to exercise that may arise such as presence of ILD in some ASSD patients. Exercise therapy should be encouraged to address both pulmonary function (50) and IIM related muscle weakness. No adverse events were reported.

Inclusion body myositis background

IBM is unlike other forms of myosi-

Table IV. Effects of exercise on patients with IBM.

Author/study design	IIM	Exercise type	Intensity	Treatment	Primary outcome measures	Results	Adverse events
Jorgensen *et al*. (57) 2018, RCT	IBM ex=11 IBM CON=11	BFR 12 weeks, 2 days/week	3 sets of 25RM Resistance training all major lower-body muscle groups 110 mmHg vascular occlusion	N/A	SF-36 Muscular strength	No change in SF-36 No change in strength in ex group. Decrease in strength in CON (P=0.02)	2 dropouts from ex group: 1 due to severe fatigue 1 due to fall caused by severe fatigue
Wallace *et al*. (61) 2019 Cross-over	IBM n=17	Endurance, 12 weeks, 3 days/week	30-minute cycling 60% $Vo2_{max}$ for 4 weeks 70%$Vo2_{max}$ for 4 weeks 80% $Vo2_{max}$ for the last 4 weeks	N/A	$Vo2_{max}$	Relative $Vo2_{max}$ (ml/kg/min) increase 17.4%	Injurious fall prevented 1 participant from continuing ex post-intervention
Jensen *et al*. (67) 2019, RCT	IBM ex=11 IBM CON=10	BFR 12 weeks, 2 days/week[d]	3 sets of 25RM Resistance training all major lower-body muscle groups 110 mmHg vascular occlusion †		Muscle biopsy of either VL or TA: CD3-, CD8+, CD68-, CD206-, CD244- and FOXP3-positive cells	Increased CD3-/CD8+ in ex group No changes in macrophage or T cell infiltration in ex group (no adverse immune or inflammatory response elicited by BFR)	
Connor *et al*. 2023 (58) RCT cross-over	IBM total=14 Ex+ testosterone=7 Ex+placebo=7	RT 12 weeks, 3 days/week	2 sets of 8 reps per exercise 8–9 exercise per session progressed to 3 sets of 12 reps by week 12	Transdermal testosterone 100 mg (AndroForte 5TM 50 mg/ml) CON=placebo	SF-36 Quadriceps isokinetic muscle strength	Treatment-related increase in well-being (p=0.034) No treatment-associated change in quadriceps strength	4 falls, 1 calf swelling, pain or cramping, and 1 muscle or bone injury reported during ex+placebo

RCT: randomised control trial; IBM: inclusion body myositis; ex: exercising group; CON: healthy controls; VRM: voluntary repetition maximum; reps: repetition; 1RM: 1 repetition maximum; $Vo2_{max}$: maximal or peak volume of oxygen consumed; RT: resistance training; BFR: blood flow restricted resistance training; SF-36: quality of life questionnaire containing multiple parameters; VL: vastus lateralis; TA: tibialis anterior.
[d] Exercise intervention described by Jorgensen *et al*. (57).

tis in several ways. Muscle weakness is typically asymmetrical, affecting distal arm muscle groups such as the forearm finger flexors (51). Histology of muscle tissue is characterised by endomysial inflammatory infiltrates in non-necrotic muscle fibres with several histologic features of degeneration and mitochondrial abnormalities, including rimmed vacuoles, p62 inclusions, and COX-negative fibres (51, 52). Diagnosis typically occurs past the age of 50, but onset may begin prior. Reported sex differences vary, but generally appears to favour increased diagnosis in men (51, 53) with the ratio of men to women in North America at 2:1 (54). Treatment with immunosuppressants is ineffective; however, various therapies including exercise may play a role in management (51).

Fitness profile in IBM

Patients with IBM have a fitness level below the threshold for independence during ADLs, with a $Vo2_{max}$ of 14.3 ml/kg/min and anaerobic threshold lower than normative predicted values (23, 55). The advanced age of onset in IBM patients exposes this subset to increased risk of age-related fat infiltration of skeletal muscle tissue (56), compounding the effects of disease-related muscle weakness. Interventions reporting outcomes on IBM participants are presented in Table IV.

Summary

While not having a significant impact on muscular strength in IBM patients, low resistance blood flow occlusion training may preserve existing strength (57). Reports of the negative impact of fatigue caused by the introduction of a training program on IBM patients merits caution while prescribing exercise to prevent falls (57, 58). Age-related declines in $Vo2_{max}$ and skeletal muscle strength in addition to disease-related muscle weakness is a concern in IBM due to the age of onset (24). The ACSM recommendations for physical activity in adults discussed in the introduction section are the same as the recommendations for older adults with the intent to combat age-related declines (24). It is of particular importance to encourage IBM patients to engage in adapted regular physical activity to preserve independence and mitigate fall risk.

Overall summary and recommendations

Table V displays a summary of recommended weekly exercise prescription for IIM patients. Aerobic capacity increases can be elicited by interventions prescribing aerobic activity for three or more days per week (6, 8, 27), but not two days per week (29). Interventions intended to increase CRF should be performed three days per week or more at an intensity of 70% of $Vo2_{max}$ for at least 30 minutes (27). In prescriptions in which patients exercise at least five days per week, a 15-minute brisk walk at 50-70% of $Vo2_{max}$ may significantly increase aerobic capacity. Combined aerobic and resistance training at least two days per week decreased fat infiltration in skeletal muscle in PM, DM,

Table V. Recommendations for exercise prescription in IIM based on combined experiences of clinicians and exercise physiologists, ACSM recommendations, and previous myositis literature.

Exercise Type	Duration	Intensity	Sessions per week	Recommended outcome measures	Recommended exercise test
Aerobic	≥30min	50-70% $Vo2_{max}$ Or 64-76% maximal heart rate	≥3-5	$Vo2_{max}$ Molecular pathways of research interest (muscle biopsy)	Graded cycle ergometer[c] Modified Bruce treadmill[c]
Resistance	≥3 sets in all major muscle groups with ≥ 1 minute rest	8-12RM Or 30-40% 1RM	≥2	1RM Molecular pathways of research interest (muscle biopsy)	1 or 10RM Grip strength[c]

$Vo2_{max}$: heart rate during exercise should coincide with documented heart rate at the recommended $VO2_{max}$ during exercise testing; RM: repetitions maximum.
[c]: exercise test described in detail by van der Stap *et al*. (65).

and IMNM patients (9). Adverse events due to exercise were minimal throughout studies included in this review.

Pain is commonly reported in IIMs and muscle soreness can be expected upon adopting an exercise regime as well as for a short period after increasing loads, but exercise is otherwise well-tolerated (6, 59). Patients should be encouraged to continue exercise and advised to adjust intensities as tolerated. Developing positive exercise behaviour is important for continued therapy. Exercise intervention that transitions from supervised to unsupervised has lasting effects for long-term physical activity habituation and adherence in IIM patients (60). A fitness centre group exercise setting promotes participation and IBM patients of one study reported a desire to continue exercising post-intervention (61), reflecting the benefits of non-researcher supervised exercise. IIM patients exhibit high adherence to wearing accelerometer devices to track daily activity levels (62), and as such are a prime population for implementing semi-supervised activity interventions. Unsupervised physical activity engagement should be encouraged at-home or gym that is enjoyable to patients and meets the base recommendations presented in Table V.

Developing a belief in one's own ability to carry out exercise sessions, or exercise self-efficacy, in patients is critical for long-term adoption of physical activity habits (63). Barriers to exercise vary individually. A specific barrier given as a reason to cease unsupervised exercise in IIM patients was a lack of free gym membership (61). Financial burden is high in myositis patients due to the costs of treatment and recovery (64). Strategies for building self-efficacy and combatting the monetary costs of independent exercise should be considered while encouraging exercise in IIM patients.

Individual IIM subset characteristics such as arthritis, finger flexor weakness, or ILD must be accounted for to create personalised exercise prescriptions that are manageable for each individual and boost self-efficacy and adherence. For instance, weakness of forearm finger-flexors in IBM (51) presents the need to prescribe activities that avoid the necessity of holding objects such as bands or bars. As such, exercise interventions may vary across subsets.

Limitations and future directions

Current limitations in studies of exercise interventions in myositis are a lack of standardised exercise fitness testing and outcome measures as well as disease and age diversity in IIM. Delphi consensus on fitness testing in IIM concluded several objective outcome measures (65) that are included in the recommendations in Table V.

Standardised volumes of resistance training should be reported in sets, repetitions, and intensities. Resistance volumes reported in the interventions within this narrative review vary across studies. Future studies should strive to fulfil a quantifiable volume modelled after ACSM standards (24) or as suggested in the recommendations in Table V.

Another limitation is that a small portion of original studies have recently begun reporting outcomes by myositis subgroup (22, 30) whereas many studies reported in this narrative review did not. The scope of heterogeneity in IIM was not as well-established during early interventions as it currently is. While the goal of attenuating disease progression in all IIM patients is universal, the importance of characterising individuals of each IIM subgroup is highlighted by this narrative. Maintaining statistical power despite the rarity of presentation in each IIM subset is a limitation in experimental trials. However, future research requires subgroup analysis and reporting while investigating molecular mediators of exercises' benefits. Additionally, a greater understanding of the role of exercise early in disease may further improve long-term prognosis.

Conclusion

Exercise intervention results and their overall safety are evidence for encouraging clinicians to utilise physical therapy and fitness professionals as resources to assist patients in developing lifelong exercise behaviours outside of the research setting. While the benefits of exercise are clear, adherence remains an issue. Further research should help identify ideal exercise programs in the acute and chronic phases of disease, potential modulation of the molecular mediators of exercise due to muscle inflammation, and adherence methods specific to the context of IIM patients. Exercise should be a cornerstone of treatment in myositis.

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