Blended therapy

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Blended Therapy

An innovative approach to implement
and promote adherence to physical
exercise training in patients with
Inflammatory Myopathy

Pierrette Baschung Pfister

**Blended Therapy - an innovative approach to
implement and promote adherence to
physical exercise training in patients with
Inflammatory Myopathy**

Pierrette Baschung Pfister

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Blended Therapy - an innovative approach to implement and promote adherence to physical exercise training in patients with Inflammatory Myopathy

DISSERTATION

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List of abbreviation

ACR	American College of Rheumatology
app	application
AUC	Area Under the Curve
COSMIN	COnsensus-based Standards for the selection of health status Measurement INstruments
DM	Dermatomyositis
EULAR	European League Against Rheumatism
FITT	Frequency, Intensity, Type and Time
FI-2	functional index 2
GC	Glucocorticoids
HAQ	Health Assessment Questionnaire
HHD	hand-held dynamometry
HR _{max}	maximum Heart Rate
HRQOL	health related quality of life
IBM	Inclusion Body Myositis
IM	inflammatory myopathy
IVIG	intravenous immunoglobulins
MAP	Myositis Activity Profile
MMT	Manual Muscle Testing
MSA	myositis-specific autoantibody
PM	Polymyositis
PROM	patient reported outcome measure
SF-36	Short-Form-36
SEM	Standard Error of Measurement
SDC	Smallest Detectable Change
TPs	Training Principles
TR	Telerehabilitation
USZ	University Hospital Zurich
VO _{2max}	maximum oxygen consumption

CHAPTER 1

General Introduction

Idiopathic inflammatory myopathy

The term Inflammatory Myopathy (IM), more generally known as myositis, refers to a group of rare heterogeneous neuromuscular disorders characterized by chronic proximal muscle inflammation and weakness. Patients with IM share a common clinical presentation of skeletal muscle weakness leading to functional disability and increased morbidity and mortality. The rarity of the disease and its heterogeneity makes the diagnosis and the treatment both complex and challenging. Physical exercise is indicated for all subtypes of IM to counteract the illness itself, but also to reduce side effects from medical treatments, to prevent common comorbidities such as heart or lung involvement, and to enhance general health. Due to its different manifestations, diagnosis of the disease is often delayed, by which time muscle weakness is more pronounced.

Diagnosis and classification criteria

Traditionally, IM has been classified and diagnosed into five major subgroups, according to the Bohan and Peter criteria (1). These subgroups include polymyositis (PM), dermatomyositis (DM), juvenile dermatomyositis, overlap myositis (myositis combined with another distinct rheumatological diagnosis), and myositis associated with cancer. Later on, an additional subgroup named Inclusion Body Myositis (IBM) was described (2). Due to a deeper understanding of the pathophysiology involved, clinical features, and myositis-specific autoantibodies (MSAs), various new IM subtypes, such as immune-mediated necrotizing myopathy (IMNM) and antisynthetase syndrome (ASS), have been discovered (3), and several new classification systems based on experts' opinions were thus proposed (4). Despite these new developments, the Bohan and Peter Criteria have continued to be the most widely used criteria for more than 40 years, even though they have some limitations (4).

The strong need for new, more generally accepted classification criteria was recognized and international experts in adult and pediatric rheumatology, neurology, dermatology, epidemiology and biostatistics agreed in 2004 to develop these for IM and its major subgroups. The goal was to develop criteria that would distinguish IM from other neuromuscular diseases and at the same time categorize them into major subgroups (5). In 2017, these EULAR/ACR (European League Against Rheumatism / American College of Rheumatology) Classification criteria, based on age of onset, muscle weakness, skin manifestation, dysphagia or esophageal dysmotility levels, laboratory measurements and muscle biopsy results, for Adult and Juvenile IM

and its subgroupings, were finally published. Based on sixteen variables, the probability of having an IM can be defined by adding up the score values as illustrated in figure 1. Depending on the availability of muscle biopsy testing, individual criteria contribute differently to the total score. Probable IM corresponds to a probability of between 55 and 90% (score of 5.5 without biopsies; 6.7 with biopsies), while definite IM corresponds to a probability of at least 90% (score of 7.5 without biopsies; 8.7 with biopsies) (6).

Figure 1: The EULAR-ACR classification criteria for adult and juvenile IM and their major subgroups (6)

Variable	Score points	
	A: Without muscle biopsy	B: With muscle biopsy
Age of onset		
Age of onset of first symptom assumed to be related to the disease ≥ 18 and < 40 years	1.3	1.5
Age of onset of first symptom assumed to be related to the disease ≥ 40 years	2.1	2.2
Muscle weakness		
Objective symmetric weakness, usually progressive, of the proximal upper extremities	0.7	0.7
Objective symmetric weakness, usually progressive, of the proximal lower extremities	0.8	0.5
Neck flexors are relatively weaker than neck extensors	1.9	1.6
In the legs, proximal muscles are relatively weaker than distal muscles	0.9	1.2
Skin manifestation		
Heliotrope rash	3.1	3.2
Gotttron's papules	2.1	2.7
Gotttron's sign	3.3	3.7
Other clinical manifestations		
Dysphagia or esophageal dysmotility	0.7	0.6
Laboratory measurements		
Anti-Jo1 autoantibody present	3.9	3.8
Elevated serum levels of CK or LDH* or ASAT/AST/SGOT* or ALAT/ALT/SGPT*	1.3	1.4

Figure 1: continued

Variable	Score points	
	A: Without muscle biopsy	B: With muscle biopsy
Muscle biopsy features—presence of:		
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibres		1.7
Perimysial and/or perivascular infiltration of mono nuclear cells		1.2
Perifascicular atrophy		1.9
Rimmed vacuoles		3.1

Legend: *Serum levels above the upper limit of normal, ACR: American College of Rheumatology, EULAR: European League Against Rheumatism, IM: inflammatory myopathy, CK: creatine kinase, LDH: lactate dehydrogenase, ASAT/AST/SGOT: aspartate aminotransferase, ALAT/ALT/SGPT: alanine aminotransferase

Patients who meet the EULAR-ACR classification criteria (probability of IM $\geq 55\%$) can be classified in different subgroups according the classification decision tree (see figure 2).

The development of the EULAR-ACR classification criteria was a protracted but very important process. In the meantime, new MSAs and clinical presentations were discovered and thus some patient categories were still excluded (for example those with only interstitial lung disease and MSAs or the anti-synthetase syndrome) (4, 7). Therefore, it is important to update the classification criteria regularly.

The existence of different classification criteria led to inconsistent classification in published studies. Inflammatory myopathies have long been designated under the generic terms PM and DM and newer syndromes such as immune-mediated necrotizing myopathy or anti-synthetase syndrome were subsumed within the PM classification (8, 9).

Figure 2: Classification tree for subgroups of IM (6)

Legend: *finger flexor weakness and no improved response to treatment, **rimmed vacuoles in muscle biopsy, ACR: American College of Rheumatology, ADM: amyopathic dermatomyositis, DM: dermatomyositis, EULAR: European League against Rheumatism, IBM: inclusion body myositis, IM: inflammatory myopathy, IMNM: immune-mediated necrotising myopathy, JDM: juvenile dermatomyositis, PM: polymyositis.

Prevalence and incidence

The worldwide reported overall IM incidence, between 1957 and 2010, was estimated at 7.98 cases/million/year (95% CI 7.38, 8.66), with an overall prevalence rate of 14 cases per 100.000 habitants (95% CI 12.84, 15.46). Due to different case identification (surveys constructed from health system administrative databases generally found higher incidence and prevalence than those from hospital records) and diagnosis criteria, the variation in reported incidence (1.16 to 19/million/year) and prevalence (2.4 to 33.8/1000.000) values was considerable (8). Also recently published studies have shown different overall IM incidence and prevalence rates. For example, the Swedish nationwide population-based register study reported higher incidence and prevalence rates (11 per million person years and 14 per 100.000 respectively), in comparison with incidence and prevalence rates of 2.9–5.2 per million person years and 2.3–4.4/100.000 persons respectively, in a Korean study (10, 11).

Considering only adult IM, the review from Meyer et al. revealed an even larger incidence and prevalence range than for overall IM. Whereas the majority of the studies (12-18) reported incidence rates between 3.7 and 10.7, two studies from the USA reported much higher incidence rates of 66 and 42.7/million year (19, 20). Also two recently published regional studies from Salford (UK) and Ljubljana (Slovenia) including only adult IM cases revealed rather high incidence rates of 17.6/million person years and 11.5/million person years, respectively, although not as high as the USA-studies (21, 22). This substantial variability could be attributed to methodological heterogeneity. Higher estimates are reported in register-based studies where cases are defined using administrative codes, thus potentially overestimating the true incidence or prevalence. Conversely, lower estimates are found in studies where cases are defined using classification criteria and biopsy findings, thus potentially underestimating the true incidence/prevalence (11). Other reasons could be age and sex of the included population, or increased awareness of the diseases (20). Although there is a broad variation in the reported data there is no clear geographical disparity (8, 10). However, all studies evaluating time course agreed that recent publications show a higher incidence rate than previous ones, indicating increased awareness of these diseases but also improved medical record indexing and diagnostic tool usage (8, 22, 23). Another similarity is that IM is more prevalent in women than in men (8, 21, 22).

Clinical manifestation

The cardinal symptom of IM is progressive muscle weakness (24). In general, proximal region muscle groups are weaker than distal regions, lower extremity groups are weaker than upper extremity groups, and no significant asymmetry is detected. Hip flexors, hip extensors, hip abductors, neck flexors and shoulder abductors are the five most affected muscle groups for all IM subgroups (25). However, many people with IM may have the added burden of distal weakness (26). In DM the wrist flexors and in PM the knee extensors and ankle plantar flexors are all known to be additionally affected (25), while in both groups grip force is significantly lower compared to gender- and age-matched healthy controls (27). This muscle weakness leads to functional limitations such as getting up from a chair, lifting objects or combing hair (28, 29). Not only isometric muscle strength, but also dynamic repetitive muscle function, is impaired (30, 31). This reduction of muscle endurance may be more clinically relevant than decreased muscle strength. Limitations in activities requiring muscle endurance, such as walking, biking,

climbing stairs and running, are very common (32, 33). IBM is also considered an IM. It has specific clinicopathological features, separate classification criteria (2) and these patients are more disabled compared to those with DM, PM and other connective tissue disorders (34). In IBM an early involvement of the finger flexors and quadriceps muscles is common (35). The latter leads to increased risk of falling, walking difficulties and frequent need for walking devices (24, 36). However, patients with IBM presented lower mean values for myositis-related pain than the other subtypes (34).

In addition, patients with IM have decreased aerobic capacity with reduced peak oxygen consumption (37, 38). This decrease in aerobic capacity may be related to an impaired skeletal muscle oxidative capacity presenting as elevated levels of blood lactate and a low proportion of type 1 muscle fibers (39, 40). It may also be a consequence of lung and cardiac involvement in this disease (41). Due to the systemic nature of IM, a broad spectrum of organ manifestation is common. Depending on the subtypes, skin, joints, lung, gastrointestinal tract and/or heart can be affected (4).

These muscle and extra-muscular organ impairments contribute to various clinical features such as fatigue (34, 42), pain (28, 34, 43), disability (34, 44, 45), decreased health-related quality of life (27, 29, 44, 46-50) and high mortality rates (29, 45, 48, 51). In addition, patients with IM have a higher risk of venous thromboembolism, pulmonary embolism and deep vein thrombosis (52).

Treatment

Due to a lack of randomized controlled trials and the rarity and heterogeneity of the disease, there are no standardised therapeutic guidelines (53, 54). Glucocorticoids (GC) are the anchor drug of initial treatment for myositis, but due to its side effects, additional medication is needed to suppress or modify the immune system (55). It is generally agreed that first-line therapy should include glucocorticoids in combination with immunotherapeutic agents such as methotrexate or azathioprine. GC are able to reduce muscular inflammation and improve muscle symptoms in more than 60% of treated patients. Due to the known side effects of this effective drug, high dosage of GC should gradually be reduced. Tapering schemes vary, but a reasonable approach is to maintain a high dose for 2-4 weeks before then gradually reducing this by 20-25% monthly until a daily intake of 5-10 mg of prednisone or equivalent dose is achieved. As second-line therapy, the immunosuppressive drug mycophenolate mofetil or calcineurin inhibitors (ciclosporin or tacrolimus) are recommended. In refractory patients who have not responded

to these second line drugs, biologic agents such as rituximab or cyclophosphamide are indicated (53, 54). An additional promising medical treatment is intravenous immunoglobulin (IVIG), which suppress immune-mediated processes. IVIG therapy can be used either in combination with immunosuppressive agents or else alone and can even be used in pregnancy. Because of the extremely high financial costs involved, this agent is mainly used in severe and refractory patients (56). While most subtypes of IM react well to medical treatment, most patients with IBM are refractory to pharmacological intervention. There is no evidence that any specific treatment is effective for this disease (57, 58). As medications only reduce inflammation but do not restore muscle performance, physical exercise is an important component in the treatment of myositis (7). Exercise may not only optimize physical function and quality of life and reduce disease activity, but also helps to prevent some steroidal side effects such as weight gain, osteoporosis and type 2 atrophy (28, 59).

Physical exercise

Nowadays, physical exercise is a well accepted and essential part of current treatment recommendations (7, 28, 53, 54). Historically, patients with IM have been discouraged to exercise due to the fear that it could damage muscles and might aggravate inflammation (54). Until the nineteesixties, the majority of physicians accepted immobilisation and even bed rest as the principle treatment for inflammatory diseases (60). As recently as 1993, the first case studies approving the safety of resistance training in the management of active as well as chronic IM emerged (61, 62). Five years later, the first study confirming the safety of endurance training was published (63). Since then, several studies have found beneficial effects of resistance and endurance training without exacerbation of disease progression. Interestingly, physical exercise may not only improve muscle function, aerobic capacity, pain, fatigue, activities of daily living and health related quality of life (64), but might also have the capacity to reduce disease activity and inflammatory markers (38, 65-67), normalize high blood lactate levels (68), and increase the number of capillaries in the muscles (66).

Physical exercise is defined for the purpose of this thesis as physical activity that is planned, structured, repetitive, and designed to improve or maintain physical fitness, physical performance and health. It is in turn a subcategory of physical activity, which is defined as any bodily movement produced by skeletal muscles that results in energy expenditure (69). A physical exer-

cise program can include several subtypes, such as cardiorespiratory, resistance, flexibility, and neuromotor (e.g. balance, agility, coordination) training (70), and should consider training principles which include specificity, progression, and overload (71). A physical exercise program can only be replicated if it specifically describes the frequency, intensity, type and time of the included exercises (70). Although physical exercise is an established adjunct in the treatment of IM, there is no consensus about the best kind of training regime. Therefore, there is a strong need for specific training recommendations that go beyond the general advice of exercising and staying active.

Outcomes Measures

In previous decades, there were only a few commonly used outcome measures and most of them were not validated for patients with IM (72). Therefore, to improve and standardize the conduct and reporting of clinical trials and to enhance the identification of effective treatment, the International Myositis Assessment and Clinical Studies Group (IMACS) developed consensus core set domains and measures for the assessment of disease activity, disease damage and patient-reported outcomes (73, 74). Disease activity is defined as the reversible manifestations resulting directly from inflammatory process, whereas disease damage is reflected in persistent changes in anatomy, physiology, pathology or function resulting from prior active disease as well as from complications of therapy or other events (73). Table 1 presents the partially validated core set domains and measures for the assessment of disease activity, disease damage and patient-reported outcomes in adult patients with IM.

Table 1: core set domains and measures (75)

Disease Activity Core Set Measures
<ul style="list-style-type: none">• Physician Global Activity - 10cm Visual Analogue Scale• Patient/Parent Global Activity - 10-cm Visual Analogue Scale• Muscle Strength - Manual Muscle Testing (MMT)• Physical Function - Health Assessment Questionnaire (HAQ)• Laboratory - At least 2 of CK, LDH, AST, ALT, or aldolase tests• Extra-Muscular Activity - Extramuscular portion of the Myositis Disease Activity Assessment Tool
Disease Damage Core Set Measures
<ul style="list-style-type: none">• Myositis Damage Index• Physician Global Damage - Visual Analogue Scale• Patient/Parent Global Damage - Visual Analogue Scale• Muscle Strength - MMT• Physical Function - HAQ
Patient Reported Outcomes
<ul style="list-style-type: none">• Health Related Quality of Life using SF-36

For all measures of the disease activity core set, the degree of clinically meaningful improvement was defined. For domains of muscle strength and physical function, a minimum improvement of 15%, for physician and patient global assessment a minimum improvement of 20% and for serum levels of muscle associated enzymes a minimum improvement of 30% were each considered to be clinically meaningful (76). Because no single core set outcome adequately covers all important domains, a set of composite response criteria was developed based on these defined amounts of improvement. These preliminary defined response criteria, published in 2004, were as follows: three out of any six measures improved by at least 20%, with no more than two measures worsened by 25% (which cannot be MMT) (77). These preliminary criteria were not prospectively validated and had potential limitations including equal weights being applied to each core set measure, a lack of quantitative or continuous outcomes, and ceiling effects in some core sets measures (7, 9). Therefore, revised response criteria for minimal, moderate and major clinical improvement were developed and validated through a complex data and consensus-driven process involving multiple clinical data sets and the international myositis community. These new improvement criteria, generating a total improvement score between 0 and 100, were released in 2017. The total score is the sum of the improvement reflected in each of the six core set measures (table 2). In order that those measures deemed to be more important can provide a greater contribution to the final score, the single core set measures were weighted (9). These new response criteria also have limitations; most notably some core set measures on which

the criteria are based are subjective and evaluator dependent and fail to differentiate between no change and worsening, thus being of no use for disease flare or remission state (75).

Table 2: Final myositis response criteria for minimal, moderate, and major improvement (75)

Core set measure, level of improvement based on absolute percent change	Improvement score
Physician global activity	
Worsening to 5% improvement	0
>5–15% improvement	7.5
>15–25% improvement	15
>25–40% improvement	17.5
>40% improvement	20
Patient global activity	
Worsening to 5% improvement	0
>5–15% improvement	2.5
>15–25% improvement	5
>25–40% improvement	7.5
>40% improvement	10
Manual muscle testing	
Worsening to 2% improvement	0
>2–10% improvement	10
>10–20% improvement	20
>20–30% improvement	27.5
>30% improvement	32.5
Health Assessment Questionnaire	
Worsening to 5% improvement	0
>5–15% improvement	5
>15–25% improvement	7.5
>25–40% improvement	7.5
>40% improvement	10
Enzyme (most abnormal)	
Worsening to 5% improvement	0
>5–15% improvement	2.5
>15–25% improvement	5
>25–40% improvement	7.5
>40% improvement	7.5
Extramuscular activity	
Worsening to 5% improvement	0
>5–15% improvement	7.5
>15–25% improvement	12.5
>25–40% improvement	15
>40% improvement	20

Legend: The total improvement score is the sum of all six improvement scores associated with the change in each core set measure. A total improvement score of ≥ 20 represents minimal improvement, a score of ≥ 40 represents moderate improvement, and a score of ≥ 60 represents major improvement.

Beside these core set measures which should be used in all trials, additional assessment may be useful depending on the aim and nature of the study. On the one hand, affected domains that are not included in the core

set need to be further explored. On the other hand, more illness-specific, reliable, valid and responsive measures that evaluate core domains should be developed, evaluated and implemented. In studies evaluating physical exercise, these additional assessments should focus on physical impairments such as muscle weakness / reduced muscle strength or decreased peak oxygen consumption, on functional limitations resulting from these impairments, on subsequent disabilities, and on potentially affected health-related quality of life.

The outcome 'muscle strength' is not easy to operationalize because the term has no single meaning (78). In general, muscle strength is defined as the capacity of muscle to produce force and generate muscle tension (79). For some authors muscle strength is a generic term and they include several subtypes such as isometric, dynamic and explosive strength in the definition (80), whereas other authors define it more specifically as the maximal force the muscle can exert isometrically in a single effort (81). According to the American College of Sports Medicine (ACSM) 'muscular fitness' is composed of the functional parameters of strength (ability to generate the maximal amount of muscle force), endurance (ability to produce and maintain muscle force over a sustained period of time) and power (ability to generate enough force to move weight in the shortest amount of time possible) (70). Furthermore, muscle strength can be measured with either dynamic or static muscle contraction. Whereas dynamic muscle contraction contains both concentric and eccentric action, static measurements record the greatest voluntary muscle tension the patient can exert against immovable resistance. A special kind of dynamic test is isokinetic measurement: This is an elaborate method using apparatus in which dynamic force development is measured at constant speed (79). To prevent any possibility of confusion it is better to use the term 'muscular fitness' or 'muscle performance' when talking about general muscle strength and otherwise to use specific terms such as for example 'isometric maximal strength' or '12 repetition maximum'.

In IM-trials, different kinds of muscle strength tests were applied, but generally, isometric maximum strength was assessed. The most frequently used assessment, however, is Manual Muscle Testing (MMT) (75). This is also the only assessment that directly captures muscle weakness. The other tests used in IM-trials (hand-held or fixed dynamometry) measure muscle weakness indirectly, by recording the peak force a subject can generate.

MMT has high practicality, low testing time and few equipment requirements, but dynamometry is more objective and less examiner dependent. So far, the clinimetric properties of MMT and dynamometry in IM have not been

tested conclusively and the two tests have never been compared to each other. Therefore, it is not known which test should be preferred in IM trials. A sophisticated but more expensive and time-consuming method is isokinetic testing. It might be more reliable than other tests and could therefore provide a useful instrument for monitoring therapy progress (82). However, because of the high costs of isokinetic test systems, they are less suitable in clinical practice.

In addition to isometric strength testing, muscle endurance testing is – although not a core set measure – a well established one within the myositis community. The Functional Index 2 (FI-2) is a valid and reliable tool testing muscle endurance of seven muscle groups (shoulder flexion, shoulder abduction, neck flexion, hip flexion, step test, heel lifts, toe lifts) (83). The FI-2 is well tolerated by patients and does not require expensive equipment (75). As this test is rather time consuming (20-30 minutes) a shorter version, FI-3, has been developed and is now undergoing validation (7). Aerobic capacity, also called cardiovascular endurance, is the ability of the heart and lungs to provide the body with oxygen and can be expressed as maximum oxygen consumption (VO_{2max}). Tests of cardiovascular endurance can be divided into maximal aerobic tests, which determine VO_{2max} directly, and submaximal aerobic tests, which predict aerobic capacity using a submaximal exercise protocol (84). There are many different test protocols available, but so far none of them have been evaluated in patients with IM.

In 2016 a candidate core set of fitness and muscle strength tests was published. This core set includes 1) the (treadmill) modified Bruce protocol, 2) the (cycle ergometer) incremental exercise test, 3) the 6 minute walking test for aerobic capacity, 4) handgrip strength and MMT for muscle strength, and 5) FI-2 for muscle function. Initially, the expert panel suggested performing an additional test when an MMT score of ≥ 6 is achieved in a particular muscle group. However, none of the proposed tests reached consensus (84). Although not included in this core set, different tests to assess functional limitations were used, but none of them became widely accepted. Two promising assessments with good reliability and validity in patients with IM are the 30-second chair stand and the 30 second arm curl (85).

Whereas muscle impairment and functional limitations can be tested with objective assessments, disability and health-related quality of life are more complex constructs that must be captured through patient-reported outcome measures (PROMs). Two often used PROMs are the Short-Form-36 (SF-36) and the Health Assessment Questionnaire (HAQ) (72). The main advantages of these PROMs are their generic, universal, multidimensional character and

their availability in many languages. Therefore, they are suitable tools to compare different diseases. The HAQ captures disability in eight functional domains, consisting of dressing, arising, eating, walking, hygiene, reach, grip and social activities (86) and is well validated in patients with IM (75). The SF-36 is aimed at quantifying health related quality of life (HRQOL) and includes 36 questions divided into eight subscales: limitations in physical activities because of health problems, limitations in social activities because of physical or emotional problems, limitations in usual role activities because of physical health problems, bodily pain, general mental health (psychological distress and well-being), limitations in usual role activities because of emotional problems, vitality (energy and fatigue), and general health perceptions. The eight subscales can be divided into two main components: physical component summary (PCS) and mental component summary (MCS) (87). The only disease-specific PROM is the Myositis Activity Profile (MAP). In this, patients indicate their limitations in 32 different activities which are divided into four subscales (movement activities, activities of moving around, personal care, and domestic activities) and four single items (keeping in touch with close friends and relatives, avoiding overexertion during daily activities, being able to cope with work and/or housework to a satisfactory degree, and being able to undertake recreational activities of choice). The MAP assesses activity limitation with a broader perspective, meaning that “difficulty” pertains both to how hard it is for the patient to complete an activity, as well as to how important it is to the individual to be able to perform that particular activity. Patients have to weigh their difficulties with their needs when answering the questions. The MAP was developed in Sweden and later translated into English (32, 88). As these currently used PROMs do not cover the symptoms and effects of the disease that are most important for patients with IM (33, 89), the Outcome Measures in Rheumatology (OMERACT) working group defined a research agenda to develop adequate PROM (90).

Telerehabilitation

Despite the encouraging effects seen in patients with IM who exercised, it remains a challenge for these patients to start and maintain a physical exercise program. In addition to muscle weakness and low endurance, caused by the chronic inflammation of skeletal muscle and microangiopathy with loss of capillaries, patients with IM often suffer from fatigue. Besides these disease-intrinsic features, the tendency of patients with IM to avoid strenuous physical activity further exacerbates the physical deconditioning process.

This vicious circle is worsened even more by the common catabolic side effect of steroids on muscle metabolism and may be supported by the patient's fear of disease exacerbation. This fear may be reasoned by the fact that until the 1990s patients with an inflammatory disease were discouraged from physical exercise because it was believed that it would worsen inflammation. Furthermore, physiotherapists trained in the treatment of patients with IM are relatively rare, which in turn makes it difficult to ensure an appropriate, standardized and high-quality therapy to address problems of physical activity. Additionally, clinical experience from Alexanderson & Lundberg (2012) revealed problems with sustained adherence to home based physical exercise programs, suggesting that future research should focus on sustained physical activity and exercise in these patient groups (91).

It is a challenge not only to maintain but also to start a physical exercise program, particularly for inactive persons (92). Interventions with integrated assistive technology devices have, in this context, the potential to help in overcoming some of the barriers to starting training (93). From two studies we know that it is feasible to apply assistive technology devices with the aim of encouraging performance of physical exercise with the use of motivational strategies in independently living older adults (93, 94).

Telerehabilitation (TR), a subfield of telemedicine, may help to overcome some of the barriers to regular exercise. TR may be defined as the provision of rehabilitation services from a distance using telecommunication technologies as the delivery medium. This approach may optimize the timing, intensity and sequencing of interventions and provide opportunities for individuals to receive specialised care rehabilitation in their own social and professional environments, thus enhancing the availability and capacity of rehabilitation programs. Initial promising positive experience with TR has already been gained in different therapeutic settings, such as stroke rehabilitation (95-100), knee arthroplasty (101, 102), chronic obstructive pulmonary disease (103, 104), multiple sclerosis (99, 105), and cerebral palsy (106). An additional advantage of TR is the possibility of implementing different persuasive technologies such as personalisation, self-monitoring, tailoring, goal setting, comparison and conditioning through positive and negative reinforcement in the development of physical exercise programs. These technologies help to make such programs more enjoyable and, therefore, potentially enhance patients' motivation to exercise regularly (107).

The effect size comparison in the use of web-based interventions compared to non-web-based interventions shows an improvement in outcomes

for individuals using the former approach, in terms of achievement of specified knowledge and/or behavioural change (108). Furthermore, the importance of individual and social support has been highlighted in several reviews evaluating health behaviour change (108-111). This kind of support can be integrated in the design of web-based interventions and it can further be enhanced by blending such interventions with face-to-face sessions. The so-called blended therapy is a promising approach, combining the advantages from traditional rehabilitation and new technologies (112, 113).

The usage of interactive health care applications has often been hampered by poor design, making them complicated to use. Consequently, usability testing is an essential step for developing usable and enjoyable products and for identifying flaws in an early system's design (114, 115). Usability, defined as the extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency and satisfaction in a specific context of use, is a fundamental step in the user-centred design process (116). Therefore, it seems necessary to perform an exploratory pilot study to test usability of newly developed health care applications (117).

Objectives of the thesis

The primary objectives of the thesis were to develop an interactive, tablet-based exercise application (app), to test its usability, to explore therapists' opinion for using this new app in a clinical setting and to evaluate feasibility of a blended therapy approach, combining this app with face-to-face physiotherapy sessions in patients with IM. The secondary objectives were to evaluate the most effective physical exercise program and to develop evidence-based training guidelines for patients with IM. Finally, the tertiary objectives were to evaluate clinimetric properties of two maximum strength tests and to translate and validate the Myositis Activity Profile.

Outline of the thesis

The safety and beneficial effects of physical exercise in patients with IM have been acknowledged and resulted in the inclusion of physical exercise in recognized treatment recommendations. Nevertheless, study results were not consistent. One reason for this might be the application of different training protocols. Therefore, this thesis started with a systematic review about the relevance of applying exercise training principles and the reporting of FITT components (frequency, intensity, time, and type) in the training prescription and the adherence to the training in IM (**Chapter 2: The relevance of applying exercise training principles when designing therapeutic interventions for patients with inflammatory myopathies: a systematic review**). Subsequently, evidence-based training guidelines were developed (**Chapter 3: Entwicklung eines Trainingsleitfadens für Patienten mit entzündlicher Muskelerkrankung / Development of an Exercise Guideline for Patients with Myositis**). As the training protocols of the published studies were insufficiently reported, clinical experience from specialist physiotherapists and the general training guidelines of the American College of Sports Medicine were also considered to develop these guidelines.

Although muscle strength is the core symptom of IM, there exist no valid and reliable assessments to measure it. MMT is the most used assessment for evaluating muscle strength, despite known uncertainties concerning reliability and validity. Another promising and more objective assessment is hand-held dynamometry (HHD). The clinimetric properties of HHD in IM are also insufficiently investigated. Furthermore, it is not known if both assessments measure the same outcome, namely maximum muscle strength, and could therefore be used interchangeably. To know which assessment we should use in the feasibility study, we evaluated reliability of MMT and HHD as well as correlation between these two maximum strength tests (**Chapter 4:**

Manual muscle testing and hand-held dynamometry in people with inflammatory myopathy: An intra- and interrater reliability and validity study). Physical exercise is not only expected to improve muscle strength, but also to reduce disability. Therefore, we needed a reliable and valid assessment to evaluate disability in IM. The only appropriate disease-specific questionnaire which was available was not yet translated and validated in German. Therefore, we translated the MAP and assessed validity and reliability of this new German version. (**Chapter 5: Reliability and validity of the German version of the Myositis Activities Profile (MAP) in patients with inflammatory myopathy**). Even though individually tailored, therapeutic exercise is safe and recommended for patients with IM it is still challenging to start and maintain a physical exercise program. Unfortunately, physical exercise has almost no depot effect, meaning that it should be continuously performed to maintain the benefits. Therefore, ideally it needs to become a part of the daily routine. Such a change of lifestyle behavior is very demanding and needs the support of (health) professionals. In our digital era, the use of new telecommunication technologies is a good way to help accomplish such a behavioral change process. With a blended therapy approach, we can combine the advantages from new technologies and personal support. With this in mind, we developed an interactive, tablet-based, exercise application (app), tested its usability and explored therapists' opinion for using this new application in a clinical setting (**Chapter 6: Usability and acceptance of an interactive tablet-based exercise application: a mixed methods study**). Finally, based on the results of the previous study, we evaluated feasibility of a blended therapy approach, combining this app with face-to-face physiotherapy sessions in patients with IM (**Chapter 7: Feasibility of a blended therapy approach in the treatment of patients with inflammatory myopathies**). This study evaluated feasibility in terms of recruitment rate, attrition rate, adherence, acceptance of the app and satisfaction with the blended approach. Furthermore, potential impacts on muscle strength, muscle function, activity limitation, disability and HRQOL were evaluated. Figure 3 illustrates the outline of this thesis. The last chapter (**Chapter 8: general discussion**) provides a general discussion of this thesis, including implications for clinical practice and recommendations for future research.

Figure 3: flow chart summarising the outline of this thesis

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CHAPTER 2

The relevance of applying exercise training principles when designing therapeutic interventions for patients with inflammatory myopathies: a systematic review

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Abstract

Physical exercise seems to be a safe and effective intervention in patients with inflammatory myopathy (IM). However, the optimal training intervention is not clear. To achieve an optimum training effect, physical exercise training principles must be considered and to replicate research findings, FITT components (frequency, intensity, time, and type) of exercise training should be reported. This review aims to evaluate exercise interventions in studies with IM patients in relation to (1) the application of principles of exercise training, (2) the reporting of FITT components, (3) the adherence of participants to the intervention, and (4) to assess the methodological quality of the included studies. The literature was searched for exercise studies in IM patients. Data were extracted to evaluate the application of the training principles, the reporting of and the adherence to the exercise prescription. The Downs and Black checklist was used to assess methodological quality of the included studies. From the 14 included studies, four focused on resistance, two on endurance, and eight on combined training. In terms of principles of exercise training, 93% reported specificity, 50% progression and over- load, and 79% initial values. Reversibility and diminishing returns were never reported. Six articles reported all FITT components in the prescription of the training though no study described adherence to all of these components. Incomplete application of the exercise training principles and insufficient reporting of the exercise intervention prescribed and completed hamper the reproducibility of the intervention and the ability to determine the optimal dose of exercise.

Abbreviations

DM	Dermatomyositis
FITT	Frequency, intensity, time, and type of exercise
IBM	Inclusion body myositis
IM	Inflammatory myopathies
PE	Physical exercise
PM	Polymyositis
RCT	Randomised controlled trail
RPE	Rating of perceived exertion and pain

Introduction

Dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM) belong to inflammatory myopathies (IMs), a group of autoimmune syndromes leading to chronic diseases of the musculature characterised by proximal muscle weakness. IM may also be present as a part of a multisystem disorder in other connective tissue diseases, most commonly scleroderma, systemic lupus erythematosus, mixed connective tissue diseases, and Sjögren Syndrome [1]. Several epidemiological studies report incidence rates varying widely between 0.1 and 7.89 cases per 100,000 annually [2–4]. Interestingly, recent publications show a higher incidence rate than previous studies, indicating increased awareness of this disease but also improved screening methods [5]. Although relatively rare, IMs pose a significant economic burden causing increased medical costs and resource usage as well as high patient burden [6, 7]. The most prominent clinical features in all sub-categories of IM are proximal and (often) symmetric muscle weakness and low muscle endurance, combined with progressive decline over a period of weeks or months. These features result in significant disabilities [8, 9]. Patients often report increasing difficulties in performing everyday tasks, such as self-care or household chores, combined with limited community mobility [1, 8]. Additionally, muscle weakness is a known risk factor for postural instability and falls [10, 11], and there is evidence that falling is common in patients with IBM [8]. The benefit of targeted physical exercise (PE) in patients with IM has been acknowledged and resulted in the inclusion of physical training which aims to improve performance without exacerbating disease progression in recognised treatment recommendations [2, 12, 13]. PE is a safe intervention and may not only improve strength and endurance but also seems to have anti-inflammatory, anti-fibrotic, and positive metabolic effects [2, 14–19]. An important prerequisite for PE to be effective is, however, the adherence to principles of exercise training [20–22]. A systematic review investigating the safety and efficacy of exercise in IM patients reported indecisive results [23]. Up to now, the published reviews describing exercise training in IM focused on safety and efficacy of physical exercise interventions, but did not critically evaluate the application of the principles of exercise training or the adherence to the prescribed exercise programme in a structured manner.

When reporting the results of a PE intervention, it is important to provide precise information regarding the core principles of PE training that were used and considered [20, 21]. Without a detailed and comprehensive description of the interventions, research findings cannot be used for replication

in other studies or implementation in clinical daily routine [24]. The recognised principles of PE are specificity, overload, progression, initial values, reversibility, and diminishing returns (Table 1) [25]. Their implementation in the design of a PE intervention helps to ensure that an appropriate dose and type of exercise is utilised to achieve a desired outcome, be this improvements in cardiorespiratory endurance, muscular strength, or balance. Besides considering these core principles, it is also important to report the components of the exercise programme. Only if training is reported with this level of detail can appropriate study conclusions be drawn as well as intervention replication guaranteed. The components of a PE programme can be reported using the FITT components (frequency, intensity, time, and type of exercise) [26]. Furthermore, the adherence to the described FITT components should be captured and reported. Without reporting the adherence to the prescribed exercise programme, the dose that was delivered remains unclear. Therefore, the prescription of the components of the exercise programme as well as participants' adherence to that exercise prescription need to be reported in sufficient detail. Moreover, when principles of exercise training are applied to the development of exercise protocols, clinicians can assume that studies where the intervention of interest demonstrates a lack of significant effects reveal shortcomings in exercise efficacy rather than shortcomings in exercise prescription [21, 22]. Some of the shortcomings of knowledge related to exercise implementation in IM patients might relate to the lack of consideration of exercise principles in the trials published so far.

Besides a specific and clearly planned and described intervention, other factors such as the design and methodological quality of a trial may influence study outcome. Well-designed randomised controlled trials provide the best evidence regarding the effectiveness of health-care interventions, whilst inadequate methodological approaches may overstate treatment effects and bias results [27]. Although non-randomised studies are more susceptible to confounding, their results in comparison with those of randomised trials may sometimes differ [28]. Furthermore, for some rare diseases, there may in any event be too few RCTs to answer the question of interest, thus necessitating that non-randomised trials also be included in review work. Irrespective of study design, study quality should be evaluated in a standardised manner.

This review evaluates exercise interventions in populations suffering from IM in randomised controlled, non-randomised controlled, and uncontrolled trials investigating the effect of resistive, endurance, or balance training alone or in combination in relation to (1) the application of principles of exercise

training in developing the exercise prescription, (2) the reporting of FITT components of the exercise prescriptions, (3) the adherence of participants to the prescribed intervention and to gauge (4) the methodological quality of the included studies.

Methods

Search strategy

An electronic search strategy was developed and performed by a librarian of Zurich University for the databases MEDLINE/PreMEDLINE, CINAHL, PsychINFO, EMBASE, and the Cochrane Library. The search was restricted to English, German, French, and Dutch language literature from inception of the databases up to January 2015. Combinations of medical subject headings (MeSH) and free text words related to inflammatory myopathy (inflammatory myopathy, dermatomyositis, polymyositis, inclusion body myositis, scleroderma, systemic sclerosis, systemic lupus erythematosus, Sjögren's syndrome) and exercise (e.g. exercise, endurance training, cardiovascular training, cardiopulmonary training, cardiorespiratory training, aerobic training, endurance exercise, ergometry, cycling, rowing, treadmill, resistive strength training, muscle strength training, weight-lifting strengthening programme, weight-bearing strengthening programme, flexibility training, balance training, physical exercise principles, specificity, overload, progression, initial values, reversibility, diminishing returns) were used. The search results were supplemented by articles found through hand searching by scanning reference lists of identified studies.

Eligibility criteria

Studies were eligible for inclusion if they: (1) included adult (18 years) patients with an idiopathic or an associated inflammatory myopathy, (2) were randomised controlled trials, non-randomised controlled trials, or uncontrolled trials, (3) evaluated the effect of resistive, endurance, or balance training alone or in combination, (4) included aerobic capacity and/or aerobic endurance, muscle strength and/or balance as a primary outcome measurement. Case series or case reports were excluded. Hands-on intervention therapies alone (i.e. mobilisation, passive movements, stretching without physical exercise), as well as relaxation training, were not considered in this review.

Table 1: Exercise training principles [25]

Principle	Criteria for this review	Example
Specificity Training adaptations are specific to the system or muscles trained with exercise	Appropriate population targeted and intervention given based on primary outcome	Aerobic exercise such as brisk walking is more appropriate for an intervention aimed at increasing cardiovascular fitness than strength training
Progression Over time, the body adapts to exercise. For continued improvement, the volume or intensity must be increased	Stated exercise programme was progressive and outlined training progression	A walking intervention 2x /week at 60% of maximum heart rate for 30 min, adds 5 min/week over 6 weeks
Overload For an intervention to improve fitness, it must be greater than what the individual is already doing	Rationale provided that programme was of sufficient intensity/exercise prescribed relative to baseline fitness	An individual currently cycles 30 min 2x /week; the exercise intervention must be of greater volume to see a significant improvement in fitness
Initial values Improvements in the outcome of interest will be greatest in those with lower initial values	Selected population with low level of primary outcome measure and/or baseline physical activity levels	Those with lowest level of fitness have greatest room for improvement. A sample with high fatigue level will be more likely to see a significant change than a sample with low baseline fatigue
Reversibility Once a training stimulus is removed, fitness levels will eventually return to baseline	Performed follow-up assessment on participants who decreased or stopped exercise training after conclusion of intervention	"Use it or lose it". Strength gains achieved over 1 year of resistance exercise may completely reverse within a number of months of inactivity
Diminishing returns The expected degree of improvement in fitness decreases as individuals become fit, thereby increasing the effort required for further improvements	Performed follow-up assessment of primary outcomes on participants who continued to exercise after conclusion of intervention	Non-exercisers who begin an exercise programme are likely to experience large initial gains, but the magnitude of change will decrease over time. Also known as the "ceiling effect"

Study selection

After removal of duplicates, the search results were screened for eligibility by a team of two reviewers (PB/ RHK), sharing the retrieved citations. In case of disagreement between the two reviewers, a third party (BCT) served as referee. Reports of secondary analyses or on extensions from original manuscripts were not included in this review.

Data extraction and synthesis

Information on the study design, number and diagnosis of participants, type and length of intervention, and the intervention protocol were extracted from each publication. Details of the intervention protocol were abstracted using a purpose adapted data collection sheet based on systematic reviews evaluating the effects of physical exercise interventions in cancer [21] and stroke patients [22]. It included reporting of PE training principles, description of exercise training components, and participants' adherence to the training plan according to the FITT components. For each physical exercise principle, three rating categories were used, these being yes (+) "reported", no (NR) "not reported", and (?) "unclearly/inconsistently reported". Corresponding to the rating of the training principles, the description of each of the four FITT components was judged with (+) if the component of the exercise prescription was reported, (NR) if the component was not reported, and (?) if it was unclearly or inconsistently reported. Participants' adherence to the exercise prescription was judged with (+) if adherence to each component of the exercise prescription was reported, (NR) if adherence was not reported, and (?) if it was unclearly or inconsistently reported. Two reviewers (BCT, PB) independently collected and rated these data. In case of discrepancies, a third reviewer (RHK) was used as an adjudicator.

Study quality assessment

Methodological quality of all studies was assessed by two independent reviewers (PB and BCT) using the checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health-care interventions developed by Downs and Black [29]. This scale contains 27 items assessing five subscales, these being **reporting** (10 items), **internal validity-bias** (seven items), **internal validity-confounding** (six items), **external validity** (three items), and **power** (one item). We modified the scoring of the last item (*study power*) from a 0–5 scale to a 0–1 scale where 1 was scored if authors reported if and how they determined their sample size a priori [30]. Item 4 (*description of the intervention*) and 19 (*compliance with the intervention*) were scored "yes" if all FITT components were described in

the method and results, respectively. According to other recommendations [31], we scored item 26 (losses to follow-up) “yes” if the drop-out rate was <15%, or if an intention-to-treat analysis was conducted. The score from this modified version ranged from 0 to 28, with a higher score indicating higher methodological quality. For intervention studies with a one-group design, several items must be scored zero (items 5, 14, 15, 21–25), which implied a possible range score between 0 and 19 for those study designs. The arbitration of a third reviewer (RHK) was used in the event of any disagreement between the reviewers (BCT and PB) for the ratings. The percentage agreement and Cohen’s kappa were calculated and interpreted in accordance with Landis and Koch’s benchmarks for assessing the agreement between raters, categories being poor (0), slight (0.1–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect (0.81–1.0) [32]. The PRISMA statement was followed for reporting items of this review [33, 34].

Results

Study selection and characteristics

The literature search provided a total of 1371 citations. After screening and checking for duplicates, 16 reports [20, 34–48] met all of the inclusion criteria [35–50]. Two reports were classified as a secondary analysis [43] or an extension [36] from an original study and were therefore excluded from this review (Figure 1). Finally, 14 reports [35, 37–42, 44–50] evaluating 190 patients remained. Thirteen patients were evaluated in two studies; a 6-week randomised controlled trial [49] and a 6-month follow-up trial [50]. Relevant information was extracted (Table 2). Nine reports [20, 34, 36–38, 40, 46–48] investigated patients with DM and PM [35, 37–40, 42, 48–50], four reports [39, 43–45] included patients with IBM [41, 45–47], and one report [44] evaluated PM, DM, and IBM patients. In total, 161 DM and PM patients (121 in a chronic stage and 40 with recent disease onset) and 29 IBM patients were examined. Four reports (two PM/DM [38, 48], two IBM [46, 47]) focused on resistance training, two on endurance training (two PM/DM [49, 50]) and eight reports (five PM/ DM [35, 37, 39, 40, 42], two IBM [41, 45], and one PM/DM and IBM [44]) on combined interventions of aerobic and resistance exercises. No study evaluated the effects of balance training. All but five studies used a one-group study design, from which were four RCTs [35, 37, 42, 49] and one [50] was a controlled trial without randomisation procedure. One RCT [42] compared a combination of PE/oral creatine supplements against PE/placebo. Both groups performed the same exercise programme, making a comparison between the two groups concerning the effects of PE

impossible. The length of the exercise programmes varied between 3 weeks [44] and 6 months [42, 50] (median: 12 weeks). Exercise frequencies ranged from twice daily [46] to twice per week [49–51]. Half of the studies evaluated a home exercise programme [37, 39–42, 45, 46] and the other half a supervised exercise programme in dedicated training facilities [36, 38, 44, 47–50].

Figure 1: Flow chart of study selection process

Application of exercise principles

The application of exercise principles is summarised in Table 3. None of the articles reported all six training principles, five articles [20, 38, 46, 47, 50] reporting four, four articles [37, 40, 42, 48] reporting two and three articles [35, 39, 45] reporting three. The remaining two articles reported 0 [42] or 1 [39] principle. In two articles [35, 37], the training principles **Reversibility** and **Diminishing Return** were reported inconsistently. Thirteen articles [35, 37–42, 45–50] reported **Specificity**, 11 articles [35, 37–40, 42, 45–47, 49, 50] described **Initial Values**, whilst seven articles described **Progression** [38, 39, 45–47, 49, 50] and **Overload** [35, 38, 45, 47–50]. Articles focusing on one training method alone (either strength [38, 46–48] or endurance training

[49, 50]) reported more training principles (mean 3.7 ± 0.8) compared to those with a combined intervention [35, 37, 39–42, 44, 45] (mean 2.1 ± 1.2).

Reporting of the prescription of the physical exercise training

Reporting of the prescriptions of the training programme according to the FITT components as well as its adherence is presented in Figure 2. Six articles [35, 38, 47–50] reported all four FITT components, five articles [37, 39–42] described three components, two articles [45, 46] reported two components, and one article [44] described 0 components. **Frequency** and **Type** were described in 13 articles [35, 37–42, 45–50], **Time** in 11 articles [35, 37–42, 47–50], and **Intensity** in seven articles [35, 38, 45, 47–50]. The quality of reporting of the intervention was better in studies focusing on only one training method compared to those including a combination of strength and endurance training (mean of 3.7 ± 0.8 vs. 2.6 ± 1.2 FITT components out of four).

Figure 2: Reporting of the planned exercise prescription components

Legend: (+) The percentage of studies that reported the component of exercise prescription. (?) The percentage of studies that was unclear or inconsistently with their reporting of the exercise prescription. (NR) The percentage of studies that did not report the component of the exercise prescription

Table 2: Description of studies

Study	Design	N and diagnosis	Type of intervention	Control	Length	TP	FITT rep	FITT adh	D&B
Aerobic and resistance									
Alexanderson et al. [40]	1 group	10 PM/DM (chronic) (5 PM/5 DM)	Home exercise programme (strength and mobility exercises and 15 min walk)	–	12 weeks	2	3	0	11/19
Alexanderson et al. [39]	1 group	11 PM/DM (acute) (7 PM/4 DM)	Home exercise programme (strength exercises and 15 min walk)	–	12 weeks	3	3	2	14/19
Heikkilä et al. [44]	1 group	22 DM/PM/IBM (15 PM/4 DM/3 IBM)	Exercise-based multidisciplinary inpatient course	–	3 weeks	0	0	0	13/19
Amaróttir et al. [41]	1 group	7 sporadic IBM (chronic)	Home exercise programme (strength and mobility exercises and 15 min walk)	–	12 weeks	1	3	2	12/19
Chung et al. [42]	RCT	37 PM, DM (chronic) (22 PM/15 DM)	Home exercise programme (strength and mobility exercises and 15 min walk) and oral creatine supplements	Home exercise programme and placebo	6 months	2	3	0	24/28
Johnson et al. [45]	1 group	7 sporadic IBM (chronic)	Home exercise programme (functional exercise programme and aerobic training)	–	12 weeks	3	3	0	12/19
Munters et al. [35]	RCT	21 PM, DM (chronic) (9 PM/12 DM)	Supervised exercise programme (cycling and muscular endurance)	Non-intervention group	12 weeks	4	4	0	22/28

Table 2 (continued)

Study	Design	N and diagnosis	Type of intervention	Control	Length	TP	FITT rep	FITT adh	D&B
Alexanderson et al. [37]	RCT	19 PM, DM (acute) (10 PM/9 DM)	Home exercise programme (resistive exercise programme and brisk walking)	Range of motion exercise programme	24 weeks	2	3	2	21/28
Resistance only									
Spector et al. [47]	1 group	5 sporadic IBM (chronic)	Supervised exercise programme (progressive resistive training)	–	12 weeks	4	4	0	12/19
Variju et al. [48]	1 group	21 PM, DM Acute: 4 PM/6 DM Chronic: 5 PM/6 DM	Supervised exercise programme (bending and stretching exercise, isotonic muscle training and respiratory training)	–	3 weeks	2	4	0	14/19
Alexanderson et al. [38]	1 group	9 PM, DM (chronic) (4 PM/5 DM)	Supervised exercise programme (intensive muscular training)	–	7 weeks	4	4	1	15/19
Johnson et al. [46]	1 group	7 sporadic IBM (chronic)	Home exercise programme (functional exercise programme)	–	16 weeks	4	2	2	12/19
Aerobic only									
Wiesinger et al. [49]	RCT	14 PM, DM (chronic) (4 PM/10 DM)	Supervised exercise programme (cycling and step aerobic)	No training	6 weeks	4	4	0	22/28
Wiesinger et al. [50]	CT	8 PM, DM (chronic)	Supervised exercise programme (cycling and step aerobic)	No training	6 months	4	4	0	19/28

Adh: Reported in the result section; CT: controlled trial; DM: dermatomyositis; FITT: frequency, intensity, time, and type; D & B: Downs and Black checklist; IBM: inclusion body myositis; PM: polymyositis; RCT: randomised controlled trial; TP: training principles; rep: reported in the 'Methods' section

Table 3: Applications of the exercise training principles

Study	Sp	Pr	Ov	IV	Rev	DR
<i>Aerobic and resistance</i>						
Alexanderson et al. [40]	+	NR	NR	+	NR	NR
Alexanderson et al. [39]	+	+	NR	+	NR	NR
Heikkilä et al. [44]	?	?	NR	?	NR	NR
Arnardottir et al. [41]	+	NR	NR	?	NR	NR
Chung et al. [42]	+	NR	NR	+	NR	NR
Johnson et al. [45]	+	+	?	+	NR	NR
Munters et al. [35]	+	?	+	+	?	?
Alexanderson et al. [37]	+	NR	?	+	?	?
<i>Resistance only</i>						
Spector et al. [47]	+	+	+	+	NR	NR
Varju et al. [48]	+	?	+	?	NR	NR
Alexanderson et al. [38]	+	+	+	+	NR	NR
Johnson et al. [46]	+	+	+	+	NR	NR
<i>Aerobic only</i>						
Wiesinger et al. [49]	+	+	+	+	NR	NR
Wiesinger et al. [50]	+	+	+	+	NR	NR

Legend: +: reported, NR: not reported, ?: unclearly or inconsistently reported

Adherence to the exercise prescription according to the FITT components

Four articles [37, 39, 41, 46] reported two out of four training components, one report [38] described one component, and nine reports [35, 40, 42, 44, 45, 47–50] did not describe the adherence of the patients to the PE programme. **Frequency** was reported in five [37–39, 41, 46] and **Type** in four reports [37, 39, 41, 46]. **Intensity** and **Time** were not mentioned in any of the included reports.

Methodological quality

The methodological quality varied widely between the reports (Figure 3). Studies using a one-group design [38–41, 44–48] scored between 11 and 15 (mean 12.75 ± 1.3) points (maximum possible score 19). Reports with a two-group design [35, 37, 42, 49, 50] scored between 19 and 24 (mean 21.6 ± 1.8 ; maximum possible score 28). The subscales **internal validity-confounding** had the highest quality score (86% yes answers), followed by the subscales **internal validity-bias** and **reporting** (each 78% yes answers), whilst **external validity** and **power** scored lowest (only 48% respectively 40% yes answers). In the subscale **reporting**, the item “intervention of interest” was described in six reports [35, 38, 47–50] and “actual p-values” were stated in five reports [35, 42, 44, 45, 50]. The items “hypothesis/aim/objective”, “main outcomes to be measured”, and “main findings” were described

in all 14 reports. In the subscale **external validity**, eight reports [37–39, 42, 44, 48–50] stated if the subjects asked to participate were representative of the entire population, whilst only four reports [44, 48–50] described whether participants were representative of this population. One report [42] described the blinding of their patients regarding intervention. None of the reports provided an account of participant adherence. The total inter-rater agreement was good (kappa 0.62, SE of kappa: 0.054, 95%CI 0.51–0.72). The number of observed agreements between the two raters was 86.93% of the judgements. The kappa of the subscales varied between poor (kappa 0.05, external validity) to very good (kappa 0.80, confounding).

Figure 3: Methodological quality assessed with the Downs and Black checklist.

Legend: *Maximal possible point score: 28. **Maximal possible point score: 19

Discussion

The results of this review demonstrated that application of training principles and methodological quality were both reported inconsistently in those papers studied, whilst FITT components were reported more consistently in training prescriptions than in result sections. Eighty per cent of studies applied at least three out of four FITT components in their exercise prescriptions. However, none of the studies provided complete accounts of the level of adherence to the PE protocol. Sixty-four per cent of the studies provided no details on adherence to their training protocol.

Regarding IM patients, there were only three RCTs comparing a PE intervention with a non-exercising control group. The majority of the published studies were performed as a one-group design. Furthermore, the sample sizes of the included studies were low and varied between five and 37 patients, whereas half of the studies included 10 or less participants. In addition, the involved studies investigated different subcategories of IM (chronic or recent onset) and different types of intervention. Taken together, the evidence for PE in IM is still weak and it is not yet known which training prescription is the most effective. Therefore, no final conclusion regarding the evidence for PE in IM patients can be drawn. These facts are indicative of the still sparsely investigated topic of exercise interventions for patients with inflammatory disease [18, 19].

Application of the principles of exercise training

Specificity was the most commonly applied training principle. Ninety-three per cent of the reviewed trials matched the training mode with their primary outcome measure. This result is in agreement with previous studies about the application of principles of PE training in cancer [20, 21] and stroke [22] survivors. Although lower values (89 and 64%, respectively) were reported in cancer and stroke survivors, *specificity* was the most applied exercise training principle. In our review, only one study [44], assessing an exercise-based multidisciplinary inpatient course, did not report *specificity*. In this study, PE was a single part of a comprehensive rehabilitation programme and each participant performed different components of exercise. In contrast, *progression* and *overload* were reported in only 50% of the included studies. Other authors found comparable values for the principle *progression* (41, 26, and 76%, respectively) and lower values for the principle *overload* (31, 37, and 49%, respectively) [20–22]. The principle of *overload* states that, to improve fitness, the intervention must be greater than what the individual is

already doing (Table 1). Therefore, without knowing the baseline fitness levels of studied individuals, it is impossible to determine whether adequate training intensities and volumes have been used. In studies evaluating resistance training, a valid and feasible way to assess baseline value is to perform a 1, 5, or 10 voluntary repetition maximum test for the target muscle groups [35, 38, 47] or to count the maximum number of times that participants were able to repeat the exercise in the initial assessment session [46, 48]. In studies investigating aerobic exercise, VO_{2max} [35] or maximum heart rate [49, 50] could be used to assess *initial value*. If the training matches the baseline level of the individual, improvement will occur. Thus, to assure continued improvement, the training intensity and/or volume must be adjusted after a certain period of training. *Progression* can be conducted in different ways. In order to maintain the same absolute training stimulus, the intensity or volume of an exercise must be increased continuously. Muscular strength training in IM patients can be modulated by increasing the level of resistance or the number of exercises, repetitions or sets [38, 45–47]. In cycle training, the resistance can be increased [49, 50]. The principle of *initial value* was considered in 79% of the included studies. This rate is higher compared to studies including cancer [20–22] and stroke patients [26]. One reason for this difference could be that our reviewed studies included patients with muscular diseases. These patients have by definition impaired muscle function [9] and therefore a low *initial value* in muscle strength. This allows greatest room for improvement. *Reversibility* and *diminishing return* can only be judged in studies that investigate a follow-up after conclusion of the initial intervention. The two studies [35, 37] which performed a follow-up after the end of the intervention did not report whether the patients continued, stopped, or decreased with the PE programme. For that reason, both principles could not be judged unambiguously.

An explicit conclusion concerning efficacy of a specific exercise programme can only be drawn if at least the first four principles (*specificity, progression, overload, initial value*) are clearly stated. Otherwise it is not possible to distinguish if exercise training per se is not indicated or if the prescribed exercise programme was inadequate or under dosed. Lack of attention to these principles may affect the study impact and effect of exercise training may thus be underestimated. To investigate long-term effect, the two principles of reversibility and diminishing return need to be included in PE studies. Knowing that exercise has no depot effect [25], it would be important to study how patients can be motivated to continue exercise training after study conclusion.

Reporting of the prescription of the physical exercise training and adherence

Whilst only one paper [44] failed to report frequency and type of exercise prescribed, eight out of 14 reports did not adequately report the complete FITT components. Although intensity is a key component, it was the least reported one. If intensity is under a certain threshold, patients will probably not benefit from their training effort. Conversely, if the PE intensity is too high, patients' safety could be impaired. Due to the lack of equipment, it is not always feasible to measure intensity in absolute values, e.g. maximal oxygen consumption or measurement units such as watt, newton, or maximum peak torque. Nevertheless, intensity can always be described in a relative way. For resistance training, a 1, 5, or 10 repetition maximum can be tested. Then percentages of these results can be taken for the desired training intensity. For aerobic exercise, the percentage of the theoretical maximum heart rate could be used. Furthermore, a subjective way to measure intensity is the Borg's Rating of Perceived Exertion and Pain (RPE) Scales [52]. This scale values range from 6 to 20, where 6 is a very, very light and 20 a very, very hard exertion. This scale is an affordable, practical, and valid tool to monitor and prescribe exercise intensity. Exercise at an RPE of 11–13 (low) may be recommended for less trained individuals, whilst a RPE of 13–15 may be recommended where training should be more intense whilst still retaining an aerobic training effect [53].

Whilst reporting the PE training prescription is important, it is also necessary to identify which patients actually undertook PE and persisted with it. Only if adherence to the FITT components is completely covered and reported will the actual performed PE training be evident and thus conclusions for further research or practice be more safely drawn. To start and maintain an exercise programme is a huge challenge, particularly for inactive persons [54]. Therefore, it is important to know which PE training programme participants actually perform and how often they have performed it. If participants do not exercise regularly, the training goal may not be achieved. Additionally, it is important to know if participants had to modify their programme, for example because they were unable to perform the original planned intensity or training period. Therefore, besides information on frequency and type of exercise, additional information about intensity and time needed to perform the exercises is fundamental. Unfortunately, none of our included studies reported this information in sufficient detail. The poor reporting of adherence seems to be a common weakness in PE studies. This was also highlighted in studies with other diseases [20–22]. It is a challenge to control and verify

adherence, especially in home-based training programmes. Patients could be motivated to fill out training logs and to send them back regularly. As known from questionnaires relating to physical activity, people tend to give socially desirable answers [55]. This risk also exists in diaries, as people may overestimate the level of performed exercises. One possibility for overcoming this shortcoming could be an e-health home-based training programme, using telecommunication technologies [56]. Such a programme would allow patients to report their performed exercise volume, intensity and perceived exertion immediately. Based on this information they receive direct feedback and their training programme could be adapted regularly. The training volume and intensity would be transparent and rehabilitation specialists would be able to react immediately if some patients did not adhere to the PE programme. In a recently published study investigating independent living, older adults showed that adoption of assistive technology devices for physical intervention tends to motivate and retain exercising for longer periods of time [57].

Methodological quality

One of the most prevalent methodological shortcomings was the insufficient power of the studies, only two of which reported how sample size was determined a priori. In the subscale **internal validity-confounding**, the items concerning the different intervention groups (four out of five items) could not be scored for those studies which had a one-group design. Because controlling for extraneous variables is not possible in studies with only one group, these are susceptible to confounding and tend to exaggerate the beneficial effects of interventions [58].

The item “lost to follow-up” was scored positive in 86% of all studies. Compared with other exercise studies, attrition bias is not so prevalent in our review. This may be because the intervention durations of our studies were rather short and study samples small. This makes it easier to support and motivate individual participants. A common problem in the subscale **internal validity-bias** in studies with exercise interventions is the blinding of the participants and the reliability of compliance reporting. It is almost impossible to blind participants regarding an exercise intervention [59]. Only one RCT was able to blind its participants, and this was because it compared exercise training in combination with oral creatine supplements with exercise training in combination with placebo. The subscale **external validity** is scored between 4 and 8 points. Although external validity is important for ascertaining implications for clinical practice, most checklists in fact ignore this aspect. To date,

the best way to assess external validity is still unknown [29]. In the subscale **reporting**, the “description of the intervention” and “actual probability value” are the weakest scored items. The methodological quality of future studies may be improved if authors provide all of the information requested by the Risk of Bias checklist for RCTs [60] or the Downs and Black checklist [29] for non-randomised studies.

Strength and limitations

Although the intervention is the essence of each experimental study, its detailed description is often neglected in those trials evaluating the effect of PE training. Poor reporting of the intervention may bias the study outcomes in a way which is comparable to poor reporting of the methodological quality [24]. The strength of our study is that we evaluated the quality of the reporting and performing of the intervention as well as the methodological quality. Furthermore, we used a comprehensive search strategy in standard bibliographic databases to identify potential studies. Nevertheless, some limitations remain. Firstly, as we had to include studies with different study designs, nine out of 14 studies had no control group. Therefore, the risk of selection bias and confounding is greater than in a review of RCTs [58]. To address these limitations, we used a comprehensive quality checklist which deals with randomised and non-randomised studies. Secondly, we included different subtypes and phases of myositis. Thus, the included participants were very heterogeneous and training modalities could not be compared between the included studies. As a result, it was not possible to perform a meta-analysis. Thirdly, we could only judge the information authors described in their published articles. Hence, it is possible that some studies considered the principles of PE but did not report it. Such studies would thus be under-rated in our review. Fourthly, we did not focus on the outcome measures of the included studies. All studies reported aerobic capacity, aerobic endurance, or muscle strength as a primary outcome measurement. As reported in a previous review, both aerobic and strength training seems to have a beneficial effect on strength and endurance [23]. Additionally, all included studies evaluated laboratory measurement such as erythrocyte sedimentation rate, C-reactive protein or creatinine phosphokinase and/or inflammatory cell infiltrates. None of the reports found an aggravation of these muscle enzymes or of the inflammatory cell infiltrates.

Finally, we were unable to determine whether applying the exercise training principles explicitly influenced outcomes. Our studies were heterogeneous concerning design, sample size, and methodological quality. This means

that too many factors had the potential to influence the outcome of the study. Thus, no conclusion could be drawn regarding the impact of the application of principles of exercise training on outcome.

Call for transparency to facilitate evidence-based practice

The steadily growing health market calls for effectively and efficiently performed PE interventions. Therefore, it is important that the goals for PE training are reasonable and attainable [25]. Whilst fitness levels of patients vary widely, these aims are best achieved with a custom-made and individually tailored training programme, with parameters that can be adjusted from workout to workout. These parameters include type, volume, intensity, and order of physical exercise as well as the frequency and length of training and the length of rest periods [25]. To achieve the desired training effect, PE programmes should consider the training principles [25] and the training parameters should be reported, e.g. by use of FITT components [26]. Only with a complete description of the PE strategy can clinicians reliably implement interventions that are effective. Furthermore, investigators can replicate or further develop research findings. To improve the completeness of reporting, and ultimately improve replicability of exercise interventions with IM patients, the Template for Intervention Description and Replication (TIDieR) checklist and guide might prove useful [24]. Using this checklist in conjunction with the CONSORT checklist [27] makes it easier for authors to structure description of their interventions, for reviewers and editors to assess the descriptions, and for clinicians to replicate the interventions. Thus, future methodological well-designed RCTs, including a detailed prescription of the physical exercise intervention, should be designed and evaluated in patients with IM.

Conclusion

This review showed that exercise training principles and FITT components in intervention studies for myositis patients were not systematically reported. When failing to apply the training principles, exercise interventions may be of insufficient intensity or may be executed under suboptimal circumstances. As a result, the effect of the physical exercise intervention may be underestimated and time allotted for therapy is not used effectively and efficiently. Furthermore, if the FITT components of physical exercise training and the adherence to these components are not explicitly reported, the intervention is not reproducible and it is difficult to transfer the results to the clinical setting. Therefore, future studies should consider the Template for Intervention Description and Replication checklist and guide in order to describe

the training principles and report FITT prescriptions and, thus, allow development of replicable exercise recommendations for IM patients.

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CHAPTER 3

Entwicklung eines Trainingsleitfadens für Patienten mit entzündlicher Muskelerkrankung / Development of an Exercise Guideline for Patients with Myositis

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Zusammenfassung

Hintergrund: Inflammatorische Myopathien (IM) sind eine Gruppe seltener entzündlicher Muskelerkrankungen. Verminderte Kraft und Ausdauerfähigkeit stellen die Hauptsymptome dar. Diverse Studien konnten positive Effekte einer Trainingstherapie nachweisen, es existieren jedoch keine krankheitsspezifischen Trainingsrichtlinien.

Ziel: Erstellung einer Übersicht der vorhandenen Trainingsstudien mit Fokus auf erwachsene Patienten mit IM, um daraus einen evidenzbasierten, krankheitsspezifischen Trainingsleitfaden abzuleiten.

Methode: In einem ersten Schritt erfolgte eine systematische Literaturübersicht. Sie diente als Basis, um den Trainingsleitfaden zu entwickeln. Die langjährige klinische Erfahrung spezialisierter Physiotherapeuten sowie die Trainingsrichtlinien des American College of Sports Medicine fanden ebenfalls Berücksichtigung.

Ergebnisse: In die systematische Übersicht wurden 24 Studien mit insgesamt 151 Patienten mit IM eingeschlossen. Alle Studien zeigten positive Effekte eines Kraft- und/oder Ausdauertrainings auf. Unerwünschte Ereignisse traten nicht ein. Der Trainingsleitfaden besteht aus einem Einführungsteil zu allgemeinen Trainingsprinzipien sowie zwei weiteren Teilen über Kraft- und Ausdauertraining für jede Krankheitsaktivität (früh-aktiv, aktiv, stabil).

Schlussfolgerungen: Obwohl die Trainingsprotokolle im Bereich der Myositis unterschiedlich sind, weisen alle Studien konsistent darauf hin, dass das Training sicher und effektiv ist. Der Trainingsleitfaden ermöglicht Therapeuten einen raschen Überblick über evidenzbasierte Trainingsrichtlinien. Die Richtlinien sollten in weiteren Studien angewendet, überprüft und abschliessend verfeinert werden.

Abstract

Background: Inflammatory myopathies (IM) are a group of rare inflammatory muscle diseases. Reduced strength and endurance are the main symptoms. Although various studies show positive effects of exercise, there are no disease-specific training guidelines.

Objective: Providing an overview of exercise studies in adult patients with IM to derive evidence-based, disease-specific training guidelines.

Method: At first a systematic literature review was performed. Based on the results, training recommendations were then developed. Long-lasting clinical experience of specialist physiotherapists and the training guidelines of the American College of Sports Medicine were also incorporated.

Results: The systematic literature review included 24 studies with a total of 151 IM patients. All studies showed positive effects for strength and/or endurance training. No adverse events were reported. The training guidelines consist of an introduction part on general training principles and two further parts on strength and endurance training for each disease activity (early-active, active, stable).

Conclusions: Although training protocols related to myositis are varying, all studies consistently indicate that the training is safe and effective. The training recommendations allow therapists a quick overview of evidence-based training guidelines. The guidelines should be applied, reviewed, and refined in further studies.

Einleitung

Inflammatorische Myopathien (IM) – auch Myositiden genannt – sind eine heterogene Gruppe seltener autoimmuner entzündlicher Muskelerkrankungen, die vor allem die quergestreifte Muskulatur betreffen. Auch innere Organe wie die Lunge, das Herz, der Gastrointestinaltrakt oder die Haut können von der Entzündung betroffen sein [1]. Die Inzidenz variiert je nach Studie zwischen 0,1 und 7,89 Fällen pro Jahr, wobei Frauen häufiger erkranken als Männer. Damit gehören IM zu den seltenen Erkrankungen. IM können in jedem Alter auftreten, manifestieren sich jedoch am häufigsten in der 5. und 6. Lebensdekade [2–4]. Je nach Entzündungsaktivität und Krankheitsdauer wird zwischen einer früh-aktiven, einer aktiven und einer stabilen Phase unterschieden. Die früh-aktive Phase ist definiert durch eine Krankheitsdauer von weniger als drei Monaten. Eine Krankheitsdauer von mehr als drei Monaten mit instabilem Krankheitsverlauf, wobei Therapieänderungen in den letzten drei Monaten erfolgten, wird als aktive Phase bezeichnet. Eine stabile Phase ist charakterisiert durch einen stabilen Krankheitsverlauf ohne Therapieänderungen in den letzten drei Monaten [5].

Zu den häufigsten IM-Formen bei Erwachsenen zählen die Dermatomyositis (DM), die Polymyositis (PM) und die Einschlusskörpermyositis (Inclusion Body Myositis: IBM). Es existieren weitere seltenere Formen, beispielsweise krebsassoziierte Myositis, nekrotisierende Myositis, Overlap-Syndrom (Myositis assoziiert mit anderen entzündlichen rheumatischen Erkrankungen) oder fokale Varianten [6]. Die gemeinsamen Hauptsymptome, die sich innerhalb von Wochen und Monaten entwickeln, sind proximal betonte und meist symmetrische Muskelschwäche, verminderte muskuläre Ausdauerfähigkeit und Fatigue. Dadurch sind Patienten mit IM häufig auch im Alltag eingeschränkt, beispielsweise beim Gehen, Treppensteigen, Aufstehen von einem Stuhl oder Haare waschen. Zusätzlich berichten insbesondere Patienten mit IBM von regelmäßigen Stürzen [7]. Ebenso besteht ein höheres Risiko, an Komorbiditäten zu erkranken, zum Beispiel an kardiovaskulären Erkrankungen oder malignen Tumoren [8, 9]. Myositis ist mit erhöhter Mortalität sowie verminderter gesundheitsbezogener Lebensqualität assoziiert [10–12].

Ursprünglich wurden Patienten mit IM ausschließlich medikamentös mit Kortikosteroiden, Immunsuppressiva und Immunglobulinen behandelt [13]. Erst in den letzten Jahren fand ein Paradigmenwechsel statt. Entgegen der bisherigen Überzeugung, dass sich Patienten mit IM schonen und körperliche Aktivitäten meiden sollen, ist heute bekannt, dass Kraft- und Ausdauer-

training sicher bzw. effektiv sind und keine negativen Effekte auf die Entzündungsaktivität haben [14, 15]. In diversen Studien war sogar ein entzündungshemmender Effekt des Trainings nachweisbar [16, 17]. Kraft- und Ausdauertraining ist nicht nur wegen der Grunderkrankung wichtig, sondern kann auch das Komorbiditätsrisiko reduzieren sowie die katabolen Nebeneffekte der Kortikosteroidtherapie positiv beeinflussen. Zusätzlich kann eine Trainingstherapie die physische Belastbarkeit und die Lebensqualität verbessern sowie Fatigue reduzieren [18, 19].

Obwohl diverse Studien die positiven Effekte einer Trainingstherapie nachweisen konnten und die Wichtigkeit der körperlichen Aktivität und des Trainings inzwischen anerkannt ist, existieren aktuell keine krankheitsspezifischen Trainingsrichtlinien. Um Patienten mit Myositis sicher und effektiv behandeln zu können, sind in der Physiotherapie jedoch klar definierte Trainingsrichtlinien, die auf der momentan besten verfügbaren Evidenz beruhen, erforderlich [20].

Methode

In einem ersten Schritt erfolgte eine systematische Literaturübersicht zum Thema „Training bei entzündlichen Muskelerkrankungen“. Dabei wurden die verschiedenen Trainingsprotokolle anhand beschriebener Trainingskomponenten (Methode, Intensität, Frequenz und Umfang) analysiert. Für jede eingeschlossene Studie wurde die Evidenzstufe angegeben. Die höchste Evidenzstufe (Level 1) bezog sich auf randomisierte kontrollierte Trials (RCTs) mit geringem Konfidenzintervall und auf qualitativ hochwertige systematische Reviews von RCTs. Level 2 umfasste Kohortenstudien (inklusive RCTs von geringerer Qualität) sowie systematische Reviews solcher Arbeiten. Level 3 beinhaltete Fall-Kontroll-Studien und Reviews von Fall-Kontroll-Studien. Level 4 bezog sich auf Fallserien und Level 5 auf Expertenmeinungen [21]. Auf der Basis dieser Analyse erfolgte die Entwicklung eines Trainingsleitfadens.

Literatursuche

Die Literatursuche erfolgte in den Datenbanken MEDLINE/ PreMEDLINE, Cochrane Library, Embase und PEDro mit folgenden Schlagwörtern und Kombinationen: inflammatory myopathy (z. B. myositis, dermatomyositis, polymyositis, inclusion body myositis, systemic sclerosis, Sjögren's syndrome, systemic lupus erythematosus) and exercise (z. B. exercises, physical exercise, physiotherapy, training, strength training, strengthening, resistive training, endurance training, cardiovascular training, cardiorespiratory training, aerobic training, cycling).

Ein- und Ausschlusskriterien

Eingeschlossen wurden deutsch- und englischsprachige Interventionsstudien, die bis Dezember 2018 publiziert wurden und den Effekt von Kraft- und/oder Ausdauertraining auf die aerobe Kapazität, die muskuläre Ausdauerfähigkeit oder die Maximalkraft bei erwachsenen Personen mit IM untersuchten. Ausgeschlossen wurden Studien mit Patienten, die von einer juvenilen entzündlichen Muskelerkrankung betroffen waren, sowie Studien, die von konventionellem Krafttraining abweichen (z.B. Blutfluss-Restriktions-Training (Okklusionstraining) oder Training der Handkraft).

Datensammlung

Folgende Informationen wurden aus den Studien extrahiert und tabellarisch dargestellt: Studiendesign, Stichprobengröße, Diagnosen, Krankheitsaktivität, Krankheitsdauer, Studiendauer und Trainingskomponenten.

Entwicklung des Trainingsleitfadens

Zur Erstellung konkreter Trainingsrichtlinien für ein Kraft- und Ausdauertraining bei Patienten mit IM, erfolgte ein Rückgriff auf die langjährige klinische Erfahrung der Physiotherapeuten des Myositisteam im Universitätsspital Zürich, auf Trainingsrichtlinien des American College of Sports Medicine (ACSM) [18] sowie auf eine aktuelle narrative Übersichtsarbeit zum Thema [22]. Die Erstellung der Trainingsrichtlinien orientierte sich an der Checkliste zur Qualitätsbeurteilung von Leitlinien, AGREE Instrument (Appraisal of Guidelines, Research & Evaluation), die sechs Bereiche mit insgesamt 23 Elementen enthält [23].

Ergebnisse

Übersicht der Trainingsstudien

Seit den ersten beiden Fallbeschreibungen im Jahr 1993 sind insgesamt 28 Studien zum Thema „Training bei Erwachsenen mit einer entzündlichen Muskelerkrankung“ erschienen: fünf randomisierte kontrollierte Studien [24–28], zwei nicht randomisierte kontrollierte Studien [29, 30], 12 unkontrollierte Studien [31–42] und neun Fallstudien [43–51]. Fünf Studien [27, 33, 45, 48, 51] untersuchten Patienten in der aktiven Krankheitsphase, 22 Studien [24–26, 28–32, 34–41, 43, 44, 46, 47, 49, 50] solche in einer stabilen Phase und eine Studie [42] schloss Patienten aus beiden Phasen ein.

Trainingskomponenten für Patienten in der aktiven Krankheitsphase

Die sechs Studien mit Bezug auf die aktive Phase schlossen insgesamt 52 Patienten mit labornachweislicher Krankheitsaktivität ein (Tabelle 1). Eine

Studie [27] war randomisiert kontrolliert (Evidenzlevel 1B), zwei Studien [33, 42] waren unkontrolliert (Evidenzlevel 2C) und bei drei Studien [45, 48, 51] handelte es sich um Fallserien (Evidenzlevel 4). Eine Studie [42] untersuchte ein betreutes Krafttraining, drei Studien [45, 48, 51] ein betreutes Kraft- und Ausdauertraining und zwei Studien [27, 33] ein Heimprogramm (Kraft- und Ausdauertraining). Die Kontrollgruppe der randomisierten kontrollierten Studie führte ein Training zur Verbesserung der Beweglichkeit durch. Obwohl alle Studien Patienten in der aktiven Krankheitsphase einschlossen, unterschied sich die Krankheitsdauer bei den einzelnen Studien. In den beiden Untersuchungen von Alexanderson et al. [27, 33] trainierten Patienten mit einer Krankheitsdauer zwischen 0,5 und 3 Monaten, bei Mattar et al. [51] und Hejazi et al. [48] hingegen solche mit einer Krankheitsdauer zwischen 48 und 72 Monaten. Die Dauer der Trainingsprogramme variierte zwischen 2 und 24 Wochen, wobei das Training täglich bis zweimal wöchentlich erfolgte. Bei keiner Studie kam es während des Trainings zu unerwünschten Ereignissen (adverse events), beispielsweise zu einer Erhöhung der Entzündungsaktivität.

Krafttraining: Um die Intensität im Kraftbereich zu bestimmen, erfolgte in einer Studie ein Manueller Muskeltest (MMT) [45] und in zwei Studien [27, 33] kam der krankheitsspezifische Funktionelle Index (FI) zum Einsatz.

- Beim MMT sind die Probanden aufgefordert, einen Muskel unter Aufhebung der Schwerkraft oder gegen diese bis zum maximalen Widerstand anzuspannen. Die Ausgangsstellung der Probanden ist dabei standardisiert [52]. Die Einschätzung der Muskelkraft basiert auf drei Kriterien: (1) Der Muskel oder die Muskelgruppe zeigt keine Kontraktion oder nur eine Muskelzuckung (keine Gelenkbewegung), (2) der Muskel oder die Muskelgruppe kann einen Körperabschnitt bis zum vollen Bewegungsausmaß bewegen (entweder gegen die Schwerkraft oder unter Abnahme der Eigenschwere), (3) der Muskel oder die Muskelgruppe kann einen Körperabschnitt gegen Widerstand bewegen. Es gibt verschiedene Skalen, um die Muskelkraft zu dokumentieren. Die häufig eingesetzte Skala des Medical Research Council (MRC) umfasst fünf Stufen (0 = keine Kontraktion sicht- oder fühlbar, 1=sicht- oder tastbare Kontraktion, 2 = Bewegung unter Aufhebung der Schwerkraft möglich, 3 = Bewegung gegen Schwerkraft möglich, 4 = Bewegung gegen Schwerkraft und Widerstand möglich, 5 = normale Muskelkraft) [53].

- Der FI wurde entwickelt, um die Muskelfunktion bei Personen mit Myositis zu messen. Er bezieht sich auf die Muskelausdauer in den Extremitäten, im Nacken und im Rumpf, die Griffstärke, den maximalen Ausatemungsfluss sowie das Drehen im Bett und auf den Übergang vom Liegen zum Sitzen. Erreichbar ist eine Punktzahl zwischen 0 und 64, wobei 64 die maximale Kapazität bedeutet [54].

In der Regel erfolgte ein dynamisches Krafttraining mit/ohne Gewicht oder mit Unterstützung eines Schlingentisches. Escalante et al. beschreiben jedoch, dass bei sehr abgeschwächter Muskulatur (MRC-Grad 1 beim MMT) auch ein isometrisches Training erfolgte [45]. Der Umfang des Krafttrainings variierte zwischen einer Serie à 5–10 Wiederholungen und drei Serien à 8–12 Wiederholungen. In der Studie von Alexanderson et al. wurde die Intensität als „moderat“ bezeichnet [33]. Ansonsten fehlten Angaben zur Trainingsintensität im Kraftbereich.

Die Resultate im Kraftbereich waren nicht einheitlich. Vier Studien protokollierten einen Kraftzuwachs, in zwei Studien war jedoch nicht in allen untersuchten Muskelgruppen eine Kraftverbesserung festzustellen. Beispielsweise verbesserte sich in der Studie von Mattar [38] nur die untere Extremität, nicht aber die obere Extremität. In der randomisierten kontrollierten Studie war kein signifikanter Gruppenunterschied nachweisbar.

Ausdauertraining: In einer Studie [51] war die Intensität anhand eines vorgängig durchgeführten maximalen Ausdauertests festgelegt. Hier erfolgte ein Training mit einer Herzfrequenz (HF) zwischen der ersten ventilatorischen Schwelle (anaerobic threshold) und 10% unter der zweiten ventilatorischen Schwelle (respiratory compensation point) [51]. In einer zweiten Studie war ein Trainingsbereich zwischen 50 und 70% der geschätzten maximalen Herzfrequenz (HFmax) angegeben [27]. In allen anderen Studien war die Trainingsintensität nicht beschrieben. Das Ausdauertraining nahm zwischen zehn und sechzig Minuten in Anspruch. Alle Studien konnten eine Steigerung der Ausdauer nachweisen.

Tabelle 1: Übersicht der Trainingsstudien (mit Trainingskomponenten) bei aktiver entzündlicher Muskelerkrankung

Studie/Design/ Evidenzlevel	Diagnose/Krank- heitsdauer (in Monaten)	Trainingskomponenten			Resultate	
		Methode	Intensität	Umfang	Frequenz	Dauer
Escalante et al. [45] Fallserie Evidenzlevel 4	3 PM 1 DM 1 aM median: 9 min/max: 3/10	Krafttraining: funktionelles Training plus Krafttraining mit Widerstand Ausdauertraining: Fahrrad- ergometer oder Stepper (isokinetisch)	kA	2–3× 5–10 Wiederholungen	kA	mind. 2 Wo. MMT+ bei 4 von 5 Probanden
Alexanderson et al. [33] Prä-post-Vergleich Evidenzlevel 2C	7 PM 4 DM 3 aM median: 2 min/max: 1/2	dynamisches Krafttraining (jedenach individuellem FI- Score Training mit oder ohne Gewicht): • obere/untere Extremität • Rumpfkraft Ausdauertraining: Walking	„moderat“ kA	1 × 10 Wiederho- lungen pro Übung (to- tal 9 Übungen) • total 15 Minuten	5 ×/Wo. kA	12 Wo. FI2 +*
Varju et al. [42] Prä-post-Vergleich Evidenzlevel 2C	4 PM 6 DM kA	dynamisches Krafttraining: • obere/untere Extremität • Rumpfkraft	kA	2× 65–70% der maxi- mal möglichen Wieder- holungen • total 40–60 Minuten	5 ×/Wo. kA	3 Wo. • Dynamometrie • Kniestreckung+ • Schulterabduktion+* • Ellenbogenflexion • Handflexion+*
Hejazi et al. [48] Fallbericht Evidenzlevel 4	1 PM 60	Krafttraining: • untere Extremität • Gehtraining Ausdauertraining: Fahrrader- gometer	kA	kA 15–20 Minuten	täglich kA	4 Wo. MMT+ Gehdistanz+

Tabelle 1 (Fortsetzung)

Studie/Design/ Evidenzlevel	Diagnose/Krank- heitsdauer (in Monaten)	Trainingskomponenten			Resultate	
		Methode	Intensität	Umfang	Frequenz	Dauer
Alexanderson et al. [27] RCT Evidenzlevel 1B	10 PM 9 DM median: 3 Q1–Q3: 2–3	dynamisches Krafttraining (jedenach individuellem FI- Score Training mit oder ohne Gewicht) • obere/untere Extremität • Rumpfkraft Ausdauertraining: Brisk Walking	kA	• 1 x 10 Wiederho- lungen • 6 Übungen	• 12 Wo.: 5 x/Wo. • 12 Wo.: 2 x/Wo.	24 Wo. F12 + (in IG und KG)
Mattar et al. [38] Fallserie Evidenzlevel 4	3 PM median: 60 min/max: 48/72	dynamisches Krafttraining: • obere/untere Extremität • Rumpfkraft Ausdauertraining: Laufband	50–70% der ge- schätzten maxi- malen HF	15 Minuten		aerobe Kapazität+ (in IG und KG)
			kA	• 3 x 8-12 Wiederho- lungen • total 40 Minuten	2 x/Wo.	12 Wo. Kraft ±
			HF-Bereich zwii- schen aerober Schwelle und 10% unter der anaero- ben Schwelle	40 Minuten		aerobe Leistungs- fähigkeit+

*signifikant; +Verbesserung; –keine Verbesserung; aM: assoziierte Myositis; DM: Dermatomyositis; F12: Funktioneller Index 2; HF: Herzfrequenz; IG: Interventionsgruppe; kA: keine Angaben; KG: Kontrollgruppe; max: Maximum; min: Minimum; MMT: Manueller Muskel Test; PM: Polymyositis; Q1: 1. Quartile; Q2: 2. Quartile.

Trainingskomponenten für Patienten mit stabiler Krankheitsaktivität

19 von 23 Studien mit Patienten in stabiler Krankheitsphase untersuchten ein allgemeines Kraft- und/oder Ausdauertraining. Zwei Studien bezogen sich auf ein Okklusionstraining [38, 46], eine Studie auf ein Handtraining [40], bei einer Studie handelte es sich um eine Sekundäranalyse [39]. Aufgrund der Einschlusskriterien finden diese Studien im Folgenden keine weitere Beachtung. Die anderen 19 Studien schlossen insgesamt 199 Patienten mit IM ein. Es handelte sich um vier randomisierte kontrollierte Studien (Evidenzlevel 1B) [24–26, 28], zwei Studien [29, 30] waren nicht randomisiert und kontrolliert (Evidenzlevel 2C), bei acht Studien [31, 32, 34–37, 41, 42] handelte es sich um Prä-Post-Vergleiche (Evidenzlevel 2C) und bei fünf Studien [43, 44, 47, 49, 50] um Fallberichte/Fallserien (Evidenzlevel 4). Bei drei der vier randomisierten kontrollierten Studien führte die Kontrollgruppe kein Training durch. Bei einer RCT absolvierten beide Gruppen dasselbe Trainingsprogramm, eine Gruppe erhielt zusätzlich orales Kreatinin, die andere Gruppe Placebo [28]. Sechs Studien untersuchten ein Krafttraining [32, 37, 41, 42, 47, 49], vier Studien ein Ausdauertraining [24, 29, 43, 44] und acht Studien ein kombiniertes Kraft- und Ausdauertraining [25, 26, 28, 30, 34–36, 50]. Eine Studie evaluierte ein multidisziplinäres Programm mit jeweils unterschiedlichen Aktivitäten [31] (Tabelle 2). Auch bei stabiler Krankheitsaktivität wurden keine unerwünschten Ereignisse beschrieben.

Tabelle 2: Übersicht der Trainingsstudien bei stabiler entzündlicher Muskelerkrankung

Studie/Design/ Evidenzlevel	Diagnose/ Krankheitsdauer (Jahre)	Art der Intervention	Kontrolle
Hicks et al. [49] Fallbericht Evidenzlevel 4	- 1 PM - 4	betreutes Krafttraining	
Spector et al. [41] Prä-post-Vergleich Evidenzlevel 2C	- 5 IBM - Mittelwert: 6.2	betreutes Krafttraining	
Wiesinger et al. [24] RCT Evidenzlevel 1B	- IG: 5 DM, 2 PM KG: 5 DM, 2 PM - > 6 Monate	betreutes Ausdauertraining	kein Training
Wiesinger et al. [29] kontrollierte Studie Evidenzlevel 2B	- IG: 6PM, 2 DM KG: 5 PM/DM - Mittelwert±SD: 7.25±8	betreutes Ausdauertraining	kein Training
Alexanderson et al. [34] Prä-post-Vergleich Evidenzlevel 2B	- 5 PM, 5 DM - median: 4 min/max: 2/10	Kraft- und Ausdauertraining (Heimprogramm)	
Karper et al. [50] Fallbericht Evidenzlevel 4	- 1 DM - 4	betreutes Kraft- und Ausdauertraining	
Heikkilä et al. [31] Prä-post-Vergleich Evidenzlevel 2B	- 15 PM, 4 DM, 3 IBM - Mittelwert ±SD: 6.4 ± 6.1	multidisziplinäres Programm (unterschiedliches Atvi- tätsangebot)	
Arnardottir et al. [35] Prä-post-Vergleich Evi- denzlevel 2B	- 7 IBM - median: 2 min/max: 2/6	Kraft- und Ausdauertraining (Heimprogramm)	
Varju et al. [42] Prä-post-Vergleich Evidenzlevel 2B	- 5 PM, 6 DM - kA	betreutes Krafttraining	
Harris-Love et al. [47] Fallbericht Evidenzlevel 4	- 1 PM - 1	Phase 1: betreutes Krafttrai- ning, gefolgt von Heimpro- gramm Phase 2: betreutes exzentri- sches Krafttraining	
Chung et al. [28] RCT Evidenzlevel 2B	- IG: 10 PM, 9 DM KG: 12 PM, 6 DM - IG: median: 9.2; min/max: 1/52 KG: median: 8.6; min/max: 1/23	Kraft- und Ausdauertraining (Heimprogramm) plus orales Kreatin	Kraft- und Ausdauer- training (Heimpro- gramm) plus Placebo
Dastmalchi et al. [30] kontrollierte Studien Evidenzlevel 2B	- 5 PM, 4 DM - median: 3.6 min/max: 1.5/8.5	Kraft- und Ausdauer- training (Heimpro- gramm)	gesunde Kontroll- gruppe
Alexanderson et al. [32] Prä-post-Vergleich Evidenzlevel 2B	- 5 DM, 3 PM, 1aM - median: 4.5 min/max: 2.7/29	betreutes Krafttraining	
Johnson et al. [37] Prä-post-Vergleich Evidenzlevel 2B	- 7 IBM - median: 11 min/max: 4/17	Krafttraining (Heimprogramm)	

Tabelle 2 (Fortsetzung)

Studie/Design/ Evidenzlevel	Diagnose/ Krankheitsdauer (Jahre)	Art der Intervention	Kontrolle
Johnson et al. [36] Prä-post-Vergleich Evidenzlevel 2B	- 7 IBM - min/max: 5/9	Kraft- und Ausdauer- training (Heimpro- gramm)	
Dalise et al. [44] Fallbericht Evidenzlevel 4	- 1 PM - 3	betreutes Ausdauertraining	
Alemo Munters et al. [25] RCT Evidenzlevel 1B	- IG: 4 PM, 5 DM KG: 3 PM, 4 DM - IG: median: 8; min/max: 1/13 KG: median: 7; min/max: 2/33	Kraft- und Ausdauer- training (2 x/Wo. be- treut, 1 x/Wo. selbst- ständig)	kein Training
Alemo Munters et al. [26] RCT, plus 1-Jahres-(of- fenes)-Follow-up Evidenzlevel 1B	- IG: 4PM, 5DM KG: 3PM, 4 DM - IG: median: 8; IQR: 8 KG: median: 8; IQR: 6	betreutes Kraft- und Ausdauertraining	kein Training
Bertolucci et al. [43] Fallserie Evidenzlevel 4	- 4 PM - > 6 Monate	betreutes Ausdauertraining	

Legende: aM: assoziierte Myositis; DM: Dermatomyositis; IBM: Eischlusskörpermyositis; IG: Interventionsgruppe; KA: keine Angaben; KG: Kontrollgruppe; max: Maximum; min: Minimum; PM: Polymyositis; QR: Inter-Quartile-Range; RCT: randomisierte kontrollierte Studie; SD: Standard Deviation.

Krafttraining: Die Trainingskomponenten der Studien, die sich auf die stabile Phase beziehen, sind in Tabelle 3 dargestellt. Das Krafttraining erfolgte in den meisten Studien dynamisch, in der Regel mit 1–3 Serien zwischen 8 und 20 Wiederholungen. Nur eine Studie untersuchte die Wirkung eines isometrischen Krafttrainings [49]. Vier Studien verwendeten dasselbe Trainingsprotokoll [28, 30, 34, 35]. Es beinhaltete ein 30-minütiges Heimprogramm (15 Minuten Krafttraining, gefolgt von 15 Minuten Ausdauertraining). Patienten mit starken funktionellen Einschränkungen (FI-Score < 38) trainierten die Handmuskulatur, die vordere Oberschenkel-, Hüft- und Bauchmuskulatur, diejenigen mit nur leichten bis moderaten funktionellen Einschränkungen (FI-Score ≤ 38) trainierten zusätzlich mit Gewichten (0,25–2 kg) [34]. In drei Studien war die Intensität anhand 1 RM bzw. 3 oder 10 RM definiert [32, 41, 47], bei vier Studien anhand der maximal möglichen Anzahl der Wiederholungen [25, 26, 36, 37]. Beim Krafttraining sind die Resultate auch in der stabilen Phase nicht konsistent. Zwar zeigen alle Studien in gewissen Muskelgruppen einen Kraftzuwachs. Bei einzelnen Muskelgruppen ließ sich jedoch insbesondere mit dem Manuellen Muskeltest kein Effekt nachweisen [35, 41].

Tabelle 3: Trainingskomponenten bei stabiler entzündlicher Muskelerkrankung

Studie	Methode	Intensität	Umfang	Frequenz	Dauer	Resultate
Hicks et al. [49]	isometrisches Krafttraining: obere/untere Extremität	max isometrische Kon- traktionen	2 Übungen à 6 x 6 Sekunden	3 x/Wo.	4 Wo.	IP1+
Spector et al. [41]	dynamisches Krafttraining: obere/untere Extremität	75% des 3 RM	<ul style="list-style-type: none"> • kA • 4 Übungen à 3 x 10,15, 20 Wiederholungen 	3 x/Wo.	12 Wo.	<ul style="list-style-type: none"> • MMT– • 3RM+
Wiesinger et al. [24]	Ausdauertraining: <ul style="list-style-type: none"> ■ Fahrradergometer ■ Step Aerobic 	<ul style="list-style-type: none"> • Ergometer: bis 60% max HR • Step Aerobic: kA 	<ul style="list-style-type: none"> • Ergometer: 20 Minuten • Step Aerobic: 30 Minuten • total: 60 Minuten (mit Aufwärmen, Cool-down und Stretching) 	<ul style="list-style-type: none"> • Wo. 1–2: 2 x/Wo. • Wo. 3–6: 3 x/Wo. 	6 Wo.	<ul style="list-style-type: none"> • VO_{2max} (KG-G)+* • IPT (KG-G)+*
Wiesinger et al. [29]	Ausdauertraining: <ul style="list-style-type: none"> ■ Fahrradergometer ■ Step Aerobic 	<ul style="list-style-type: none"> • Ergometer: bis 60% max HR • Step Aerobic: kA 	<ul style="list-style-type: none"> • Ergometer: 20 Minuten • Step Aerobic: 30 Minuten • total: 60 Minuten (mit Aufwärmen, Cool-down und Stretching) 	<ul style="list-style-type: none"> • Wo. 1–2: 2 x/Wo. • Wo. 3–6: 3 x/Wo. • Wo. 7–24: 1 x/Wo. 	6 Monate	<ul style="list-style-type: none"> • VO_{2max} (KG-G)+* • IPT (KG-G)+*
Alexanderson et al. [34]	Ausdauertraining: <ul style="list-style-type: none"> ■ Walking dynamisches Krafttraining (jeden individuellen FI2-Score wurde mit oder ohne Gewicht trainiert): <ul style="list-style-type: none"> ■ untere/obere Extremität ■ Rumpfmuskulatur 	kA „leicht bis moderat“	15 Minuten • 15 Minuten • 10 Wiederholungen pro Übung	5 x/Wo.	12 Wo.	FI2+* Gehdistanz+*
Karper et al. [50]	Ausdauertraining: <ul style="list-style-type: none"> ■ Walking Krafttraining: <ul style="list-style-type: none"> ■ obere Extremität ■ Rumpfmuskulatur 	„etwas anstrengend“ kA	30–40 Minuten • kA • 6 Übungen à 1 x 8–10 Wiederholungen pro Übung	4–5 x/Wo. 3 x/Wo.	12 Monate	<ul style="list-style-type: none"> • Handkraft+ • Kraftausdauer (M. biceps)* • Gegeschwindigkeit+

Tabelle 3 (Fortsetzung)

Studie	Methode	Intensität	Umfang	Frequenz	Dauer	Resultate
Varju et al. [42]	dynamisches Krafttraining: • untere/obere Extremität • Rumpfmuskulatur	kA	• 40–60 Minuten • 2 x 65–70% der maximal möglichen Wiederholungen	5 x/Wo.	3 Wo.	Dynamometrie+*
Arnardottir et al. [35]	s. Alexanderson [34]				12 Wo.	• MMT+/- • FI2 +/-
Harris-Love et al. [47]	dynamisches Krafttraining: • Phase 1: isotonisches Krafttraining: untere Extremität • Phase 2: exzentrisches Krafttraining: untere Extremität	• kA • Wo. 1: 2 Serien à 40–50% des exzentrischen 1 RM • Wo. 2–3: 2–3 Serien à 50–60% des exzentrischen 1 RM • Wo. 4–12: 70% des exzentrischen 1 RM	• kA • 2–3 x 12 Wiederholungen • kA	• 2–3 x/Wo. • 2 x/Wo.	• 6 Monate • 12 Wo.	• IPT+ • CPT+
Chung et al. [28]	s. Alexanderson [34]				6 Monate	FI2: • IG: +* • KG: +* • IG-KG: +/- MMT: • IG: + • KG: +/- • IG-KG: +/-
Dastmalchi et al. [30]	s. Alexanderson [34]				12 Wo.	FI+*

Tabelle 3 (Fortsetzung)

Studie	Methode	Intensität	Umfang	Frequenz	Dauer	Resultate
Alexanderson et al. [32]	dynamisches Krafttraining: • untere/obere Extremität • Rumpfmuskulatur	• Wo. 1: 3 x 15 mit 50% vom 10 VRM • Wo. 2-7: 3 x 10 mit 100% vom 10 VRM	• 45 Minuten Krafttraining 3 x 10-15 Wiederholungen • total: 60 Minuten (inklusive Aufwärmen und Stretching)	3 x/Wo.	7 Wo.	10-15 VRM+*F12 +*
Johnson et al. [37]	dynamisches Krafttraining: • untere/obere Extremität • Rumpfmuskulatur	• Wo. 1-2: Angewöhnungs- phase mit tiefer Intensität • Wo. 3-16: 2 Wiederholungen weniger als maximal möglich wäre (maximal 3-15)	• kA • max. 6 Übungen à 3 x 15 Wiederholungen	2 x/Tag	16 Wo.	■ Dynamometrie+* ■ Gegeschwindigkeit+
Johnson et al. [36]	Ausdauertraining: • Fahrradergometer	80% der maximalen HF	• Wo. 1-2: 2 Minuten weniger als beim Maxi- maltest möglich war • Wo. 3-12: alle 2 Wochen 2 Minuten länger • kA • 4-6 Übungen à 3 x 6-15 Wiederholungen	6 x/Wo.: • 3 x/Wo. Kraft • 3 x/Wo. Ausdauer	12 Wo.	VO _{2max} +*
	dynamisches Krafttraining: • untere/obere Extremität • individuelle Übungen	• Wo. 1-2: tiefe Intensität • Wo. 3-12: 2 Wiederholungen weniger als maximal möglich				Dynamometrie +*/+/-

Tabelle 3 (Fortsetzung)

Studie	Methode	Intensität	Umfang	Frequenz	Dauer	Resultate
Dalise et al. [44]	Ausdauertraining: • Laufband (Walking) • Armergometer	• Walking: 65–80% max HF • Armergometer: RPM: 35–40, „very low load“	• Laufband: mind. 20 Minuten • Armergometer: 15 Minuten • total: mind. 35 Minuten	5 x/Wo.	5 Wo.	• Dynamometrie+ • 10 MWT+ • 6 MWT–
Alemon Munters et al. [25]	Ausdauertraining: Fahrradergometer	70% der VO_{2max}	30 Minuten	3 x/Wo.	12 Wo.	• TG: VO_{2max}^{+*} • KG: VO_{2max}^{-} • TG-KG: kA
Alemon Munters et al. [26]	dynamisches Kraftausdauertraining: untere/obere Extremität	30–40% der maximal möglichen Wiederholungen	• 20 Minuten • total: 60 Minuten (mit Aufwärm-, Cool-down und Stretching)			VO_{2max}^{+} • IG: + • KG: – • TG-KG: + MMT: • IG: + • KG: – • IG-KG+ 5 VRM (kg): • IG: + • KG: + • IG-KG: left+, right+
Bertolucci et al. [43]	Ausdauertraining: Laufband (Walking)	60–75% max HF	30–40 Minuten	3 x/Wo.	6 Wo.	• 10 MWT+ • 6 MWT+ (in 3 von 4 Muskeltests)

Legende: *: signifikant; +: Verbesserung, -: keine Verbesserung; aM: assoziierte Myositis; CPT: concentric peak torque; DM: Dermatomyositis; F/2: funktioneller Index 2; HF: Herzfrequenz; IBM: Einschlusskörpermyositis; IG: Interventionsgruppe; IPT: isometric peak torque, kA: keine Angaben; KG: Kontrollgruppe; max: Maximum; min: Minimum; PM: Polymyositis; Q1: 1. Quartile; Q2: 2. Quartile; 6 MWT: 6 Minutes Walking Test; VO_{2max} : prozentuale maximale Sauerstoffaufnahme; VRM: Voluntary Repetition Maximum; Wo.: Woche; 10 MWT: 10 Meters Walking Test.

Ausdauertraining: Ein Ausdauertraining erfolgte zwischen 1–5 × wöchentlich und dauerte zwischen 15 und 50 Minuten. In den meisten Studien fand das Training mit 60–80% der (geschätzten) maximalen Herzfrequenz statt, was einem moderaten bis hohen Anstrengungsempfinden entspricht. In den Studien von Munters et al. trainierten die Probanden mit 70% der maximalen Sauerstoffaufnahme (VO_{2max}), was einer hohen Intensität entspricht [25, 26]. Ein Vergleich der unterschiedlichen Intensitätsangaben bietet Tabelle 4. Durch Ausdauertraining war in fast allen Studien ein positiver Effekt auf die Ausdauerleistung nachweisbar. Lediglich in einer Fallbeschreibung verbesserte sich die Gehdistanz im 6-Minuten-Gehtest nicht [44]. 2 von 3 Studien mit randomisierter Kontrollgruppe zeigten einen signifikanten Gruppenunterschied zugunsten der Trainingsgruppe [24, 25].

Tabelle 4: Vergleich der Intensitätsparameter im Ausdauerbereich (ACSM)

Intensität	$VO_{2max}\%$	$HF_{max}\%$	Borg-Skala
sehr leicht	< 37	< 57	< 9
leicht	37–45	57–63	9–11
moderat	46–63	64–76	12–13
schwer	64–90	77–95	14–17
sehr schwer bis maximal	≥ 91	≥ 96	≥ 18

Legende: VO_{2max} : prozentuale maximale Sauerstoffaufnahme; $HF_{max}\%$: prozentuale maximale Herzfrequenz; Borg-Skala: subjektives Anstrengungsempfinden.

Trainingsleitfaden

Der Trainingsleitfaden besteht aus einem Einführungsteil zu allgemeinen Trainingsprinzipien und je zu einem Teil über Kraft- und Ausdauertraining, individuell abgestimmt auf Patienten mit IM. Im Einführungsteil ist die Bestimmung des Ausgangswertes beschrieben, ebenso die allgemeine Trainingsgestaltung (Abbildung 1). Aufgrund der unterschiedlichen Krankheitsdauer in der aktiven Phase ist der Trainingsleitfaden in eine früh-aktive Phase (Krankheitsaktivität < 3 Monate) und eine aktive Phase (Krankheitsaktivität > 3 Monate mit instabilen Krankheitsverlauf) unterteilt. Die Trainingskomponenten sind für Kraft- und Ausdauertraining für jede Krankheitsaktivität (früh-aktiv, aktiv, stabil) beschrieben. In Bezug auf die Ausdauer ließen sich die Empfehlungen direkt aus den Studien ableiten (Tabelle 5). Da die Angaben hinsichtlich des Krafttrainings in den Studien teilweise unvollständig und vor allem unterschiedlich waren, war es schwierig, spezifische Empfehlungen zu formulieren. Deshalb wurden im Trainingsleitfaden die Studienergebnisse durch Empfehlungen des ACSM sowie durch Angaben aus einer narrativen Übersichtsarbeit und Erfahrungen aus dem Klinikalltag ergänzt.

Zum Krankheitsbild Myositis gehört neben abnehmender Muskelkraft auch verminderte Kraftausdauer. Deshalb enthält der Trainingsleitfaden sowohl Empfehlungen für ein Training der Muskelkraft als auch für Kraftausdauer. In beiden Kraftbereichen sollten die Übungen – wenn immer möglich – in allen Krankheitsphasen dynamisch erfolgen. Ist die Muskelschwäche so stark ausgeprägt, dass keine aktive Bewegung gegen die Schwerkraft möglich ist, kann das Training mit therapeutischer Unterstützung oder mittels eines Schlingentischs schwerkraftneutral erfolgen. Ist dies ebenfalls nicht möglich, ist zu Beginn ein statisches Training empfehlenswert (6–10 Sekunden halten, 5–10 Wiederholungen). Die empfohlenen Trainingskomponenten für das Krafttraining sind in Tabelle 6 dargestellt.

Abbildung 1: Trainingsleitfaden: Trainingsprinzipien

Trainingsprinzipien

- Jedes Trainingsprogramm sollte individuell sein und die Intensität sollte an den Fitnesszustand angepasst sein. Dabei sind Faktoren wie Trainingserfahrung, Krankheitszustand, Komorbiditäten, Alter, Schmerzen und Fatigue zu beachten. Um die richtige Intensität zu finden wird idealerweise eine Leistungsdiagnostik durchgeführt. Ist dies nicht möglich, sollte die Intensität anhand theoretischen Vorgaben abgeschätzt bzw. berechnet werden.
 - Für das Ausdauertraining kann die Trainingsherzfrequenz anhand der theoretisch maximalen Herzfrequenz (theoretisch maximale Herzfrequenz = $220 - \text{Alter}$) abgeschätzt werden. Da diese Formel nicht für alle Personen gilt, ist immer auch auf das subjektive Anstrengungsempfinden zu achten (Borg-Skala).
 - Im Kraftbereich wird die Intensität häufig als Prozent der Maximalleistung angegeben. Die Maximalleistung (1 Repetition Maximum) ist definiert als das Gewicht, welches bei einmaliger Ausführung maximal bewältigen werden kann. Bei untrainierten Personen ist die Testung des Wiederholungsmaximums nicht immer möglich. Als Alternative kann nach einer Angewöhnungsphase ausgetestet werden mit welchem Gewicht bzw. mit welcher Ausgangsstellung die gewünschte Anzahl Wiederholungen durchgeführt werden können. Dies dient dann als Ausgangsgewicht. Auch im Kraftbereich sollte das subjektive Anstrengungsempfinden (Borg-Skala) beachtet werden.
- Um langfristig einen Trainingseffekt aufrecht zu erhalten sollte das Training progressiv sein, d.h. die Trainingsbelastung sollte regelmässig angepasst werden. Idealerweise wird zuerst der Trainingsumfang (Anzahl Wiederholungen, Serien oder Zeitdauer) und erst dann das Gewicht bzw. die Intensität gesteigert. Um die Trainingsbereitschaft zu verbessern und das Verletzungsrisiko zu senken, ist bei untrainierten Personen insbesondere für das Krafttraining eine Angewöhnungsphase sinnvoll.
 - Angewöhnungsphase (1. und 2. Woche)
 - Während der Angewöhnungsphasen ist die Intensität gering, der Übungsumfang ist dafür höher. Das Ziel hierbei ist sich an das Training zu gewöhnen. Es werden vor allem koordinative Anpassungen des Nervensystems erwartet d.h. dass die Innervation sowie die inter- und intramuskuläre Koordination verbessert werden.
 - Trainingsphase (ab der 3. Woche)
 - Die Wiederholungsanzahl wird zu Gunsten des Gewichts reduziert. Angaben zur Intensität sind im Trainingsleitfaden beschrieben. Begonnen wird mit 2 Serien und jeweils 30 Sekunden Pause dazwischen. Sobald der Patient 2 Serien ausführen kann, wird eine 3. Serie dazu genommen. Danach kann das Gewicht entsprechend gesteigert werden.
- Leider ist beim Training nur mit einer kleinen Depotwirkung zu rechnen. Nach dem Prinzip «use it or lose it» geht das Leistungsniveau, sobald der Trainingsreiz ausbleibt, wieder auf das Ausgangsniveau zurück, bzw. nimmt langsam ab. Gerade bei chronischen Erkrankungen bei denen es auch immer wieder zu Krankheitschüben kommen kann, ist ein regelmässiges Training eine Herausforderung. Wichtig ist, dass das Training immer dem jeweiligen Gesundheitszustand angepasst wird und dass Schmerzen richtig eingeordnet werden. Ungewohnte, neue Aktivitäten können im Sinne eines Muskelkaters zu harmlosen Muskelschmerzen führen. Ansonsten sollte aber ein Training nicht zu erhöhten Schmerzaktivität führen. Dabei ist die Betreuung einer erfahrenen Fachperson wichtig. Zusätzlich kann eine übersichtliche und exakte Trainingsdokumentation die Trainingskontrolle und -planung erleichtern.

Borg-Skala	
6	
7	sehr, sehr leicht
8	
9	sehr leicht
10	
11	ziemlich leicht
12	
13	etwas anstrengend
14	
15	Anstrengend
16	
17	sehr anstrengend
18	
19	Sehr, sehr anstrengend
20	

Tabelle 5: Trainingsleitfaden: Trainingskomponenten des Ausdauertrainings

Krankheitsaktivität	Intensität	Frequenz	Umfang	Trainingsmittel (Beispiele)
früh-aktiv: Krankheitsaktivität < 3 Monate	<ul style="list-style-type: none"> 50–60% der maximalen Herzfrequenz Borg-Skala: 9–11/20 	3–5 x pro Woche	5–10 Minuten	Laufband Fahrradergometer Stepper/Cross-trainer Walking
aktiv: Krankheitsaktivität ≥ 3 Monate mit instabilem Verlauf (d. h. Therapieänderung in den letzten 3 Monaten)	<ul style="list-style-type: none"> 60–70% der maximalen Herzfrequenz Borg-Skala: 11–13/20 	3x pro Woche	15–30 Minuten	
stabil: Krankheitsaktivität ≥ 3 Monate mit stabilem Verlauf (d. h. keine Therapieänderung in den letzten 3 Monaten)	<ul style="list-style-type: none"> 70–85% der maximalen Herzfrequenz Borg-Skala: 13–17/20 	3x pro Woche ¹	20–45 Minuten	

Legende: ¹nicht an denselben Tagen wie die Kraftübungen durchführen.

Tabelle 6: Trainingsleitfaden: Trainingskomponenten des Krafttrainings

Krankheitsaktivität	Intensität und Dauer zur Verbesserung der Muskelmasse und -stärke	Intensität und Dauer zur Verbesserung der Kraftausdauer	Frequenz	Umfang und empfohlene Muskelgruppen
früh-aktiv: Krankheitsaktivität < 3 Monate	leicht: • 40–60% der Maximalleistung • 5–10 Wiederholungen/ Serie • 1–3 Serien • Borg-Skala: 9–11/20		5 x pro Woche	6–8 Muskelgruppen: Schulterabduktoren Flexoren Hand Fingerflexoren (Faustschluss) Beine
aktiv: Krankheitsaktivität ≥ 3 Monate mit instabilem Verlauf (d. h. Therapieänderung in den letzten 3 Monaten)	moderat: • 40–60% der Maximalleistung* • 8–15 Wiederholungen/ Serie • 1–3 Serien • Borg-Skala: 11–13/20	moderat: • 20–40% der Maximalleistung* • 15–25 Wiederholungen/ Serie • 2–3 Serien • Borg-Skala: 11–13/20	3–5 x pro Woche	Knieextensoren Knieflexoren Fußflexoren Fußextensoren Hüftabduktoren Becken/Rumpf
stabil: Krankheitsaktivität ≥ 3 Monate mit stabilem Verlauf (d. h. keine Therapieänderung in den letzten 3 Monaten)	schwer (submaximal): • 60–80% der Maximalleistung* • 8–15 Wiederholungen/ Serie • 2–3 Serien • Borg-Skala: 13–17/20	schwer (submaximal): • 30–50% der Maximalleistung* • 15–25 Wiederholungen/ Serie • 2–3 Serien • Borg-Skala: 13–17/20	3 x pro Woche	Beckenheben (Bridging) Rumpfbeugen (Sit-ups)

Legende: * definiert als Gewicht, das die trainierende Person bei einmaliger Ausführung maximal bewältigen kann.

Diskussion

Die aktuelle Datenlage deutet darauf hin, dass sowohl Kraft- als auch Ausdauertraining bei Patienten mit IM indiziert sind. Für Ausdauertraining sind bei aktiver und stabiler Krankheitsaktivität positive Effekte auf die Leistungsfähigkeit nachweisbar. In Bezug auf Krafttraining sind die Resultate weniger einheitlich. Ein Kraftzuwachs lässt sich meist nur in einzelnen Muskelgruppen nachweisen. Da jedoch alle Studien gewisse positive Effekte eines Kraft- und/oder Ausdauertrainings und keine trainingsbedingten unerwünschten Ereignisse (adverse events) aufzeigen, ist ein Kraft- und Ausdauertraining bei Patienten mit entzündlicher Muskelerkrankung empfehlenswert. Insgesamt ist das Evidenzlevel bei stabiler Krankheitsaktivität höher als bei aktiver Krankheitsaktivität. Somit lassen sich die Empfehlungen für die stabile Krankheitsaktivität als stark und diejenigen für die aktive Phase als moderat bezeichnen.

Anhand der Studien wird jedoch nicht deutlich, welches Trainingsprotokoll sich am besten eignet. Deshalb ist im Leitfaden die verfügbare Evidenz mit den Angaben der allgemeinen Trainingsrichtlinien des ACSM [18] und dem Fachwissen der spezialisierten Physiotherapeuten kombiniert. Die Trainingskomponenten für Kraft- und Ausdauertraining sind jeweils für die drei Krankheitsphasen früh-aktiv, aktiv und stabil beschrieben.

Da die Studien auch in Bezug auf die eingeschlossenen Probanden, die untersuchten Endpunkte sowie das Studiendesign heterogen sind, lassen sich die Resultate nicht in einer Metaanalyse zusammenfassen. Die meisten Studien untersuchten nur eine kleine Stichprobe und hatten keine Kontrollgruppe. Somit bleibt unklar, ob die ermittelten Effekte tatsächlich auf das Training zurückzuführen sind oder ob andere Faktoren, beispielsweise veränderte Medikation oder Zufall, den Effekt beeinflussten. Um die Wirksamkeit einer Intervention nachzuweisen, wird idealerweise eine Trainingsgruppe mit einer nicht trainierenden Kontrollgruppe verglichen [55]. Insgesamt liegen für Patienten mit IM bis zum heutigen Zeitpunkt fünf RCTs vor. Bei der RCT mit der größten Stichprobe (N: 37) führte sowohl die Interventions- als auch die Kontrollgruppe dasselbe Heimprogramm durch [28]. Da bei dieser Studie jedoch keine nicht trainierende Kontrollgruppe vorhanden war, ist keine definitive Aussage zur Wirksamkeit eines Trainings möglich. In vier Studien mit einer Probandenzahl zwischen 14 und 19 erfolgte ein Vergleich der Trainingsgruppe mit einer nicht trainierenden Kontrollgruppe.

Im Gegensatz zum Ausdauertraining ist im Kraftbereich kein signifikanter Gruppenunterschied bezüglich der Zunahme der Muskelkraft nachweisbar. Dafür gibt es verschiedene Erklärungen. Ein Grund kann darin bestehen,

dass diese Studien infolge der kleinen Stichprobengröße nicht genügend Power aufweisen, um einen Unterschied im Kraftbereich aufzuzeigen. Das Problem der dürtigen Datenlage ist typisch für seltene Erkrankungen. Besondere Hindernisse sind unter anderem Rekrutierungsschwierigkeiten. Aufgrund der geringen Populationsgrößen sowie der klinischen Heterogenität besteht ein Bedarf an angepassten Studiendesigns und an multinationalen randomisierten klinischen Studien [56]. Ein zweiter Grund könnte darin bestehen, dass das untersuchte Krafttraining zu wenig intensiv war, um eine effektive Verbesserung der Kraft zu erreichen. Da die Trainingsintensität in den meisten Studien nicht ausreichend beschrieben ist, bleibt unklar, ob ein intensiveres Training einen besseren Effekt hat als ein weniger intensives Training. Das Problem der ungenauen Dokumentation der Trainingskomponenten ist bekannt – sowohl in Trainingsstudien mit Patienten mit Myositis [57] als auch in Studien mit anderen Gruppen von Patienten, beispielsweise bei Personen mit Hirnschlag oder einer Krebserkrankung [58, 59].

Ein weiterer Grund für dieses Ergebnis könnte auch die gewählten Assessments sein. In den meisten Studien erfolgte die Messung der Kraft mit dem MMT. Er zeigt hohe Deckeneffekte und die Reliabilität einzelner Muskelgruppen ist ungenügend [60]. Eventuell ist der MMT bei einzelnen Muskelgruppen zu wenig sensitiv, um eine Verbesserung aufzuzeigen. Im Ausdauerbereich konnten Wiesinger et al. den Effekt eines 60-minütigen Ausdauertraining mit leichter Intensität (60% der maximalen Herzfrequenz) auf die aerobe Leistungsfähigkeit nachweisen [24]. Diese Dosierung entspricht den Empfehlungen des ACSM für Ausdauertraining bei dekonditionierten gesunden Personen [18]. Da Patienten mit Myositis häufig eine verminderte körperliche Leistungsfähigkeit aufweisen [25, 61], ist es angebracht, die Empfehlungen für dekonditionierte Personen zu befolgen.

Zusätzlich zur Verbesserung der Kraft und Ausdauer ließen sich in verschiedenen Studien auch subjektive Parameter (Patient Reported Outcomes [PRO]) verbessern, beispielsweise Lebensqualität, Alltagsaktivitäten (Gehen, Treppensteigen und Rennen), Vitalität und körperliche Funktionsfähigkeit [25, 26, 61]. Im einzigen RCT mit Patienten in der aktiven Krankheitsphase verbesserten sich die Kraft- und Ausdauerparameter in beiden Gruppen vergleichbar. Im Langzeit-Follow-Up zeigte sich jedoch, dass Patienten, die frühzeitig mit einem Trainingsprogramm starteten, nach zwei Jahren körperlich aktiver und leistungsfähiger waren, als diejenigen der Kontrollgruppe [27]. Diese Beobachtung würde deshalb bei der momentanen Datenlage eher für einen Trainingsbeginn in einer frühen Krankheitsphase sprechen.

Trainingsleitfaden

Da das Krankheitsspektrum umfassend und die individuelle körperliche Leistungsfähigkeit bei vergleichbarer Krankheitsaktivität unterschiedlich ist, findet sich im Trainingsleitfaden jeweils eine große Bandbreite der Trainingsdosierung. Sie setzt sich aus der Trainingsintensität (z. B. Prozent der maximalen HF für ein Ausdauertraining bzw. Prozent des 1 RM für ein Krafttraining) und des Trainingsumfangs (z. B. Zeit bzw. Serien und Wiederholungen) zusammen. Normalerweise ist die Dosierung zu Beginn tief und je nach Möglichkeit erfolgt eine Steigerung. Damit ein Training effektiv ist, sind auch Trainingsprinzipien wie Spezifität, Ausgangswert, Overload sowie Progression zu berücksichtigen [62]. Ebenfalls bedeutsam sind individuelle und krankheitsbedingte Faktoren wie Schmerz, körperliche Einschränkungen, Komorbiditäten und Fatigue. Fachpersonen, die Patienten bei ihrem Training begleiten, sollten sich sowohl mit der vorhandenen Pathologie als auch mit der Trainingslehre auskennen. Die Angaben im Trainingsleitfaden sind als mögliche Zielvorgaben zu verstehen und sollten an die individuelle Situation der Patienten angepasst werden. Die Kombination aus klinischer Expertise der Fachpersonen, Wünschen bzw. Erfahrungen der Patienten sowie aktuellem Forschungsstand ist ein wichtiges Merkmal der evidenzbasierten Arbeitsweise [63].

Die Intensität im Ausdauerbereich ist im Trainingsleitfaden anhand der theoretisch maximalen Herzfrequenz (theoretisch maximale Herzfrequenz = $220 - \text{Alter}$) sowie des subjektiven Anstrengungsempfindens mittels Borg-Skala [64] angegeben. Diese Kombination ist in jeder Praxis anwendbar. Da die Formel zur Berechnung der theoretisch maximalen HF nicht für alle Personen gilt, ist bei diesen Angaben immer auch auf das subjektive Anstrengungsempfinden (Borg-Skala) zu achten. Um diese Angaben mit eventuellen $\text{VO}_{2\text{max}}$ -Messungen einer Leistungsdiagnostik vergleichen zu können, erfolgt in Tabelle 4 ein Vergleich der unterschiedlichen Möglichkeiten zur Intensitätssteuerung. Die Intensitätsbereiche von 60–80% der maximalen HF für die aktive und die stabile Phase entsprechen den allgemeinen Empfehlungen des ACSM [18]. Diese schlagen für dekontionierte Erwachsene eine Intensität zwischen 57 und 76% der maximalen HF und für die meisten gesunden Erwachsenen eine Intensität zwischen 64 und 95% der maximalen HF vor. Es ist bekannt, dass viele Patienten mit Myositis eine reduzierte Fitness besitzen [25, 61]. Daher ist für das Ausdauertraining eine Intensität von höchstens 80% der maximalen HF empfehlenswert. In den untersuchten Studien wurde deutlich, dass ein Intensitätsbereich zwischen 60 und 80% der maximalen HF sicher ist und sich positiv auf die aerobe Leistungsfähigkeit

auswirkt. Die Praxis zeigt jedoch, dass Patienten in einer früh-aktiven Phase mit stark erhöhten Entzündungsparametern, Fatigue und/oder stark reduziertem Allgemeinzustand bereits eine minimale Intensität von 60% der maximalen HF nicht bewältigen können. Deshalb ist im Trainingsleitfaden die Dosierung für diese Phase auf 5–10 Minuten mit 50–60% maximaler HF angepasst. Der Umfang eines alleinigen Ausdauertrainings beinhaltet in allen Studien 30–60 Minuten. Dies entspricht den allgemeinen Trainingsempfehlungen des ACSM. Der gesamte Trainingsaufwand wird dadurch bei einem kombinierten Kraft- und Ausdauertraining umfangreich. Für untrainierte Patienten kann dies aufgrund der Fatigue schwierig zu bewältigen sein [58]. Deshalb ist das Ausdauertraining im Trainingsleitfaden auf 15– 45 Minuten beschränkt. Eine erfolgsversprechende Alternative zu den bisher untersuchten kontinuierlichen Ausdauertrainings könnte ein hochdosiertes Intervalltraining sein. Diese Trainingsmethode hat sich im Vergleich zu einem kontinuierlichen Ausdauertraining als wirksamer erwiesen, um die körperliche Leistungsfähigkeit bei Gesunden sowie bei Patienten mit chronischen Erkrankungen zu verbessern [65–68]. Bisher liegen für diese Trainingsart bei Patienten mit IM noch keine Untersuchungen vor.

Im Trainingsleitfaden sind aus Gründen der Vergleichbarkeit die Intensitätsangaben für den Kraftbereich in Prozentwerten der Maximalleistung angegeben. Diese Maximalleistung (1 RM) ist definiert als das Gewicht, das bei einmaliger Ausführung maximal bewältigt werden kann. Bei untrainierten Personen sowie Patienten ist die Testung des Wiederholungsmaximums häufig nicht möglich, da bei reduzierter Belastungsverträglichkeit gesundheitsgefährdende Begleiterscheinung wie Pressatmung, hoher Blutdruck oder orthopädisch bedenkliche Belastungsspitzen im Stütz- und Bewegungsapparat auftreten können. Zudem sind Trainingsanfänger meist nicht in der Lage, eine Übung mit der maximalen Belastung korrekt auszuführen. Um das passende Trainingsgewicht zu finden, gilt es deshalb, zuerst das angestrebte Wiederholungsmaximum zu bestimmen. Dies erfordert, auszu- testen, mit welchem Ausgangsgewicht bzw. in welcher Ausgangsstellung die gewünschte Anzahl der Wiederholungen durchführbar ist. Auch im Kraftbereich ist das subjektive Anstrengungsempfinden (Borg-Skala) bei der Trainingsdosierung zu berücksichtigen. Tabelle 7 zeigt die unterschiedlichen Methoden der Intensitätssteuerung im Kraftbereich. Da aus der Literatur nicht hervorgeht, welche Intensität im Kraftbereich zum besten Trainingsresultat führt, orientiert sich der Trainingsleitfaden an den ACSM-Empfehlungen. Je nach Trainingserfahrung und Alter sind für ein Training der Muskel-

kraft 8–15 Wiederholungen mit 40– 80% des 1 RM empfohlen. Diese Dosierung gilt auch für die aktive und stabile Phase. Analog zum Ausdauertraining ist für Patienten in der früh-aktiven Phase die Trainingsintensität auf 5–10 Wiederholungen mit 40–60% der Maximalleistung nach unten angepasst. Bei weniger intensivem Training ist die Regenerationszeit verkürzt. Deshalb ist es in dieser Phase möglich, häufiger zu trainieren. Da Patienten mit IM eine verringerte Maximalkraft und Kraftausdauer haben, finden sich im Leitfaden zusätzliche Angaben zur Kraftausdauer. Lediglich in zwei Studien erfolgte ein Kraftausdauertraining [25, 26]. Leider fehlen in diesen beiden Studien konkrete Angaben zum Umfang des Trainings. Deshalb besteht die momentan bestmögliche Evidenz aus der Übernahme der ACSM-Empfehlungen (< 50% des 1RM, 15–20 Wiederholungen). Sobald wie möglich sollte ein dynamisches Krafttraining erfolgen. Dies entspricht der Muskelaktionsform, die in den meisten Studien beschrieben ist. Patienten mit entzündlichen rheumatologischen Erkrankungen tolerieren diese gut [69]. Ein Vorteil des dynamischen Krafttrainings besteht darin, auch Koordination zu trainieren. Um den Transfer in den Alltag zu gewährleisten, erfolgt idealerweise eine Instruktion funktioneller Übungen. Falls nötig, ist die Ausgangsposition so zu wählen, dass sich einzelne Übungen schwerkraftneutral (mit/ohne Gewicht, z. B. mithilfe eines Schlingentischs) ausführen lassen.

Im Trainingsleitfaden sind bewusst keine Empfehlungen für exzentrisches Training enthalten. Exzentrisches Training ist mit hohen Trainingsbelastungen verbunden. Dabei ist die Verletzungsgefahr bei trainingsunerfahrenen Personen erhöht. Beim Training mit Patienten mit IM gilt es, eine allzu starke Belastung zu vermeiden. In einer Studie [49] erfolgte exzentrisches Training bei stark abgeschwächten Muskelgruppen. Bei einem MRC-Wert von 1 ist keine aktive Bewegung möglich, weshalb lediglich ein statisches oder exzentrisches Training erfolgen kann.

Die Empfehlungen des Trainingsleitfadens beziehen sich explizit auf Patienten mit IM. Je nach Gesundheitszustand und Beschwerden kann auch lediglich ein Krafttraining oder Ausdauertraining erfolgen. Die Bewegungsempfehlungen der WHO sollten ebenfalls Beachtung finden [70]. Sie beinhalten mindestens 150 Minuten pro Woche moderate körperliche Aktivität. Insbesondere bei älteren Personen ist regelmäßige körperliche Aktivität wichtig – nicht nur zur Prävention verschiedener chronischer Erkrankungen wie Herz-Kreislauf-erkrankungen, Diabetes Typ II oder Krebs, sondern auch, um Stürze zu vermeiden sowie die Selbstständigkeit im Alter und das psychische Wohlbefinden zu erhalten [71].

Eine Herausforderung beim Erstellen des Trainingsleitfadens bestand darin, dass die meisten untersuchten Studien die Trainingsprotokolle nur ungenau beschreiben. Deshalb war es notwendig, die fehlenden Trainingsangaben anhand allgemeingültiger Trainingsrichtlinien und -prinzipien zu ergänzen. Empfehlungen bezüglich des Trainingsumfangs fehlen im Trainingsleitfaden teilweise, zum Beispiel Angaben bezüglich der Übungsanzahl. Diese gilt es anhand von Informationen aus zukünftigen Studien anzupassen. Ein Vorteil der Trainingsrichtlinien besteht darin, dass sich Kraft- und Ausdauertraining flexibel kombinieren lassen und der Leitfaden als Grundlage für zukünftige Trainingsstudien dienen kann. Zum Beispiel kann in der früh-aktiven Krankheitsphase der Kraftverlust dominant sein und in einer späteren Krankheitsphase die verminderte muskuläre sowie kardiopulmonale Ausdauerfähigkeit. So lässt sich je nach Hauptproblematik und den individuellen Bedürfnissen der Patienten der Trainingsschwerpunkt auf das Krafttraining oder die kardiopulmonale Ausdauerfähigkeit legen.

Schlussfolgerungen

Obwohl die verwendeten Protokolle der Trainingsstudien im Bereich der Myositis unterschiedlich sind, weisen alle Studien konsistent darauf hin, dass das Training sicher und effektiv ist. Erstmals sind die verschiedenen Trainingsprotokolle für alle Krankheitsaktivitäten in einem Trainingsleitfaden zusammengefasst. Dies ermöglicht Physiotherapeuten einen raschen Überblick über evidenzbasierte Trainingsrichtlinien bei Patienten mit IM in allen Krankheitsphasen, wodurch eine bessere Versorgung der Patienten von der Diagnosestellung bis zur Rehabilitation möglich ist. Die Richtlinien sollten nach Möglichkeit in weiteren Studien angewendet, überprüft und anschließend verfeinert werden. Am Universitätsspital Zürich findet aktuell eine Machbarkeitsstudie statt, um ein tabletbasiertes Heimprogramm bei Patienten mit IM zu überprüfen. Dieses Vorgehen erlaubt, die Trainingsrichtlinien an die Bedürfnisse und Möglichkeiten der Patienten anzupassen. Dabei sollte bei der Beschreibung der Intervention die TiDieR-Checklist Berücksichtigung finden [72], um die spätere Reproduzierbarkeit für die Forschung und die klinische Praxis zu gewährleisten. Diese Liste beinhaltet 12 Items, die es bei der Beschreibung der Intervention zu berücksichtigen gilt und die eine Replizierung der Ergebnisse in der Praxis und Forschung erlauben. In einem weiteren Schritt sollte die Wirksamkeit dieses Heimprogramms in einer größeren randomisierten kontrollierten Studie untersucht werden. Bei seltenen Erkrankungen wie Myositis ist dies nur im Rahmen einer internationalen multizentrischen Studie möglich.

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CHAPTER 4

Manual muscle testing and hand-held dynamometry in people with inflammatory myopathy: An intra- and interrater reliability and validity study

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Abstract

Manual muscle testing (MMT) and hand-held dynamometry (HHD) are commonly used in people with inflammatory myopathy (IM), but their clinic-metric properties have not yet been sufficiently studied. To evaluate the reliability and validity of MMT and HHD, maximum isometric strength was measured in eight muscle groups across three measurement events. To evaluate reliability of HHD, intra-class correlation coefficients (ICC), the standard error of measurements (SEM) and smallest detectable changes (SDC) were calculated. To measure reliability of MMT linear Cohen's Kappa was computed for single muscle groups and ICC for total score. Additionally, correlations between MMT8 and HHD were evaluated with Spearman Correlation Coefficients. Fifty people with myositis (56 ± 14 years, 76% female) were included in the study. Intra- and interrater reliability of HHD yielded excellent ICCs (0.75–0.97) for all muscle groups, except for interrater reliability of ankle extension (0.61). The corresponding SEMs% ranged from 8 to 28% and the SDCs% from 23 to 65%. MMT8 total score revealed excellent intra- and interrater reliability (ICC > 0.9). Intrarater reliability of single muscle groups was substantial for shoulder and hip abduction, elbow and neck flexion, and hip extension (0.64–0.69), moderate for wrist (0.53) and knee extension (0.49) and fair for ankle extension (0.35). Interrater reliability was moderate for neck flexion (0.54) and hip abduction (0.44); fair for shoulder abduction, elbow flexion, wrist and ankle extension (0.20–0.33); and slight for knee extension (0.08). Correlations between the two tests were low for wrist, knee, ankle, and hip extension; moderate for elbow flexion, neck flexion and hip abduction; and good for shoulder abduction. In conclusion, the MMT8 total score is a reliable assessment to consider general muscle weakness in people with myositis but not for single muscle groups. In contrast, our results confirm that HHD can be recommended to evaluate strength of single muscle groups.

Introduction

Inflammatory myopathies (IMs), including dermatomyositis (DM), polymyositis (PM) and associated myopathies, are systemic rheumatic muscle diseases characterized by chronic muscle inflammation [1]. With a worldwide average annual incidence rate ranging from 0.2 to 8 in 100'000, IMs are relatively rare. However, the burden of the disease for affected patients is considerable. The most prominent clinical features in IM are muscle weakness and low muscle endurance, which progresses over a period of weeks or months [2, 3]. Most commonly, the weakness is symmetrical, proximal extremity muscles appear to be more affected, and neck flexors are weaker than extensors [4]. As a consequence of muscle weakness, people with myositis often report difficulties with activities of daily living, e.g., getting up from a chair, going up- or down the stairs, getting into a car, stepping onto a curb, lifting objects, washing hair, brushing teeth, and gripping objects [1, 2].

The International Myositis Assessment and Clinical Study Group (IMACS) defines muscle strength as one of the core outcomes to be measured for assessing myositis disease activity and damage [5]. As the limb-girdle muscles and anterior neck flexors are among the leading indicators of myositis [6], the measurement of muscle strength in these muscle groups is a relevant parameter when diagnosing IM. Furthermore, muscle strength should also be used as an intervention outcome to evaluate the effects of progressive resistance training in rehabilitation programs. The foregoing emphasizes the necessity for a widely-accepted assessment to measure muscle strength in people with myositis. To date, however, there is no consensus about the most accurate way to assess muscle strength in this patient group.

Manual muscle testing (MMT), which is scored using a 0–5 point Medical Research Council muscle strength scale or a 0–10 point Kendall grading scale and hand-held dynamometry (HHD) which measures the peak isometric force generated from a muscle group, are two common methods to assess muscle strength in therapeutic IM trials [7]. MMT is less time consuming and, therefore, less stressful for people with myositis but has decreased sensitivity and specificity in detecting mild weakness and exhibits ceiling effects. Furthermore, the grading system of MMT is subjective and varies with the strength of the examiner [5, 8]. Despite this deficiency, the MMT8, a myositis specific subset of MMT, is the most frequently used assessment in myositis trials [5, 7]. HHD is used less commonly than MMT, but being an objective measure of muscle strength, it has the potential to overcome some of the limitations of the latter. HHD may detect mild deteriorations or improvements during the course of IM or after a resistive strength training program [5].

These low-cost and portable devices assess muscle strength reliably in clinical settings when using specific procedures [9]. Furthermore, HHD has demonstrated to have good concurrent validity when compared with laboratory-based isokinetic dynamometry testing [10–12]. Although MMT and HHD are both supposed to measure muscle weakness, reports about the relationship between the two methods show conflicting results. Whilst some authors concluded that these methods measure the same construct [13, 14], other authors indicated no clear relationships between MMT and HHD [15, 16].

Clinimetric properties, in particular reliability and concordance between the MMT8 and the HHD, have never been conclusively determined in people with myositis. Two studies, each with seven patients, investigated the relative reliability of the MMT8 and the HHD. ICCs between 0.28 and 0.85 were reported for the MMT8 whilst reliability values of the HHD ranged from 0.88 to 0.98 [4, 17]. Absolute agreement parameters have, to the best of our knowledge, not been reported. Although both measures (MMT8 and HHD) are used to assess maximal voluntary isometric muscle contraction it is not investigated whether the results of MMT8 and HHD in people with myositis are comparable.

The first aim of the present study was, therefore, to evaluate intra- and interrater reliability of the MMT8 and HHD in adults with myositis. Secondly, this study aimed to determine concordance between MMT8 and HHD. It was hypothesised that HHD would demonstrate excellent reliability ($ICC > 0.75$), that MMT8 would demonstrate substantial reliability (Kappa values between 0.61 and 0.8) and that the concordance between HHD and MMT8 would be good (Spearman correlation between 0.7 and 0.9) for all tested muscle groups.

Material and methods

Participants

A convenience sample of 50 people with myositis was recruited from the Department of Rheumatology of the University Hospital Zurich, Switzerland between August 2014 and May 2016. All patients presenting for evaluation of myositis were asked by their physician if they would be interested to participate in this study. Interested patients were then contacted by one of the researchers and checked for inclusion and exclusion criteria. Inclusion criteria were diagnosis of polymyositis, dermatomyositis or a myositis associated disorder (scleroderma, systematic lupus erythematosus, Sjögren's syndrome), age over 18, and ability to read and understand German. Exclusion criteria were diagnoses of inclusion body myositis, pulmonary hypertension,

osteoporosis, severe cardiovascular and/or pulmonary disease, pain syndrome, and paresis. The participants gave their signed informed consent to participate, and the study was approved by the local ethics committee (registration no. 2014–0022 of the Cantonal Ethics Committee Zurich, Switzerland). The individual in this manuscript demonstrating a measurement set-up has given written informed consent (as outlined in PLOS consent form) to publish these case details. This study is registered at the ClinicalTrials.gov (registration number: NCT0 3059394).

Out of 76 people with myositis who met all inclusion criteria, 50 agreed to participate. Four dropped out after the first measurements. Therefore, reliability was analyzed with data from 46 participants. Due to pain or incapacity to perform certain test positions, some muscle groups could not be tested in all participants. The detailed sample selection process is shown in Figure 1.

Figure 1: Sample selection

Legend: From 76 people with myositis fulfilling all inclusion criteria 50 agreed to participate. After the first measurement four participants dropped out.

Testers

The measurements were performed by two senior physiotherapists, experienced with treatment and measurement of people with rheumatologic diseases. The female physiotherapists were 35 and 47 years old, had a body height of 162 cm and 175 cm and weighted 49 kg and 60 kg, respectively. The two testers were instructed and trained in the use of the MMT8 and the HHD before study start.

Procedures

Each participant was measured three times. At time point 1 demographic data (gender, age, BMI, diagnosis, disease stage, time since diagnosis) were collected and tester 1 conducted the MMT8 and the HHD (Measurement 1).

For intrarater reliability, at time point 2 (one week later), MMT8 and HHD were performed by the same tester (Measurement 2). After a one-hour break, the MMT8 and HHD were conducted by tester 2 for interrater reliability (Measurement 3, Figure 2). Measures were performed in the same order, in the same test room and if possible at the same time of the day, to optimize the standardisation of the test procedure.

Figure 2: Procedure of the intra- and interrater reliability.

Legend: Each patient was measured three times. For intrarater reliability MMT8 and HHD were performed by the same tester (Measurement 1 and 2) and for interrater reliability MMT8 and HHD were performed by two different testers (Measurement 2 and 3). Abbreviations: MMT8: Manual muscle test 8, HHD: Hand-held dynamometry.

Manual muscle testing (MMT8): The dominant side of the following eight muscle groups was tested in a standardised order: shoulder abduction, elbow flexion, ankle extension, hip abduction, hip extension, knee extension, wrist extension and neck flexion. The dominant side was based on the self-declared hand preference. Detailed description of the participants' and therapist's position and the precise test instructions for each muscle group is described in the "manual muscle testing procedure for MMT8 Testing". Each muscle group was scored according the Kendall 10-point Scale (Table 1) [18]. Scores between 0–3, 4–6, and 7–9 indicate severe, moderate and mild weakness, respectively and a score of 10 means that there is no detectable weakness [19]. The single scores were added to receive a total score varying from 0 to 80 (0 = no muscle contraction, 80 = normal strength).

Hand-held dynamometry: Muscle strength of the same muscle groups that were included in the MMT8 was assessed using the MicroFET2 hand-held dynamometer. The MicroFET2 is a battery operated hand-held device which measures peak force in Newtons (N), up to a value of 890N (Force

Evaluating and Testing, Hoggan Health Industries Inc. West Draper, UT, USA). Each muscle action was measured in a gravity-neutralized position. Testing procedure and test position were performed according to standardised protocols [20–22]. After at least one familiarization trial, each muscle group was assessed twice. Isometric “make” tests were used [20]. Peak force values were recorded for each trial. Participant position, placement of the dynamometer, verbal instruction and location of stabilisation provided for each tested muscle group are described in the “Manual Quantitative Muscle Testing”. The individual in this manuscript demonstrating a measurement set-up has given written informed consent (as outlined in PLOS consent form) to publish these case details.

Table 1: Kendall 10-point scale.

test procedure	function of the muscle	raw score	graded scored
no movement	No visible movement of the part	0	severe weakness
test movement	Movement in horizontal plane		
	Moves through partial range of motion	1	
	Moves through complete range of motion	2	
	Movement against gravity		
	Moves through partial range of motion	3	
test position	gradual release from test position	4	moderate weakness
	Holds test position (no added pressure)	5	
	Holds test position against slight pressure	6	
	Holds test position against slight to moderate pressure	7	mild weakness
	Holds test position against moderate pressure	8	
	Holds test position against moderate to strong pressure	9	
	Holds test position against strong pressure	10	no weakness

Data analysis

Demographic data (gender, age, BMI, diagnosis, disease stage, time since diagnosis) were defined using descriptive statistics. Normality of the data was evaluated using Shapiro Wilk test. The level of significance was set to $\alpha \leq 0.05$ (with Bonferroni correction for multiple comparisons). No imputation was performed. A case was deleted when a variable was missing for a particular analysis, however, this case was included in analyses for which all required variables were present. Due to this pairwise deletion, the total N was not consistent across all analyses. SPSS version 22.0 (SPSS Inc, Chicago, Illinois) was used for data analysis.

Hand-held dynamometry: Data of each muscle group and total score were summarized by mean and standard deviation. To compute total scores, the values of each muscle group were added and this sum was divided by eight. The peak force of the best trial (peak force) and the averaged force of the two performed trials (averaged peak force) were used for data analysis.

Relative reliability, which expresses how well participants can be distinguished from each other despite the presence of measurement error, was determined by calculating intraclass correlation coefficient (ICC) [23]. The ICC₂ (A,1) formula for reliability of the highest score and the ICC₂ (A,k) formula for reliability of the average score were used [23, 24]. For interpretation of ICC values, the following classification was considered: >0.75 excellent reliability, 0.40–0.75: fair to good reliability, and <0.40 poor reliability [25].

To evaluate changes over time, variability between participants and, therefore, relative reliability is not particularly informative. In this case absolute measurement error, also called agreement parameters, are indicated [26]. Therefore, the standard error of measurement (SEM) and the smallest detectable change (SDC) were calculated. The SEM represents the standard deviation of repeated measures of one individual and is calculated with the formula $SEM_{\text{agreement}} = \sqrt{(\sigma_{\text{pt}}^2 + \sigma_{\text{residual}}^2)}$ [26]. The SDC represents the minimal change that must be overcome to ensure real change and is calculated with the formula $SDC = 1.96 \times \sqrt{2} \times SEM$ [26]. To evaluate a systematic failure between strength measures, Bland Altman plots were drawn with the free Medcalc statistic software (MedCalc Software, Ostend, Belgium) [27].

Manual muscle testing (MMT8): Raw MMT scores (0–10) as well as graded MMT scores (0–3: severe weakness, 4–6: moderate weakness, 7–9: mild weakness, 10: no weakness) [19] are ordinal scales and, therefore, summarized by medians and interquartile ranges for single muscle groups and for the graded total score. Floor and ceiling effects were determined by calculating the number of individuals obtaining, respectively, the highest or lowest scores, where a limit of 15% should not be exceeded [28].

To measure reliability of single muscle groups and for the graded total score weighted Cohen's Kappa was computed using the GraphPad software (<http://faculty.vassar.edu/lowry/kappa.html>). Because misclassifications between adjacent categories are less serious than those between more distant categories we used a linear Kappa [23]. To interpret kappa values we applied Landis and Koch benchmarks (>0.8: almost perfect, 0.61–0.8: substantial, 0.41–0.6: moderate, 0.21–0.4: fair, <0.2 slight) [29]. For ordinal data there are no parameters of measurement error that quantify the measurement error in units of measurement [23].

Raw MMT total scores are summarized as means and standard deviations and parametric statistics was used because they approximated interval data. Reliability of the raw total score was determined by calculating intraclass correlation coefficient (ICC₂ (A,1), SEM and SDC.

Concordance between HHD and MMT8: Correlations between HHD and MMT8 were calculated with Spearman's rho. When scoring the MMT, raters might consider participant's body weight. Therefore, absolute force as well as normalized force (absolute force divided by body weight) of HHD were correlated with the MMT. A Spearman correlation coefficient greater than 0.9 was considered 'excellent', a coefficient between 0.7 and 0.9 'good' and one between 0.5 and 0.7 'moderate' [30]. Additionally, the associations between the two muscle strength assessments are depicted with boxplots with strength values of each muscle group displayed for the MMT grades.

Results

The demographic and health related data of the 50 participants are summarized in Table 2.

Table 2: Demographic and health related data of the participants (n = 50).

Characteristics	Values
Sex, n (%)	female
	38 (76)
	male
	12 (24)
Age, in years	mean $\pm$ SD
	56 $\pm$ 14
	range
	21–82
BMI, in kg/cm ²	mean $\pm$ SD
	26 $\pm$ 5
Diagnosis, n (%)	DM
	22 (44)
	PM
	17 (34)
	Associated
	11 (22)
Disease stage, n (%)	Acute
	9 (18)
	(0–3 weeks after an active disease stage)
	Subacute
	9 (18)
	(between 3 and 12 weeks after an active disease stage)
	Chronic
	32 (64)
	(more 12 weeks after an active disease stage)
Time since diagnosis (months)	mean $\pm$ SD
	36 $\pm$ 18
	range
	0.25–240

Legend: n: number, SD: standard deviation, DM: Dermatomyositis, PM: Polymyositis

Hand-held dynamometry

The muscle strength values (M1, M2, and M3) and the reliability parameters (ICC, SEM and SDC) for peak force are presented in Table 3. The mean peak forces ranged from 55 N (wrist extension) to 219 N (knee extension) and the standard deviations ranged from 25 (neck flexion) to 92 N (knee extension). All strength measurement data were normally distributed and there was no significant difference between measurement 1 and 2 or between 2 and 3 (t-test, $p \geq 0.003$; corrected for 16 comparisons). For all muscle groups, except for elbow flexion and for knee extension, intrarater reliability

of peak force (ICCs between 0.71 and 0.86) was higher than interrater reliability (ICCs between 0.45 and 0.9). For elbow flexion and knee extension, the ICCs for intrarater reliability were lower than those for interrater reliability (0.83 versus 0.9, and 0.82 versus 0.87, respectively). Six out of eight measured muscle groups showed excellent intrarater reliability. Hip abduction and neck flexion had fair to good intrarater reliability. Interrater reliability was excellent for three muscle groups (shoulder abduction, elbow flexion, and knee extension) and fair to good for the other five muscle groups (ankle extension, hip abduction, hip extension, wrist extension and neck flexion). Intra- and interrater reliability was excellent for total score (0.92 and 0.94). The corresponding SEMs for single scores varied between 12 and 37 Newton and the SDCs% ranged from 40 to 70% for intra- and from 33 to 78% for interrater reliability. The SEM for the total score was 12 N and the SDC 27% for intrarater reliability and 10 N and 23% for interrater reliability.

The results and reliability parameters of averaged peak force are shown in Table 4. Intrarater and interrater ICCs for single muscle groups and for the total score were excellent (0.75–0.97), except for interrater reliability of ankle extension (0.61) which was fair to good. All SEMs (8–30N) and SDCs% (23–65%) for single muscle groups and for the total score (SEM: 7–8, SDC%: 16–19) were smaller for averaged peak force than for peak force values.

Bland Altman plots between M1 and M2 (intrarater) and between M2 and M3 (interrater) are shown for peak force (Figure 3 and Figure 4). For all comparisons, most of the data were within two standard deviations in the Bland-Altman plots. The plots illustrated small, but non-systematic errors between test and retest. Limits of agreement were always greater for intra- than for interrater reliability and visual inspection showed no tendency towards heteroscedasticity.

Table 3: Peak force at M1, M2 and M3 plus intra- and interrater reliability measured with hand-held dynamometry (N = 46).

muscle groups	M 1		M 2		M 3		Intrater reliability			Interrater reliability		
	Newton mean $\pm$ SD		Newton mean $\pm$ SD		Newton mean $\pm$ SD		ICC (95%CI)	SEM (SEM%)	SDC (SDC%)	ICC (95%CI)	SEM (SEM%)	SDC (SDC%)
S_ABD	97 $\pm$ 43		92 $\pm$ 36		95 $\pm$ 43		0.86** (0.75–0.92)	15 (16)	41 (43)	0.78** 0.64–0.87)	19 (20)	52 (55)
E_FLEX	131 $\pm$ 57		133 $\pm$ 49		128 $\pm$ 50		0.83** (0.91–0.83)	22 (17)	61 (46)	0.90** (0.83–0.95)	15 (12)	43 (33)
A_EXT	144 $\pm$ 47		142 $\pm$ 51		128 $\pm$ 47		0.82** (0.70–0.90)	21 (14)	57 (40)	0.45* (0.19–0.65)	36 (27)	101 (75)
H_ABD	123 $\pm$ 46		122 $\pm$ 42*		133 $\pm$ 53		0.71+ (0.53–0.83)	23 (19)	65 (53)	0.61* (0.40–0.77)	29 (23)	81 (64)
H_EXT	143 $\pm$ 59		143 $\pm$ 65*		151 $\pm$ 60*		0.83** (0.72–0.91)	25 (18)	70 (49)	0.65* (0.44–0.79)	37 (25)	104 (71)
K_EXT	216 $\pm$ 86		210 $\pm$ 89		219 $\pm$ 92		0.82** (0.69–0.90)	37 (17)	103 (48)	0.87** (0.78–0.93)	32 (15)	90 (42)
W_EXT	55 $\pm$ 28		60 $\pm$ 30		60 $\pm$ 31		0.83** (0.72–0.91)	12 (21)	33 (57)	0.69* (0.51–0.82)	17 (28)	47 (78)
N_FLEX	58 $\pm$ 28		68 $\pm$ 33*		62 $\pm$ 25**		0.72* (0.51–0.85)	16 (25)	44 (70)	0.65* (0.44–0.79)	17 (26)	47 (73)
total score	121 $\pm$ 40		122 $\pm$ 41		124 $\pm$ 43***		0.92** (0.85–0.96)	12 (10)	32 (27)	0.94** (0.89–0.97)	10 (8)	29 (23)

Legend: M: measurement, SD: standard deviation, 95%CI: 95% confidence interval, ICC: intraclass correlation coefficient, SEM: standard error of measurement, SDC: smallest detectable change, S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion, *1 missing values, **2 missing values, ***3 missing values, +fair to good reliability, ++excellent reliability

Table 4: Averaged peak force at M1, M2 and M3 plus intra- and interrater reliability measured with handheld dynamometry (N = 46).

muscle groups	M 1		M 2		M 3		intrarater reliability			interrater reliability		
	Newton mean $\pm$ SD		Newton mean $\pm$ SD		Newton mean $\pm$ SD		ICC (95%CI)	SEM (SEM%)	SDC (SDC%)	ICC (95%CI)	SEM (SEM%)	SDC (SDC%)
S_ABD	92 $\pm$ 39		88 $\pm$ 35		89 $\pm$ 42		0.94 ⁺⁺ (0.87-0.97)	9 (11)	26 (29)	0.88 ⁺⁺ (0.78-0.93)	13 (15)	37 (42)
E_FLEX	125 $\pm$ 53		128 $\pm$ 47		123 $\pm$ 47		0.90 ⁺⁺ (0.82-0.95)	16 (12)	43 (34)	0.95 ⁺⁺ (0.91-0.97)	10 (8)	29 (23)
A_EXT	135 $\pm$ 45		136 $\pm$ 51		122 $\pm$ 46		0.91 ⁺⁺ (0.84-0.95)	14 (11)	40 (29)	0.61 ⁺ (0.31-0.78)	30 (23)	84 (65)
H_ABD	114 $\pm$ 40		114 $\pm$ 37 [*]		125 $\pm$ 51		0.84 ⁺⁺ (0.70-0.91)	16 (14)	43 (38)	0.75 ⁺⁺ (0.55-0.86)	22 (18)	61 (51)
H_EXT	134.3 $\pm$ 58		134 $\pm$ 61 [*]		141 $\pm$ 57 [*]		0.91 ⁺⁺ (0.83-0.95)	18 (13)	50 (37)	0.77 ⁺⁺ (0.58-0.87)	28 (20)	78 (57)
K_EXT	205 $\pm$ 83		199 $\pm$ 85		207 $\pm$ 88		0.92 ⁺⁺ (0.85-0.95)	24 (12)	68 (33)	0.94 ⁺⁺ (0.89-0.97)	21 (10)	58 (29)
W_EXT	52 $\pm$ 27		55 $\pm$ 27		56 $\pm$ 29		0.92 ⁺⁺ (0.86-0.96)	8 (14)	21 (39)	0.84 ⁺⁺ (0.72-0.91)	11 (20)	31 (55)
N_FLEX	54 $\pm$ 25		63 $\pm$ 29 [*]		59 $\pm$ 24 ^{**}		0.87 ⁺⁺ (0.72-0.93)	10 (17)	27 (46)	0.82 ⁺⁺ (0.66-0.90)	11 (19)	31 (52)
total score	114 $\pm$ 38		115 $\pm$ 39		117 $\pm$ 41 ^{***}		0.96 ⁺⁺ (0.92-0.98)	8 (7)	21 (19)	0.97 ⁺⁺ (0.94-0.98)	7 (6)	19 (16)

Legend: M: measurement, SD: standard deviation, 95%CI: 95% confidence interval, ICC: Intraclass correlation coefficient, SEM: standard error of measurement, SDC: smallest detectable change, S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion, *1 missing values, **2 missing values, ***3 missing values, +fair to good reliability, ++excellent reliability

Figure 3: Bland and Altman plots of hand-held dynamometry (peak force)

Legend: The blue continuous horizontal line shows the mean difference between tests. The dashed orange horizontal lines show the upper and lower 95% limits of agreement (bias $\pm 1.96 \times$ standard deviation). Abbreviations: M: measurement, S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion.

Figure 4: Bland and Altman plots of hand-held dynamometry (peak force)

Legend: The blue continuous horizontal line shows the mean difference between tests. The dashed orange horizontal lines show the upper and lower 95% limits of agreement (bias $\pm 1.96 \times$ standard deviation). Abbreviations: M: measurement, S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion.

Manual muscle testing

The results of the raw MMT8 score (M1, M2, M3, intrarater Kappa, and interrater Kappa) are presented in Table 5 (single muscle groups) and Table 6 (total score) and those from the graded score in Table 7.

MMT-scores were between 1 and 10 for the weakest muscle group (hip extension) and between 7 and 10 for the strongest muscle group (knee extension and ankle extension). No differences between the measurements over time (M1, M2, M3) were seen (Wilcoxon, $p \geq 0.003$). All but one muscle group (hip extension) showed ceiling effects of 22 to 82% (Figure 5) with medians of the raw scores ranging from 8 to 10 points. The total raw score had no ceiling effect and varied from 46 to 80 with a mean of 70 points. The three muscle groups with the lowest score were neck flexion, hip abduction, and hip extension with moderate to severe weakness of 18%, 20%, 26%, respectively. Most of the participants had mild weakness (total graded score).

Figure 5: Ceiling effects of MMT8

Legend: All but one muscle group (hip extension) showed ceiling effects of 22 to 82%. Abbreviations: A_EXT: ankle extension, E_FLEX: elbow flexion, W_EXT: wrist extension, K_EXT: knee extension, N_FLEX: neck flexion, S_ABD: shoulder abduction, H_ABD: hip abduction, H_EXT: hip extension.

Intrarater reliability of the single muscle groups (raw as well as graded score) were substantial for shoulder abduction, elbow flexion, neck flexion, hip abduction, and hip extension (linear weighted Kappa varying from 0.61 to 0.69); moderate for wrist extension and knee extension (linear weighted Kappa varying from 0.49 to 0.53) and fair for ankle extension (linear weighted Kappa varying between 0.35 and 0.37). Interrater reliability (raw and graded scores) were moderate for neck flexion and hip abduction (linear weighted Kappa from 0.44 to 0.58); fair for shoulder abduction, wrist extension, and ankle extension (linear weighted Kappa varying from 0.20 to 0.35); and slight

for knee extension (linear weighted Kappa of 0.08 and 0.18). Graded scores showed better Interrater reliability than row scores for elbow flexion (0.43 versus 0.3) and for hip extension (0.65 versus 0.59).

Intrarater and interrater reliability for total weakness score was substantial (0.88) and moderate (0.42), respectively. Intrarater and interrater reliability of the raw total score were excellent (ICC > 0.9 for both measures), and SEM and SDC% were 1.8 N and 6.9% and 2.2 N and 8.6%, respectively.

Concordance between MMT and HHD

Analysis of inter-muscle-assessment-method showed low correlations for four muscle groups (wrist, knee, ankle and hip extension), moderate correlations for three muscle groups (hip abduction and elbow and neck flexion) and a good correlation for shoulder abduction between results obtained by the MMT8 and HHD, for both absolute force and force normalized to body weight (Table 8).

Table 8: Correlations (Spearman's rho) between peak force (averaged and normalized) and MMT8 (N = 50)

muscle groups	averaged force	normalized force
S_ABD	0.85 ⁺	0.75 ⁺
E_FLEX	0.55 ⁻	0.54 ⁻
W_EXT	0.27	0.19
K_EXT	0.28	0.27
A_EXT	0.24	0.09
N_FLEX	0.62 ⁻	0.57 ⁻
H_ABD	0.61 ⁻	0.65 ⁻
H_EXT	0.28	0.38

Legend: S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion, -low correlation, +moderate correlation

Figure 6 illustrates no consistent association between results from the MMT8 and the HHD in the different muscle groups. In elbow flexion, knee extension and neck flexion the median strength value is higher for a higher MMT score. However, the distribution of strength values for each muscle group showed a large range with considerable overlaps in the interquartile ranges. For the other four muscle groups (shoulder abduction, ankle extension, hip abduction, hip extension, wrist extension) the median strength value did not progressively increase between the consecutive score categories of MMT. Markedly, the median strength value is higher for grade seven than grade eight and nine in hip abduction, hip extension and wrist extension.

Table 5: MMT8 single muscle groups at M1, M2, M3 plus intra- and interrater Kappa values (N = 46)

muscle groups	M1		M2		M3		intratester	intertester
	median	(min,max)	(25%, 75%)	median	(min, max)	(25%, 75%)	Kappa	Kappa
S_ABD	9	(6,10)	(8, 10)	9	(6, 10)	(8, 10)	0.64***	0.33*
E_FLEX	10	(6, 10)	(9, 10)	10*	(6, 10)	(9, 10)	0.66***	0.30*
W_EXT	10	(6, 10)	(9, 10)	10	(7, 10)	(9, 10)	0.53**	0.24*
K_EXT	10	(7, 10)	(9, 10)	10	(6, 10)	(9, 10)	0.49**	0.08*
A_EXT	10	(7, 10)	(10, 10)	10	(7, 10)	(10, 10)	0.35*	0.20*
N_FLEX	9	(3, 10)	(7, 10)	8	(3, 10)	(7, 10)	0.64***	0.54**
H_ABD	9	(3, 10)	(7, 9)	9*	(3, 10)	(8, 9.5)	0.66***	0.44**
H_EXT	8	(1, 10)	(6, 9)	8*	(1, 10)	(7, 9)	0.69***	0.58**

Legend: M: measurement, min: minimum, max: maximum, S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion, *1 missing values, **2 missing values, *fair reliability, **moderate reliability
 ***substantial reliability

Table 6: MMT8 total score at M1, M2, M3 plus intra- and interrater reliability (N = 46)

	M1		M2		M3		intratester reliability			interrater reliability		
	mean (±SD)	mean (±SD)	mean (±SD)	mean (±SD)	mean (±SD)	mean (±SD)	ICC (95%CI)	SEM SEM%	SDC SDC%	ICC (95%CI)	SEM SEM%	SDC SDC%
total score	70±8	71±7*	72±7*	72±7*	72±7*	72±7*	0.94** (0.90–0.97)	1.8 (2.5)	4.9 (6.9)	0.91** (0.83–0.95)	2.2 (3.1)	6.2 (8.6)

Legend: M: measurement, SD: standard deviation, 95%CI: 95% confidence interval, ICC: Intraclass correlation coefficient, *3 missing values, **excellent reliability

Table 7: MMT8 graded score at M1, M2, M3 plus intra- and interrater Kappa values (N = 46)

muscle groups	M1				M2				M3				Intratester	intertester
	no_w %	mi_w %	mo_w %	s_w %	no_w %	mi_w %	mo_w %	s_w %	no_w %	mi_w %	mo_w %	s_w %	Kappa	Kappa
S_ABD	28.0	58.0	14.0	0.0	32.6	58.7	8.7	0.0	37.0	52.2	10.9	0.0	0.66+++	0.35+
E_FLEX	73.5	22.4	4.1	0.0	71.1*	22.2	6.7	0.0	73.9*	26.1	0.0	0.0	0.61+++	0.43++
W_EXT	63.3	32.7	4.1	0.0	69.6	30.4	0.0	0.0	71.7	26.1	2.2	0.0	0.55++	0.21+
K_EXT	62.0	38.0	0.0	0.0	71.7	26.1	2.2	0.0	60.9	39.1	0.0	0.0	0.49++	0.18
A_EXT	82.0	18.0	0.0	0.0	73.9	26.1	0.0	0.0	80.4	19.6	0.0	0.0	0.37+	0.20+
N_FLEX	32.0	50.0	16.0	2.0	28.3	60.9	8.7	2.2	34.1**	45.5	20.5	0.0	0.68+++	0.58++
H_ABD	22.0	58.0	18.0	2.0	24.4*	64.4	8.9	2.2	46.7*	37.8	11.1	4.4	0.65+++	0.46++
H_EXT	12.0	62.0	22.0	4.0	22.2*	57.8	17.8	2.2	33.3*	48.9	15.6	2.2	0.63+++	0.65+++
Total score	4.1	89.8	6.1	0.0	4.5**	90.9	4.5	0.0	15.9**	79.5	4.5	0.0	0.88++++	0.42++

Legend: M: measurement, no_w: no weakness, mi_w: mild weakness, mo_w: moderate weakness, s_w: severe weakness, S_ABD: shoulder abduction, E_FLEX: elbow flexion, A_EXT: ankle extension, H_ABD: hip abduction, H_EXT: hip extension, K_EXT: knee extension, W_EXT: wrist extension, N_FLEX: neck flexion, *1 missing, values, **2 missing values, -slight reliability, +fair reliability, ++moderate reliability, +++substantial reliability, ++++almost perfect reliability

Figure 6: Muscle strength measured by hand-held dynamometry (in Newton) and MMT8 (MMT-Scale)

Legend: The association between results from MMT8 and HHD are not consistent.

Discussion

This study evaluated the intra- and interrater reliability of the MMT8 and a HHD, and the concordance between these two measures in a consecutively recruited convenience sample ($n = 50$) of people with myositis. In our sample, 76% of the participants were female. This gender distribution reflects the known higher prevalence of IM in females compared to males [31, 32].

The results of this study revealed excellent ($ICC > 0.7$) intra- and interrater reliability of the averaged peak force, except for the interrater reliability of ankle extension ($ICC = 0.61$). For peak force measurement, excellent ICCs were found for intrarater reliability for all muscle groups and the total score. Conversely, only three single muscle groups and the total score yielded excellent peak force interrater reliability scores. The SEMs and SDCs varied widely between single muscle groups. The SEMs% of the individual muscle groups ranged from 8 to 25% and the SDCs% from 23 to 78%. The SEMs% for the total score varied between 6 and 10% and the SDCs% between 16 and 27%. For the MMT8, the total score showed excellent intra- and interrater reliability ($ICC > 0.9$), the single muscle group revealed Kappa values of 0.35–0.69 for intrarater reliability and values of 0.08–0.58 for interrater reliability, however, considerable ceiling effects (22–82%) were determined.

Hand-held dynamometry

Our findings are in accordance with the findings from Stoll et al., who also reported excellent intra- and interrater reliability (ICCs intrarater: 0.88–0.98, ICCs interrater: 0.81–0.98) in seven people with myositis [17]. These results are only partially comparable, because different muscles groups were assessed. Neck flexion, shoulder elevation, elbow flexion and extension, hip flexion, and knee flexion and extension were evaluated by Stoll et al. while the muscle groups in our study were equal to those measured in the MMT8. Furthermore, no data about absolute reliability (measurement error) were reported by Stoll et al. [17]. Thus, it is not yet possible to compare the measurement errors of both studies and we cannot conclusively determine what measurement protocol leads to the optimal values to measure change in a patient's strength values. Whether or not a measurement error is acceptable, depends on the amount of improvement or deterioration that one wants to detect [33]. The observed change in muscle strength must, therefore, be larger than the threshold of the SDC to ensure a real change in muscle strength. As $\geq 15\%$ improvement in muscle strength is defined to be clinically relevant [18], an estimated SDC of $\leq 15\%$ may be acceptable. The observed

SDC measures in our study showed considerably higher values (SDCs between 29 and 65%) than the recommended 15%. However improvements of muscle strength varying between 38 and 62% are common [34, 35], therefore, dynamometry is capable to capture these improvements. These considerable improvements may be explained by the training principles of initial values, i.e. people with lowest level of fitness have greatest room for improvement [36].

As intrarater reliability is superior to interrater reliability, we recommend measurements to be performed by the same tester, a recommendation of particular importance when considering measurement error. Furthermore, reliability might be improved by using the average value of multiple measurements at each time point, instead of the peak force values [37]. We could confirm that ICCs and measurement errors were better for the averaged value of two performed measurements than for the maximum value. In clinical practice and research trial even three to four measurements were performed [9, 38].

A well-known problem of hand held dynamometry is that the testers are often too weak to provide counterbalance to test certain lower extremity muscles [39]. Stone et al hypothesized that reliability was compromised by inadequate tester strength even in frail populations [40]. We tried to overcome this limitation by using a belt to stabilize the dynamometer or the examiner where this seemed necessary. When measuring knee extension, the dynamometer was always fixed with a belt (Figure 7). When measuring hip abduction and extension in strong participants the examiners stabilized themselves with a belt (Figure 8). Although measurement of knee extension could not be limited by the strength of the examiner, the reliability parameters were not superior for these measures compared to the other muscle groups. If the examiners' strength were too low to assess actual strength, we would anticipate detection of a ceiling effect. As our data did not show any ceiling effect, we concluded that the force of the examiners was not a limiting factor.

Figure 7: Measuring knee extension using a belt to stabilize the dynamometer

Legend: Standard body position of the patient and the device are shown with knees and hips flexed to 90°

Figure 8: Measuring hip extension using a belt to stabilize the examiner

Legend: Standard body position of the patient and the device are shown with stretched hip and knees.

Manual muscle testing

Compared to other IM-trials, our participants showed relatively low muscle weakness. The median score of MMT8 in our sample was 10 to 50% higher than the score reported by Harris- Love et al. [19], and our total score exceeded the score reported by Rider et al. (87.5% versus 76.5%) [4]. We could confirm or even exceed known ceiling effects [5]. In seven out of eight muscle groups more than 20% of the included participants revealed the highest scores, which theoretically implies that these participants had no muscle weakness at the time of measurement. Conversely, Anderson et al. demonstrated a substantial number of participants (28– 41%) classified with 'normal' MMT values had muscle weakness following evaluation with isokinetic dynamometry. Therefore, the MMT cannot differentiate mild muscle weakness from normal muscle strength [41]. This finding was confirmed by Bohannon et al., who examined participants from four different studies with a manual muscle grade 5 (grade 5 of the Medical Research Council Scale equals 10 in the Kendal scale) and revealed that the highest grade encompassed a broad range of forces between 85N and 650 N. They concluded that MMT may lack the sensitivity to properly assess relatively strong muscle groups [42].

Whereas intrarater reliability of five single muscle groups was substantial, those of interrater reliability were only slight to moderate. One study, that evaluated reliability in adult people with myositis reported higher interrater reliability. The authors identified excellent interrater reliability for shoulder abduction, elbow flexion, knee extension and hip abduction, fair to good interrater reliability for hip extension, neck flexion and wrist extension, and poor for ankle extension [43]. This study included seven participants and used ICCs to calculate reliability, although MMT scores are ordinarily scaled. Therefore, these results should be interpreted with caution. The results of our study were partially in line with one report in which juvenile people with myositis ($n = 10$) were tested for intra-and interrater reliability. The intrarater reliability was also higher (Spearman's rank correlation coefficient: 0.8) than interrater reliability (Kendall's W: 0.72). In contrast to our study, the study of Rider et al. revealed acceptable interrater reliability [4]. Despite a detailed test protocol, standardised test environment, defined test order, and experienced and trained examiners, we could not reach satisfying interrater reliability for single muscle groups.

Nevertheless, intrarater as well as interrater reliability of the total score was excellent. These findings were supported by one report evaluating reliability in children with juvenile DM. The authors emphasized that it is important to use MMT summary scores, because the interrater reliability varies between individual muscle groups [44].

Absolute reliability could only be calculated for the total score. SDC and SDC per cent were lower for intrarater reliability (4.9 points, respectively 7%) than for interrater reliability (6.2 points, respectively 9%). A consortium of rheumatologists and neurologists has reached consensus that MMT8 should improve by $\geq 15\%$ to classify adult people with PM/DM as improved [18]. According to our calculations, the MMT8 total score is capable of capturing such improvements.

Concordance between HHD and MMT8

Although the QMT and the MMT8 were both supposed to measure maximum isometric muscle strength the correlation for the majority of single muscle groups and the total score were only moderate or even worse. Additionally, graphical presentation of the data showed variable relationship between MMT and HHD. If MMT and HHD would measure the same construct of isometric muscle strength, we would expect that an increase in MMT scores correspond with an increase in the median of peak force of HHD and that the interquartile ranges between MMT scores would not overlap. In our data, only three muscle groups showed a constant increase in peak force and MMT-scores, but interquartile ranges were overlapping in all muscle groups. We could therefore confirm the variable relationship found by Noreau et al. for upper extremities [15]. In contrast to our results, previous studies reported good correlations (>0.7) between manual muscle test and HHD for knee extension [13, 14].

There are several possible explanations for these low correlations: First, high ceiling effects could be responsible for the low correlations. With the MMT8 no differences were seen for a considerable amount of participants (22–82%) whereas HHD gives different values for these participants. It seems to be difficult to detect and grade mild symmetrical muscle weakness with the MMT, partly because the examiner must consider the normal variation in strength in relation to age, weight, height, and gender [41]. Then, variations in the weight of the participant's extremities, the force applied by the examiner, and the strength of the examiner could affect the subjective scoring of MMT8. Next, participant's test position is different for MMT8 and HHD.

While for the HHD, a gravity-neutralized position is needed, the MMT 8-test-position varies depending on the degree of weakness (from movement in horizontal plan to an antigravity position). For grades 5 and higher, participants have to hold the extremity against gravity and then the tester has to add pressure. The force needed to hold the extremity against gravity is not considered in scoring the MMT. Taken together, our results indicate that MMT does not measure the same parameter measured by HHD. Previous studies revealed that HHD is an appropriate method to assess isometric muscle strength compared with the gold standard isokinetic testing. Therefore, we conclude that MMT8 is an inadequate method to assess isometric muscle strength of individual muscle groups.

Limitations and future research

This study had several limitations. First, a heterogeneous sample of people with myositis was included. Our participants suffer from different kind of myositis in different disease stages (acute, sub-acute and chronic). Due to inadequate sample size for a reliable subgroup analysis, we could not evaluate more homogeneous subsamples. Second, we did not record medications of our participants. Third, the measurements of this study were performed by two female examiners with several years of clinical experience and training in muscle strength assessment. Including more examiners in the reliability study would improve external validity of the results. Since strength assessment is exhausting for the people with myositis, we decided not to include more than two examiners in our study. Fourth, as no generally valid test protocol for HHD exists we developed our own measurement protocol, which hampers the comparison with other study results. Fifth, whilst MMT8-scores can be interpreted (severe, moderate, mild, no weakness), this is not possible with the HHD. However, individual strength values could be compared with normal reference values. Different authors published such reference values for shoulder abduction [20–22, 45–47], elbow flexion [20–22, 45–48], ankle extension [20–22, 45–48], hip abduction [20–22, 45, 47, 48], hip extension [47], knee extension [20–22, 45–48], wrist extension [20–22, 45–47], and neck flexion [22, 46, 47]. Because the published reference values were captured with different devices, in different test positions and with different placement of the devices, a direct comparison may not be adequate. None of these previous studies used the same device as we did and, to the best of our knowledge, there exists no reference values for this device. Bo-

hannon et al emphasized that dynamometers should not be used interchangeable, because the magnitude of the force measured with two different devices differed significantly although they demonstrated good to high reliability and correlations [49]. Therefore, it is not possible to consider conclusively if a muscle group is weakened or not. Last, we did not include a gold standard for strength measurement.

To overcome these limitations future research should compile gender and age specific reference values for key muscles in people with myositis. Thereby the use of a generally accepted standardised protocol is important. These reference values may help to judge strength values of people with myositis. Furthermore, the validity of these muscle tests needs further investigation.

Conclusion

The fact that the correlation between HHD and MMT8 is not satisfactory raises doubt as to whether the MMT8 measures the same construct (isometric strength) as HHD. The MMT8 total score is a reliable and time efficient assessment to consider general muscle weakness in people with myositis. However, since only the total score of MMT8 showed good reliability parameters MMT8 should not be used to evaluate changes (either improvement or deterioration) in single muscle groups of people with myositis. On the contrary, HHD could be recommended to evaluate isometric muscle strength of single muscle groups in people with myositis if the following important aspects are considered: examiners are experienced and trained in muscle testing, a standardised protocol is followed, a belt to stabilize examiner or the device is used, and the average of at least two measures is applied.

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5

CHAPTER 5

Reliability and validity of the German version of the Myositis Activities Profile (MAP) in patients with inflammatory myopathy

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Abstract

The Myositis Activity Profile (MAP) is the only disease-specific questionnaire to assess limitations in activities of daily living (ADL) in patients with inflammatory myopathy (IM). Because a German version does not currently exist, this study's aim was to translate the MAP and assess reliability and construct validity of the new version. Therefore, a cross-cultural adaptation was performed following international guidelines. Forty-eight patients with IM completed the German-MAP, twice within two weeks. They were also assessed using the Health Assessment Questionnaire (HAQ), 36-Item Short Form Survey (SF36), Manual Muscle Test (MMT8), Quantitative Muscle Testing (QMT) and Functional Index (FI-2). For discriminant validity, 48 age- and gender-matched healthy controls completed the German- MAP. Reliability was assessed using weighted kappa (Kw). Correlations between the MAP and the HAQ, the physical (PCM) and mental (MCS) component scores of SF36 and the MMT8 and QMT muscle tests were assessed using Spearman correlation analysis. Discriminative validity was assessed by calculating the Area under the Curve (AUC). The German- MAP showed substantial reliability for the four subscales (Kw: 0.65–0.71) and moderate to substantial reliability for the single items (Kw: 0.57–0.77). The MAP showed good construct validity (high correlations with HAQ and PCM, moderate with FI-2, QMT and MMT8 and poor with MCS and pain) and acceptable discrimination for three subscales and two single items (AUC: 0.65–0.79). In conclusion, the German-MAP appears to be a reliable and valid questionnaire to assess ADL-limitations in patients with IM. Further research is required, both to substantiate these results and to evaluate responsiveness.

Introduction

Inflammatory myopathies (IMs), including polymyositis (PM) and dermatomyositis (DM), are chronic, idiopathic inflammatory muscle diseases characterized by decreased muscle strength and endurance, general fatigue, and, in some cases, muscle pain and extra-muscular manifestations such as lung fibrosis [1]. Epidemiological studies have reported widely varying incidence rates between 0.1 and 7.89 cases per 100,000 annually [2–4]. Although relatively rare, IMs pose a significant socioeconomic burden causing increased medical costs and resource usage. Moreover, there is substantial disease morbidity [4, 5]. The most prominent clinical features in all subcategories of IMs are proximal and (often) symmetric muscle weakness and low muscle endurance, combined with progressive decline of functional performance over a period of weeks or months. This results in significant difficulties in everyday tasks, such as self-care or household chores, combined with limited community mobility [6, 7].

Until recently, activity limitation in patients with IM has been assessed with the Health Assessment Questionnaire (HAQ). Arthritis-specific instruments such as the HAQ permit comparisons between different rheumatologic diagnoses. However tools like this may be insufficiently sensitive to capture activity limitations caused by a specific non-arthritic condition [8]. The Myositis Activity Profile (MAP) was the first disease-specific activity limitation questionnaire for use with patients who have IM. It was developed in Sweden and later translated into the English language [8, 9]. Both the Swedish and English versions showed promising, preliminary psychometric properties in patients with IM. The MAP correlated well with the HAQ and showed fair-to-moderate correlation with muscle endurance (assessed with the functional index in myositis) and muscle strength (assessed with the manual muscle test) [8, 9]. To date, correlations between the MAP and health-related quality of life (HRQL) and pain have, to the best of our knowledge, not been determined. Because the MAP focusses on activity limitation and correlates with muscle endurance and strength, it can be hypothesized that the MAP tends rather to correlate with physical components of HRQL (e.g. with the physical component of the SF36 questionnaire), than with those components reflecting mental and pain aspects of life quality.

The MAP is based on the International Classification of Impairments, Disabilities and Handicaps-2 (ICIDH) Beta-2 draft, an earlier version of the In-

ternational Classification of Functioning, Disability and Health (ICF). It includes 32 items, which are each answered on a seven-point Likert scale; where one equals no difficulty to perform and seven equals impossible to perform. These items are divided into four subscales (movement activities, activities of moving around, personal care, and domestic activities) and four single items (keeping in touch with close friends and relatives, avoiding over-exertion during daily activities, being able to cope with work and/or housework to a satisfactory degree, and being able to do recreational activities of choice). The four subscales are scored using the median value of item responses within each, while the four single items are scored using the actual item response value. Additionally, a total median score across the four subscales and the four single items is also calculated [10]. Overall, the MAP assesses activity limitation within a broad perspective, meaning that patients weight their difficulties against their needs when answering the questions [11].

To date and to the best of our knowledge, a German version of the MAP has not been developed. Therefore, the aim of this study was to translate and cross-culturally adapt the MAP into German following international guidelines [12, 13], and then evaluate construct validity and reliability of this new version. We hypothesized that the total median score across the four subscales and the four single items of the German-MAP would correlate highly with the HAQ and the physical component of the SF36, moderately with muscle function (strength and endurance), but lower with pain and the mental component of the SF 36. Furthermore, we hypothesized acceptable discriminant validity, substantial reliability with no systematic variations between test and retest, no internal redundancy or poor internal consistency.

Material and methods

Participants

Patients with IM were recruited from the Department of Rheumatology at the University Hospital Zurich. Inclusion criteria were diagnosis of PM, DM or associated myositis, age over 18, and ability to read and understand German. Excluded were patients diagnosed with inclusion body myositis, osteoporosis, severe cardiovascular and/or pulmonary disease, pain syndrome, and paresis. To evaluate discriminative validity, a healthy control group individually matched by age and gender was recruited. Healthy was defined as not having any disease diagnosed by a medical doctor.

Cross-cultural translation

The cross-cultural translation into German was performed in four steps, in accordance with international guidelines and with permission for translation from the original MAP developers [12, 13]. In step 1, two independent investigators each independently translated the MAP from English into German (T1 and T2). One of the translators was aware of the questionnaire concept. The second step was the synthesis of these two German versions, achieved by consensus discussion between the two translators. This produced a consensus German version (T1/2). In the third step, T1/2 was independently translated backwards by two native English-speaking persons, to produce two further English language versions (BT1 and BT2). Both persons were unaware of the questionnaire concept and were unfamiliar with the original English questionnaire. In step four, all four translators discussed any discrepancies retrieved between the original and the translated versions and produced a pre-final version. The understanding of this pre-final version was tested in practice with three patients with IM, before a final German version (S1 Appendix) was arrived at. This was then tested for validity and reliability.

Assessments

The HAQ consists of 20 questions divided into eight sections: dressing, rising, eating, walking, hygiene, reaching, gripping objects, and performance of activities. Scoring within each section varies from zero (without any difficulty) to three (unable to do) [14].

The SF-36 is a generic patient-reported outcome measure aimed at quantifying health-related quality of life (HRQOL). The questionnaire includes 36 questions, divisible into a physical component summary (PCS) and a mental component summary (MCS). In both of these components, higher scores indicate better HRQOL [15].

The Functional Index in Myositis (FI-2) is a disease-specific observational tool to measure muscle endurance. The FI-2 measures the number of repetitions performed in seven muscle groups/activities on the dominant side of the body. Each muscle group is scored by the number of correctly performed repetitions, ranging from 0–60 for shoulder flexion, shoulder abduction, neck flexion, hip flexion, knee extension and step test, and from 0–120 for heel and toe lifts. Sixty and 120 repetitions respectively indicate normal endurance [16]. To compute a total percentage score for all performed repetitions, all individual muscle group scores are summed and then divided by seven.

The MMT8 is a disease specific subset of eight proximal, distal, and axial muscle groups tested unilaterally to measure muscle strength. Each muscle group is scored from 0–10 on the Kendall scale. Zero indicates no muscle contraction and ten equals normal strength. The scores are summed up to a total score with a range varying from 0–80 [17].

Quantitative Muscles Testing (QMT) was performed with the microFET2. Maximum muscle strength of each of the muscle groups included in the MMT8 (shoulder abduction, elbow flexion, ankle extension, hip abduction, hip extension, knee extension, wrist extension, neck flexion) was tested on a continuous scale (Newton). To compute a total score, values of each muscle group were summated and this sum was then divided by eight.

Pain was measured using a Visual Analog Scale (VAS). A ten centimetres horizontal line with the anchors ‘no pain’ (score of zero) and ‘worst pain’ (score of 100) was used [18].

Experimental procedures

Patients attended the university hospital Zurich on two occasions, to provide data to test construct validity and reliability. During the first visit, patients’ demographic data were collected, questionnaires (MAP, HAQ, SF36, pain) were completed and strength assessments (MMT8, QMT, FI-2) were performed by one of two experienced physiotherapists. The latter had both received instruction and training prior to the investigation. All patients, whose health status remained unchanged, received a further copy of the MAP at their second visit. This was to provide data for reliability assessment. The time interval between the two visits ranged from one to two weeks. Health status was assessed with the question: did your health status change since the last visit to the hospital? The healthy control group individuals each received a copy of the MAP by post at home and were requested to complete and return it via registered post-paid mail envelope.

Data analysis

As the MAP uses an ordinal scale, nonparametric statistical analysis was used. Data are presented as median value with lower and upper quartiles and analyzed accordingly. Analysis was performed using SPSS version 23.0.

Construct validity: Convergent validity was assessed by determining the Spearman correlation coefficient for the relationship between the median scores of subscales and single items of the German MAP and the HAQ, the physical and mental component score of the SF36, the pain scale, the FI-2,

the MMT8 and the QMT. A Spearman correlation coefficient of 0–0.25 was considered as no or very low correlation, 0.26–0.4 as low correlation, 0.41–0.69 as moderate correlation, 0.70–0.89 as high and 0.90–1.0 as very high correlation [19].

The discriminative value of the MAP based on the gold standard (healthy by self-report) was assessed by plotting the receiver operating characteristic (ROC) curve and by calculating the area under the curve (AUC). The greater the area under the curve, the more accurate the test is. We used the following classification proposed by Hosmer and Lemeshow: AUC = 0.5: no discrimination, 0.7 to < 0.8: acceptable discrimination, 0.8 to 0.9: excellent discrimination and > 0.9 outstanding discrimination [20].

Reliability: To determine reliability, the weighted kappa coefficients (K_w) of subscales and the single items were computed using GraphPad software (<http://faculty.vassar.edu/lowry/kappa.html>). To interpret kappa values we applied the classification from Landis and Koch (>0.8: almost perfect, 0.61–0.8: substantial, 0.41–0.6: moderate, 0.21–0.4: fair, <0.2 slight) [21]. The Mann-Whitney-U test was used to analyse systematic variations between test and retest of the MAP. The level of significance was set to $p \leq 0.05$.

Based on the evaluation of the original Swedish version, internal redundancy and internal consistency were analyzed [8]. For internal redundancy, correlations between questions in the subscales and for internal consistency correlations between individual items and their subscales, after the actual item had been removed from the score, were computed. Spearman correlation coefficients (r_s) >0.90 were considered to indicate internal redundancy, and r_s <0.50 to indicate poor internal consistency [8].

Additionally, Cronbach's alpha coefficient was calculated to evaluate item fit within subscales. Cronbach's Alpha values between 0.7 and 0.9 were considered as acceptable [22].

The study complied with the Helsinki Declaration and was approved by the local ethics committee (registration no. 2014–0022 of the Cantonal Zurich Ethical Committee). All participants signed an informed consent.

Results

From the 76 patients invited to participate in this study, 28 declined because of “lack of time”, “bad health condition” or “no interest”. Baseline characteristics of the 48 patients and 48 healthy controls are summarized in Table 1. Healthy controls had a significant lower BMI than patients (median of 23

Table 1: Baseline characteristics

	patients with IM N:48	healthy controls N: 48
Sex, n (%)		
female	36 (75)	36 (75)
male	12 (25)	12 (25)
Age, in year		
median (Q1-Q3)	60 (51–66)	60 (51–66)
BMI, in kg/cm ²		
median (Q1-Q3)	26 (22–29)	23 (20–25)
Diagnosis, n (%)		
PM	17 (35.4)	
DM	20 (41.7)	
Associated	11 (22.9)	
Disease stage, n (%)		
acute	9 (18.8)	
subacute	7 (14.6)	
chronic	32 (66.7)	
Time since diagnosis (months)		
median (Q1-Q3)	18 (3–54)	
HAQ, 0.00–3.00		
median (Q1-Q3)	0.81 (0.13–1.38)	
pain, VAS, 0–100		
median (Q1-Q3)	14 (0–31)	
SF36		
PCS		
median (Q1-Q3)	35 (30–49)	
MCS		
median (Q1-Q3)	51 (42–58)	
FI-2		
hip flexion		
median (Q1-Q3)	13 (5–27)	
shoulder flexion		
median (Q1-Q3)	22 (10–55)	
total score		
median (Q1-Q3)	25 (16–46)	
MMT8 total score		
median (Q1-Q3)	71 (67–76)	
QMT total score		
median (Q1-Q3)	106 (91–137)	

Legend: PM: polymyositis, DM: dermatomyositis, FI-2: Functional Index 2, HAQ: Health Assessment Questionnaire, PCS: physical component score, MCS: mental component score, Q1: lower quartile, Q3: upper Quartile

versus 26, p -value < 0.01). Score distribution of the subscales and single items of the MAP are shown in Figure 1.

Figure 1: Score distribution of the subscales and single items of the Myositis Activity Profile in patients with IM and healthy controls

Legend: 1 = no difficulty, 7 = impossible to do.

Construct validity

Convergent validity: The median of subscales and single items of the German MAP correlated highly with the HAQ and the physical component score of the SF36; moderately with the total scores of the FI-2, the QMT and the MMT8; and poorly with the mental component score of the SF36 and with pain scale scoring (Table 2). Correlation coefficient values between the MAP and the SF36 (PCS and MCS), the MMT8 and the FI-2 were all negative, as these are all inverse relationships.

Table 2: Correlations between the total median score across the four subscales and the four single items of the German Myositis Activity Profile (MAP) and other measures

Measure	German MAP r_s	CI
Health Questionnaires, N:46		
HAQ	0.77	0.60–0.91
SF 36: PCS	-0.78	-0.87 - -0.63
SF 36: MCS	-0.28	-0.55–0.27
Muscle strength, N: 47		
MMT8	-0.59	-0.76 - -0.34
QMT_total score	-0.59	-0.76 - -0.34
Muscle endurance, N:45		
FI-2 total score	-0.64	-0.44 - -0.78
Pain (during last week), N: 46	0.38	0.10–0.62

Legend: r_s : Spearman correlation coefficient; MMT8: Manuel Muscle Test; FI-2: Functional Index 2; HAQ: Health Assessment Questionnaire

Discriminative validity: The ROC curves are shown in Figure 2. Three out of four subscales and two out of four single items achieved acceptable AUC values (0.72–0.79). Subscale “personal care” and single questions “social” and “avoid overexertion” indicated no acceptable discrimination (AUC between 0.65 and 0.69), as illustrated in Table 3.

Figure 2: Receiver operating characteristic (ROC) curve

Table 3: Area under the curve

German MAP	AUC	CI
Subscales		
Movement	0.78	0.68–0.87
Moving around	0.78	0.69–0.88
Personal Care	0.69	0.58–0.79
Domestic	0.79	0.70–0.88
Single Items		
Social	0.65	0.54–0.76
Avoid overexertion	0.68	0.57–0.79
Work/school	0.72	0.62–0.82
Recreational	0.75	0.66–0.85

Legend: MAP: Myositis Activity Profile; AUC: Area under the Curve, CI: Confidence Interval

Specificity and Sensitivity of possible cut-off values are presented in Table 4. For the subscales/single items a cut-off level of two points and for the total median a cut-off value of 1.5 points leads to highest sensitivity. When considering the specificity, cut-off levels of 3 points for the subscales/single item values and 3.5 points for the total median values are therefore ideally required.

Table 4: Sensitivity, specificity at different cut-offs

German MAP	cut-off	Sensitivity	Specificity
Subscales			
Movement	2.00	68.75	75.00
	3.00	52.08	95.83
Moving around	2.00	64.58	87.50
	3.00	50.00	95.83
Personal care	2.00	45.83	89.58
	3.00	33.33	95.83
Household	2.00	68.75	83.33
	3.00	43.75	95.83
Single Items			
Social	2.00	41.67	83.33
	3.00	31.25	97.92
Avoid overexertion	2.00	75.00	50.00
	3.00	50.00	75.00
Work/school	2.00	68.75	64.58
	3.00	43.75	89.58
Recreational	2.00	68.75	75.00
	3.00	54.17	87.50
Total median	1.50	70.83	81.25
	2.00	66.67	85.42
	0.50	47.92	93.75
	3.00	41.67	95.83
	3.50	22.92	97.92
	4.00	18.75	97.92
	4.50	6.25	97.92

Legend: MAP: Myositis Activity Profile

Reliability

Forty-four patients declared no change in their health status and were, therefore, included in the reliability analysis. Weighted kappa coefficient values ranged from 0.65 to 0.71 for the MAP subscales and 0.57 to 0.77 for the single items. No systematic differences between the two test occasions were recorded (Table 5).

Table 5: Test retest reliability of subscales and single items of the German MAP

MAP	Test Median (Q1-Q3) N: 44	Retest Median (Q1-Q3) N: 44	K _w	95%CI	Sign Test p
Subscales					
Movement	3.3 (1.0–3.0)	2.0 (1.0–4.0)	0.67	0.54–0.81	0.34
Moving around	2.5 (1.0–4.0)	2.0 (1.0–3.0)	0.65	0.54–0.75	0.09
Personal Care	1.0 (1.0–3.0)	1.0 (1.0–3.0)	0.7	0.55–0.84	0.31
Domestic	2.0 (1.0–3.8)	3.0 (1.0–4.0)	0.71	0.61–0.82	0.78
Single Items					
Social	1.0 (1.0–3.0)	1.0 (1.0–3.0)	0.77	0.63–0.92	0.57
Avoid overexertion	2.5 (1.3–4.0)	2.5 (1.0–4.0)	0.57	0.41–0.74	0.35
Work/school	2.0 (1.0–3.8)	2.5 (1.0–4.0)	0.67	0.53–0.81	0.2
Recreational	3.0 (1.0–4.0)	3.0 (1.0–4.0)	0.71	0.55–0.87	0.27

Legend: MAP: Myositis Activity Profile; Q1: lower quartile, Q3: upper Quartile; K_w: weighted kappa coefficient; CI: Confidence Interval

Internal redundancy: Spearman Correlation Coefficients between items in the subscale “movement activities” (n: 9) varied between 0.29 and 0.81, in the subscale “moving around” (n: 4) between 0.60 and 0.76, in the subscale “personal care” (n: 9) between 0.33 and 0.91, and in the subscale “household” (n: 6) between 0.41 and 0.88. The two questions about “washing and combing hair” were considered redundant ($r_s = 0.91$).

Internal consistency: Correlations between individual items and their subscales after the actual item had been removed from the score ranged from $r_s = 0.45$ to 0.83 for the subscale “movement activities”, $r_s = 0.70$ to 0.78 for the subscale “moving around”, $r_s = 0.45$ to 0.76 for the subscale “personal care”, and $r_s = 0.48$ to 0.87 for the subscale “household”. Three items (standing for longer period, wiping yourself after bathroom, putting plates and glasses away) indicate poor consistency.

Cronbach’s alpha coefficient values for the four subscales ranged between 0.89 and 0.94 (movement: 0.94, moving around: 0.89, personal care: 0.94, and household 0.93).

Discussion

The German-MAP is the first disease-specific questionnaire for assessing limitations in activities of daily living in German-speaking patients with IM. This new German version of the MAP revealed acceptable construct validity: the majority of our hypotheses for discriminative validity were confirmed. Good test retest reliability was recorded. Kappa values for all subscales and

three out of the four single items were substantial. The single question “avoid overexertion” just failed to reach substantial reliability. Cronbach’s Alpha was acceptable for the subscale “moving around”. For the three other subscales Cronbach’s Alpha was higher than expected.

Our results for the convergent validity are in line with previous studies. All three versions of the MAP demonstrated higher correlations with a generic activity limitation questionnaire (HAQ) than with muscle function assessment scores. The correlations between the two questionnaires (MAP and HAQ) were similar in all three countries (Spearman correlation coefficients ranging between 0.69 and 0.77). For muscle function, the correlations were more heterogeneous across the different language versions. While the correlation coefficients of the MAP with muscle endurance in the Swedish and German cohorts were moderate (0.55 and 0.64), those in the English cohort were lower and poorer (between 0.29 and 0.47). Correlations between the MAP and muscle strength were solely determined in the English and German cohorts. Also for muscle strength, the English cohort showed lower correlations with the MAP compared to the German cohort (0.35 versus 0.59, respectively). Reasons for these lower correlations between the MAP and muscle function in the English cohort are unclear. The subject sample in the German cohort is slightly older than the two other cohorts (60 years versus 55 and 52 years), however, the Swedish cohort has the highest MAP scores. Concerning muscle strength, the English and German cohorts were comparable [8, 9]. Future studies with larger samples may shed greater light on this issue. The current correlation is an estimate and only with increasing sample size can we hope to progress towards a more stable and representative value [23].

In general, muscle strength and muscle endurance values correlated only moderately with the MAP. This emphasizes the importance of using Health-Related Patient-Reported Outcomes as well as assessments of physical performance. This was the first time that the MAP has been compared with the SF36 and with pain scores. The higher correlation found with the physical component summary than with the mental component summary of the SF36 supports the notion that the MAP does measure activity limitation. Although pain is an important outcome measure in patients with IM, it did not seem to affect activity limitation in our sample. The reason for this could be that our sample reported rather low pain levels on the VAS.

The gender and age matched control group indicated lower scores in all subscales/single items when compared with patients (Figure 1). Nevertheless, three items did not reach acceptable discriminative validity. One of these items was “avoid overexertion”. This is the only item that has a median higher than one in the healthy control group. Avoid overexertion does not seem to be an illness-related problem, but rather an individual or age-related challenge. Although our controls had to be healthy (by self-report), it is not impossible that they suffered from age-related problems such as physical deconditioning or arthritis, especially as half of our sample was older than 60. The remaining two items with low discriminative validity were “personal care” and “social”. These were the two items with the lowest rating in our patients group (median of one) as well as in the American and Swedish cohort [8, 9]. Patients seem to manage their personal care despite physical limitations. Perhaps this is because they have developed good coping strategies and/or have adapted their personal environments in such a way that they can live independently. For example, one woman in our sample told us that because she had problems drying her long hair she had it cut short. The item “social” is defined as “to keep in touch with and meeting friends or relatives”. It appears that, despite their physical limitations, the social lives of people who have IM are not strongly affected.

The level at which the cut-off value should be set for discrimination between patients and healthy persons is not obvious. When considering only the sensitivity, the cut-off should be at 2 points, but when considering the specificity, the cut-off would be at 3 points. Therefore, it is questionable if the MAP should be used as a screening tool. In actuality, the MAP was developed for assessing activity limitation among patients with IM [8], rather than a discriminatory tool.

Assessment items “washing hair” and “combing hair” both demonstrated high internal redundancy. In fact, these two activities are very similar. Because the item “washing hair” is rated lower, it could potentially be excluded from the questionnaire. In three out of the four subscales, one item indicated poor internal consistency: “standing for long period” from the subscale “movement”, “wiping yourself after bathroom” from the subscale “personal care” and “putting plates and glasses away” from the subscale “household”. For the items “standing for a longer period” and “putting plates and glasses away” it is questionable whether they belong to their current subscales. “Standing for a longer period” is the only item in the subscale “movement”

that is a static rather than a dynamic activity. All the other activities are dynamic ones. This may be a reason why this item does not appear to fit this subscale. In the subscale “household” all activities other than “putting plates and glasses away” demand predominantly lower rather than upper extremity performance, or else focus on the body as a whole. Because the activity involves putting plates and glasses away in the top of a cupboard, other attributes such as adequate upper limb strength and range of motion are required.

As might be anticipated, our study had certain strengths as well as limitations. One strength is that we were almost able to recruit the COSMIN initiative minimum recommended number of 50 participants [24], despite IM being a relatively rare disease. Sixty-three percent of the patients, who visited our department and who were informed about this study, satisfied our selection criteria and agreed to participate. Another strength is the inclusion of a healthy control group. This is the first time that the MAP has been compared across both patients and healthy individuals. A limitation may be that the healthy controls and patients were only matched by age and gender and not by other possibly biasing factors; e.g. their physical activity level. The healthy control group had a significant lower BMI than patients; this may be an indication that the former were more active than the latter. Therefore, we do not know if healthy controls have fewer activity limitations than patients because they are more active, or if they are more active because they do not have muscle symptoms. To definitively exclude the influence of physical activity, its level across both patients and healthy controls should ideally be controlled for. Another possible limitation is that the study was performed in the German speaking part of Switzerland. To avoid a Swiss bias to the translation, one translator had a German background. Nevertheless, participants from other German speaking countries, such as Germany or Austria, might have judged certain items differently. A further limitation of our study is that we could not conduct a factor analysis. For this analytical approach, a minimum of four to ten cases per item is required [22], a participant number that was beyond our project’s capacity. Based on the encouraging findings of our study an international multicenter study might be considered to assess the replicability of our findings.

Although the MAP showed acceptable validity, there are some ambiguities concerning the structure and scoring of this questionnaire, which should also be considered in any future studies. The score of a subscale is the median of the scores from all items within it. Because the median is unaffected

by extreme scores in such a scoring strategy, easier items have greater influence in the scoring of a subscale. This leads to the fact that all patients, who have no difficulty in more than fifty percent of the activities of a subscale end up having the same score, independently of the scoring of the other items. This scoring approach may lead to underestimation of the activity limitation of participants. Another pitfall of the MAP could be the fact that patients have to weight their difficulties against their needs when answering questions. Patients' abilities to reliably weight both the importance and the difficulty of their own performance has yet to be investigated [8].

This initial validation of the German version of the MAP revealed acceptable validity and good reliability for assessing activity limitation among German speaking Swiss patients with IM. Further validation is required to fully verify these results, using German and/or Austrian participant groups. Furthermore, structure and scoring as well as responsiveness of the MAP should ideally be evaluated in a larger multicenter study.

Acknowledgments

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Supporting information: S1 Appendix. German-MAP

Identifikationsnummer: _____

Name Untersucher/in: _____

Datum: _____

Myositis-Aktivitätenprofil (MAP)
(Fragebogen über tägliche Aktivitäten)

(adaptiert nach Alexandersen H et al. The myositis activity profile – initial validation for assessment of physical activities in patients with myositis. J Rheumatol 2012;39:11; Alexandersen H et al. Development of the myositis activities profile – validity and reliability of a self-administered questionnaire to assess activity limitations in patients with polymyositis/dermatomyositis. J Rheumatol 2002;29:11)

German-MAP

Bewegung

- 1) Wie schwierig ist es für Sie in Ihrem Alltag während längerer Zeit zu stehen (z.B. in einer Schlangenlinie)?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 2) Wie schwierig ist es für Sie in Ihrem Alltag beim Vordersitz eines Autos ein bzw. auszustiegen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 3) Wie schwierig ist es für Sie in Ihrem Alltag einen Gegenstand vom Boden aufzuheben (zum Beispiel etwas vom Boden auf den Tisch zu heben)?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 4) Wie schwierig ist es für Sie in Ihrem Alltag eine Umhängetasche oder einen Rucksack mit mehr als einem Kilo Gewicht zu tragen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 5) Wie schwierig ist es für Sie in Ihrem Alltag eine volle Einkaufstasche vom Ladentisch oder vom Auto auf den Boden zu stellen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 6) Wie schwierig ist es für Sie in Ihrem Alltag ein Kind, Haustier oder Gegenstand in Ihre Arme hochzunehmen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich

German-MAP

- 7) Wie schwierig ist es für Sie in Ihrem Alltag Gegenstände mit einer oder beiden Händen zu greifen (beispielsweise eine Bratpfanne oder einen Hammer)?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 8) Wie schwierig ist es für Sie in Ihrem Alltag Konfigurationsgläser, Frischhalteboxen (z.B. Tupperware) oder Verpackungen zu öffnen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 9) Wie schwierig ist es für Sie in Ihrem Alltag eine schwere Türe zu öffnen (beispielsweise eine Auto-, Restaurant-, oder Ladentüre)?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich

Aktivitäten der Fortbewegung

- 10) Wie schwierig ist es für Sie in Ihrem Alltag mehr als 800 Meter auf einem ebenen Boden zu gehen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 11) Wie schwierig ist es für Sie in Ihrem Alltag zu rennen (beispielsweise auf einem Bus rennen oder zu joggen)?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich
- 12) Wie schwierig ist es für Sie in Ihrem Alltag ein Stockwerk Treppe ohne Geländer zu steigen?
(1)	☐	(2)	☐	(3)	☐	(4)	☐	(5)	☐	(6)	☐	(7)	☐
	Gar nicht		sehr wenig		wenig		mässig		schwierig		sehr		extrem
	schwierig		schwierig		schwierig		schwierig		schwierig		schwierig		unmöglich

German-MAP

- 13) Wie schwierig ist es für Sie in Ihrem Alltag öffentliche Verkehrsmittel wie einen Bus, einen Zug oder ein Flugzeug zu benutzen?
(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

Körperpflege und -hygiene

- 14) Wie schwierig ist es für Sie in Ihrem Alltag Ihre Haare zu waschen?
(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich
- 15) Wie schwierig ist es für Sie in Ihrem Alltag ein Bad in einer Badewanne zu nehmen?
(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 16) Wie schwierig ist es für Sie in Ihrem Alltag Ihre Haare zu kämmen oder zu föhnen?
(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 17) Wie schwierig ist es für Sie in Ihrem Alltag Ihre Zehennägel zu schneiden oder zu feilen?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 18) Wie schwierig ist es für Sie in Ihrem Alltag Ihren Rücken zu waschen (eventuell mit einer Rückenbürste)?
(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

German-MAP

- 19) Wie schwierig ist es für Sie in Ihrem Alltag sich nach dem Gang zur Toilette selbst zu reinigen?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 20) Wie schwierig ist es für Sie in Ihrem Alltag einen Pullover an- bzw. auszuziehen?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 21) Wie schwierig ist es für Sie in Ihrem Alltag Hosen oder Strumpfhosen an- bzw. auszuziehen?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 22) Wie schwierig ist es für Sie in Ihrem Alltag Schuhe oder Stiefel an- bzw. auszuziehen?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

Arbeiten im Haushalt

- 23) Wie schwierig ist es für Sie in Ihrem Alltag tägliche Einkäufe nach Hause zu transportieren?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

- 24) Wie schwierig ist es für Sie in Ihrem Alltag Teller oder Gläser in den oberen Teil des Schrankes zu versorgen?

(1)	(2)	(3)	(4)	(5)	(6)	(7)
☐	☐	☐	☐	☐	☐	☐
Gar nicht
schwierig	sehr wenig
schwierig	wenig
schwierig	mässig
schwierig	sehr
schwierig	extrem
schwierig	unmöglich

German-MAP

25) Wie schwierig ist es für Sie in Ihrem Alltag den Boden nass aufzunehmen?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

26) Wie schwierig ist es für Sie in Ihrem Alltag zu staubsaugen?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

27) Wie schwierig ist es für Sie in Ihrem Alltag Ihr Haus und Garten oder Ihre Wohnung in Stand zu halten (beispielsweise Fenster zu putzen oder den Rasen zu mähen)?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

28) Wie schwierig ist es für Sie in Ihrem Alltag Haushaltsgeräte zu reinigen und in Stand zu halten (beispielsweise einen Staubsauger, einen Ofen oder elektrische Geräte)?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

29) Wie schwierig ist es für Sie in Ihrem Alltag den Kontakt mit Freunden und Verwandten aufrecht zu erhalten bzw. sie zu treffen?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

30) Wie schwierig ist es für Sie in Ihrem Alltag Überanstrengung zu vermeiden?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

German-MAP

31) Wie schwierig ist es für Sie in Ihrem Alltag Ihre Arbeit, Schule und/oder Hausarbeit zu bewältigen?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

32) Wie schwierig ist es für Sie in Ihrem Alltag Freizeitaktivitäten, die Ihnen Spass machen, ausführen zu können?

(1) ☐ (2) ☐ (3) ☐ (4) ☐ (5) ☐ (6) ☐ (7) ☐
 Gar nicht sehr wenig wenig mässig sehr extrem unmöglich
 schwierig schwierig schwierig schwierig schwierig schwierig

Besten Dank für das Ausfüllen des Fragebogens!

German-MAP

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6

CHAPTER 6

Usability and acceptance of an interactive tablet-based exercise application: a mixed methods study

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Abstract

Purpose: To investigate usability and acceptance of a newly developed interactive, tablet-based exercise app and to explore personal opinions of therapists when using this app in the clinical setting.

Methods: Twenty participants (10 therapists and 10 inactive healthy adults) tested usability of this app performing different test tasks, using the think aloud method, and rated overall satisfaction with the System Usability Scale and acceptance with a modified Technology Acceptance Model Questionnaire. Personal opinions of therapists were evaluated with two focus groups, one for team leaders and one for team members.

Results: Overall, the app was judged to be usable. Effectiveness varied between 73% and 90%, overall satisfaction between 70.5 and 85.5/100 points and acceptance between 74% and 80%. Team leader and team member focus groups considered the app as providing a great opportunity for therapy extension, especially because of its blended character. Barriers to its implementation were seen in the existing clinical working processes, personal attitudes of therapists and uncertainty of who would cover expenses for this new form of therapy. Some improvements such as using videos instead of photos, the integration of more interactive tools and the possibility to add additional exercises were suggested in both settings.

Conclusion: The app showed high acceptance and usability in trainees and therapists, although some ideas for upgrading functions were formulated. Before this app can be used in clinical practice, feasibility of this blended approach should be evaluated in a clinical setting.

Abbreviation

app	application
ETH	Eidgenössische Technische Hochschule
RT	resistance training
TT	telecommunication technologies
SUS	system usability scale
TAM	Technology Acceptance Model
TL	team leaders
TM	team members
USZ	University Hospital Zurich

Introduction

Resistance training (RT) is a crucial element of the general health enhancing physical activity recommendations and guidelines suggest that every adult should perform activities that maintain or increase muscle strength and endurance at least twice a week (1). Such a regular RT program can not only minimize age-related musculoskeletal alterations, thus reducing their impact on health and the aging process, but also improve physical and mental health, as well as quality of life (2, 3). In addition, RT has potential in the prevention and management of several chronic diseases (4, 5). There is broad evidence that RT increases muscle strength, reduces pain and improves functional ability in patients suffering from chronic low back pain, knee osteoarthritis, chronic tendinopathy and in those recovering after hip replacement surgery (6). RT may also improve health-related quality of life in patients with rheumatic diseases (7) and has positive effects on muscle strength and functional outcomes related to mobility in patients with Parkinson's Disease (8). Furthermore, RT enhances physical functioning and reduces the risk of condition-related lymphedema in patients with breast cancer (9), and can also improve multi-dimensional function, pain, tenderness, and muscle strength in women with fibromyalgia (10).

Despite these positive effects of RT, it remains difficult to motivate inactive individuals to participate regularly in physical exercise (11). For (chronic) patients the barriers to starting exercising may be even higher. Physical deconditioning discourages patients from exercising, which in turn worsens the overall deconditioning and creates a vicious cycle (12). The use of telecommunication technologies (TT) – for example the internet, software applications or SMS messaging - may help to promote health behaviour change (13, 14). These technologies have the advantage of implementing different persuasive features that may help exercise programs to be more enjoyable and, thereby, enhance motivation to exercise on a regular basis. Examples of these persuasive features include personalisation, self-monitoring, tailoring, goal-setting and comparison through positive and negative reinforcement in the development of physical exercise programs (15, 16). Evidence shows that web-based compared to non-web-based interventions are more effective in achieving behavioural change (e.g. increased exercise time) (17) and in improving home exercise adherence for people with musculoskeletal conditions (18).

One of the disadvantages of using TT for home exercises is the lack of face-to-face contact with a professional, which may reduce adherence to training (19). Several studies highlight the importance of personal support when exercising, both in disease prevention and management (20-22). Via such personal contact, the definition of personalised goals, the consideration of individual fitness levels and disabilities within the exercise prescription, and necessary exercise adaptations are all feasible.

Therefore, an interactive, tablet-based exercise app (called “Fit”) was developed. The aim of this exercise app is to assist and monitor physical exercise novices during an individually tailored home-based progressive resistance training program with remote support. This interactive approach not only allows additional supervision, but also combines the advantages of new technologies with the personal support of a health professional.

Although it is well known that convincing system designs are crucial for adherence to web-based interventions, the usage of interactive health care applications has often been hampered by their poor design (23). Consequently, usability testing is an essential step for developing usable and enjoyable products and for identifying flaws in an early system’s design (24, 25). Usability is defined as the extent to which a product can be used by predefined users to achieve particular goals with effectiveness, efficiency and satisfaction in a specific context of use (26). Therefore, it is necessary to perform an exploratory study to test usability of this newly developed interactive, tablet-based exercise app in untrained healthy individuals, prior to exploring its feasibility with patients in clinical practice (27). However, for a newly developed device to be successfully implemented, not only the opinions of actual end-users (individuals who want to become fitter) but also those of the actual health care providers, are crucial to such exploration. As a result, the primary objective of this study was to test usability and acceptance of the Fit app both with physio- and occupational therapists and untrained individuals. In order to increase acceptability of this novel tablet-based Fit app in therapists, who will introduce this app to their patients, the secondary objective of this study was to explore personal opinions of therapists when using it in a clinical setting.

Materials and Methods

Study design

This mixed method study consisted of a usability part followed by a focus group part. Usability was tested in two consecutive phases. After each phase the app was revised based on the feedbacks from the participants (Figure 1).

Figure 1: Explanatory design

Legend: *after each usability phase the app was revised based on the feedbacks from the participants

Participants and Recruitment

For the usability part, a sample of 20 participants was recruited (ten therapists and ten trainees). The therapists were recruited by means of an explanatory leaflet distributed at the University of Applied Science, Winterthur and the University Hospital Zurich (USZ). Therapists' inclusion criteria were that they were (i) a physiotherapist or occupational therapist and (ii) fluent in German. The healthy individuals were recruited among the social environment of the study team members. Inclusion criteria were (i) feeling healthy by self-report; (ii) no currently ongoing treatment by a physician at the time of study; (iii) able to walk independently without a walking aid; (iv) engaging in no more than one exercise session per week; (v) fluent in German. Persons with any potential health risks associated with exercise (assessed with the Physical Activity Readiness Questionnaire (28)) were excluded.

For the qualitative section, an invitation to participate in a focus group interview was e-mailed to all therapists from the Department of Physiotherapy and Occupational Therapy of the USZ. The aim was to recruit two therapists (one team leader and one team member) per unit (e.g. neurology, rheumatology, hand therapy) to achieve a broad variety of work settings and patients.

The study protocol was approved by the Research Ethics Committee of ETH Zurich, Switzerland (protocol number EK 2017-N-27) and conformed to the Declaration of Helsinki. All participants signed an informed consent declaration before study entry.

Rationale of the sample size

Successful Identification of key usability problems depends on the number of users included (24). Early studies reported that five evaluators found about two third of all usability problems (29, 30), whereas more recent literature supports the 10 ± 2 rule (31). With ten users a minimum 80% of the problems related to system use may be identified (32). Therefore, we decided to test usability of this exercise app with ten therapists and ten trainees.

For semi-structured focus group discussions, 4-12 participants are recommended for specific topic exploration (33). Less than four people is too few to be considered a “group”, whereas more than 12 is too many persons to allow equal participation in the discussion. The group members usually share certain characteristics (e.g. their profession, social background etc.) to allow a discussion on the same level, and should show interest in the chosen topic (34). It is further recommended to conduct at least two focus group discussions to cover different aspects of the chosen topic (35). Therefore, we invited seven team leaders (TL) and seven team members (TM) per focus group, each representing a therapy unit of the USZ.

Exercise app

The interactive, tablet-based exercise app was developed by scientist of the ETH, the USZ and Divdiat AG (Dividat Fit, Schindellegi, Switzerland, 93/42/EWG certified). This exercise app provides an interactive, tablet-based, progressive RT programme. “Interactive” means that the supervising therapists design the exercise program individually together with each client (hereafter called trainee) and monitor training progress remotely. During the exercise program, trainees monitor their performed exercises, while the therapists supervise and, as necessary, adapt the exercise’s level via remote monitoring.

The exercise app consists of two different parts: “manager” and “play”. “Manager” is the part where therapists record trainees, compile the exercise program for them and monitor their performed training. It is not accessible to the trainees. Based on trainees’ needs, an individually tailored exercise program can be designed and adapted to their skills. For this purpose, a pool of different single- or multiple-joint exercises, each of them at different difficulty levels, is available. For each exercise, individual training parameters (amount of series and repetitions, duration of rest between series, and target intensity using the 6-20 Borg rating of perceived exertion scale (36) can be defined. If needed, a written comment can be added by the therapists. Additionally,

therapists have the option of choosing if trainees should rate their current level of pain and mood on a visual analogue scale from 0 to 10. Once all exercises are selected and training parameters defined, the desired order of the exercise must be determined. This is important, as the app guides trainees step-by-step through the individually adjusted exercise program. As soon as the trainees have performed the first training session, the therapists can see a graphical and tabular overview of the performed training within “manager”.

“Play” is the part where trainees can see their exercise program and record their performed exercises. After finishing each exercise, trainees have to record perceived exertion (rating of perceived exertion scale from 6 to 20) for it as well as possible pain on a visual analogue scale from 0 to 10. Subsequently, they receive automatically generated feedback corresponding to their reported training intensity, as follows: (1) perceived exertion score is in the predefined level: a positive response is given; (2) perceived exertion score is higher than the predefined level: trainees are suggested to perform the exercise at a lower level; (3) perceived exertion score is lower than the predefined level: trainees are motivated to increase volume or intensity of the exercise; (4) pain is recorded: trainees are advised to perform the exercise correctly and to contact their therapists. In addition to this feedback, the app provides a short statement about the advantages of exercise or a motivational quotation. Additionally, trainees have the option to write a brief note to their therapists. Only after having recorded all training parameters is the next exercise provided. At the end of a training session, trainees receive an overview of their achieved training results. Figure 2 illustrates a screen with the exercise description, the target training parameter and the option to indicate performed repetitions and series of an exercise.

Procedures

Usability

Usability was determined by using the separate feedback from two target stakeholder populations: from the perspective of supervising therapists the “manager” component of the app was assessed, while inactive healthy adults tested usability of “play” (Figure 3).

In both phases, the two stakeholder populations tested usability separately by doing different test tasks categorized into four and five topics, respectively (Table 1 and 2). The test procedure was organized in two phases. In phase one, five therapists and five trainees tested usability. Based on their

feedback, adaptations to “manager” and “play” were implemented. In phase two, five new therapists and five new trainees tested usability of the adapted “manager” and “play” and provided feedback on usability. Based on this feedback, further adjustments were then made.

Figure 2: Screen with exercise description of “play”

Legend: (1) Exercise overview presenting the exercise description, (2) the target training parameters (series, repetitions and intensity) and (3) the possibility to indicate performed training parameters and to finish the exercise or the training.

The usability testing took place in a laboratory setting which was equipped with all necessary requirements (e.g. tablet, audio-recording system) (Figure 3). The test scenario consisted of a *briefing*, the *test session* itself and a *debriefing*.

1. The *briefing* contained the introduction to the test session process and the applied questionnaires.
2. The *test session* contained different elementary tasks for the app's usage (Table 1 and 2). Participants independently completed these tasks in a predefined sequence, while communicating when they started and finished a task. While participants performed the tasks, they were encouraged to verbalise their thoughts, and these were audio-recorded (37). The test moderator recorded the time required to complete the task and checked results after task completion. During the whole session, the test moderator sat in the same room, but out of sight of the participant, to limit interaction between moderator and participant. The moderator only intervened when the participant was unable to complete a task. After finishing all tasks, the participants

filled out the “System Usability Scale” (SUS) (38, 39) and a modified version of the “Technology Acceptance Model” (TAM) questionnaire.

3. The test scenario ended with a *debriefing* consisting of a short discussion and subsequent discharge.

Figure 3: Usability procedure

Table 1: Tasks designed for the Therapists

topics and respective tasks	estimated time for a topic
topic I: register a trainees	5 minutes
task 1: enter name of trainees	
task 2: enter birthdate of trainees	
topic II: create an individual exercise program	20 minutes
task 3: choose trainee from the list of trainees	
task 4: open standard exercise program	
task 5: change this program into an individual exercise program	
task 6: determine order of the exercises	
topic III: check training diary	10 minutes
task 7: choose trainee form the list of trainees	
task 8: open training diary	
task 9: interpret figure and table of the training diary	
topic IV: adapt individual exercises of an existing exercise program	5 minutes
task 10: add a new exercise	
task 11: change an existing exercise	
task 12: adapt repetitions and series and target intensity	
task 13: write an individual comment	

Table 2: Tasks designed for the Trainees

topics and respective tasks	estimated time for a topic
topic I: start exercise program	2 minutes
task 1: activate the tablet	
task 2: start the exercise program	
topic II: view first exercise*	3 minutes
task 3: read instruction of the first exercise	
task 4: click on the pictures to see the correct performance	
task 5: read the target training parameters (repetitions, series, break, intensity)	
topic III: record training diary*	3 minutes
task 6: record performed repetitions and series	
task 7: complete first exercise	
task 8: record intensity and if required pain of the first exercise	
task 9: write a comment	
topic IV: automatically generated feedbacks*	3 minutes
task 10: read the automatically generated feedback, the motivation or information citations and the overview of the performed exercise.	
topic V: check training diary	3 minutes
task 11: examine and interpret the training diary	

Legend: * topic 2-4 were repeated for every four exercise

Focus groups

The focus group interviews took place at the USZ. One focus group was organized for the TL and another for the TM, each lasting 90 minutes (Figure 3). Before starting with the focus group discussion, the co-moderator presented the app to the therapists by means of a power point presentation. A tablet was used to illustrate the app, which no participants had seen beforehand. The interviews were audio-recorded and filmed. As proposed by Pelz et al. (34), the moderator led the discussion, while the co-moderator took notes on flipcharts. These notes served as a summary of what has been said during the discussion.

Outcome measurements

Usability (effectiveness, efficiency and satisfaction) and acceptance

For *effectiveness* and *efficiency* of the Fit app, measurements of performance (task completion, errors, time needed) were recorded by the moderator (40), together with reasons for failed completion and relevant comments from the “think aloud” method (25).

For overall *satisfaction*, the System Usability Scale (SUS) was used (38, 39). The SUS includes 10 items about several aspects of usability, such as ease of use or complexity. Each item can be scored on a 5 point Likert scale from 1 (strongly disagree) to 5 (strongly agree). The SUS total score ranges from 10 to 100, higher scores indicating better usability.

For *acceptance*, a modified version of the Technology Acceptance Model (TAM) questionnaire (41) was used. The modified TAM consists of 20 items which can be rated on a 7 point Likert scale ranging from 1 (strongly disagree) to 7 (completely agree), together with an open question about desired additional options for the app. The items are divided into four subgroups: perceived usefulness (7 items), perceived ease of use (6 items), attitude toward using (4 items), and intention to use (3 items). The scores of the subgroups range from 1 to 7 and the total score from 20 to 140. All outcome measurements and the way they were measured and analysed are summarized in table 3.

Table 3: Outcome measurements usability

outcome	How was it measured and analysed?
Effectiveness	Quantitative: <ul style="list-style-type: none"> task completion rate Qualitative: <ul style="list-style-type: none"> reasons for failed completion description of errors comments from the think aloud method
Efficiency	Time needed to complete a task <ul style="list-style-type: none"> number of tasks that could be completed within the given time limits
Satisfaction	System Usability Scale <ul style="list-style-type: none"> mean, standard deviation and minimum/maximum of the total score
Acceptance	TAM <ul style="list-style-type: none"> mean, standard deviation and minimum/maximum of the total score and the four subscales

Focus group interview guide

The interview guide for the focus group discussion comprised four pre-defined questions, around which the discussion was shaped. These were:

- (1) What are your spontaneous thoughts after the presentation of the app?
- (2) How could you (not) envisage using this app for your patients?
- (3) Do you feel this app could influence training motivation in your patients?

- (4) What would you need / already have at your workplace for a smooth integration of this app in your clinical practice?
- (5) Can you describe your attitude towards using such exercise apps during your daily work?

Data analysis

Usability

Descriptive statistical analysis of outcome measurements was done using the software IBM SPSS statistics for windows version 22.0 (Armonk, NY, USA). Effectiveness consisted of the binary (yes/no) task completion rate (proportion of participants that completed a task correctly) and the errors detected. Additionally, participants' reasons for failed completion, together with the comments from the think aloud method, were also reported. Efficiency was rated as high when all tasks within a topic could be performed within the given time limit. For the total score of the SUS and the TAM, all item scores were summed. Additionally, the four subscales of the TAM were scored using the mean value of the respective item responses. Then the mean, standard deviation and minimum/maximum values of the total score and the subscales were calculated.

Focus group interviews

As this study aimed to summarize a broad variety of opinions rather than focusing on group interactions or single statement ("who said what and how"), the "Focus group Illustration Maps" (FIMs) method was adopted to analyse the interviews (34). The following steps of analysis were carried out:

- (1) transcribing the flipchart notes from the focus group interviews in a preliminary FIM.
- (2) listening to the audio-recording of the focus group discussion; incorporating statements in the preliminary FIM.
- (3) re-listening to the audio-recording, then checking the FIMs for accuracy and completeness.
- (4) grouping, organizing and giving "weight" to the correlations between the different statements.
- (5) finalizing the FIMs by re-listening to the audio-recording again.
- (6) e-mailing the FIMs to the participants for member checking.
- (7) implementing feedback from member checking.
- (8) merging FIMs from therapists and leaders.
- (9) finalizing the FIMs; translation into English language.
- (10) writing the report.

Results

For usability testing, 20 participants (10 therapists and 10 trainees) were consecutively recruited. Demographic data are presented in Table 4. Most therapists as well as trainees indicated being familiar with the internet, computer, tablets or cell phones (Figure 4). In the focus group interviews, seven TL and five TM participated. Eight participants (6 TL and 2 TM) had a Master's degree and four (1 TL and 3 TM) a Bachelor's degree. Five participants (3 TL and 2 TM) described personal use of exercise apps and three of them (1 TL and 2 TM) indicated using exercise apps in their clinical settings. The remaining seven participants did not use apps at all. Demographic data are presented in Table 5.

Figure 4: Familiarity with technology

Table 4: Demographic data of usability participants

	trainees (n=10)	therapists (n=10)
gender female/male		
all	7/3	8/2
phase 1	3/2	5/0
phase 2	4/1	3/2
age in years mean (SD)		
all	57 (10)	38 (9)
phase 1	59 (13)	38 (12)
phase 2	55 (8)	38 (3)
BMI mean (SD)		
all	26.2 (4.7)	23.6 (3.6)
phase 1	24.0 (3.1)	22.8 (4.0)
phase 2	28.4 (5.3)	24.5 (3.3)
professional experience in years mean (SD)		
all		10 (7)
phase 1		12 (10)
phase 2		9 (4)

Legend: n: number, BMI: body mass index; SD: standard deviation

Table 5: Demographic data of focus group participants

	team members (n =5)	team leaders (n =7)
gender female/male	2/3	6/1
age in years mean (SD)	32 (5)	46 (8)
professional experience in years mean (SD)	7 (5)	20 (8)
percentage of employment mean (SD)	82 (4)	83 (13)
work time dedicated for patients in % mean (SD)	80 (7)	36 (19)

Legend: n: number, SD: standard deviation

Usability

Effectiveness

Tasks completion rate, reasons for failed completion, errors and comments are presented in Table 6 for therapists and in Table 7 for trainees. In both phases, the trainees needed a short period of instruction before starting with the test tasks.

Efficiency

In both phases, therapists and trainees could fulfill all but one task within the estimated time limit. For therapists, it was task 9 “interpret figure and table of the training diary,” which was problematic, while for trainees it was task 11 “examine and interpret the training diary for trainees”. Therefore, the topic “check training diary” could not be completed within the predefined timeframe.

Satisfaction

Therapists from phase one rated satisfaction with the app higher than those from phase two, whereas the reverse was the case in trainees (Table 8).

Table 8: System Usability Scale (SUS)

	phase 1		phase 2	
	mean (SD)	min/max	mean (SD)	min/max
trainees	70.5 (11.1)	52.5 / 80.0	81.5 (12.8)	67.5 / 97.5
therapists	85.5 (10.5)	67.5 / 92.5	73.5 (10.8)	62.5 / 87.5

Table 6: Tasks completion rate, reasons for failed completion, errors and comments of the therapists

topic	phase 1		phase 2	
	tasks completion rate (reason for failed completion)	errors	tasks completion rate (reason for failed completion)	errors
register new trainees	task 1: 100% task 2: 0%	<ul style="list-style-type: none"> unfamiliar format of birth date 	task 1: 100% task 2: 100%	
create an individual exercise program	task 3: 100% task 4: 100% task 5: 100% task 6: 100%	<ul style="list-style-type: none"> therapists did not see the photos and description of the exercises some instructions were written in English (even though the program was in German) values higher than 20 could be recorded for the 9-20 Borg-scale in the input window the series and breaks were numbered continuously, although only the series should be numbered the exercises were numbered, but this number had no meaning 	task 3: 100% task 4: 100% task 5: 100% task 6: 100%	<ul style="list-style-type: none"> the first digit of the repetitions could not be deleted the order of the training parameters was not consistent within the different exercises when a new exercise was added to the exercise program, it appears in the first place instead of at the end of the exercise program
check a training diary	task 7: 100% task 8: 100% task 9: 0% (figures and tables were too crowded and confusing)	<ul style="list-style-type: none"> the order of the list with the participants could not be changed 	task 7: 100% task 8: 100% task 9: 60% (no scales for the x-y-axes, colours of the lines were not distinguishable from each other)	<ul style="list-style-type: none"> "this is not clear, the colours of the lines are confusing" "I think this should be a target-performance comparison" "there are too many lines, it is not obvious which line represents what"
adapt individual exercises	task 10: 100% task 11: 100% task 12: 100% task 13: 100%	--	task 10: 100% task 11: 100% task 12: 100% task 13: 100%	--

Table 7: Tasks completion rate, reasons for failed completion, errors and comments of the trainees

topic	phase 1			phase 2		
	task completion rate (reason for failed completion)	errors	comments	task completion rate (reason for failed completion)	errors	comments
start exercise program view first exercise	task 1: 100%	--	--	task 1: 100%	--	
	task 2: 100%			task 2: 100%		
	task 3: 100%	--	--	task 3: 100%	--	• "it would be nice to have videos instead of photos"
	task 4: 100%			task 4: 100%		
	task 5: 100%			task 5: 100%		
record training diary	task 6: 80% (it was not clear where to report the performed repetitions)	• no possibility to add series	• "where can I click?"	task 6: 100%	--	--
	task 7: 100%	• no "return" button	• "it is not clear where it is possible to insert something"	task 7: 100%		
	task 8: 60% (very low sensitivity of the touch screen for the Borg-Scale)	• no text was see-able while writing a note	• "when I was too fast: is there no "return" button?"	task 8: 100%		
	task 9: 80%	• "I hoped I could see anywhere what I'm writing"		task 9: 100%		
	task 10: 60% (screen disappeared too fast)	--	• "oh, that's too fast"	task 10: 100%	--	• "it's cool to have these feedbacks"
automatically generated feedbacks						
check training diary	task 11: 0% (screen with the training diary was very crowded and disappeared after a few seconds)	• figure could be enlarged with two digits but then not mini-mized to the original size	--	task 11: 60% (axis were not clearly labelled)	--	• "I normally like statistics and figures, but here I needed help"
		• axis were not labelled				

Acceptance

The TAM included one question about the usefulness of videos, which was redundant, as there were no videos integrated in the app. Additionally, the two questions about the ease of use of photos could not be answered by the therapists, as there were no photos integrated in the “manager”. Thus, the possible maximum scores for trainees and therapist were 133 and 119 respectively. The percentage of the total score was computed to allow comparison of results between trainees and therapists (Table 9).

Table 9: Technology Acceptance Model (TAM)

		phase 1		phase 2	
		mean (SD)	min / max	mean (SD)	min / max
trainees	perceived usefulness	5.5 (0.5)	4.6 / 5.9	6.6 (0.4)	6.0 / 7.0
	perceived ease of use	6.0 (0.2)	5.8 / 6.4	6.1 (1.1)	4.4 / 7.0
	attitude toward using	6.4 (0.5)	5.8 / 7.0	6.3 (0.7)	5.5 / 7.0
	intention to use	5.7 (0.4)	5.3 / 6.3	6.2 (0.8)	5.3 / 7.0
	total score (max: 133)	111 (4)	106 / 115	120 (12)	104 / 133
	total score (%)	84 (3)	80 / 86	90 (9)	78 / 100
therapists	perceived usefulness	6.1 (0.5)	5.4 / 6.6	5.9 (0.5)	5.4 / 6.8
	perceived ease of use	5.4 (1.4)	3.0 / 6.6	5.8 (0.9)	4.6 / 6.6
	attitude toward using	6.4 (0.9)	4.8 / 7.0	5.9 (0.9)	4.8 / 7.0
	intention to use	6.2 (0.6)	5.3 / 7.0	5.3 (1.0)	4.0 / 6.7
	total score (max: 119)	101 (12)	88 / 114	97 (14)	83 / 115
	total score (%)	85 (10)	74 / 96	81 (11)	70 / 97

Therapists as well as trainees identified several ideas for improvements for the app. For the “manager” therapists proposed (i) the possibility to filter the exercises’ overview for individual use, (ii) the inclusion of videos instead of photos, (iii) other exercises and help functions and (iv) other training parameters, e.g. heart rate or blood pressure. For the “play”, the trainees proposed (i) help functions, (ii) exercise instruction by videos instead of photos, (iii) return buttons and (iv) the possibility to contact the therapists via e-mail.

Focus groups

Usefulness

In general, both TL and TM perceived the Fit app as a useful therapy supplement which they could contemplate introducing to different patient

groups (Figure 5). Aside from certain specific reservations for its use – e.g. for “technically disinclined patients” – they believed that up to 90% of myositis patients could benefit from this app. The focus group members highlighted that most of these patients travelled from all over Switzerland to the USZ for single therapy sessions. Therefore, use of the app could increase training intensity, as patients could work from home, while simultaneously being offered professional assistance from the USZ thanks to its division into “manager” and “play” components. Both TL and TM liked the need of the presence of an expert - the therapist - which was seen as an important difference when compared with other fitness apps without a “professional” feedback function. The use of “blended therapy” increased the acceptability of the app among the focus group members, because it reduced their fear of being replaced by technical applications. Particularly for TM, it was seen as important that use of the app should not consume the whole therapy time, but rather serve as part of a therapy session alongside “face-to-face” treatment. During the interview, it became evident that all members would have preferred the use of videos instead of pictures to illustrate the exercises, because “everyone likes watching videos”. Further ideas for improvement mostly aimed at increasing the app’s advantages over the common use of hardcopies to illustrate the prescribed exercises (as “stick figure”). Other provided examples included integrating push news as a memory function to contact the patient, and the app’s availability via smartphone rather than tablet-computer.

Training motivation

The TL all agreed on the app’s feasibility for increasing training motivation in comparison with the current wide use of hardcopies to present home exercise programs (Figure 6). For example, they emphasized the app’s positive commitment to training due to its active therapist involvement in support and control of progress of patients’ home exercises. However, they imagined this involvement as rather time-consuming for their already very busy therapists. They further liked the app as a tool of evidence for the effectiveness of therapy thanks to its immediate provision of training progress. In comparison to the TL, the TM took a more critical stance towards the app’s ability for increasing training motivation. They doubted that patients would increase their exercise volume when using the app instead of hardcopy exercise schedules, and were reluctant to promote extrinsic rather than intrinsic training motivation. In addition, they feared being restricted in their choice of exercises

to design individually adjusted exercise programs when using the preset exercises of the app. Ideas for improvements to increase training motivation when using this app were plentiful (Figure 6). The focus group members, however, did not reach consensus regarding whether implementation of rewarding games would really increase training motivation. Some stated that rewarding games are no valuable feedback for training quality, but rather trigger extrinsically motivated training aspects, e.g. to please the therapist. Others missed the playfulness of gaming when using the app for training at home, and advocated a bonus when exercising, emphasizing “everybody likes collecting things”.

Smooth integration

The focus group members mainly mentioned environmental factors that could facilitate a smooth integration of the Fit app into their clinical practice, e.g. a laptop per therapist (Figure 7). Most of the TM appreciated the app’s potential for remote support, but had reservations regarding personal time resources for coaching and monitoring patients. The TL, however, put more emphasis on the uncovered costs and missing work processes involved in implementing the app. Some of the latter feared that this innovation is “just one more thing I have to do”, expressing reservations for its use, while some of the former stated that “having no time” is not an excuse for non-usage. Other concerns mentioned included the fear of not being able to address patients’ technical problems when using this app and when precisely to use it who best to use it for. Besides rising concerns, the focus group members also created new ideas for this app’s usage, e.g. as an option for Telemedicine (“call center”) and the related possibility for therapists to do more home-office working.

Attitude

Most of the focus group members shared a positive attitude towards using such apps for therapeutic purposes (Figure 8). They all agreed that therapists should stay alert to new therapy developments. To date, they described mostly using hardcopies to compose individualized home exercise programs for their patients, together with the smartphone of the patient to take pictures or make videos. Exercise apps on the computer were rarely used, because they were described as being more time-consuming than using hardcopy training schedules or oral instructions during therapy. The TL highlighted the importance of such apps running smoothly, as technical diffi-

culties often reduce their usability. The protection of data privacy was an important issue for all therapists. Those members of the focus group with a reluctant and ambivalent attitude mentioned that they perceived it difficult to change and adjust to the “digital world”. They stated that they do not perceive computer work as dedicated time to patients, experiencing a barrier to using IT in their presence. One advantage for using the Fit app was seen in its ability to stay up-to-date with patients’ progress, while exercises on paper bear the risk of patients still performing exercises at home that have ceased to be effective. Nevertheless, they preferred using both digital and handwritten exercise programs.

Figure 5: Therapists’ perceived usefulness of the Fit app for daily work

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Figure 8: Therapists' attitude for using the Fit app during daily work

Discussion

Overall, the app has demonstrated to be usable for both therapists and trainees. Effectiveness measured by task completion rate improved from phase one to phase two from 73% to 90% and from 85% to 92% for the “play” and “manager” components respectively. In contrast, because in both phases there was one task which was not completed within the expected timeframe, efficiency did not change. Whereas satisfaction with “play” improved (from 70.5 to 81.5), it decreased with “manager” (from 85.5 to 73.5) from phase one to phase two. Overall acceptance with the app showed the same pattern as satisfaction. Acceptance of “play” improved from 111 to 120 points and decreased for “manager” from 101 to 97. Therapists from the focus group interviews perceived this app suitable for different patient groups and appraised it worth trying in their clinical practice.

Although most of the detected errors from phase one could be remedied before phase two started, satisfaction and acceptance improved only for “play” (assessed by trainees) but not for “manager” (assessed by therapists). One reason that satisfaction and acceptance of the “manager” decreased in phase two might be that some errors were only detected in the second

phase, although they already existed in the first phase. It seems that therapists from the second phase were more critical than those from the first phase. This interpretation is confirmed by the fact that therapists from phase two made more critical comments during the task “create an individual exercise program” than those from phase one. In comparison, the trainees detected no further errors in the second phase and comments were less critical than in phase one. One explanation for this result is that therapists indicated being more familiar with technology than trainees, especially for handling tablet computers. Perhaps, therefore, the former expected less from this app and were thus less critical. Another reason for decreased satisfaction and acceptance of the “manager” in phase two might be that some problems could only be seen in the second phase. For example in the first phase the overview of the training diary was so unclear that therapists did not go into details, but just accepted that this part requires improvement. In phase two, the overview improved slightly, but was still not satisfying. Therapists tried hard to interpret the figures and tables, but since it was still very confusing, they were not successful. This may be more frustrating and therefore they were less satisfied and consequently less convinced that they would use the app.

Although trainees were not able “to check the training” (task 11) in “play”, it seems that therapists weight this task as more important than do trainees. For the latter, it was important to understand the exercise and be able to record their training diary. They were not very interested in the overview. Perhaps this was also because they did not perform a real training session but recorded only one virtual one. Therefore, progress could not be seen in the training overview. For the therapists, the training diary was one of the most important tasks of this app. They can only coach their trainees adequately when they have a good overview of the performed training sessions. Therefore, the failure of this task might have a higher impact on satisfaction and acceptance than the failure of task 2 (enter birthdate of the trainees). In addition, the fact that SUS as well as TAM-scores were at a high level in the first phase made it difficult to further improve scores in the second phase. SUS scores for example were higher than the described average score of 68 from normative data (42). Scores from therapists even reached the threshold of 82 points, which is important for a system to be recommended to a friend (39).

In general, trainees as well as therapists judge the Fit app as usable and also had a positive attitude toward its use. This is consistent with the overall judgement from the participants of the focus groups. Some points were emphasized in both settings, such as participants preferring videos to photos, wishing to have more interactive tools such a push news or e-mail contact and wanting to have the scope to add additional exercises. In addition, focus group members emphasized the importance of the ease of use of such an app. This aspect was rated as good in the usability part of this study.

Besides the device itself, the focus group members discussed also contextual factors related to the acceptance of innovative digital tools. The results showed that the focus group members liked the app thanks to its blended character in offering a patient (“play”) and therapist (“manager”) station. With the feature of remote support of the patient, this app provides an opportunity of therapy extension between patient’s home and clinic, allowing maintenance of contact with patients from wherever they are. Our results corroborate previous studies that reported high acceptance and satisfaction of blended therapy (defined as the combination of face-to-face therapy and remote support via TT) in patients with anterior cruciate ligament reconstruction, multiple sclerosis and hip/knee osteoarthritis (21, 43, 44).

Despite the high acceptance of the Fit app among therapists, they also raised some concerns regarding its use. Barriers were seen in its implementation in the clinic (work processes need to be adjusted; data protection), in the personal attitude of therapists (change management), together with uncertainties regarding payment of costs and invested therapy time. Kloek et al. also revealed some of these concerns: some therapists perceived the evaluated web-based application as an additional burden within the busy work schedule and their fear that this approach could substitute face-to-face sessions (45). Nevertheless, the therapists had diverse ideas for improvements of this app, putting emphasis on revising the many advantages of an app in comparison with non-technological approaches (e.g. using videos instead of photos, including push-news, providing an interface with the clinic’s network to exchange data). This is in line with the therapists’ feedback during the usability part of this study. Because the Fit app is part of a bigger software program and all functions and features must be compatible with these other applications, it was not possible to insert photos in the “manager” during the usability study. To overcome this failing, a leaflet with the overview of the

exercises was given to the therapists. In the meantime, the software engineers developed a solution to include photos of exercise in the “manager”.

As blended therapy is a relatively new therapy option, it is unclear which patient groups could benefit the most from such an approach. One group might be patients with a relatively long rehabilitation period such as, for example, anterior cruciate ligament reconstruction. Patients with rare diseases, e.g. inflammatory myositis or haemophilia, could also benefit from blended therapy, as specialized and experienced health professionals are mostly available in major health centers only. Therefore, access to high quality care is limited by travel distance and travel costs. In this situation, the blended therapy approach may optimize the timing, intensity and sequencing of interventions and provide opportunities for individuals to receive specialised care rehabilitation in their own social and professional environments (46). A recently conducted RCT reported blended therapy to be equally effective as usual physical therapy with respect to physical functioning and free-living physical activity. Both interventions led to similar clinical improvements (22). Results of blended therapy and usual care were also comparable with respect to cost. While intervention costs of a blended therapy approach are significantly lower when compared to usual therapy, overall societal and healthcare costs were not significantly different statistically (47). Therefore, the authors concluded that blended therapy could be used as a suitable alternative for usual care. While digital health options do not interest all patients and not all patients are suitable for a digital tool, decisions about which intervention should be used can be based on patients’ preferences, as well as prerequisites such as sufficient internet skills, technology affinity and self-discipline (21, 44, 47).

Our study also had some limitations. First, trainees received a virtual exercise program and had to imagine doing the exercises and then record the virtually performed training parameters. For some trainees, it would have been easier to record an effectively performed training session. However, this would have been too time consuming for this usability study. Second, the app is part of a blended intervention in which therapists examine their trainees, design an individual exercise program and instruct the Fit app for each trainee within one or two face-to-face sessions. Only after these face-to-face sessions can trainees then start their individual program at home. This usability study did not evaluate the interaction between therapists and trainees

in the blended intervention process but only the handling of the app in a laboratory setting. Third, the results should be considered with caution because of the small sample size of five end-users within each phase. Nevertheless, tests with five participants are usually able to uncover two thirds of usability issues (29). As we included five trainees and therapists in each phase, most of the usability problems are likely to have been revealed. Fourth, combining our results with other usability methods such as heuristic evaluation or cognitive walkthrough would have strengthened our results (25). As we only had limited financial and personal resources for the development of this app and because we considered the opinion of end-users as the most important benefit, we decided to apply a user-based testing method. Only with the involvement of end-users in the development can users' perspectives such as their needs, expectations, problems and attitudes be considered (48). Finally, the first and second authors of this article conducted the focus group interviews. This might have influenced the participants' expressions of opinions in two ways: firstly, the authors and participants knew each other from daily work, which might have hindered some of the latter to issue critical statements. Secondly, as the first author was also one of the joint inventors of the Fit app, participants might have felt disinclined to fully express their opinions, for fear of causing offence. As the first authors of this study were aware of this bias, they addressed the issue before the interviews, highlighting that all opinions were welcome.

A strength of this study was the two-phase approach for the usability part, whereby end-users could be involved in the stepwise development process and adaptations of the first prototype of the app could be evaluated directly within the next phase. Another strength is the combination of usability testing with the evaluation of the opinions of therapists. Therapists have an important role as facilitator – or if they are insufficiently engaged – as preventer of the usage of such tools (21, 44). Therefore, for successful implementation of this app within daily clinical business, not only ease of use, but opinions of therapists and contextual factors have also to be considered. So far, blended therapy is not a standard approach in hospital settings, therefore it is important to learn what requirements are necessary to implement it in clinical practice.

Although the Fit app is relatively low-key and various ideas for upgrading functions of the app were suggested, end-users judged it as usable. In par-

ticularly, the blended therapy approach was perceived as a promising therapy development. In order that implementation of this approach will be successful, clearly defined work processes are needed and it has to be clarified how costs of this innovative therapy option will be managed. Before the app can be used in daily practice, feasibility of this blended therapy approach in a clinical setting should be evaluated.

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Contribution to the Field Statement

Technical developments can enable innovative possibilities in the field of rehabilitation. In particular, the combination of telecommunication technologies and face-to-face therapy sessions could be a promising procedure in initiating and supervising therapeutic exercise programs. Such approaches have proved to be effective in settings such as cognitive behavioural therapy, but are relatively new in the field of therapeutic exercise training. With the development of this app we wanted to fill this gap.

As new devices are only used in everyday practice if they are user-friendly and accepted by end-users, we tested usability and acceptance of this app and explored personal opinions of therapists using it. With this app it is possible for therapists to coach their patients remotely. Such an approach helps to guarantee access to health professionals for people who are unable to regularly attend hospital. Furthermore, barriers and facilitators identified in this study can also be helpful in the development of other technology-based approaches. We consider that this work has made an important contribution to the implementation of new technologies in the field of physical exercise therapy.

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CHAPTER 7

Feasibility of a blended therapy approach in the treatment of patients with inflammatory myopathies

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Abstract

Background: Inflammatory myopathies (IMs) are a group of rare conditions characterized by proximal and often symmetrical muscle weakness and reduced muscle endurance. The recommended medical treatment is based on corticosteroids in combination with immunosuppressants. This anti-inflammatory therapy serves to inhibit and prevent inflammation but does not influence impaired muscle strength. Exercise, particularly progressive resistance training, therefore plays an important role in IMs management. Blended therapy, a combination of face-to-face treatment and telerehabilitation, may be a powerful therapy option in improving exercise program adherence in these patients.

Methods: The feasibility of a 12-week interactive tablet-based home exercise program combined with face-to-face therapy sessions – a ‘blended therapy’ approach - was evaluated using a quasi-experimental one-group pre-post comparison design. Primary outcomes were recruitment, attrition and adherence rates, plus measures of acceptance (Technology Acceptance Model Questionnaire (TAM)) and satisfaction (satisfaction questionnaire). Secondary outcomes comprised potential effects of the intervention on muscle strength and function, activity limitation, disability and health-related quality of life.

Results: Thirteen of the included 14 participants completed the study without any related adverse events. Mean adherence to exercise program was 84% (range: 25-100%) and participants indicated high acceptance of the intervention with mean TAM scores between 6.1 and 6.5 points. Overall satisfaction with the therapy sessions, the home program, and the technology was good. Approximately half the participants wished for longer training periods and more training sessions per week. There were inconsistent effects on muscle strength, muscle function, activity limitation, disability and health-related quality of life.

Conclusion: Blended therapy combining the use of an interactive tablet-based resistance training program with face-to-face therapy sessions is feasible and safe and participants’ acceptance with this approach was high. Furthermore, results were obtained that might be useful in selecting appropriate assessments and sample sizes in future trials.

Abbreviations

app	Application
DM	Dermatomyositis
ETGUG	Expanded Timed Get-up-and-Go
FI2	Functional Index
HAQ	Stanford Health Assessment Questionnaire Disability Index
HHD	Hand-Held Dynamometry
HRQOL	Health-Related Quality of Life
IMs	Inflammatory Myopathies
MAP	Myositis Activity Profile
MMT	Manual Muscle Testing (MMT8)
PM	Polymyositis
PROM	Patient-Reported Outcome Measures
RPE	Rated Perceived Exertion
SF36	Short Form (36) Health Survey
TAM	Technology Acceptance Model
TR	Telerehabilitation

Background

Inflammatory myopathies (IMs) are composed of rare and heterogeneous subgroups of neuromuscular disorders characterized by proximal and often symmetrical muscle weakness and low muscle endurance, progressing over a period of weeks or months (1, 2). The recommended medical treatment is based on high-dose corticosteroids in combination with immunosuppressive agents (3). However, the effects of pharmacological therapy on restoring muscle strength and endurance are limited, as anti-inflammatory therapy can only inhibit and prevent inflammation but cannot directly restore damaged muscle fibres. Therefore, exercise plays a pivotal role in restoring muscle strength and performance in adult patients with IM at all disease stages (4-6). Furthermore, there is evidence for beneficial effects of supervised and home-based exercise programs on disease activity, impairment, activity limitation and quality of life (7, 8).

Despite these encouraging effects seen in patients with IM who do exercise, there are several barriers to start and maintain an exercise program for these patients. In addition to muscle weakness and low endurance caused by chronic inflammation of skeletal muscle and microangiopathy with loss of capillaries, patients with IM often suffer from fatigue and pain (9, 10). Besides these disease-intrinsic features, the tendency of patients with IM to avoid strenuous physical activity further exacerbates the physical deconditioning process. This vicious circle is even more aggravated by the common catabolic side effect of corticosteroids on muscle metabolism and may be reinforced by the patient's fear of disease exacerbation (11). This fear may be explained by the fact that until the 1990s, patients with an inflammatory disease were discouraged from exercise, assuming that it would increase inflammation (12). However, recent studies have shown that exercise is safe and may even have an anti-inflammatory effect in patients with an inflammatory rheumatic disease (13, 14). There are some uncertainties regarding exercise adherence in these populations. A recently published systematic review revealed that only 29% and 36% of included studies reported performed type of exercise and frequency, respectively. No information was provided concerning time and intensity of the completed training sessions (15). Furthermore, problems with sustained adherence to home based exercise programs were also reported in clinical experience in patients with IM (16).

Blended therapy may be a powerful approach to improve adherence to an exercise program, because conventional face-to-face care and telerehabilitation (TR) are combined (17, 18). TR, defined as the provision of remote rehabilitation services via telecommunication technologies (19), may optimize the timing, intensity and sequencing of interventions. It provides the opportunity to receive rehabilitation at home (20) as a complement to conventional face-to-face sessions. Promising results of a blended approach were achieved in supporting older adults performing an exercise program (21), and in varied rehabilitation settings such as post anterior cruciate ligament reconstruction (22) and hip and knee osteoarthritis (23).

We hypothesised that a TR approach might support patients with IM to sustain an individual exercise program while being remotely monitored and coached. To the best of our knowledge, a TR program especially designed for patients with IM does not currently exist. For this reason we developed a tablet-based exercise application (called Dividat Fit), tailored for patients with IM, which considered the best available evidence (24). The aims of this study were [1] to evaluate the feasibility of our newly developed blended therapy approach, combining a tablet-based exercise application (app) with face-to-face physiotherapy sessions in patients with IM, and [2] to evaluate potential impacts on muscle strength, muscle function, activity limitation, disability and health-related quality of life (HRQOL). We adopted the NHR (National Institute for Health Research Evaluation) definition of a feasibility trial (25), stating “Feasibility Studies are pieces of research done before a main study in order to answer the question “Can this study be done?”, focusing on assessment of the intervention process (26).

Methods

Study Design

All participants took part in the study for a period of 12 weeks using a quasi-experimental one-group pre-post comparison design. The study was performed from February to November 2019. The study protocol was approved by the Cantonal Ethics Committee of Zurich (Protocol No. 2018-00970) and conforms with the Declaration of Helsinki. All participants were informed about the study procedure prior to participation and signed informed consent forms. All instruction sessions and measurements were performed at the University Hospital Zurich, Switzerland.

Participants

The study was designed for patients with the diagnosis of IM. Patients were considered eligible if they fulfilled all of the following inclusion criteria: (1) diagnosis of an IM (Polymyositis (PM) or Dermatomyositis (DM) or IM associated disorders), (2) age over 18, (3) able to walk 20 meters without walking aids, (4) not currently participating in other resistance training, (5) maintained a stable medical regimen for four weeks prior to study initiation and (5) considered capable of maintaining a stable regimen for the course of the study. Criteria for exclusion were: (1) clinically significant concomitant disease states (e.g. renal failure, hepatic dysfunction, severe cardiovascular and/or pulmonary disease, severe osteoporosis, pulmonary hypertension, pain syndrome, paresis), (2) contraindications to physical exercise (e.g. acute exacerbation of inflammation), (3) known or suspected non-compliance, (4) drug or alcohol abuse, (5) inability to follow the procedures of the study (e.g. due to language problems, psychological disorders, dementia), (6) participation in an investigational drug study within the 30 days preceding and during the current study, (7) known pregnancy or breastfeeding, and (8) intention to become pregnant during the course of the study.

Sample size considerations

For testing the feasibility of our new blended therapy approach, a relatively small sample was deemed appropriate (27). For pilots and feasibility studies a rule-of-thumb advice lies around 12 participants (28). We chose, therefore, to recruit 10-15 patients with IM.

Recruitment

The recruitment process was performed stepwise. In a first step, a letter with the study information was sent to a random sample of 15 patients from the IM registry of the University Hospital Zurich. Interested patients could return an application form or contact the study team by phone or by e-mail. All patients who did not respond to this letter were contacted by phone and asked if they were interested in taking part in the study. Depending on the recruitment rate, in further steps another random sample of 10-15 patients was contacted. This procedure was repeated until the required number of participants was recruited. All patients who were interested and met all inclusion criteria were invited to the first assessment.

Study intervention

The study intervention comprised a blended therapy approach, combining face-to-face physiotherapy sessions with an interactive tablet-based exercise program. Overall, three or four 45-minute individual physiotherapy sessions were planned. The exercise program consisted of a 12-week home based progressive resistance training program (figure 1).

Figure 1: Procedure of the blended therapy

During the first two face-to-face sessions, the physiotherapist examined the participant, designed an individually tailored resistance training program based on that examination, demonstrated the selected exercises and then explained how to use the app. With the completion of these steps, the participant started the 12-week home-based resistance training program. After the first two weeks of training (familiarization phase), the third face-to-face session took place, aiming to check exercise performance and adapt the exercise program as necessary. If required, another follow-up session or phone call was added during the remaining ten weeks of training (main phase). During the whole exercise program, the physiotherapist tele-monitored each participant weekly by checking the training diary and by adapting or commenting on the training by remote access.

Each individually tailored resistance training program was designed based on a pool of various exercises. This pool contains open and closed chain exercises for the most commonly affected muscle groups in IM (29, 30), set at different difficulty levels. An overview of the exercises is presented in table 1.

Table 1: Pool of exercises of different difficulty levels

	Level 1	Level 2	Level 3	Level 4
Bridging	Arms beside the upper body (to stabilize)	Arms on your chest	With one leg only	
Hip abduction	Standing upright, abduct one leg	Lateral position, abduct one leg (knee in 90° flexion)	Lateral position, abduct one leg (knee in extension)	
Hip extension	Standing upright, extend one leg backwards	Support upper body on a table, extend one leg backwards	All-four position, extend one leg backwards	
Knee extension	Sitting on a chair, extend knee without extra weight	Sitting on a chair, extend knee with extra weight		
Squats	Squats in front of a table (limited ROM)	Deep squats in front of a chair (max. 90°)	Lunges	
Heel lift	Calf raises (with both legs)	Calf raises (with one leg)		
Neck flexion	Head lifts, sitting on a chair (recliner)	Head lifts, supine position	Sit-ups, supine position	
Press-up	Press-ups against a wall	Press-ups against a table	Press-ups on your knees	Press-ups normal version
Shoulder abduction	Elbows in 90° flexion (with or without extra weight)	elbows extended (with or without extra weight)	Overhead	
Shoulder flexion	Limited ROM, with or without extra weight	Full ROM, with or without extra weight		
Elbow flexion	Limited ROM, with or without extra weight	Full ROM, with or without extra weight		

Legend: ROM=range of motion

Based on the training guidelines (24) and the individual's personal requirements, an exercise program which included 6 to 8 exercises was tailored for each participant. Since all participants were medically stable, we aimed for the following training parameters: 2-3 sets with 8-15 repetitions at perceived intensities between levels 13 and 17 on the 6 to 20 points Borg scale (31). Level 13 on the Borg Scale indicates "somewhat hard" intensity while levels between 15 and 17 indicate a "hard" to "very hard" intensity. This is also considered to provide an optimal strength training 'zone' (31). In the familiarization phase, the intended perceived exertion was at the lower end of the recommendations (RPE Scale 13) and if the participants tolerated these intensities without pain and signs of an inflammation, the intensity was

increased to 15 to 17. The progression of the exercises was adapted individually, first by increasing the amount of repetitions and sets, and then by choosing a more difficult exercise level. In addition, a personal comment could be added to each exercise.

Training app

When participants opened the app on their tablet, they were guided through their individual exercise program in a stepwise manner. On the first screen, photos and a description of the first exercise as well as the target training parameters and personal comments from the physiotherapists were displayed. Once the first exercise was completed, participants had to record their performed repetitions, sets, perceived exertion (RPE-scale) and (if present) pain. Additionally, participants could write a brief note addressed to their physiotherapist. Dependent on the self-reported perceived exertion and pain levels, an automatically generated feedback was sent to participants: (a) if the perceived exertion is within the predefined range of intensity level, they got a positive response, (b) if the exertion is higher than the predefined range of intensity level, they were advised to exercise less, (c) if the exertion is lower than the predefined range of intensity level, they were motivated to increase the volume or intensity of the exercise. If pain is recorded, they were advised to perform the exercise correctly and if pain remains, they were prompted to contact their physiotherapist. In addition, short information about the advantages of exercise or a motivational quotation and an overview of the performed exercise parameters were provided. The participants were guided in the same way as explained above through the entire exercise program. After having finished the last exercise, an overview of the completed training session was displayed on the tablet. In this overview, participants could also see the progress they had made during the entire exercise program.

Outcomes

The primary outcomes were the feasibility parameters of recruitment rate (and reasons for exclusion), attrition rate (and reasons for dropping out), adherence to the intervention, plus acceptance of and satisfaction with the blended therapy approach.

Acceptance was measured with a modified version of the Technology Acceptance Model (TAM) questionnaire (32). This consists of 20 items, which

are each rated on a seven-point Likert scale ranging from one (strongly disagree) to seven (completely agree), plus an open question about desired additional options for the app. The items are divided in four subgroups: perceived usefulness (seven items), perceived ease of use (six items), attitude toward using (four items), and intention to use (three items). The scores of the subgroups range from one to seven and the total score from 20 to 140.

Satisfaction was measured with a questionnaire developed by the research team, based on previous literature on program satisfaction (33). The 30 questions were divided into four sections: individual physiotherapy sessions (five questions), home-training program (ten questions), statements about technology (three questions), and motivation (eight questions). Participants were asked to agree or disagree with several statements, using a five-point Likert scale ranging from one (agree completely) to five (disagree). In every section, participants were also invited to answer an open question.

Secondary outcomes comprised potential effects of the interventions on isometric muscle strength and muscle function, as well as on patient reported outcome measures (PROM) including activity limitation, disability and health-related quality of life (HRQOL). All tests and questionnaires were completed before the first physiotherapy session (pre-intervention) and after the last home exercise session (post-intervention). The main goal of these outcomes was not to assess effectivity per se, but see whether it was feasible from a routine collecting data point of view. The same experienced assessor, who was not involved in the intervention, performed all measurements. Isometric muscle strength was measured with Manual Muscle Testing (MMT8) and hand-held dynamometry, while muscle function was evaluated with Expanded Timed Get-up-and-Go (ETGUG), 30-second chair stand, 30-second arm curl, and functional index (FI2). Activity limitation was assessed using the Myositis Activity Profile (MAP), disability with the Stanford Health Assessment Questionnaire Disability Index (HAQ), and HRQOL with the Short Form (36) Health Survey (SF36).

The Manual Muscle Testing 8 (MMT8), an IM specific subset of the MMT, is the most commonly used strength test in IM trials (30). MMT8 measures and scores weakness of the dominant side of eight muscle groups (shoulder abduction, elbow flexion, wrist extension, neck flexion, hip abduction and hip extension, knee extension, and ankle flexion) according to the Kendall 10-point Scale. Scores between 0-3, 4-6, and 7-9 indicate severe, moderate and

mild weakness, respectively, and a score of 10 means that there is no detectable weakness. The single scores were added to obtain a total score varying from 0 to 80 (0 = no muscle contraction, 80 = normal strength) (29).

Isometric peak force of the same muscle groups was assessed using the MicroFET2 hand-held dynamometer (Force Evaluating and Testing, Hoggan Health Industries Inc. West Draper, UT, USA). Each muscle group was measured according to a standardised protocol (34). The average of three measurements was used for data analysis.

The ETGUG (35) requires participants to stand up from a seated position, walk a distance of six meters at a comfortable pace, make a 180-degree turn, return to the start and sit down. The total time taken to complete the ETGUG was recorded and the gait speed was also calculated.

The 30 second chair stand measures the number of times that the participant rises to a full stand from a seated position, with arms folded, within 30 seconds, when moving at a comfortable pace (36).

The 30 second arm curl test measures the numbers of times a participant can lift a 1 kg weight above the head until the elbow is fully extended in a 30 second period, when moving at a comfortable pace. The number of times the weight is lifted above the head in a 30 s period is recorded for each arm, and the final score is the mean of the two measurements (36).

The functional index evaluates muscle endurance of seven muscle groups (shoulder flexion, shoulder abduction, neck flexion, hip flexion, step test, heel lift, and toe lift) (37). For each task, participants perform as many repetitions as possible until the predefined maximal number of repetitions is reached (60 repetitions for shoulder flexion, shoulder abduction, head lift, hip flexion and step test and 120 repetitions for heel lift and toe lift). The numbers of correct repetitions achieved, following five learning repetitions, are then registered for each task (0 = severe limitation and 60 (or 120) = no limitation).

The Myositis Activity Profile (MAP) is a disease-specific activity limitation questionnaire for patients with IM (34, 38, 39). The MAP includes 32 items which can be answered on a 7-point Likert scale; where 1= no difficulty to perform and 7= impossible to perform. These items are divided into four subscales (movement activities, activities of moving around, personal care and hygiene, and domestic activities) and four single items (keeping in touch with close friends and relatives, avoiding overexertion during daily activities, being able to cope with work and/or housework to a satisfactory degree, and being able to do recreational activities of choice).

The Stanford Health Assessment Questionnaire Disability Index (HAQ) consists of 20 questions divided into eight sections: dressing, rising, eating, walking, hygiene, reaching, gripping, and performing activities. Scoring within each section ranges from 0 (without any difficulty) to 3 (unable to do) (40).

The SF36 is a generic patient-reported outcome measure aimed at quantifying health-related quality of life (HRQOL). The questionnaire includes 36 questions that are divided into eight subscales: limitations in physical activities due to health problems, limitations in social activities due to physical or emotional problems, limitations in usual role activities due to physical health problems, bodily pain, general mental health (psychological distress and well-being), limitations in usual role activities due to emotional problems, vitality (energy and fatigue), and general health perceptions. The eight subscales are divided into the two main components, these being a physical component summary (PCS) and a mental component summary (MCS). Higher scores within the main components indicate a better HRQOL (41).

Analysis:

Demographic data (age, sex, BMI, diagnosis, years since diagnosis, physical activity, and medication) and the primary feasibility outcomes were reported using narrative and descriptive statistics. For attrition rate, defined as the percentage of dropouts, a 10% drop out rate was deemed acceptable. Adherence rate was calculated as the number of completed training sessions in relation to the scheduled sessions, with an adherence rate of 80% being considered acceptable (42). Results from the satisfaction questionnaire were given as percentage of agreement with the single items. For the total TAM score, all item scores were summated. Additionally, the four subscales of the TAM were scored using the mean value of the respective item responses. Thereafter, mean, standard deviation and minimum/maximum values of the total score and the subscales were calculated.

For the secondary outcomes, descriptive statistics (mean and standard deviation for interval data and median and inter-quartile range for ordinal data) and existing floor or ceiling effects (more than 15% of the participants achieve the lowest or highest possible score) (43) were reported. The normality of the data was evaluated using the Shapiro–Wilk test. Depending on whether data were considered normally, or non-normally distributed, paired t-tests or Wilcoxon signed-rank tests were used to compare pre- and post-intervention measurements. Only data from participants who adhered to the

training protocol and did not drop out were analysed (per protocol analysis). Because the focus of statistical analysis of secondary outcomes is not on significance, effect sizes (ES) were calculated for within-group differences. Since effect size depends on the dispersion, which gets artificially low when the ceiling effect is high, thus resulting in a falsely high ES, we only calculated ES for assessments without ceiling effects at baseline. For non-normal data, it is expressed as $r = z/\sqrt{N}$, where z is the approximation of the observed difference in terms of the standard normal distribution and N is the total number of samples. To enable interpretation, the following classification was assumed: 0.1 for small effect, 0.3 for medium effect, and 0.5 for large effect (44). For normal data, Cohen's d was calculated as follows: pre-post ES = (post-test mean – pre-test mean)/pre-test standard deviation. Here, 0.2 indicated a small, 0.5 a medium and 0.8 a large effect (45, 46). IBM SPSS Version 25.0 software (SPSS, Inc., Chicago, IL, United States) was used for data analysis.

Results

Sixty out of the 75 selected patients from the IM registry could be reached and were asked whether they would be interested to participate in this study. Finally, 14 patients were included in the study, resulting in a recruitment rate of 23%. The detailed recruitment process is illustrated in Figure 2.

Figure 2: recruitment process

Table 2 provides demographic and clinical characteristics of the participants. One participant experienced a serious adverse event (renal colic) that was not related to the study intervention, however, was able to continue with the scheduled training. One participant dropped out because of frustration with problems manipulating the tablet, resulting in an attrition rate of 7%. Ten participants (77%) completed at least 80% of all training sessions and 8 participants completed more than the expected 24 sessions. The mean adherence rate was 84% (range 25-100%, table 3).

Each individual home program consisted of a warm-up session and 6-8 exercises for the hip, shoulder, knee, ankle, neck/abdomen, and elbow (table 3). Individual training volume varied between 6 (2x3) repetitions and 100 (4x25) repetitions and perceived exertion between 10 and 16. Mean perceived exertion fell within a range of ± 1 of the expected exertion in 63% of the 90 performed exercises. In 19% of the exercises, the perceived exertion was higher than planned, while in 18% it was lower. Details of performed and expected volume (repetitions and sets) as well as perceived and expected exertion of each exercise are illustrated in the additional file 1.

Table 2: Demographic and clinical characteristics of the participants (N: 14)

Participant	Age	Sex	BMI	Diagnosis	Years since diagnosis	Physical activity	Medication
1	72	male	24	PM	4	active	steroid / immunosuppressive
2	40	male	28	DM	2	partially active	steroid
3	54	female	22	PM	28	inactive	steroid
4	56	female	22	DM	0.3	inactive	immunosuppressive / anti-malarial
5	60	male	23	DM	2	active	biologic agents
6	74	female	19	Statins-induced Myositis	7	active	biologic agents / immunosuppressive
7	55	male	17	PM	7	active	steroid / immunosuppressive
8	49	male	21	PM	7	active	steroid
9*	64	female	35	DM	13	partially active	steroid
10	65	female	23	Overlap Syndrom	5	partially active	--
11	57	female	35	Associated Myositis	7	partially active	steroid / immunosuppressive
12	71	female	28	Associated Myositis	6	active	steroid
13	54	male	27	DM	14	trained	anti-malarial
14	51	male	30	Anti Synthetase Syndrom	3	inactive	steroid / immunosuppressive
Total	59 (10)	7 male 7 female	25 (5)	4 PM 5 DM 5 other	7.5 (6.6)	6 active 4 partially active 3 inactive 1 trained	
Mean (SD)							

Legend: *: dropout, BMI: body mass index, PM: polymyositis, DM: dermatomyositis, SD: standard deviation, trained: vigorous intensity activities at least three days per week, active: recommended amount of physical activity per week (150 minutes of moderate activity), partially active: certain activities but do not meet the recommended amount of physical activity per week, inactive: less than half an hour per week.

Table 3: Overview of the performed exercises during the 12-week resistance training of every participant

Participant	Adherence rate	Bridging	Hip abd	Hip ext	Knee ext	(adapted)		Heel lift	Neck flex / sit ups	(Adapted) Press ups	Shoulder abd	Shoulder flex	Elbow flex
1	100	x	x	x			Squat/ Lunge	x	x	x			
2	100	x	x					x	x	x			
3	100	x	x		x					x	x		
4	100	x	x	x						x			
5	67	x	x					x		x			
6	100	x	x	x				x	x	x			x
7	88	x	x					x	x	x	x		x
8	100	x			x				x	x			x
9*	na		x		x					x		x	
10	100	x	x					x	x	x			
11	83		x	x				x	x	x		x	
12	29		x	x	x			x	x	x	x		
13	100	x	x	x				x	x				
14	25	x	x					x	x	x	x		

Legend: *drop out, abd: abduction, ext: extension, flex: flexion, x means that this exercise was performed, na: not applicable

Acceptance

Table 4 presents the mean and standard deviation values for the TAM questionnaire subgroups and the scoring from each participant. In general, acceptance of this blended therapy approach was high, with mean scores of the TAM subscales between 6.1 and 6.5 and a mean total score of 128 (from a theoretical maximum of 140) points. One participant was not convinced of the usefulness of this blended approach, was reluctant to use it and stated that he would not use it again (score <4). Participants mentioned the following desirable options for the app: “videos instead of photos”, “more space for writing messages”, “back button (to go back to the previous exercise)”, “a simple password to enter the program”, “possibility of downloading the program on the mobile phone and possibility of checking if the exercise is performed correctly (video feedback)”.

Table 4: Results of the Technology Acceptance Model (N:13)

Participant	Perceived ease of use	Perceived usefulness	Attitude toward using	Intention to use	Total score
1	7.00	6.33	7.00	6.33	134
2	6.43	3.00	3.25	1.00	79
3	6.29	7.00	7.00	7.00	135
4	5.71	6.50	7.00	7.00	128
5	6.86	6.33	6.25	4.67	127
6	6.86	7.00	7.00	7.00	139
7	6.43	7.00	6.25	7.00	133
8	6.86	7.00	5.50	7.00	139
10	7.00	7.00	6.75	7.00	139
11	6.86	6.50	7.00	7.00	136
12	5.29	6.17	6.00	7.00	119
13	7.00	7.00	7.00	7.00	140
14	6.14	6.00	6.25	4.00	116
Mean scores	6.5	6.4	6.3	6.1	128
(SD)	(0.5)	(1.1)	(1.0)	(1.8)	(17)

Legend: The scores of the TAM subscales may range between one to seven (mean value of the respective items) and the total score range between 20 to 140 (sum of all 20 items), SD: standard deviation, N: number

Satisfaction

The results of the satisfaction questionnaire are illustrated in figure 3. More than 80% of the participants were satisfied with the number and content of the three face-to-face therapy sessions and their individual exercise programs. Two training sessions per week was deemed insufficient for most of the participants (70%) and the training period of 12 weeks was too short for 45%. Ninety percent of all participants liked the support provided during the

program, the comments of the physiotherapist, the automatic feedback from the app, the scale for perceived exertion and the combination of physiotherapy sessions with the tablet-based home-program. Three of the participants found that the pain scale was not useful. These results were confirmed by comments from the participants. Statements from the open questions revealed that the participants were satisfied with the therapy sessions and the home program: “I am very satisfied, feel I’m in good hands” (participant 4), “training at home without any problems, but maybe I would have needed one or two checks to see if I am doing the exercises correctly” (participant 4), “very good, because specific muscles can be trained” (participant 9), “was a good mix of self-check and monitoring throughout the training program” (participant 8), “I think it’s a very good thing” (participant 0), “I find the program very good” (participant 13), “motivational slogans are not needed” (participant 3), “the control with the tablet is useful and helps ensure I really do the training; I could do the exercises at home, it does not need much space” (participant 4), “I think the home program is very good, I can train without equipment and save expensive gym subscriptions, and thanks to the control of the tablet I am also motivated to train” (participant 4).

All participants considered the tablet a suitable training medium, although three participants mentioned that there were some technical issues with their devices. Individual statements were rather heterogeneous. Although some flaws occurred, most participants managed the tablet without any problems. Comments were: “if you are kicked out of the program you have to enter everything all over again” (participant 4), “program could be improved” (participant 7), “very good, although I am not a computer freak” (participant 10) and, “easy and not too complicated” (participant 16). Only one participant was overwhelmed, ceasing the training program and commenting: “with the tablet, there always occurred situations I couldn’t manage” (participant 12).

The most motivating aspects were perceived to be the written feedback provided by the physiotherapist, knowing that the physiotherapist monitored the training and the fact that participants were taking part in a study. Other motivational aspects were: “I can exercise at home any time” (participant 10), “The combination of the home training program and therapy sessions was perfect” (participant 8), “I hope that thanks to the training I will get stronger again and change the course of the disease” (participant 4), “supervision and training tips” (participant 5).

Figure 2: Satisfaction questionnaire

Legend: PT: physiotherapist

Secondary endpoints

Results of the secondary endpoints are summarized in table 5. Since data for isometric peak force, chair stand, arm curl and ETGUG had a normal distribution parametric statistical analysis was used. All other results were presented using nonparametric statistics. Scatterplots showing the distribution of all secondary endpoints and the pattern of change are illustrated in the additional file 2.

Muscle strength

The MMT8 revealed ceiling effects between 50 and 100% for single muscle groups and 33% for the total score. The median difference for all single muscle groups and the total score was zero. At baseline, 12 of 14 (86%) participants demonstrated no or only mild muscle weakness (grade 7-10). Only two participants had severe muscle weakness (grade 4-6) in one muscle group each (knee extension and neck flexion). There was a slight, not significant increase in isometric peak force measured with the hand-held dynamometer in five muscle groups. Effect sizes were small (0.02 – 0.28). Mean strength of shoulder flexion, hip abduction and hip flexion was slightly reduced after 12 weeks of training.

Muscle function

On average, participants increased the amount of performed repetitions after the intervention, as measured with the chair stand and the arm curl, by 1.5 and 2.3 repetitions respectively. The difference represents a medium effect for the arm curl and the chair stand (ES: 0.54 and 0.52). The overall time to perform the ETGUG and the walking speed did not show consistent change. Data of FI-2 showed ceiling effects in all muscle groups. There was a non-significant increase of the repetitions for neck flexion (median difference of five repetitions) and for toe lift (median difference of three repetitions).

Patient reported outcome measures

Four out of the eight subscales of the SF36 revealed ceiling effects between 23 and 69%. Only the subscales physical functioning and vitality improved slightly by 5 and 10 points, respectively. The increase of the PCS (one point) and the MCS (two points) were not significant. Floor effects between 15 and 62% were present in the subscales of the MAP (except subscale overexertion) and the HAQ. The median difference of all subscales of the MAP and the HAQ were zero.

Table 5: Results of secondary endpoints before the first physiotherapy session (pre-intervention) and after the last exercise session (post-intervention), N: 13

	ceiling effect number (%)	pre-intervention mean (SD)	post-intervention mean (SD)	mean difference (pre-post)	95%CI	p-value	effect size
Isometric peak force							
Shoulder abduction (Newton)*	na	131 (51)	128 (49)	-2	-16 / 12	0.759	0.04
Elbow flexion (Newton)**	na	154 (65)	158 (54)	4	-17 / 24	0.709	-0.05
Wrist extension (Newton)*	na	83 (32)	90 (35)	7	-3 / 16	0.169	-0.20
Knee extension (Newton)*	na	254 (153)	258 (149)	4	-29 / 36	0.806	-0.02
Ankle extension (Newton)*	na	141 (50)	155 (55)	15	0 / 29	0.046	-0.29
Neck flexion (Newton)*	na	81 (37)	91 (30)	10	-3 / 23	0.107	-0.28
Hip abduction (Newton)**	na	172 (63)	161 (46)	-11	-33 / 11	0.293	0.17
Hip extension (Newton)**	na	176 (62)	168 (36)	-8	-31 / 16	0.483	0.12
Chair stand							
Repetitions	na	11.2 (2.8)	12.6 (3.6)	1.5	0.0 – 2.9	0.046	0.52
Arm curl							
Repetitions	na	18.1 (4.2)	20.3 (7.1)	2.3	-0.7 – 5.2	0.120	0.54
ETGUG							
Overall time (seconds)	na	17.1 (2.4)	16.6 (2.4)	0.6	-1.0 – 2.1	0.462	-0.23
Speed (meter/second)	na	1.5 (0.2)	1.5 (0.3)	-0.04	-0.22 – 0.14	0.670	-0.14

Table 5 (continued)

	ceiling effect number (%)	pre-intervention median (Q1/Q3)	post-intervention median (Q1/Q3)	median difference (pre-post)	95%CI	p-value	effect size
Manual Muscle Testing							
Shoulder abduction (points)	11 (85)	10 (10/10)	10 (9.5/10)	0	na	0.317	na
Elbow flexion (points)	10 (77)	10 (9.5/10)	10 (10/10)	0	na	0.157	na
Wrist extension (points)	11 (85)	10 (10/10)	10 (10/10)	0	na	0.564	na
Knee extension (points)	10 (77)	10 (9/10)	10 (10/10)	0	na	0.180	na
Ankle extension (Points)	13 (100)	10 (10/10)	10 (10/10)	0	na	0.317	na
Neck flexion (points)	7 (54)	10 (7.5/10)	10 (10/10)	0	na	0.057	na
Hip abduction (points)*	7 (58)	10 (8/10)	10 (9.25/10)	0	na	0.214	na
Hip extension (points)*	6 (50)	9.5 (9/10)	10 (10/10)	0	na	0.408	na
Total score (points)*	4 (33)	77 (73/80)	79 (76/80)	0	na	0.514	na
Functional Index 2							
Shoulder abduction (repetitions)**	7 (64)	60 (24/60)	60 (56/60)	0	na	0.144	na
Shoulder flexion (repetitions) **	7 (64)	60 (29/60)	60 (41/60)	0	na	0.715	na
Neck flexion (repetitions)*	2 (17)	15 (7/40)	24 (10/58)	5	na	0.021	na
Hip flexion (repetitions)*	2 (17)	39 (12/45)	33 (18/60)	2	na	0.333	na
Step up (repetitions)*	6 (50)	58 (33/60)	60 (27/60)	0	na	0.416	na
Heel lift (repetitions)*	5 (42)	57 (37/120)	90 (39/120)	0	na	0.173	na
Toe lift (repetitions)*	3 (25)	37 (20/104)	64 (25/120)	3	na	0.109	na

Table 5 (continued)

	ceiling effect number (%)	pre-intervention median (Q1/Q3)	post-intervention median (Q1/Q3)	median difference (pre-post)	95%CI	p-value	effect size
SF36							
Physical functioning (points)	1 (8)	65 (45/83)	80 (55/90)	5	na	0.219	-0.24
Role-physical (points)	4 (31)	50 (0/100)	100 (0/100)	0	na	0.034	na
Bodily pain (points)	3 (23)	62 (47/87)	72 (37/100)	0	na	0.553	na
General health (points)	0	47 (39/54)	52 (44/55)	0	na	0.694	-0.08
Vitality (points)	0	50 (38/70)	65 (38/78)	10	na	0.031	-0.42
Social functioning (points)	4 (31)	75 (63/100)	100 (75/100)	0	na	0.107	na
Role-emotional (points)	9 (69)	100 (50/100)	100 (100/100)	0	na	0.102	na
Mental health (points)	1 (8)	76 (58/88)	80 (70/86)	0	na	0.959	-0.01
Physical component summary	0	40 (33/47)	42 (28/51)	2	na	0.152	-0.28
Mental component summary	0	53 (41/59)	55 (54/61)	1	na	0.152	-0.28
MAP subscales							
Movement (points)	3 (23)	2 (1.5/3.0)	1 (1.0/3.5)	0	na	1	na
Moving around (points)	3 (23)	3 (1.5/3.0)	1 (1.0/3.0)	0	na	0.043	na
Personal care and hygiene (points)	8 (62)	1 (1.0/2.0)	1 (1.0/2.0)	0	na	0.739	na
Domestic (points) (points)	5 (38)	2 (1.0/4.0)	1 (1.0/3.5)	0	na	0.160	na
MAP single items							
Social (points)	6 (46)	2 (1.0/3.0)	1 (1.0/2.5)	0	na	0.792	na
Avoid overexertion (points)	1 (8)	4 (2.0/4.0)	3 (1.5/4.5)	0	na	1	0
Work/school (points)	3 (23)	3 (1.5/4.0)	3 (1.0/4.0)	0	na	0.564	na
Recreational (points)	2 (15)	3 (2.0/4.0)	3 (2.5/4.0)	0	na	0.773	na
HAQ (points)	4 (31)	0.5 (0.0/1.0)	0.25 (0.0/0.9)	0	na	0.558	na

Discussion

This study evaluated the feasibility of a blended therapy approach, combining face-to-face sessions with a tablet-based exercise program, while also gathering data on potential impacts of the intervention on muscle strength, muscle function, activity limitation, disability and HRQL. The clinical focus was patients with IM. With an attrition rate of 7%, a mean adherence rate of 84% and no related (severe) adverse events, we demonstrated that this blended approach is feasible. Furthermore, this conclusion gains support by way of participants' acceptance of and satisfaction with a blended therapy approach, both of which were high. The results of secondary endpoints were not conclusive: the results for muscle strength and function tests were rather mixed, and only the subscales physical functioning and vitality of the SF36 improved significantly.

Feasibility

Out of the initial 75 potential participants, 33% were interested in joining our study. One pitfall was that our patient list was insufficiently up-to-date, so 60 patients were actually contacted. Out of those 60 patients, 25 (42%) were interested in participating in the study, resulting in 14 fulfilling the inclusion criteria and starting the exercise program. In our sample, men were over-represented. Generally, prevalence in IM is higher in females than in males (47, 48). This known sex distribution was also seen in one of our previous studies at the University Hospital Zürich. In that study, 76% of the 50 participants were female (34).

Overall, the mean adherence rate of 84% was acceptable. This rate is comparable with the reported adherence of 79% during a 12-week resistance home exercise program with telephone support for patients with recent onset PM and DM (49), but lower than the one reported in another 12-week resistive home exercise program. In this study, one of the 12 initially included participants dropped out and 10 of the remaining 11 participants performed all of the planned 60 training sessions, resulting in an adherence rate of 95% (50). In contrast to our study, both of these studies included recent onset patients and patients exercised 5 days a week. In our study, there were considerable differences in adherence between individuals. Two participants did not manage to exercise in a regular manner, only completing 6 and 7 of the 24 expected training sessions each during the 12-week exercise program, whereas all other participants completed at least 16 of all 24 scheduled training sessions. Our high adherence rate is in line with the high acceptance of

the app indicated by the TAM questionnaire. As we had no control group with a traditional home program, we do not know whether the app influenced adherence. From other settings, we know that persuasive technologies including personalisation, self-monitoring, tailoring or goal setting, help to make exercise programs more enjoyable and therefore enhance patients' motivation to exercise regularly (51).

Although different ideas for improvements were suggested, the participants were convinced that this app was useful and easy to use, and they felt that they would continue using it in the future. Interestingly, the two participants with low adherence rated acceptance of the app with 116 and 119 points, respectively, which was lower than the average of all other participants (128 points). Only one participant (participant 2) was even less convinced by the app. Whereas the TAM questionnaire focused mainly on the app, the satisfaction questionnaire evaluated the blended approach in its entirety. Despite the identified flaws of the app, the participants were satisfied with this tablet-based exercise program. Only one participant dropped out because she could not manipulate the app, while all other emerging technical problems could be solved without taking too much time. Participants appreciated the different motivational aspects, but interestingly, the personal contact – even though performed remotely – was judged to be the most important part. This kind of support is also emphasized in other studies. Mehra et al. described remote feedback (beside individual needs, demonstrations of functional exercises, and self-monitoring) as one of the key components of a tablet-supported exercise intervention (52) and de Vries et al. highlighted the importance of the physiotherapists' role as facilitator by monitoring progress and rewarding adherence of the exercise program (53). Regarding the length of the training program and the frequency of the training sessions, the participants had different opinions. Fifty percent would have preferred a longer training period and thirty percent requested more training sessions. Since the guidance for prescribing exercise from the American College of Sports Medicine recommends two to three training sessions per week (54), and we wanted to avoid discouraging participants from taking part in this study by too much training, we instructed our participants to exercise at least twice a week. Exercise more than twice per week was explicitly allowed however and eight participants trained more than the minimum recommendations. With hindsight, it would have been better to recommend three training

sessions a week, especially since some meta-analyses indicate that untrained individuals should do resistance training three days a week (55, 56). Considering that not all patients adhere 100% to the prescribed program, the recommendation of three sessions may ensure that patients are exercising at least twice a week.

Different ideas for improvement suggested by the participants showed that our app could be developed further, but unfortunately, not all suggestions can be implemented. Since this resistance exercise program is a part of a multimodal training system, which includes exergame-driven high-intensity interval training (42) and exergame-based balance training (57), all adaptations of this app must be compatible with all parts of the system. Therefore, the development process is rather arduous, and some desirable adaptations cannot be implemented.

One important advantage of this app is that each participant must record the performed volume and intensity of each exercise. Without filling in this information, the next exercise will not be displayed in the app. In this way a detailed training diary is generated, and the physiotherapist has real-time feedback about the volume and intensity of training. So far, unreported or unknown adherence to home based exercise programs has been a weakness in many published studies (15). Such a mandatory digital diary might be a suitable solution to overcome this issue.

We are aware of the fact that in feasibility trials an emphasis should not be placed on statistical significance (58), however, quantitative data permit the creation of sample size tables for various effect values or variance estimates (59), thus warranting the inclusion and discussion of some effect measures that may be of interest for inclusion in future randomised clinical trials.

Muscle strength and function

The two most used assessment in patients with IM, the MMT and the FI-2, both showed high ceiling effects. Therefore, they were not suitable to measure improvement in our sample. In case these measures are taken as primary outcome in a future randomised trial with patients with IM the researchers are advised to pay attention to their inclusion criteria, which should focus on strength-impaired individuals. One of the advantages of HHD, chair stand, arm curl and ETGUG is that muscle strength and function is measured with an open-ended ratio scale, without any possible ceiling effect. These assessments are, therefore, inherently capable of detecting changes over

time, regardless of their extent. Nevertheless, for isometric peak force we detected only small changes. The generally small effect sizes (for improvement as well as for deterioration) indicate that maximum peak force did not change considerably. This may be explained by the fact that the participants performed dynamic progressive resistance training with a volume of between 6 and 100 repetitions and a subjective intensity of between light to somewhat hard (RPE Scale 10-16). This kind of training might have insufficient impact on maximum peak force. To improve maximum peak force, higher loads with fewer repetitions (1-6 repetitions with 80-90% of the one repetition maximum) would be more suitable (60). However, for individuals having no experience with resistance training, such a heavy intensity is not indicated. Furthermore, maximum strength tests are highly dependent on motivation and “form of the day”, and it is uncertain whether inexperienced individuals are able to develop maximum strength (61). Consequently, it is questionable whether a maximum strength test is suitable for this group of patients. The chair stand and arm curl seem to be more adequate to capture changes of a dynamic resistance training. Besides the advantage of the continuous, open-ended scale, they are examiner independent as well as quick and easy to perform. So far, these two promising assessments are relatively unknown and rarely used in IM trials (62). The ETGUG was unable to detect any limitations, and our sample showed no reduction in walking speed or the overall time to perform the ETGUG as compared to healthy elderly (35). We, therefore, conclude that this test was too easy to perform for our participants and would not recommend using the ETGUG for future IM trials.

PROMs

The SF36 revealed modest positive effects on the physical and the mental component summary. An improvement of some aspects of HQOL was also reported in two other studies evaluating a home based resistance training program in chronic patients with IM (63, 64). Like our own study, Alexanderson et al. identified major improvements in the subscales of physical functioning and role-physical (63). These results indicate that resistance training mostly influences the physical parts of QOL. Another similarity between these two studies is that role-emotional has high ceiling effects and therefore appears to be a less impaired part of QOL in these samples (63). Results of the MAP and HAQ revealed high floor effects and all participants scoring the lowest possible score at baseline cannot exhibit any further improvement.

We understand our research has some limitations. Firstly, our participants seem to have had better muscular fitness compared to many patients with IM. One reason might be that our inclusion criteria regarding physical activity were too broad. Only concomitant resistance training was prohibited and all forms of exercise other than resistance training (e.g. endurance or coordination) was allowed. Unfortunately, we recorded baseline physical activity of our participants only with categorical data. Based on these categories, only a participant who exercised three times a week is considered “trained” and we do not know how many participants exercised once or twice a week. The fact that muscular fitness was relatively high contributed to the second limitation that was the high ceiling effects for some of the secondary outcome measures, especially in the MMT8 and the FI-2. These high ceiling effects affected the assessment responsiveness, since no improvements could be detected with the applied measurement methods, thus increasing the effect size by keeping the dispersion artificially low. Thirdly, our training program only contained resistance exercise, although endurance training is recommended for these patients. However, since our primary aim was to evaluate feasibility of the app, we focused on traditional resistance training only. Nevertheless, participants could perform (or continue) endurance training. It would therefore have been useful to monitor additional activities.

We included several secondary quantifiable outcome measures in our study, with which we expected to gather useful mean and variance values for some potentially important outcomes that may be used in future clinical trials. With this information, researchers might calculate necessary sample sizes for future trials. However, the approach to calculating the sample sizes required for such trials from feasibility studies, using statistical analysis, is seen with scepticism by some researchers (65). These researchers state that clinical judgement prevails over statistical analysis for a main trial sample size calculation (65). Finally, our study results may have been influenced by volunteer bias, assuming that our volunteer participants were more interested in technology or convinced about resistance training than the average patient. This might explain the high level of acceptance and satisfaction with both the app and the blended therapy approach.

Conclusions

This study demonstrates that a blended therapy approach, combining a tablet-based exercise app with face-to-face physiotherapy sessions, is feasible and that this innovative approach was highly acceptable for the study participants. To further evaluate the advantages of this approach, comparison regarding adherence between traditional home programs with paper leaflets and web-based applications should be evaluated in larger randomized controlled trials. As IM is a rare disease, this would only be possible with an international multi-centre study. Based on our results, no clear conclusion about the most adequate assessment can be drawn, even though the chair stand and arm raise appear to be the most promising assessments to evaluate muscle outcomes. Measurement of maximum peak force seems to be inadequate for dynamic resistance training. To include patients' perspectives, these assessments should be supplemented by PROMS, such as the SF36. Future exercise studies should consider whether muscle strength or muscle endurance should be exercised and adapt the dosage of sets and repetitions accordingly. Furthermore, measurement properties, especially responsiveness should be defined for all assessments.

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Additional File 1: Performed and expected volume (repetitions and sets) and perceived and expected exertion of each exercise

subject	time	bridging				hip abduction				hip extension			
		exercise level	summary (performed repetitions/ expected repetitions)	mean perceived borg	mean expected borg	exercise level	summary (performed repetitions/ expected repetitions)	mean perceived borg	mean expected borg	exercise level	summary (performed repetitions/ expected repetitions)	mean perceived ad borg	mean expected borg
1	week 1	2	15/15 - 15/15 - 15/15			2	10/10 - 10/10 - 10/10 - 10/10			2	10/10 - 10/10 - 10/10 - 10/10		
	week 3	3	10/10 - 10/10 - 10/10 - 10/10	12.7	12.7	3	10/10 - 10/10 - 10/10 - 10/10	12.6	12.7	2	10/10 - 10/10 - 10/10 - 10/10	12.2	11.1
	week 12	3	15/15 - 15/15 - 15/15 - 15/15			3	15/15 - 15/15 - 15/15 - 15/15 - 15/15			2	15/15 - 15/15 - 15/15 - 15/15 - 15/15		
2	week 1	2	8/8 - 8/8			2	8/8 - 8/8 - 8/8 - 8/8						
	week 3	2	8/8 - 8/8	15	14.5	1	6/6 - 6/6 - 6/6 - 6/6	14.6	14.5				
	week 10	2	10/10 - 10/10			1	8/8 - 8/8 - 8/8 - 8/8						
3	week 1	2	12/12 - 12/12			1	5/5 - 5/5 - 5/5 - 5/5						
	week 2	2	15/15 - 15/15	12.7	14.8	1	5/5 - 5/5 - 5/5 - 5/5 - 5/5 - 5/5	12.7	15				
	week 12	2	14/14 - 14/14 - 14/14			1	14/14 - 14/14 - 14/14 - 14/14 - 14/14						
4	week 1	2	15/15 - 15/15 - 15/15			3	12/12 - 12/12 - 12/12 - 12/12			1	8/8 - 8/8 - 8/8 - 8/8		
	week 3	2	20/20 - 20/20 - 20/20	12.3	13	3	12/12 - 12/12 - 12/12 - 12/12 - 12/12	13	13	2	8/8 - 8/8 - 8/8 - 8/8	12.5	13
	week 12	2	20/20 - 20/20 - 20/20			3	20/20 - 20/20 - 20/20 - 20/20			2	12/12 - 12/12 - 15/12 - 15/12		
5	week 1	2	12/12 - 12/12 - 12/12			1	6/6 - 6/6 - 6/6 - 6/6						
	week 3	2	8/8 - 8/8 - 8/8	10	11.5	3	6/6 - 6/6 - 6/6 - 6/6 - 6/6	10	11.5				
	week 12	2	12/12 - 12/12 - 12/12			3	12/12 - 12/12 - 12/12 - 12/12						
6	week 1	2	12/12 - 12/12 - 12/12			1	12/12 - 12/12 - 12/12 - 12/12			3	10/10 - 10/10		
	week 3	2	14/14 - 14/14 - 14/14	14.2	15	3	12/12 - 12/12 - 12/12 - 12/12 - 12/12	13.7	14.6	3	15/15 - 15/15	14.1	14.3
	week 12	2	14/14 - 14/14 - 14/14			3	14/14 - 14/14 - 14/14 - 14/14 - 14/14			3	15/15 - 15/15		
7	week 1	1	15/15 - 15/15			3	12/12 - 12/12 - 12/12 - 12/12						
	week 3	1	15/15	14.8	14.6	3	12/12 - 12/12 - 12/12 - 12/12	15.4	14.6				
	week 12	2	22/22 - 22/22 - 22/22			3	24/22 - 24/22 - 24/22 - 24/22						
8	week 1	2	12/12 - 12/12										
	week 4	2	15/15 - 15/15 - 15/15	11.6	12.5								
	week 12	2	15/15 - 15/15 - 15/15										
9	week 1					1	10/10 - 10/10 - 0/10 - 0/10	15.8	12				
	week 3					1	10/10 - 10/10 - 0/10 - 0/10						
	stop												
10	week 1	2	15/15 - 15/15 - 15/15			3	10/10 - 10/10 - 10/10 - 10/10						
	week 3	3	3/3 - 3/3 - 3/3 - 3/3	12.2	14.3	3	15/15 - 15/15 - 15/15 - 15/15	11.5	14.3				
	week 12	3	6/6 - 6/6 - 6/6 - 6/6			3	30/30 - 30/30 - 30/30 - 30/30						
11	week 1					3	10/10 - 10/10 - 10/10 - 10/10			2	10/10 - 10/10 - 10/10 - 10/10		
	week 3					3	8/8 - 8/8 - 8/8 - 8/8	13.6	12.8	2	8/8 - 8/8 - 8/8 - 8/8	13	12.8
	week 12					3	11/11 - 11/11 - 11/11 - 11/11			2	14/14 - 14/14 - 14/14 - 14/14		
12	week 1					1	10/10 - 10/10 - 10/10 - 0/10			1	10/10 - 10/10 - 10/10 - 10/10		
	week 4					1	10/10 - 10/10 - 8/10 - 8/10	13	12.4	1	10/10 - 10/10 - 10/10 - 10/10	12.4	12.4
	week 8					1	10/10 - 10/10 - 10/10 - 10/10			1	10/10 - 10/10 - 0/10 - 0/10		
13	week 1	2	15/15 - 15/15										
	week 4	3	8/8 - 8/8 - 8/8 - 8/8	14.6	14.5	3	8/8 - 8/8 - 8/8 - 8/8	14.9	13	3	8/8 - 8/8 - 8/8 - 8/8	14.1	15
	week 12	3	9/9 - 9/9 - 9/9 - 9/9			3	10/10 - 10/10 - 10/10 - 10/10			3	9/9 - 9/9 - 9/9 - 9/9		
14	week 1	2	15/15 - 15/15			3	10/10 - 10/10 - 10/10 - 10/10						
	week 6	2	15/15 - 15/15	14.7	14	3	10/10 - 10/10 - 10/10 - 10/10	14	14				
	week 10	2	15/15 - 15/15			3	10/10 - 10/10 - 10/10 - 10/10						

subject	time	knee extension			(adapted) squat			heel lift		
		exercise level	summary (performed repetitions / expected repetitions)	mean perceived borg	exercise level	summary (performed repetitions / expected repetitions)	mean perceived borg	exercise level	summary (performed repetitions / expected repetitions)	mean perceived borg
1	week 1				1	15/15 - 15/15 - 15/15	12.6	1	15/15 - 15/15 - 15/15	
	week 3				2	15/15 - 15/15 - 15/15	12.7	1	20/20 - 20/20 - 20/20	11.8
	week 12		--		2	20/20 - 20/20 - 20/20		1	22/22 - 22/22 - 22/22	
	week 10				1	6/6 - 6/6	13.6	1	15/15 - 15/15	14.5
2	week 1				1	6/6 - 6/6	14.5	1	8/8 - 8/8 - 8/8	
	week 3				1	6/6 - 6/6		1	12/12 - 12/12 - 12/12	
	week 10				1	8/8 - 8/8		1		
	week 12		5/5 - 5/5 - 5/5 10/10 - 10/10 - 10/10 12/12 - 12/12 - 12/12	12.7	1	3/3 - 3/3	12.7		--	
3	week 1				1	12/12 - 12/12 - 12/12				
	week 2				2	15/15 - 15/15 - 15/15				
	week 12				2	20/20 - 20/20 - 20/20	12.9			
	week 10				2	20/20 - 20/20 - 20/20				
4	week 1				2	10/10 - 10/10 - 10/10	9.8			
	week 3				2	10/10 - 10/10 - 10/10				
	week 12				2	12/12 - 12/12 - 12/12				
	week 10				2	10/10 - 10/10 - 10/10	11.5			13
5	week 1				2	15/15 - 15/15 - 15/15				
	week 3				2	15/15 - 15/15 - 15/15	13.9			
	week 12				2	22/22 - 22/22 - 22/22				
	week 10				2	22/22 - 22/22 - 22/22	15.7			14.6
6	week 1				1	10/10 - 10/10	12.5			
	week 3				1	12/12 - 12/12 - 12/12				
	week 12				2	9/9 - 9/9 - 9/9				
	week 10									
7	week 1				2	15/15 - 15/15	12.9			
	week 3				2	14/14 - 14/14 - 14/14				
	week 12				2	10/10 - 10/10	12.9			
	week 10				2	12/12 - 12/12 - 12/12	12.8			12.9
8	week 1				2	19/19 - 19/19 - 19/19				
	week 3				2	8/8 - 8/8	13.3			
	week 12				2	6/6 - 6/6	12.4			
	week 10				2	6/6 - 6/6				
9	week 1				2	15/15 - 15/15	14.5			
	week 3				3	5/5 - 5/5 - 5/5 - 5/5				
	week 12				3	6/6 - 6/6 - 6/6 - 6/6	14.7			
	week 10				2	15/15 - 15/15				
10	week 1				2	15/15 - 15/15	13.5			
	week 3				2	15/15 - 15/15				
	week 12				2	15/15 - 15/15				
	week 10				2	15/15 - 15/15				
11	week 1				2	15/15 - 15/15	14.3			
	week 3				2	10/10 - 10/10 - 10/10				
	week 12				2	14/14 - 14/14 - 14/14	12.9			10.8
	week 10				2	17/17 - 17/17 - 17/17 - 17/17 - 17/17				
12	week 1				2	10/10 - 10/10	12.9			
	week 3				2	12/12 - 12/12 - 12/12				
	week 12				2	19/19 - 19/19 - 19/19	12.8			13.3
	week 10				2	15/15 - 15/15				
13	week 1				2	8/8 - 8/8	13.3			
	week 3				2	6/6 - 6/6	12.4			
	week 12				2	6/6 - 6/6				
	week 10				2	6/6 - 6/6				
14	week 1				2	15/15 - 15/15	14.5			
	week 3				3	5/5 - 5/5 - 5/5 - 5/5				
	week 12				3	6/6 - 6/6 - 6/6 - 6/6	14.7			13.1
	week 10				2	15/15 - 15/15				
15	week 1				2	15/15 - 15/15	13.5			
	week 3				2	15/15 - 15/15				
	week 12				2	15/15 - 15/15				
	week 10				2	15/15 - 15/15				

subject	time	shoulder flexion				elbow flexion			
		exercise level	summary (performed repetitions / expected repetitions)	mean perceived borg	mean expected borg	exercise level	summary (performed repetitions / expected repetitions)	mean perceived borg	mean expected borg
1	Week 1		--						
	Week 3								
2	Week 1		--						
	Week 3								
3	Week 1		--						
	Week 2								
4	Week 1		--						
	Week 3								
5	Week 1		--						
	Week 3								
6	Week 1		--						
	Week 3								
7	Week 1		--						
	Week 3								
8	Week 1		--						
	Week 4								
9	Week 1	2	10/10 - 10/10	13.8	12.3				
	Week 3	2	12/12 - 12/12						
10	Week 1		--						
	Week 3								
11	Week 1		--						
	Week 3	2	10/10 - 10/10	12.9	12.9				
12	Week 1		--						
	Week 4								
13	Week 1		--						
	Week 4								
14	Week 1		--						
	Week 8								
	Week 1		--						
	Week 10								

Additional File 2: Scatterplots showing the distribution of all secondary endpoints and the pattern of change

Results of isometric peak force measured with the hand-held dynamometer

Legend: the solid lines show the mean difference.

Results of 30-second chair stand (chair stand) and 30-second arm curl (arm curl)

Legend: the solid lines show the mean difference.

Results of Expanded Timed Get-up-and-Go (ETGUG)

Legend: the solid lines show the mean difference.

Results Manual Muscle Testing

Legend: the solid lines show the median difference.

Results of Functional Index 2

Legend: the solid lines show the median difference.

Results of the Short Form Health Survey (SF36)

Legend: the solid lines show the median difference.

Results of the Myositis Activity Profile (MAP)

Legend: the solid lines show the median difference.

Results of Stanford Health Assessment Questionnaire Disability Index (HAQ)

Legend: the solid lines show the median difference.

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CHAPTER 8

General discussion

Introduction

The main objectives of this thesis were to develop an interactive, tablet-based, progressive resistant training application (app) and to evaluate feasibility of the blended therapy approach that combines this therapeutic exercise app with face-to-face physiotherapy sessions in patients with IM. To identify the most effective exercise programs for these patients we first reviewed the current literature concerning applied training principles (TPs), before developing evidence-based exercise guidelines. Secondary objectives were to evaluate clinimetric properties of assessments reporting relevant outcomes in this patient group. We evaluated reliability and concurrent validity of two simple and commonly used muscle strength tests, translated the only myositis-specific activity limitation questionnaire into German and analysed the clinimetric properties of this new version.

This chapter presents an overview of the main findings of the six studies presented in this thesis. Subsequently, limitations of the studies, implications for clinical practice, recommendations for future research and personal opinions and conclusion of this thesis are provided.

Main findings

The systematic review in **chapter 2** provides an overview of the applied TPs, the reporting of the FITT components, and the adherence of participants to the planned intervention (1). The results of this review showed that application of TPs was reported inconsistently. Studies evaluating only one aspect of physical performance (strength or endurance) described more TPs than those evaluating a combined exercise programme. Reversibility and diminishing return were always reported inadequately, and most studies did not evaluate long-term effects of exercise programmes. FITT components were neither fully described in the training outline nor in the adherence to the exercise programme. In the training outline, most studies lacked information on training intensity. Adherence was poorly described, with only four studies describing two components (type and frequency) and most of the studies not describing adherence at all. In **chapter 3** training guidelines and their development process are described (2). The guidelines include an introductory part on general TPs, plus two further parts on resistance and endurance training for each disease phase (early active – active – stable). For patients in all phases of the disease, endurance and dynamic resistance training 3-5 times a week is recommended. Depending on disease phase, endurance

training can be performed at an intensity of 50-85% of maximum heart rate (HR_{max}) for a period of 5-45 minutes. The more active the disease, the lower the intensity and volume which should be chosen (early active phase: 5-10 minutes with 50-60% of HR_{max} , active phase: 15-30 minutes with 60-70% of HR_{max} , stable phase: 20-45 minutes with 70-85% HR_{max}). Similarly, for resistance training, low intensity and volume is recommended for the early active phase (1-3 series with 5-10 repetitions at 40-60% of 1 RM (Repetition Maximum)). During the active phase, volume but not intensity should be gradually increased up to 1-3 series with 8-15 repetitions. Only in a stable phase can volume and intensity be increased (2-3 series with 8-15 repetitions at 60-80% of 1RM). Heterogeneity of study design, inclusion criteria, training modalities, and outcome measures of the 24 analysed studies meant that it was impossible to conclude which exercise program was most suitable. Therefore, the general training guidelines of the American College of Sports Medicine (3), as well as the clinical experience of specialist physiotherapists, were also considered. In **chapter 4**, intra- and interrater reliability of two commonly used assessments (MMT8 and HHD), as well as concordance between both, are evaluated in patients with IM for shoulder abduction, elbow flexion, wrist extension, knee extension, neck flexion, hip abduction, hip extension and ankle extension (4). Our results showed excellent intra- and interrater reliability of averaged peak force measured with HHD for all measured muscle groups, except for interrater reliability for ankle extension. The intra- and interrater reliability of MMT8 was excellent for the total score, whereas single muscle groups revealed only fair-to-substantial intrarater and slight-to-moderate interrater reliability. In our sample, SDC is higher for single muscle groups measured with HHD (23-78%) than for MMT8 total score (6.9-8.6%). Although both MMT8 and HHD measure isometric muscle strength, measurement concordance (assessed with Spearman's rho) between the two was low or moderate for most muscle groups. Only values of shoulder strength showed a good correlation. In **chapter 5** reliability and validity of the new German version of the Myositis Activity Profile (MAP) is reported (5). Reliability for all subscales and three of the four single items was substantial (weighted Kappa values 0.65 – 0.77). The single question “avoid overexertion” reached only moderate reliability (weighted Kappa: 0.57). The items “washing hair” and “combing hair” demonstrated high internal redundancy and in three of the four subscales one item each indicated poor internal consistency: “standing for long period” from the subscale “movement”, “wiping

yourself after bathroom” from subscale “personal care” and “putting plates and glasses away” from the subscale “household”. Despite these findings, we decided to retain all items in the questionnaire so that it remains comparable to the English and Swedish versions. As hypothesized, the MAP correlated highly with the Health Assessment Questionnaire (HAQ) and the physical component of the SF36, moderately with muscle function and poorly with pain and the mental component of the SF36. The hypothesis that the MAP can differentiate between patients with IM and healthy controls could only be partially confirmed: three subscales and two single questions revealed acceptable discriminative validity, whereas subscales “personal care”, and single items “social” and “avoid overexertion” indicated no acceptable discrimination. In **chapter 6**, the usability and acceptance of a newly developed interactive tabled-based exercise app is investigated with therapists and untrained healthy individuals. In addition, personal opinions of therapists when using it in a clinical setting is explored (6). Despite some essential suggestions for improvement, the app proved to be usable for therapists and trainees and both target groups had positive attitudes towards its use. Therapists perceive use of this app as a promising therapy enlargement for several patient groups. However, for the app to be successfully implemented in everyday practice, some barriers must be overcome: work process need to be adjusted, data privacy must be guaranteed, IT support must be clarified and coverage of costs must be regulated. In **chapter 7** feasibility of a blended approach combining this new developed app with face-to-face therapy sessions as well as potential impacts of the resistance training program on muscle strength, muscle function, activity limitation, disability and health-related quality of life (HRQOL) are reported. Both recruitment and adherence met our primarily defined feasibility criteria and patients’ acceptance and satisfaction with the blended therapy approach was high. Furthermore, there was a tendency towards better HRQOL, less limitation in daily activities and less disability. Results of muscle strength and function were less consistent. The most promising measurement instruments were the 30-second chair stand and arm curl, both showing medium-to-large effects. MMT8 and functional index 2 (Fi-2) revealed high ceiling effects, and participants’ gait speeds as measured with the Expanded Timed Get-up-and-Go test were already comparable to those from healthy adults, even before the start of the intervention. Maximum strength measured with the HHD did not change by a clinically relevant amount.

Limitations and methodological considerations

Population

Inflammatory myopathy is not only rare, but is also a very heterogeneous group of neuromuscular disorders, making it a challenge to perform clinical research with this patient group. Due to the rarity of the disease, randomized controlled trials are scarce and often small and underpowered (7, 8). This drawback also influenced the inclusion criteria of our systematic review. At the time of our literature search, only four small RCTs (sample size between 14 and 19 patients), comparing an exercise programme with a non-exercising control group, had been published (9-12). If we had only included these RCTs we would have missed important information about the application of TPs which could be gathered from other types of studies evaluating therapeutic exercise programmes. Therefore, we decided to also include non-randomised controlled and uncontrolled trials in the review. Regardless of the study design used, the quality of description of the intervention is important in order to replicate study intervention and implement interventions in clinical practice (13).

Heterogeneity of the disease

Beside the fact that the disease is rare, its clinical manifestations can vary widely across different subtypes such as overlap myositis, myositis associated with cancer, immune-mediated necrotizing myopathy or anti-synthetase syndrome (14). Nevertheless, until now most exercise studies differentiated only between PM, DM and IBM, whereby only IBM was evaluated separately. Newer syndromes such as immune-mediated necrotizing myopathy or anti-synthetase syndrome were subsumed within the PM classification (15). No study analyzed the included subgroups separately. Therefore, we do not know if certain subgroups react differently to therapeutic exercise programs. Although patients with IBM have specific clinico-pathological features and are more disabled than patients with PM and DM (16, 17), our review revealed no indication that these patients should exercise differently to those with PM or DM. Therefore, we integrated studies evaluating patients with IBM in the guideline development and our exercise guidelines are quite broad and thus applicable for all subgroups of IM. This might however be a significant limitation. In particular, it is known that subtypes can have varying patterns of muscle weakness and organ involvement (18, 19). Both the affected muscles and the organs involved might have an impact on patient trainability.

Unfortunately, no such distinction can be made based on the current literature.

In contrast to the systematic review and the exercise guidelines, we did not include patients with IBM in our intervention studies. The reason was that these patients have a different pattern of muscle involvement, leading to other functional limitations such as risk of falling and walking difficulties (20, 21). Therefore, our conclusions from the validation and feasibility study cannot be generalized to patients with IBM. We recruited our participants from the Department of Rheumatology of the USZ. As we needed almost two years to recruit the required number of participants for the validation studies, the following projects started later than originally planned. During the duration of our projects, different new IM subtypes, including immune-mediated necrotising myopathy (IMNM) and antisynthetase syndrome (ASS) were described (22), while in 2017 the new EULAR/ACR classification criteria and their major subgroups were published (23). These changes led to inconsistent classification in our studies. In the first two studies the diagnosis and classification were based on the Bohan and Peter criteria (24), whereas in the feasibility study some patients were classified based on more recent subtypes.

Selection bias

In the reliability and validity study of the MAP (5) we identified a selection bias between the patients with IM and the healthy control group. Although we matched them for age and gender, the healthy control group had a lower BMI than the included patients. As physical activity plays an important role in maintaining a healthy weight (25), we could not exclude the possibility that the former were more active than the latter. As physical activity might have an influence on activity limitation, it would be important to control for physical activity. Unfortunately, we did not assess this potential confounder.

We also observed a selection bias in the feasibility study. In this work, the proportion of men was higher than the known gender distribution in incidence and prevalence studies (26, 27). In addition, participants showed higher ceiling effects in the MMT8, indicating less muscle weakness, compared to samples from other studies (19, 28). Therefore, this sample could be criticised as being a somewhat limited representation of the general myositis population. Reasons for the high ceiling effect might be that men have lower relative muscle weakness compared to women, and that it is more difficult to detect existing weakness in males than females, although this aspect has not been

studied so far. Another explanation is that men are likely to be more interested in new technologies and that active people are more interested in participating in exercise studies.

Therapeutic exercise

The aims of the systematic review were to evaluate a) the application of TP in developing the exercise prescription, b) the reporting of FITT components in the training prescription and c) the reporting of the adherence to the prescribed intervention. From this, we wanted to work out which training protocol is most promising and whether the planned program could be carried out. Not only poor reporting of FITT principles, but also heterogeneity of study design, inclusion criteria, evaluated training intervention and outcome measures were factors which did not permit the defining of the training methodology with the greatest effectiveness. Another limitation is that, until now, only resistance and endurance training has been studied in patients with IM. So far, no study has evaluated neuromotor or balance training, even though postural control is especially affected in patients with IBM (20, 21). A promising approach that has not yet been evaluated in patients with IM is a combination of cognitive and physical training. There is growing evidence that cognitive-motor interventions can improve physical functioning (29, 30). As there is currently no evidence for balance and cognitive training in patients with IM, we did not include these interventions in our exercise guidelines. Other limitations of the exercise guidelines are that we did not evaluate methodological quality or risk of bias of the included studies, we involved neither international experts nor affected patients in the development process, and we published these guidelines only in German. Since our primary target group for these guidelines are therapists who treat patients from the USZ, we decided to publish them in a journal popular among German speaking therapists. The disadvantage is that we do not reach as many clinicians as we would when publishing in an English language journal. Another reason for focusing on German speaking therapists is that the IMACS (International Myositis Assessment & Clinical Studies Group) Rehabilitation and Exercise Scientific Interest Group decided to develop international evidence-based consensus guidelines for exercise in patients with adult and juvenile idiopathic inflammatory myopathies. The author of this systematic review and exercise guidelines will be involved in this international process and can thereby incorporate lessons learned from these two projects.

Although endurance and resistance training are both recommended for patients with IM, we only evaluated the latter in our feasibility study. The principle reason was that the current version of the app contained resistance training alone. As our main goal was to test the feasibility of this app, we refrained from including a separate endurance training component within our study intervention.

Assessments

Measurement properties of strength tests

Our study on measurement properties revealed that only the MMT8 total score but not the MMT values of individual muscle groups are reliable. Since our sample size was not large enough for subgroup analyses, we do not know if reliability would be better in specific subgroups. There is evidence that MMT cannot separate mild muscle weakness from normal strength and is therefore unsuitable for measuring the former (31, 32). In our sample, most patients had MMT-scores between 7 and 10, indicating no or mild weakness. This minimal muscle weakness might be the reason for the low reliability. Reliability might therefore be better in a patient group with more severe muscle weakness. This hypothesis is reinforced by the fact that the MMT is originally developed to assess severity of paralysis after peripheral and central nerve injuries (33). Therefore, we would not recommend MMT of single muscle groups in the general IM population.

Both the MMT and HHD measure maximum muscle strength. Nevertheless, the hypothesis of convergent validity between the MMT and HHD could not be confirmed. As we did not include a “gold standard” in our measurement setting, it is not possible to say which instrument is more adequate for assessing isometric muscle strength. However, previous studies comparing results of HHD with those of isokinetic testing (which is the gold standard) confirmed the appropriateness of the former to assess isometric muscle strength (34). Therefore, it is questionable whether the MMT is adequate for assessing maximum muscle strength.

MAP, the only disease-specific PROM

In earlier times, a non-validated German translation of the MAP was used at the USZ. As the MAP is the only disease-specific PROM for patients with IM we decided to make a new translation that followed international guidelines and then validate this new German version. In order to compare measurement properties of the new German version with the previously validated English and Swedish versions, we performed the same analysis as was done

with its predecessors. During the translation and validation process, some major limitations of the questionnaire and the analysis emerged. First, patients must weight their difficulties against the importance when answering the questions. As the questions are formulated “how much difficulty do you have....” it is uncertain if patients really weight between difficulty and importance or if they rather judge their difficulty to do a certain activity. To overcome this weakness, it should be made clear if difficulty or importance should be rated. Second, the subscales were defined based on the ICDH-2-Beta-2 draft categories. Due to the rarity of the disease, the dimensionality of the questionnaire has never been evaluated using a factor analysis. For this analytical approach, 128 to 320 participants (four to ten cases per item) are required (35), which was beyond the possibility of the research teams given the scarcity of patients. Third, MAP subscale and single items are interpreted separately and no total score is calculated and interpreted (36). Nevertheless, to analyse convergent validity, the median of all four subscales and the four single items was used. With this calculation method, the scores of the four single questions have equal weight as the score of the four subscales, although the subscales consist of four to nine different items. In addition, extreme scores do not affect the median. This may lead to the situation where a patient who indicated strong difficulties in each item of all four subscales, but no difficulty in the single items, has the same total median as a patient who indicated no difficulties in all items (subscales and single items). Based on these experiences we would recommend revisions of the MAP.

During the time of our validation study, the Outcome Measures in Rheumatology (OMERACT) Myositis Working Group explored the experience of adults living with PM and DM, concluding that the MAP does not cover the symptoms or effects of disease that are most important to patients (37). Therefore, the IMACS launched a project with the aim to develop a myositis-specific PROM for use in future clinical trials (38). Now that a new disease-specific questionnaire is being developed, it makes no sense to pursue the validation of the MAP any further.

Validity and reliability are not enough

Validity and reliability are both important and indispensable measurement properties. However, a measurement instrument is often used to evaluate whether the disease stage of a patient changed over time. Therefore, an instrument should be responsive. Responsiveness is the ability of an instrument to detect real changes over time (39). To evaluate responsiveness, a

longitudinal study in which changes of the target outcomes are expected is required (35). Such a study design was not feasible for either the strength tests or the MAP; especially because we would have needed a population where a change in muscle strength and activity limitation is expected.

Assessment in the feasibility study

High quality assessments are essential to evaluate success of a treatment. Nevertheless, in the feasibility study we used assessments in which measurement properties were insufficiently known. So far, in the field of IM, there exists no assessment which measures muscle strength or function that has acceptable validity, reliability and responsiveness (40, 41). Therefore, we had to choose the most suitable assessments. Due to this limitation, one is never sure whether the intervention did not lead to the expected change (e.g. improved muscle strength) or if an existing change could not be detected.

Telerehabilitation / blended therapy

Software application

Based on the positive experiences made with the pro-active software “Active Lifestyle”, a new app called “fit” was developed. “Active Lifestyle” used different persuasive strategies, such as conditioning through positive and negative reinforcement, goal setting, self-monitoring, social motivation, comparison and external monitoring, all intended to motivate elderly users to keep a routine of physical activity (42, 43). Originally, it was planned to adopt these proven motivational strategies in our new app. Due to technical restrictions, limited IT-personnel availability and ditto financial resources, only a “light” version could be completed. The entire aspect of social motivation and comparison (e.g. contact with peers, comparing progress of training with others) could not be implemented in our app. Also, the metaphor for conditioning through positive and negative reinforcements (in “active lifestyle” flowers grew whenever a session was completed, and mood status of this flower varied according to the adherence to the training plan) was replaced with a simpler written feedback. Finally, a simple, but clear app which guides the patients through their therapeutic exercise programme and allows therapists to monitor them remotely was developed.

In both phases of the usability study, our participants made several suggestions for improvement. Unfortunately, only a few of these proposals were finally implemented in the app. Nevertheless, participants of the feasibility

study were satisfied with the adapted version. We do not know if more sophisticated software would further improve adherence and satisfaction. Since one of the most important motivational aspects seems to be personal contact with therapists (44, 45), it is questionable if more persuasive strategies were necessary. However, some important improvements (e.g. a return button for the “play”, integration of photos of the exercise in the “manager”, clearer layout of the training overview for “play” and “manage”) should be implemented before the software can be used in clinical routine. From the focus group participants we know that such an app would only be used if it runs smoothly and error-free. Depending on whether therapists are convinced of the usability of the app, they may facilitate or restrict its use (44). Therefore, it is imperative that the proposed changes for the “Manager” and the “Play” components are implemented.

Usability and acceptance: integration of the end-user in the development process

Usability evaluation is a wide field and various methods such as heuristic evaluation, cognitive walkthrough, think-aloud and focus groups can be applied (46). For practical and time reasons we decided to use the think-aloud technique. This method allowed us to integrate end-users in the usability testing. A combination of different methods that complement each other would have been more powerfully able to detect usability flaws (47). Traditionally, to analyse the think-aloud methods, all articulated thoughts are transcribed and then analysed by codes (48). As we were primarily interested in the usability flaws and not in the thoughts of the participants, we used a simplified approach: we made notes during the test procedure and audiotaped the subjects during tasks performance. Where necessary, the notes were later supplemented using the audio files. With this method, we were able to detect various usability problems in a time-efficient way.

Implications for clinical practice

Based on current evidence, therapeutic exercise is safe and beneficial for patients with IM in all disease phases. This implies that individually tailored exercise programs including endurance and resistance training can be started as soon as the diagnosis has been made. Exercise does not aggravate inflammation processes, as it was previously feared. Before starting with an exercise session, the current physical performance should be evaluated and individual limiting factors such as pain or fatigue should be taken into consideration. Only in this way, the intensity and volume can be adapted to

the individual needs. Over the course of the disease, volume and intensity of included exercises should gradually be increased, provided that the previous training is well tolerated. For details about recommended exercise protocols and definitions of initial value and progression during the disease the exercise guidelines should be considered (2). As there are indications that balance is reduced in patients with IM, we would recommend assessing possible problems with this and, if necessary complement the therapeutic exercise programme with neuromotor exercises. To keep patients motivated and to be able to monitor and adapt the exercise programme, personal support is essential. Depending on patients' needs and preferences this support can be face-to-face (e.g. with a supervised group training) or per remote with the use of technical devices.

Reduced muscular endurance is often the first symptom of patients with IM. This may occur even before a decreased maximum force can be determined with the MMT8 (49, 50). Nevertheless, the MMT8 is the most used assessment to evaluate muscle strength in patients with IM. MMT8 is also part of the core set measures and one of the response criteria (15, 40). Our studies confirmed known limitations of the MMT. Therefore, we strongly recommend using assessments that evaluate dynamic repetitive muscle functions such as the FI-2 or the 30-second chair stand or arm curl. If maximum peak force is warranted a more objective instrument such as the HHD could be used. If only maximum force is measured using the MM8, there is a risk that initial mild muscle weakness as well as changes in muscle strength will not be detected. Therefore, in our opinion, it should be considered whether the MMT8 could be replaced within the core set measure and the response criteria, utilising a dynamic muscle test instead.

Using PROMs in clinical practice can offer important information about the impact of a disease or a treatment on patients' disability and their quality of life. The only disease-specific questionnaire in the field of myositis is the MAP. Although this questionnaire has some limitations, it can be useful in clinical practice. Not all activities that are important for patients with IM are included in this questionnaire. Nevertheless, the MAP may help to better understand patients' burden of disease and should therefore be used in addition to the more generic questionnaires as the HAQ and the SF36.

Recommendations for future research

The following recommendations for future research have emerged from this thesis:

- Exercise, more specifically resistance and endurance training, are an indispensable treatment for patients with IM. Although this is a well acknowledged fact, the most appropriate training regimen is not yet known. The currently ongoing project from the IMACS Rehabilitation and Exercise Scientific Interest Group “Development of international evidence-based consensus guidelines for exercise in patients with adult and juvenile idiopathic inflammatory myopathies” is one important step in this direction. A further challenge will then be to confirm these guidelines. Therefore, an international multi-centre randomized controlled exercise trial is needed. As myositis is a rare disease, only with this international approach it is possible to recruit a sample that is large enough to analyse subgroups of IM separately. This would contribute to the understanding of trainability of patients with different subtypes of IM and to identify if a subgroup is refractory to exercise.
- An already known but often neglected recommendation is the importance of a detailed and replicable description of the intervention. A valuable way to describe the intervention in exercise studies is by means of its FITT components. These should not only be described in the exercise prescription, but should also be reported in terms of what participants actually did. This means that adherence to these FITT components must be reported in detail.
- Beside muscle weakness and reduced aerobic capacity, there are some indications that balance is also reduced in patients with IM. So far, this aspect has received too little attention. A cross-sectional study could for example evaluate balance in patients with IM and compare the results with those of healthy controls.
- Although muscle weakness is the core symptom of myositis, there is no valid, reliable and responsive assessment to evaluate muscle strength in patients with IM that is practicable in the clinical routine. Different assessments with promising preliminary psychometric properties, such as the Fi-2, Fi-3, 30-second chair stand and HHD, have all been used, but none of them is sufficiently evaluated. Therefore, there is an urgent need for high quality studies evaluating measurement properties of these assessments. Such studies on measurement properties should consider the

COSMIN checklist (39). Assessments measuring muscle strength were not only used to evaluate treatment outcome, but also as a diagnostic tool. As an assessment that is suitable for an evaluative purpose is not automatically good for diagnostic purposes, additional measurement properties such as sensitivity, specificity, as well as positive and negative predictive values have to be evaluated if an assessment is to be used for diagnostic purposes (51).

- A new disease-specific PROM is currently being developed by an international working group (38). In order to apply this coming assessment with German speaking patients, a transcultural translation and validation into German is necessary. To avoid country-specific peculiarities in the German version, this validation should be done in cooperation with researcher from the three German speaking countries (Germany, Austria and Switzerland).
- Blended therapy is a promising new approach that is well accepted and advocated by patients. Unfortunately, in Switzerland health insurance companies do not have to cover the costs of teletherapy, even if the therapy is prescribed by a medical doctor. Therefore, studies about cost-effectiveness of this innovative approach should be carried out.

Personal opinion and conclusion

Rare diseases such as IM pose challenges to patients that are affected, to the clinicians and health professionals that take care of them and to the researchers that study their disease conditions. The broad heterogeneity of IM (wide spectrum of clinical manifestations, variable disease course, various subtypes) further complicate this challenge. While much progress in understanding the pathophysiological processes has been made in the last few years, research about clinimetric properties of outcome measurement instruments, especially measurements that assess muscle strength or weakness, remains scarce.

Although muscle weakness is the cardinal symptom of IM, there exist neither a valid, reliable and responsive assessment to evaluate changes over time in patients with IM nor an assessment with proven diagnostic accuracy such as sensitivity and specificity or predictive values. So far, the MMT8 is - despite some major known limitations - the most frequently used testing method. Our study is the first that evaluated the MMT8 in a sample that is large enough to determine clinimetric properties. Unfortunately, our results

confirmed or even exceeded the known limitations such as high ceiling effects, modest inter-tester reliability, and a broad range of muscle strength within the maximum score of MMT. Therefore, I think that the MMT8 should no longer be used as the standard measure for patients with IM. The ease of use, high practicability and low costs does not justify the use of an assessment with questionable measurement properties. Furthermore, muscle endurance is often more or earlier affected than muscle strength. With a diagnostic test of isometric maximum strength, patients with reduced muscular endurance cannot be recognised. There are other promising, simple and practical tests such as the FI-3 or the 30-second chair stand and arm raise that evaluate muscle endurance. These tests have been used in different trials, but their measurement properties are not yet sufficiently evaluated. Therefore, there is an urgent need to evaluate measurement properties of these tests in a large enough sample, so that the MMT could be replaced with a more suitable, valid and reliable test.

From the patient's perspective, activity limitations and participation restrictions might be more relevant than body functions such as muscle strength. Therefore, the use of PROMs is essential. Muscle strength may influence activity limitations, but depending on the coping strategies of patients, the limitation of activity may vary in patients with the same amount of muscle weakness. Although when muscle strength is reduced, activities do not necessarily have to be restricted. E.g., a patient who had no problems with blow-drying her hair even though she had very weak shoulder muscles. She explained that she could no longer blow-dry her long hair, therefore she had it cut and now she has no problem with combing and drying her new (short) haircut. Such discrepancy between impaired body functions and activity limitation can only be detected with PROMs. So far, the MAP is the only disease specific activity limitation questionnaire. Although this questionnaire has some limitations in its structure and does not capture all activities that are relevant for patients with IM, I would propose to use it in the clinical practice and in research as long as no other PROM is available. Currently, the Outcome Measures in Rheumatology Myositis Special Interest Group are developing a myositis specific patient reported outcome measure for use in future clinical trials and observational cohort studies (52). As soon as this PROM is developed, it should be translated in German so that this instrument can be used in German speaking countries.

In my opinion, more time should be invested in the development and validation of relevant assessments. Without reliable, valid and responsible assessments, it is not possible to record reliably treatment effects of exercise trials. If we do not know the smallest detectable change that can be captured with a certain assessment, we will not know if a possible change is within the measurement error or if it is a real change.

It is well recognized that exercise is central to patients with IM. However, it is not clear which dose and way of delivery is most effective. So far, supervised or home exercise programs have been evaluated. This thesis applied a new promising approach: blended therapy. With the combination of new technologies and face-to-face therapy, two known challenges can be solved. On the one hand, patients that often do not live near the hospital, where disease specialized therapist are available, can be supervised per remote. On the other hand, a detailed training diary is generated. Thus, deviations from the originally planned trainings regime become apparent. This allows us to draw important conclusions as to whether the planned training regimen can be performed or not. Only with this information, we can improve our knowledge about exercise in this patient group. In my opinion, it does not matter if patients exercise at home, at a gym or a hospital setting. The most important fact is that they do exercise properly and that they exercise regularly. As the effect of exercises diminishes as soon as a training is performed inappropriately or stopped, it is important that exercise becomes a normative part of daily life. Therefore, further research should address how such a behaviour change can be supported and how regular exercise can be internalized.

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English summary

The term Inflammatory Myopathy (IM) refers to a group of rare heterogeneous neuromuscular diseases characterized by chronic proximal muscle inflammation and weakness. Although IM are relatively rare, the burden of disease for the affected patients is immense. The most prominent clinical features in all subcategories of IM are proximal and often symmetric muscle weakness and low muscle endurance, which progresses over a period of weeks or months. Both features result in significant disabilities. Patients often report increasing difficulties with the activities of daily living, such as getting up from a chair, going up- or downstairs, getting into a car, stepping onto a curb, lifting objects, washing hairs, brushing teeth, and gripping objects. In addition, patients may suffer from possible systemic issues, such as dysphagia, gastrointestinal, pulmonary and cardiac dysfunction, and in DM patients, skin involvement might further contribute to the disease morbidity. The symptoms of IM may negatively influence psychological health and well-being, resulting in significantly lower health-related quality-of-life scores compared to gender- and age-matched healthy individuals. Muscle weakness and low endurance in patients with IM is multifactorial. This is mainly a consequence of the chronic inflammation of the skeletal muscle itself, but microangiopathy with loss of capillaries might also play a role. Besides disease-intrinsic features, the tendency of patients with IM to avoid strenuous physical activity due to fear of disease exacerbation further enhances the physical deconditioning process. This vicious circle is unfortunately reinforced by the common catabolic side effect of steroids on muscle metabolism. In order to interrupt the vicious circle and rectify the deconditioning syndrome, physical exercise is crucial.

Since IM is a rare disease, there are only few experienced and appropriately trained physiotherapists available, most of them working in reference centres such as the University Hospital Zurich. As many patients with IM do not live near such a reference centre, they only have limited access due to long travel distance, and high travel costs. Therefore, for patients from the USZ who are not capable of attending a supervised exercise program twice a week, a home-based exercise program is provided. Unfortunately, such a home program often results in problems with sustained adherence due to the lacking supervision and personal contact. Blended therapy, the combination of telerehabilitation using telecommunication technologies and face-to-face sessions, might be a potential therapy option. Thus, the overall aim of this

project was to evaluate the feasibility of a blended therapy approach, combining a newly developed interactive tablet-based exercise app with face-to-face physiotherapy sessions in patients with IM., Several steps were necessary to achieve this aim, and each of these steps is described in separate chapters in this thesis.

The project started with a systematic review of the relevance of applying exercise training principles, reporting the FITT components (FITT: frequency, intensity, type and time) in the training prescription as well as adhering to the training (**Chapter 2: The relevance of applying exercise training principles when designing therapeutic interventions for patients with inflammatory myopathies: a systematic review**). The systematic review revealed incomplete application of exercise training principles and insufficient reporting of the exercise prescribed and completed. From the 14 included studies, 93% reported specificity, 50% progression and overload, and 79% initial values. The training principles reversibility and diminishing returns were never reported. Interestingly, articles focusing on one training method alone (either strength or endurance training) reported more application of training principles compared to those with a combined intervention. Failure to apply the training principles may lead to under-dosed training and, as a consequence, the effect of the physical exercise intervention may be underestimated and the time allotted for therapy might not be used effectively and efficiently. FITT components were reported more consistently in the training prescription than in the result section. In the training prescription, frequency and type were described in 13 articles, time in 11 articles and intensity in 7 articles. In the results section, however, frequency was reported in 5 articles and type in 4 articles, while intensity and time never were mentioned. If the FITT components of physical exercise training and the adherence to these components are not explicitly reported, the intervention is not replicable in future studies and it is not possible to transfer the results to a clinical setting. The next step of this project entailed the development of an evidence-based exercise guideline for patients with IM (**Chapter 3: Entwicklung eines Trainingsleitfadens für Patienten mit entzündlicher Muskelerkrankung / Development of an Exercise Guideline for Patients with Myositis**). This exercise guideline was developed based on the results of a systematic review. As the study design, inclusion criteria, training modalities, and outcome measures of the 24 included studies were highly heterogeneous and the description of the study interventions were insufficient, the general training

guidelines of the American College of Sports Medicine and the clinical experience of specialist physiotherapists were consulted to complement missing information. Finally, an introductory part for general training principles and recommendations for resistance and endurance training for three different disease phases (early active, active and stable) were formulated. Patients in an early active phase (disease duration < three months) should start doing exercises to improve their cardiovascular fitness for 5-10 minutes at 50-60% of HR_{max} and perform progressive resistance training with low intensity and volume (1-3 series with 5-10 repetitions at 40-60% of 1 RM (Repetition Maximum)). In an active phase (disease duration >3 months, but unstable course of the disease), 15-30 minutes endurance training with 60-70% of HR_{max} and for progressive resistance 1-3 series with 8-15 repetitions at 40-60% of 1 RM is recommended. In a stable phase, volume and intensity of endurance and resistance training can be further increased up to 20-45 minutes with 70-85% HR_{max} for cardiovascular fitness and 2-3 series with 8-15 repetitions at 60-80% of 1RM for resistance training.

The next two studies dealt with measurement outcome instruments. The main aim of exercise studies in patients with IM is to increase the strength of affected muscle groups and to reduce disability caused by these muscle weaknesses. Treatment effects can only be verified if valid and reliable assessments are available. Therefore, we evaluated measurement properties of two strength tests and a questionnaire assessing limitations in the activities of daily living. Two practical and commonly used strength tests are the Manual Muscel Test (MMT) and the hand-held dynamometer (HHD). As both of them were insufficiently studied, we evaluated the reliability and concordance between these two tests (**Chapter 4: Manual muscle testing and hand-held dynamometry in people with inflammatory myopathy: An intra- and interrater reliability and validity study**). We tested the eight muscle groups included in the MMT8 (shoulder abduction, elbow flexion, wrist extension, neck flexion, hip abduction, hip extension, knee extension, and ankle extension) in both tests. The MMT results revealed high ceiling effects between 22% and 82% for all but one muscle group (hip extension). Intrarater reliability was substantial for shoulder abduction, elbow flexion, neck flexion, hip abduction, and hip extension (linear weighted Kappa varying from 0.61 to 0.69); moderate for wrist extension and knee extension (linear weighted Kappa varying from 0.49 to 0.53) and fair for ankle extension (linear weighted Kappa varying between 0.35 and 0.37). Interrater reliability was

moderate for neck flexion and hip abduction (linear weighted Kappa from 0.44 to 0.58); fair for shoulder abduction, wrist extension, and ankle extension (linear weighted Kappa varying from 0.20 to 0.35); and slight for knee extension (linear weighted Kappa of 0.08 and 0.18). The MMT total score showed excellent intra- and interrater reliability (ICC > 0.9) with a corresponding smallest detectable change (SDC) of 6.9% and 8.6%, respectively. The averaged peak force of two consecutive measurements assessed with the HHD revealed excellent intra- and interrater reliability (ICC between 0.75 and 0.97) for all muscle groups except for interrater reliability of ankle extension (0.61), which was fair to good. The corresponding SDC was between 23 and 65%. The correlation between the MMT and HHD was good for shoulder abduction, moderate for three muscle groups (hip abduction and elbow and neck flexion), and low for four muscle groups (wrist, knee, ankle and hip extension). These results raise doubt as to whether both tests measure the same construct (isometric maximum strength). In conclusion, only the MMT total score, but not the scores of single muscle groups, showed acceptable reliability and therefore MMT of single muscle groups should not be used to evaluate changes. In contrast, HHD could be recommended to evaluate isometric strength. If possible, the same tester should perform all tests and the average of at least two measurements should be applied. The only disease-specific patient-reported outcome measurement for patients with IM is the Myositis Activity Profile (MAP). This questionnaire includes 32 items that are divided in four subscales (movement activities, activities of moving around, personal care and hygiene, and domestic activities) and four single items (keeping in touch with close friends and relatives, avoiding overexertion during daily activities, being able to cope with work and/or housework to a satisfactory degree, and being able to do recreational activities of choice). As there was no validated German version, we translated the English MAP into German and validated this new version (**Chapter 5: Reliability and validity of the German version of the Myositis Activities Profile (MAP) in patients with inflammatory myopathy**). Our results revealed substantial reliability (weighted kappa coefficient between 0.65 and 0.77) for all MAP subscales and for three out of the four single items and moderate reliability (Weighted kappa coefficient: 0.57) for the single item “avoid overexertion”. In line with our hypothesis, the German MAP correlated highly with the Health Assessment Questionnaire (HAQ) and the physical component score of the SF36; moderately with the total scores of the Functional Index 2 (FI-2), the

HHD and the MMT8; and poorly with the mental component score of the SF36 and with pain. Three out of four subscales and two out of four single items achieved acceptable discriminative validity (area under the curve (AUC) between 0.72 and 0.79). Subscale “personal care” and single questions “social” and “avoid overexertion” indicated no acceptable discrimination (AUC between 0.65 and 0.69). Although the MAP showed good reliability and acceptable validity, there are some uncertainties concerning structure and scoring of this questionnaire. The MAP structure should be confirmed using a factor analysis, but the required sample of four to ten cases per item was far beyond our possibilities. A peculiarity of the scoring is that patients have to weight their difficulties against their needs when answering the questions. It is not known if each patient put more weight on difficulty or on their needs, and therefore it would be of considerable importance to further evaluate this scoring approach.

In the next study, we focused on the development of a tablet-based exercise app, including testing its usability and acceptance by end-users and exploring the therapists’ opinion on using this app in a clinical setting (**Chapter 6: Usability and acceptance of an interactive tablet-based exercise application: a mixed methods study**). The exercise app consists of two different parts: one for the therapists and for the trainees. In the former part, therapists can compile an individual exercise program for their trainees and monitor the performed exercises. In the latter part, the trainees can see their exercise program and record their performed exercises. The usability of the app was tested in two phases; after each phase the app was further improved based on the problems and comments of the participants. In both phases, five therapists and five trainees each performed different predefined tasks and were invited to verbalize their thoughts while performing these tasks. Effectiveness measured by task completion rate improved from 85% to 93% for the therapists, and from 73% to 90% for the patients from phase one to phase two. Therapists and trainees in both phases were satisfied with the app (70.5-85.5/100) and acceptance measured with the technology acceptance model was acceptable (101 to 120/140). As the app only will be used at the clinics if the therapists are truly convinced of its advantages, it is important to identify their opinions on the app. We therefore performed two focus group interviews; one with a group of team leaders and the other with a group of team members. In general, the team leaders and the team mem-

bers considered the app a useful therapy supplement. They especially appreciated its blended character, a distinguishing feature compared to other fitness apps, which lack a “professional” feedback function. The “blended therapy” setting also reduced their fear of being replaced by technical applications. The therapists also raised some concerns about using the app. Barriers were seen in its implementation in the clinic (data protection, uncertainties regarding payment of costs) and in the personal attitude of the therapists and patients - not all therapists and patients are technology-affine.

Finally, in the last study, we evaluated feasibility and potential impacts on muscle strength, muscle function, activity limitation, disability and health-related quality of life of a blended therapy approach, combining the app with face-to-face physiotherapy sessions in patients with IM (**Chapter 7: Feasibility of a blended therapy approach in patients with inflammatory myopathies**). The intervention consisted of three to four face-to-face therapy sessions (two sessions for compiling and introducing the individually tailored exercise program, and one to two follow-up sessions for checking the already performed exercises and adapting the training programme) and a 12-week home-based progressive resistance training which was supervised remotely. The individually tailored exercise programmes were based on recently published training guidelines and the therapists supervised each patient weekly by checking the training diary and by adapting or commenting on the training progress per remote access. The outcome of this study thus demonstrated that this blended therapy approach is feasible. The attrition rate of 7% was lower than the previously defined acceptance threshold of 10% and adherence of 84% was higher than the target adherence rate of at least 80%. Moreover, there was a high acceptance and satisfaction with this therapy approach. Nevertheless, the participants suggested some ideas for improving the app, such as “videos instead of photos”, “more space for writing messages”, “return button (to go back to the previous exercise)”, “a simple password to enter the programme”, “possibility of downloading the programme on the mobile phone and possibility of checking if the exercise is performed correctly (video feedback)”. When it comes to muscle strength and function, however, the results were inconsistent and revealed multiple levels of complexity. The MMT8 and FI-2 showed high ceiling effects, indicating that the patients achieved the highest possible score already at baseline, thus not giving the opportunity to detect any improvement even when the patients got stronger. Isometric peak force measured for patients with an adherence rate

of at least 80% showed a minor increase in six muscle groups (effect size between 0.04 and 0.42), but a decrease in two muscle groups (hip abduction and hip flexion). Higher effect sizes were revealed with the 30 second arm curl and chair stand (effect size between 0.52 and 0.88), where the participants increased the number of performed repetitions after the intervention by 1.5 and 2.3 repetitions, respectively. All three patient-reported outcomes that measured activity limitation, disability and health-related quality of life showed a tendency towards better health-related quality of life, less activity limitation and less disability. This tendency was seen despite floor effects and ceiling effects in different subscales of the MAP (used to assess activity limitation) and the HAQ (used to assess disability). In conclusion, this blended therapy approach using the newly developed tablet-based exercise app has proved to be feasible and the progressive resistance training revealed some positive impact on muscle performance and patient-reported outcomes. In addition, the study provides information that might be useful when selecting appropriate assessments and determining necessary sample sizes in future trials.

Deutsche Zusammenfassung

Der Begriff inflammatorische Myositiden (IM) bezieht sich auf eine Gruppe seltener heterogener neuromuskulärer Erkrankungen, die durch chronische proximale Muskelentzündung und -schwäche gekennzeichnet sind. Obwohl IM relativ selten sind, ist die Krankheitslast für die betroffenen Patient*innen immens. Die typischen klinischen Merkmale aller Subkategorien der IM sind proximale und oft symmetrische Muskelschwäche und eine geringe Muskelausdauer, welche über einen Zeitraum von Wochen bis Monaten fortschreiten. Beide Merkmale können zu erheblichen Behinderungen führen. Patient*innen berichten oft über zunehmende Schwierigkeiten bei Alltagsaktivitäten, wie z.B. von einem Stuhl aufstehen, Treppen hochgehen, in ein Auto steigen, auf ein Trottoir steigen, Gegenstände hochheben, Haare waschen, Zähne putzen und Objekte greifen. Darüber hinaus können Patient*innen unter möglichen systemischen Problemen wie Dysphagie, gastro-intestinalen, pulmonalen und kardialen Funktionsstörungen leiden. Bei Patient*innen mit einer Dermatomyositis kann die Hautbeteiligung die Krankheitslast zusätzlich verstärken. Die Symptome der IM können auch die psychische Gesundheit und das Wohlbefinden negativ beeinflussen. Dies führt zu einer signifikant schlechteren Lebensqualität im Vergleich zu nach Alter und Geschlecht gematchten gesunden Personen. Muskelschwäche und geringe Muskelausdauer bei Patient*innen mit IM sind multifaktoriell bedingt. Dies ist vor allem eine Folge der chronischen Entzündung der Skelettmuskulatur selbst, aber auch eine Mikroangiopathie mit einhergehendem Verlust der Kapillaren könnte eine Rolle spielen. Neben den krankheitsbedingten Folgen begünstigt die Tendenz von Patient*innen mit IM, anstrengende körperliche Aktivitäten aus Angst vor einer Verschlechterung der Krankheit zu vermeiden, die körperlichen Dekonditionierung zusätzlich. Dieser Teufelskreis wird leider durch die katabole Nebenwirkung von Steroiden auf den Muskelstoffwechsel verstärkt. Um diesen Teufelskreis zu durchbrechen und dem Dekonditionierungssyndrom entgegenzuwirken, ist körperliche Aktivität von entscheidender Bedeutung.

Da es sich bei der IM um eine seltene Krankheit handelt, gibt es nur wenige erfahrene und entsprechend ausgebildete Physiotherapeut*innen. Die meisten davon arbeiten in einem Referenzzentrum wie beispielsweise dem Universitätsspital Zürich (USZ). Viele Patient*innen mit IM wohnen jedoch nicht in der Nähe eines solchen Referenzzentrums und haben wegen der langen Anfahrtswege und der hohen Reisekosten nur begrenzten Zugang zu

diesen spezialisierten Zentren. Deshalb bekommen Patient*innen aus dem USZ, die nicht in der Lage sind, zweimal wöchentlich an einem betreuten Trainingsprogramm teilzunehmen, ein Übungsprogramm für zu Hause. Leider führt ein solches Heimprogramm aufgrund der mangelnden Kontrolle und des fehlenden persönlichen Kontakts oft zu Problemen bei der nachhaltigen Durchführung. Blended Therapie, eine Kombination von Telerehabilitation und persönlichen (Face-to-Face) Sitzungen, könnte eine mögliche Therapieoption sein. Daher bestand das Hauptziel unserer Arbeit darin, die Durchführbarkeit einer Blended Therapie bei Patient*innen mit IM zu evaluieren. Diese Blended Therapie kombiniert eine neu entwickelte interaktive, Tablet-basierte Trainingsapplikation mit persönlichen Physiotherapiesitzungen. Um dieses Ziel zu erreichen, waren mehrere Schritte notwendig. Jeder dieser Schritte wird in dieser Arbeit in separaten Kapiteln beschrieben.

Das Projekt begann mit einer systematischen Übersicht über die Anwendung von Trainingsprinzipien, die Beschreibung der verschiedenen Trainingskomponenten (Häufigkeit, Intensität, Art und Dauer) sowie die Adhärenz zum verordneten Training (**Kapitel 2: The relevance of applying exercise training principles when designing therapeutic interventions for patients with inflammatory myopathies: a systematic review**). Die systematische Übersicht zeigt auf, dass die Trainingsprinzipien zu wenig beachtet wurden und dass die Trainingskomponenten sowohl bei der Beschreibung des geplanten Trainings als auch bei den Angaben zur Adhärenz zum Training unvollständig beschrieben wurden. Von den 14 eingeschlossenen Studien machten 93% Angaben zur Spezifität, 50% zu Progression und trainingswirksamer Intensität und 79% zum Ausgangswert. Die Trainingsprinzipien Reversibilität und abnehmende Wirksamkeit wurden in keiner Studie beschrieben. Interessanterweise berichteten Artikel, die sich nur auf eine Trainingsmethode (entweder Kraft- oder Ausdauertraining) konzentrierten, über eine vermehrte Anwendung von Trainingsprinzipien im Vergleich zu denen mit einer kombinierten Intervention. Die Nichtbeachtung der Trainingsprinzipien kann zu einem unterdosierten Training führen, was zur Folge haben kann, dass die Wirkung des Trainings unterschätzt wird und die für die Therapie vorgesehene Zeit nicht effektiv und effizient genutzt wird. Trainingskomponenten wurden in der Trainingsbeschreibung konsistenter angegeben als im Ergebnisteil. In der Trainingsbeschreibung wurden Häufigkeit und Art des Trainings in 13 Artikeln, die Dauer in 11 Artikeln und die Intensität in 7 Artikeln beschrieben. Im Ergebnisteil wurde jedoch die Häufigkeit nur in 5

Artikeln und die Art des Trainings in 4 Artikeln beschrieben, während Intensität und Dauer nie erwähnt wurden. Wird das geplante sowie das effektive durchgeführte Trainingsprogramm nicht explizit beschrieben, ist die Intervention in zukünftigen Studien nicht replizierbar und es ist auch nicht möglich, die Ergebnisse in den klinischen Alltag zu übertragen.

Der nächste Schritt dieses Projekts beinhaltete die Entwicklung eines evidenzbasierten Trainingsleitfadens für Patient*innen mit entzündlicher Muskelerkrankung (**Kapitel 3: Entwicklung eines Trainingsleitfadens für Patienten mit entzündlicher Muskelerkrankung / Development of an Exercise Guideline for Patients with Myositis**). Dieser Trainingsleitfaden wurde auf der Grundlage der Ergebnisse einer systematischen Übersichtsarbeit entwickelt. Da das Studiendesign, die Einschlusskriterien, die Trainingsmodalitäten und die Outcomemessungen der 24 eingeschlossenen Studien sehr heterogen waren und die Beschreibung der Studieninterventionen unzureichend war, musste auf die allgemeinen Trainingsrichtlinien des American College of Sports Medicine und die klinische Erfahrung spezialisierter Physiotherapeut*innen zurückgegriffen werden, um fehlende Informationen zu ergänzen. Schließlich wurden ein Einführungsteil über die allgemeinen Trainingsprinzipien sowie Empfehlungen für ein Kraft- und Ausdauertraining für drei verschiedene Krankheitsphasen (früh aktiv, aktiv und stabil) beschrieben. Patient*innen in einer frühen aktiven Phase (Krankheitsdauer < drei Monate) sollten mit einem 5-10-minütigen Ausdauertraining mit einer Intensität zwischen 50-60% ihrer maximalen Herzfrequenz (HR_{max}) beginnen und ein progressives Krafttraining mit geringer Intensität und Umfang durchführen (1-3 Serien mit 5-10 Wiederholungen bei 40-60% des Ein-Wiederholungs-Maximums (repetition maximum: 1RM)). In einer aktiven Phase (Krankheitsdauer > 3 Monate, aber instabiler Verlauf der Erkrankung) wird ein 15-30-minütiges Ausdauertraining mit 60-70% der HR_{max} und für das Krafttraining 1-3 Serien mit 8-15 Wiederholungen bei 40-60% des 1 RM empfohlen. In einer stabilen Phase können Umfang und Intensität des Ausdauertrainings auf 20-45 Minuten mit 70-85% der HR_{max} gesteigert und das Krafttraining kann auf 2-3 Serien mit 8-15 Wiederholungen bei 60-80% von 1 RM für das Krafttraining weiter erhöht werden.

Die nächsten beiden Studien befassten sich mit Instrumenten zur Messung der Ergebnisse. Das Hauptziel der Trainingsstudien bei Patient*innen mit IM ist es, die Kraft der betroffenen Muskelgruppen zu erhöhen und die

durch die Muskelschwäche verursachte Behinderung zu verringern. Behandlungseffekte können nur nachgewiesen werden, wenn valide und zuverlässige Assessments vorliegen. Deshalb haben wir die Messeigenschaften von zwei Krafttests und einem Fragebogen zur Beurteilung von Einschränkungen der Alltagsaktivitäten untersucht. Zwei einfache und häufig verwendete Krafttests sind der Manuelle Muskeltest (MMT) und die Handdynamometrie. Da beide Tests nicht ausreichend untersucht waren, evaluierten wir die Reliabilität und die Übereinstimmung zwischen diesen beiden Tests (**Kapitel 4: Manual muscle testing and hand-held dynamometry in people with inflammatory myopathy: An intra- and interrater reliability and validity study**). Wir testeten die Muskelgruppen welche im MMT8 enthalten sind (Schulterabduktion, Ellenbogenflexion, Handgelenksexension, Nackenflexion, Hüftabduktion, Hüftextension, Knieextension und Fussgelenkextension) mit beiden Krafttests. Die Ergebnisse des MMT zeigten Deckeneffekte zwischen 22% und 82% für alle Muskelgruppen mit Ausnahme der Hüftextension. Die intrarater Reliabilität war substantiell für die Schulterabduktion, Ellenbogenflexion, Nackenflexion, Hüftabduktion und Hüftextension (linear gewichtete Kappa-Werte zwischen 0,61 und 0,69); moderat für die Handgelenk- und Knieextension (linear gewichtete Kappa-Werte zwischen 0,49 und 0,53) und mittelmässig (fair) für die Fussgelenkextension (linear gewichtete Kappa-Werte zwischen 0,35 und 0,37). Die interrater Reliabilität war moderat für die Nackenflexion und Hüftabduktion (linear gewichtete Kappa-Werte zwischen 0,44 und 0,58); mittelmässig für die Schulterabduktion, Handgelenksexension und Fussgelenkextension (linear gewichtete Kappa zwischen 0,20 und 0,35); und gering für die Knieextension (linear gewichtete Kappa-Werte zwischen 0,08 und 0,18). Der MMT-Gesamtscore zeigte eine ausgezeichnete intra- und interrater Reliabilität ($ICC > 0,9$) mit einer entsprechenden kleinsten nachweisbaren Veränderung (smallest detectable change: SDC) von 6,9% bzw. 8,6%. Die durchschnittliche Maximalkraft von zwei aufeinanderfolgenden Messungen bei der Handdynamometrie, ergab eine ausgezeichnete intra- und interrater Reliabilität (ICC zwischen 0,75 und 0,97) für alle Muskelgruppen mit Ausnahme der interrater Reliabilität der Fussgelenkextensoren die mit einem ICC von 0,61 als «fair to good» beurteilt wurde. Die entsprechenden SDCs lagen zwischen 23-65%. Die Korrelation zwischen dem MMT und der Handdynamometrie war gut für die Schulterabduktion, moderat für drei Muskelgruppen (Hüftabduktion und Ellbogen- und Nackenflexion) und niedrig für vier Muskelgruppen (Handgelenk-, Knie-, Knöchel-

und Hüftextension). Diese Ergebnisse lassen Zweifel aufkommen, ob beide Tests das gleiche Konstrukt, nämlich die isometrische Maximalkraft, messen. Zusammenfassend lässt sich sagen, dass nur der MMT-Gesamtscore, nicht aber die Werte der einzelnen Muskelgruppen eine akzeptable Reliabilität aufweisen, weshalb der MMT einzelner Muskelgruppen nicht zur Beurteilung von Veränderungen herangezogen werden sollte. Im Gegensatz dazu kann die Handdynamometrie zur Messung der isometrischen Kraft empfohlen werden. Wenn möglich, sollten alle Tests von derselben Testperson durchgeführt werden und es sollte jeweils der Durchschnitt von mindestens zwei Messungen berechnet werden.

Die einzige krankheitsspezifische Patient Reported Outcome Messung (PROM) für Patient*innen mit IM ist das Myositis-Aktivitäten-Profil (MAP). Dieser Fragebogen umfasst 32 Items, die in vier Subskalen (Bewegungsaktivitäten, Aktivitäten der Fortbewegung, persönliche Körperpflege und Hygiene sowie Arbeiten im Haushalt) und vier einzelne Items (soziale Kontakte, Vermeidung von Überanstrengung, Arbeit/Schule/Haushalt, Erholung) unterteilt sind. Da es keine validierte deutsche Version gab, haben wir den englischen Fragebogen ins Deutsche übersetzt und diese neue Version validiert (**Kapitel 5: Reliability and validity of the German version of the Myositis Activities Profile (MAP) in patients with inflammatory myopathy**). Unsere Ergebnisse zeigten eine substantielle Reliabilität (gewichtete Kappa-Werte zwischen 0.65 und 0.77) für alle MAP-Subskalen und für drei der vier einzelnen Items und eine moderate Reliabilität (gewichteter Kappa-Wert: 0.57) für das Item "Vermeidung von Überanstrengung". In Übereinstimmung mit unserer Hypothese korrelierte der deutsche MAP hoch mit dem Gesamtscore des Fragebogens zum Gesundheitszustand (Health Assessment Questionnaire: HAQ) und der physischen Komponente der Lebensqualität (SF36); moderat mit der Muskelausdauer gemessen mit dem funktionellen Index-2 und der Maximalkraft gemessen mit der Handdynamometrie und des MMT8; und schlecht mit der mentalen Komponente des SF36 und mit Schmerzen. Drei von vier Subskalen und zwei von vier einzelnen Items erreichten eine akzeptable diskriminierende Validität (area under the curve (AUC) zwischen 0.72 und 0.79). Die Subskala "persönliche Körperpflege und Hygiene" und die Items "soziale Aktivitäten" und "Vermeidung von Überanstrengung" zeigten keine akzeptable diskriminierende Validität (AUC-Werte zwischen 0.65 und 0.69). Obwohl der MAP eine gute Reliabilität und akzeptable Validität zeigte, gibt es einige Unsicherheiten bezüglich Struktur

und Auswertung dieses Fragebogens. Die Struktur des MAP sollte mit Hilfe einer Faktorenanalyse bestätigt werden, jedoch lag die erforderliche Stichprobengröße von vier bis zehn Fällen pro Item weit über unseren Möglichkeiten. Eine Besonderheit des Scorings ist, dass Patient*innen bei der Beantwortung der Fragen ihre Schwierigkeiten gegen ihre Bedürfnisse abwägen müssen. Es ist nicht bekannt, ob Patient*innen mehr Gewicht auf die Schwierigkeiten oder auf ihre Bedürfnisse legen, und deshalb wäre es wichtig, diesen Scoring-Ansatz weiter zu evaluieren.

In der nächsten Studie konzentrierten wir uns auf die Entwicklung einer Tablet-basierten Trainingsapplikation, einschließlich der Prüfung ihrer Benutzerfreundlichkeit und Akzeptanz durch die Endbenutzer sowie der Ergründung der Ansicht von Therapeut*innen zur Verwendung dieser Applikation (App) in einem klinischen Umfeld (**Kapitel 6: Usability and acceptance of an interactive tablet-based exercise application: a mixed methods study**). Die App besteht aus zwei verschiedenen Teilen: einem für die Therapeut*innen und einem für die Trainierenden. Im ersten Teil können die Therapeut*innen ein individuelles Trainingsprogramm für ihre Trainierenden zusammenstellen und die durchgeführten Übungen überwachen. Im zweiten Teil können die Trainierenden ihr Trainingsprogramm einsehen und die durchgeführten Übungen rapportieren. Die Benutzerfreundlichkeit der App wurde in zwei Phasen getestet; nach jeder Phase wurde die App aufgrund der Probleme und Kommentare der Teilnehmenden weiter verbessert. In beiden Phasen führten fünf Therapeut*innen und fünf Trainierende jeweils verschiedene vordefinierte Aufgaben aus und wurden eingeladen, ihre Gedanken während der Ausführung dieser Aufgaben zu verbalisieren. Die Effektivität, gemessen an der prozentualen Erfüllung der Aufgaben, verbesserte sich von 85% auf 93% für die Therapeut*innen und von 73% auf 90% für die Trainierenden von Phase eins zu Phase zwei. In beiden Phasen waren sowohl Therapeut*innen als auch Trainierende mit der App zufrieden (70,5-85,5/100). Auch die Akzeptanz gemessen mit dem Technologie Akzeptanz Modell war ausreichend mit (101 bis 120/140). Da die App nur dann im klinischen Alltag eingesetzt wird, wenn Therapeut*innen wirklich von ihren Vorteilen überzeugt sind, ist es wichtig, ihre Meinung zu der App zu ermitteln. Wir führten daher zwei Fokusgruppeninterviews durch; eines mit einer Gruppe von Leitenden und das andere mit einer Gruppe von Teammitgliedern. Im Allgemeinen hielten die Leitenden und die Teammitglieder die App für eine nützliche Therapieergänzung. Sie schätzten besonders den Blended

Charakter, also die Kombination von online Beratungen und persönlichem Kontakt dieser App. Dies wurde als wichtiges Unterscheidungsmerkmal zu anderen Fitness-Apps, denen eine "professionelle" Feedback-Funktion fehlt, genannt. Der Blended Therapie Ansatz verringerte auch ihre Angst, durch technische Anwendungen ersetzt zu werden. Die Therapeut*innen äußerten auch einige Bedenken hinsichtlich der Verwendung der App. Barrieren wurden in der Umsetzung in der Klinik (Datenschutz, Unsicherheiten bezüglich der Kostenübernahme) und in der persönlichen Einstellung der Therapeut*innen und Patient*innen gesehen - nicht alle Therapeut*innen und Patient*innen sind technikaffin.

Schließlich haben wir in der letzten Studie die Machbarkeit einer Blended-Therapie, bei der die App mit Face-to-Face-Physiotherapiesitzungen bei Patient*innen mit IM kombiniert wird, evaluiert. Zusätzlich haben wir potenzielle Auswirkungen dieser Intervention auf Muskelkraft, Muskelfunktion, Aktivitätseinschränkung, Behinderung und gesundheitsbezogene Lebensqualität untersucht. (**Kapitel 7: Feasibility of a blended therapy approach in patients with inflammatory myopathies**). Die Intervention bestand aus drei bis vier persönlichen (Face-to-Face) Therapiesitzungen (zwei Sitzungen zur Zusammenstellung und Instruktion des persönlichen Trainingsprogramms und ein bis zwei Folgesitzungen zur Überprüfung und Anpassung der bereits durchgeführten Übungen) und einem 12-wöchigen progressiven Krafttraining welches zu Hause mit Unterstützung der App durchgeführt wurde. Die individuell zugeschnittenen Trainingsprogramme basierten auf dem kürzlich veröffentlichten Trainingsleitfaden. Während des gesamten Trainings betreuten die Therapeut*innen ihre Patient*innen über Distanz, indem sie wöchentlich das Trainingstagebuch und den Trainingsfortschritt überprüften und bei Bedarf die Übungen anpassten und/oder kommentierten. Das Ergebnis dieser Studie zeigte, dass dieser kombinierte Therapieansatz machbar ist. Die Ausfallquote lag mit 7% unter der zuvor definierten Akzeptanzschwelle von 10% und die Adhärenz mit 84% über der angestrebten Adhärenz Rate von mindestens 80%. Darüber hinaus gab es eine hohe Akzeptanz und Zufriedenheit mit diesem Therapieansatz. Dennoch schlugen die Teilnehmenden einige Ideen zur Verbesserung der App vor, wie z.B. "Videos statt Fotos", "mehr Platz zum Schreiben von Nachrichten", "Zurück-Button (um zur vorherigen Übung zurückzukehren)", "ein einfaches Passwort für den Zugang zum Programm", "die Möglichkeit, das Programm auf das Mobiltelefon herunterzuladen" und "die Möglichkeit, zu überprüfen ob die

Übung korrekt durchgeführt wird (Video-Feedback)". In Bezug auf Muskelkraft und -funktion waren die Ergebnisse inkonsistent und zeigten mehrere Komplexitätsstufen. Der MMT8 und der Funktionsindex 2 zeigten hohe Deckeneffekte, was bedeutet, dass die Patient*innen bereits zu Beginn der Studie die höchstmögliche Punktzahl erreichten, so dass keine Möglichkeit bestand, eine Verbesserung festzustellen, selbst wenn die Patient*innen besser wurden. Die bei Patient*innen mit einer Adhärenz Rate von mindestens 80% gemessene isometrische Maximalkraft zeigte eine geringfügige Zunahme in sechs Muskelgruppen (Effektgrösse zwischen 0.04 und 0.42), aber eine Abnahme in zwei Muskelgruppen (Hüftabduktion und Hüftbeugung). Höhere Effektgrößen zeigten sich beim 30-Sekunden-Armhebe und Stuhlstand Test (Effektgrösse zwischen 0.52 und 0.88). Bei diesen Tests erhöhten die Teilnehmenden die Anzahl der durchgeführten Wiederholungen nach der Intervention um 1.5 bzw. 2.3 Wiederholungen. Alle drei PROMs, bei denen Aktivitätseinschränkung, Behinderung und gesundheitsbezogene Lebensqualität gemessen wurden, zeigten eine Tendenz zu besserer gesundheitsbezogener Lebensqualität, weniger Aktivitätseinschränkung und weniger Behinderung. Diese Tendenz zeigte sich trotz Bodeneffekten und Deckeneffekten in verschiedenen Subskalen des MAP (zur Beurteilung der Aktivitätseinschränkung) und des HAQ (zur Beurteilung der Behinderung). Zusammenfassend lässt sich sagen, dass sich dieser gemischte Therapieansatz unter Verwendung der neu entwickelten Tablet-basierten Trainingsapplikation als durchführbar erwiesen hat und dass das progressive Widerstandstraining einige positive Auswirkungen auf die Muskelleistung und die von den Patient*innen berichteten Ergebnisse zeigte. Darüber hinaus liefert die Studie Informationen, die bei der Auswahl geeigneter Assessments und der Festlegung der erforderlichen Stichprobengrößen in künftigen Studien nützlich sein könnten.

Impact paragraph

This thesis has generated new knowledge in the field of physical exercise training in patients with inflammatory myopathies (IM). In addition to the scientific value of this thesis, described in chapter 2-7, this section discusses the social and economic relevance of this work, identifies target groups for whom the results may be of interest, highlights innovation, and illustrates implementation and dissemination of our results.

Relevance

Physical activity and exercise has both preventive and curative effects on a number of different diseases such as diabetes, cancer (particularly breast and colon cancer), depression, dementia and cardiovascular disease (1). Furthermore, the scientific literature supports the idea that most physiologic systems are positively altered by physical activity and exercise, and thus exercise can be viewed as a medicine (2). This natural treatment enables the physiologic systems of the body to function optimally and therefore causes no side effects, as seen in traditional medicine (3). There is also evidence that exercise acts as an anti-inflammatory therapy (4, 5). As with other medications, the formulation and the dosage has to be prescribed individually for each patient. An instruction such as “you should exercise for your disease” is insufficient; the prescription must contain information about the frequency, type, intensity and duration of the exercise. According to the latest EULAR (European League Against Rheumatism) newsletter for health professionals in Rheumatology (Issue 7, 2020 spring), patients with rheumatic disease would like to be prescribed exercise as a natural medicine. They describe an unfulfilled need for advice on physical activity from their trusted healthcare professionals. On the other hand, healthcare professionals (doctors, nurses and physiotherapists) report not being confident in prescribing physical activity, due to lack in adequate knowledge. We made a similar experience in our daily practice with patients suffering from IM. Many of the patients we saw at our annual check-up were not advised and supported well enough with regards to their exercise training; they were simply told to “stay active and exercise” rather than getting clear recommendations and support. Especially in the field of rare diseases, keeping up to date with the relevant literature is a challenge for general practitioners. With this thesis, we provide two possibilities for patients with IM to get better support with their physical activities and exercise. On the one hand, there are published training guidelines which help the external therapists with giving relevant advice and supervising

their individual patients with this rare disease. On the other hand, the interactive exercise app provides specialized therapists with the possibility of giving patients remote advice and monitoring of their physical activity. In short, patients benefit from a training program that follows recognized training principles and is adapted to their individual (disease-related) needs. Physical activity and exercise is not only important as therapy, but also as prevention of secondary disease and potential disabilities. Thus, regular exercising may not only reduce the individual burden of the disease but may also decrease the consequential health care costs. Individually tailored promotion of the physical activity and exercise therefore makes an important contribution to public health.

Assessments are not only important for research, but also an essential part of evidence-based practice. Systematically measuring the effectiveness of therapeutic interventions provide an overview of the patient's progress and therefore provides a basis for adaption of the treatments procedure and possibly also a motivation for the patients. Only if we systematically record, evaluate and critically discuss our therapy results, we can prove the effectiveness of our therapies and continuously improve the quality of our treatment. This important process is only possible when valid and reliable assessments are available. Our results provide two reliable assessments for patient with IM, namely the Myositis Activity Profile and the hand-held dynamometer. Our work also demonstrated the limitations of the MMT. If muscle weakness is only measured by MMT, there is a risk that early or mild muscle weakness and moderate changes remain undetected.

Target groups

The results presented in this thesis are of interest to multiple target groups. The most important target group is people suffering from IM. While it is well accepted in popular and professional sports to take training theory into account and to adapt the training to individual needs and individual performance, it is often neglected in the therapy setting. However, the training principles need to be followed strictly in order to guarantee that the training dosage is balanced rather than under- or overdosed, which would be either a waste of time or a risk of overload for the patient. The disease-specific training recommendations given by the training guidelines described in this thesis may help the therapists in designing an efficient training program, which optimizes the chance of training success for the patients. In addition, this thesis offers a new therapy option which allows patients to exercise at

home, thereby saving time and reducing travel costs while still being supervised by a specialized therapist.

This work is also of interest for health care professionals, such as physical or occupational therapists and medical doctors. Firstly, it offers evidence-based exercise guidelines including a leaflet with the most important information about general training principles and disease-specific training recommendations for patients with IM. This leaflet can be used by medical doctors to prescribe specific exercise therapy and by therapist to compile an evidence-based, individually tailored exercise program for their patients. Secondly, our work offers new insights to outcome measurements. A validated disease-specific PROM is now also available for the German speaking countries. With this questionnaire, limitation of daily activities can be evaluated in the clinical practice. Moreover, this thesis motivates clinicians to focus not only on measuring maximum strength but also on muscle performance.

Our results may also be of interest for healthcare institutions such as hospitals, rehabilitation centers and private physiotherapy practices. Today, electronic support is an integral part of our everyday life and the digital revolution does not stop at the health care system. New technologies will influence the future of daily therapy routine, so health care institutions which deal with new technologies at an early stage will have a competitive advantage. This work therefore provides important information about the needs of patients and therapists and the conditions that must be met in order to apply new technologies in the clinical practice.

Finally, the results from the usability and feasibility studies about end-users perspectives of this exercise app and the blended therapy approach can be of interest for software designers. Such feedback is crucial for the development of effective, user-friendly and client-centered telerehabilitation (TR) solutions.

Innovation

This newly developed tablet-based exercise app and the blended therapy approach combining the use of this app with face-to-face physiotherapy sessions in patients with IM can be called innovative, as there has been no such approach for patients with IM until now. For some time now, TR has become increasingly important in the healthcare sector. Various sub-categories of TR, such as telephone counselling, online therapy via video telephony or the use of digital home programs (videos or documents that are transmitted to the patient electronically) has been evaluated. Except for the possibility of

monitoring patients per remote, the app provides detailed information about the performed training dosage and compares the performed training with the planned training prescription. It reveals whether the patients actually were able to carry out their planned training or whether they had to make adjustments to the described dosage. This particular comparison has not been possible until now, which renders this approach both valuable and innovative.

The app investigated in this thesis is part of a larger system. The goal of this system is to offer a holistic training concept, including endurance training, progressive resistance training and cognitive-motor training, which can be carried out on site or at home (with remote support). So far, the different parts have been evaluated separately, but in the future, these different parts will be put together. In this thesis we focused on RT, but future projects should combine the different training modalities.

Implementation and Dissemination

Some of the results in this thesis have already been implemented in the clinical practise at the USZ. Firstly, we adapted the assessments of the multi-professional consultation sessions for patients with IM: the older, not-validated translation of the MAP was replaced by our new validated version of the German MAP and to evaluate changes over time we now use the held-dynamometer. Secondly, we give the flyer with the training recommendations to all patients who receive physiotherapy externally. Thereby we ensure that the therapists and the patients are informed about the importance of an individually tailored exercise program and a recommended training dosage. Since some study patients wanted to continue training with the exercise app, we conducted a pilot project using the new software application in the clinical setting. Both therapists and patients appreciated this therapy option, but unfortunately this promising approach cannot be implemented for accounting reasons. In Switzerland, physiotherapy has to be prescribed by a medical doctor in order for the health insurance coverage to apply. TR is currently not included in the collective agreement and therefore, the health insurance companies do not reimburse the patients for any costs for TR.

Besides these promising experiences made with the blended therapy option, a number of other steps are crucial in order to make TR a recognized therapy offer that can be included in the collective agreement. The feasibility and acceptance of this approach has to be evaluated in other patient groups. Until now, similar feasibility studies have been performed in patients with haemophilia and in patients with End Stage Renal Disease. None of the data

from these two studies have been analysed yet. Another step would be to analyse the cost-efficiency of this approach. Such an investigation would be important for future negotiations with health insurances and people handling the collective agreements. Except for the cost-efficiency studies, clinical pilot projects in which the implementation and costs of TR are evaluated in the clinical setting are essential. A suitable target group for such implementation projects are lung transplantation patients. These patients are going through the surgery at the USZ, but they do not always live in the canton of Zurich. Since exercise training is strongly indicated after such an intervention, but their immunosuppression prevents them from training in a fitness center or a hospital, they are instructed to follow an exercise program in their homes. Many of these patients, however, do not manage to perform these exercise programs regularly, since they do not get enough support. The use of our developed exercise app could thus improve adherence to exercise programs for these patients.

The development of new technologies has increased markedly during the current Corona pandemic. This is not only seen in the office world with increased home office and video conferences, but also in the therapy setting. During the lockdown, treatment of patients on site was prohibited, so the only possibility of treating patients was per TR. During this limited period, the costs of TR were covered by the health insurance. Hopefully, this predominantly positive experience of TR will help boost its implementation, but the long-term effect of the pandemic on this development remains to be seen. Actually, everyone could benefit from TR: the patients by having a therapy option which they can perform comfortably at home and still have professional support, therapists by being able to regularly care for patients who live further away, healthcare institutions by being able to offer innovative therapies and not having to transfer patients to other institutions, and health insurance by providing better care for patients and thus preventing follow-up costs.

Based on the work of this thesis, we were unable to recommend one single assessment to evaluate muscle weakness. As we confirmed several known limitations of the MMT8, we strongly recommend critically discussing the inclusion of this assessment in the myositis core set measures. To foster such a discussion it is important to disseminate our results at national and international conferences and in scientific journals. There are several other

promising assessments for measuring muscle strength and muscle performance, but most of them have not been conclusively validated. To fill this knowledge gap regarding clinimetric properties of these outcome measures, further research is urgently warranted.

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About the author

Curriculum vitae

Pierrette Baschung Pfister was born on January 12, 1969 in Mümliswil, Switzerland. She obtained her senior high school diploma (Matura Typ D) in 1988 and studied physiotherapy at the school of physiotherapy in Leukerbad. After her graduation in 1993, she first worked as a clinical physiotherapist at a general hospital, and then continued at a private practice. Later on, she moved into a career as a team leader at a private hospital with an associated fitness center. Her main focus was musculoskeletal rehabilitation, in particular medical training therapy. During this time, she undertook many further education courses in the field of manual medicine and sport therapy and gained a certificate as a sports physical therapist at the International Academy for Sport Science in Zurzach. Working not only with patients, but also with healthy people, sparked her interest in disease prevention and health promotion. She therefore decided to continue her training, and in 2005 she awarded a Master degree in Public Health from the Universities of Zurich, Bern and Lausanne. During her master education, she became head therapist at the university hospital Zurich, where she also completed her master thesis with the title "Active over 45: a step-up jogging programme for inactive female hospital staff members aged 45+".

In 2010, she decided she needed to work with physiotherapy from a different perspective and changed her career path. She ended her management career and got a position as a scientific fellow at the Physiotherapy and Occupational Therapy Research Centre of the university hospital Zurich and at the Master of Science in physiotherapy at the University of Applied Science in Winterthur. In Winterthur, she was involved in the development of the new Master of Science in Physiotherapy program and was responsible for the scientific and leadership internships of master students. In addition, she was a lecturer in the Bachelor and the Master program and supervised students with their Bachelor and/or Master thesis. In her role as a research fellow at the university hospital, Ms Baschung was admitted as a PhD candidate at the Care and Public Health Research Institute (CAPHRI), Department of Epidemiology, Maastricht University (the Netherlands). With her thesis, she could combine two of her favourite topics: musculoskeletal diseases and physical exercise. During her time as a PhD student, she had the possibility to present her projects at the myositis conference in Washington, the annual European congress of Rheumatology in London, and in the context of an

educational visit at the Karolinska University Hospital in Stockholm. Since May 2020, Ms Baschung is part of the IMACS (International Myositis Assessment & Clinical Studies Group) Rehabilitation and Exercise SIG (Scientific Interest Group) Project “Development of international evidence-based consensus guidelines for exercise in patients with adult and juvenile idiopathic inflammatory myopathies”. Also, since January 2019, Ms Baschung has returned to work exclusively at the university hospital. In addition to her research position, she is responsible for professional leadership of physiotherapy and occupational therapy where she contributes with her combined experience of research and clinical work.

Memberships

ALUMNI ZHAW	Absolventinnen und Absolventen der ZHAW
IGPTR-B	Interessengemeinschaft Physiotherapie in der Rehabilitation, Bewegungsapparat
Physioswiss	Schweizer Physiotherapie Verband
Public Health Schweiz	The Swiss Society for Public Health
Verein hpr Schweiz	health professionals in rheumatology, Switzerland

Grants

2018 Forschungsfond Physioswiss, Sfr. 9'645.-

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2010 Swiss Foundation for Nutrition Research (SFEFS), Sfr. 10'800.-

Publications

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