

**DRIGINAL RESEARCH** 

# Effectiveness of physical training on physical performance in patients with dermatomyositis and polymyositis: systematic review and meta-analysis

Efetividade do treinamento físico sobre o desempenho físico em pacientes com dermatomiosite e polimiosite: revisão sistemática e metanálise

Eficacia del entrenamiento físico sobre el rendimiento físico en pacientes con dermatomiositis y polimiositis: una revisión sistemática y metaanálisis

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ABSTRACT | This study aimed to evaluate the impact of physical training on physical performance in patients with dermatomyositis and polymyositis. For this purpose, we conducted a systematic review and meta-analysis according to the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). The literature search was conducted in the following databases: PubMed/MEDLINE and Web of Science, using combinations of the following keywords in English: dermatomyositis OR polymyositis OR myositis AND exercise OR physical exercise OR physical therapy OR aerobic exercise OR endurance exercise OR resistance exercise. Studies that met the following criteria were included: (1) participants diagnosed with dermatomyositis or polymyositis; (2) patients that undergone a physical training protocol; (3) physical performance measured before and after the physical training protocol. A total of 14 articles were selected for inclusion in the systematic review and 10 articles were selected for inclusion in the meta-analysis. The outcomes demonstrate that physical training is effective in increasing overall physical performance in patients with dermatomyositis and polymyositis (effect size: 0.72; 95% CI 0.55; 0.89). Also, our study demonstrated that both the aerobic performance (effect size: 0.88; 95% CI 0.54; 1.21) and resistance performance variables (effect size: 0.64; CI 95% 0.43; 0.85) benefit from physical training in these patients. We concluded that physical training had a significant beneficial effect on the overall, aerobic and resistance physical performance in patients with dermatomyositis and polymyositis.

Keywords | Dermatomyositis; Exercise; Rehabilitation.

**RESUMO** | Este estudo teve por objetivo avaliar o impacto do treinamento físico sobre o desempenho físico em pacientes com dermatomiosite e polimiosite. Para tanto, uma revisão sistemática e metanálise foi conduzida de acordo com as diretrizes do PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). A pesquisa bibliográfica foi realizada nas seguintes bases de dados: PubMed/MEDLINE e Web of Science, utilizando combinações das seguintes palavras-chave em inglês: dermatomyositis OR polymyositis OR myositis AND exercise OR physical exercise OR physical therapy OR aerobic exercise OR endurance exercise OR resistance exercise. Foram incluídos estudos que atenderam aos seguintes critérios: (1) os participantes apresentavam diagnóstico de dermatomiosite ou polimiosite; (2) os pacientes foram submetidos a um protocolo de treinamento físico; (3) o desempenho físico foi mensurado antes e após o protocolo de treinamento físico. Um total de 14 artigos foram

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selecionados para inclusão na revisão sistemática e 10 artigos foram selecionados para inclusão na metanálise. Os resultados demonstram que o treinamento físico é eficaz em aumentar o desempenho físico global nos pacientes com dermatomiosite e polimiosite (tamanho do efeito: 0,72; IC 95% 0,55; 0,89). Além disso, foi demonstrado também que tanto as variáveis de desempenho aeróbio (tamanho do efeito: 0,88; IC 95% 0,54; 1,21), quanto as variáveis de desempenho resistido (tamanho do efeito: 0,64; IC 95% 0,43; 0,85) são beneficiadas com o treinamento físico nesses pacientes. Conclui-se que o treinamento físico apresentou um efeito benéfico significativo sobre o desempenho físico global, aeróbio e resistido em pacientes com dermatomiosite e polimiosite.

Descritores | Dermatomiosite; Exercício; Reabilitação.

**RESUMEN |** Este estudio tuvo como objetivo evaluar el impacto del entrenamiento físico sobre el rendimiento físico en pacientes con dermatomiositis y polimiositis. Para ello, se realizó una revisión sistemática y metaanálisis siguiendo las guías PRISMA (*Preferred Reporting Items for Systematic Reviews and Meta-Analyses*). Se hizo una búsqueda bibliográfica en las siguientes bases de datos: PubMed/MEDLINE y Web of Science, utilizando las siguientes palabras clave combinadas en inglés: dermatomyositis OR polymyositis OR myositis AND exercise OR physical exercise OR physical therapy OR aerobic exercise OR endurance exercise OR resistance exercise. Se incluyeron los estudios que cumplieron los siguientes criterios: (1) los participantes tenían un diagnóstico de dermatomiositis o polimiositis; (2) los pacientes se sometieron a un protocolo de entrenamiento físico; y (3) el rendimiento físico se midió antes y después del protocolo de entrenamiento físico. Al total se seleccionaron 14 artículos para incluir en la revisión sistemática y 10 artículos en el metaanálisis. Los resultados demuestran que el entrenamiento físico es eficaz para aumentar el rendimiento físico general en pacientes con dermatomiositis y polimiositis (tamaño del efecto: 0,72; IC 95% 0,55; 0,89). Además, tanto las variables de rendimiento aeróbico (tamaño del efecto: 0,88; IC 95% 0,54; 1.21) como las variables de rendimiento de resistencia (tamaño del efecto: 0,64; IC 95% 0,43; 0,85) mejoraron con la actividad física en estos pacientes. Se concluye que el entrenamiento físico tuvo un efecto significativo sobre el rendimiento físico global, aeróbico y de resistencia en pacientes con dermatomiositis y polimiositis. Palabras clave | Dermatomiositis; Ejercicio; Rehabilitación.

#### INTRODUCTION

Systemic autoimmune myopathies are a rare and heterogeneous group of diseases that share common characteristics, such as involvement of the striated musculature, which can involve the cardiopulmonary, gastrointestinal, and integumentary system, besides being an autoimmune and chronic condition. They can be classified clinically into several subtypes that are differentiated by their clinical, laboratory, and histological characteristics and physiopathogenesis<sup>1-3</sup>.

Dermatomyositis (DM) and polymyositis (PM) are included in this group, being associated with immunological disorders and genetic predisposition, besides being triggered by factors, such as malignancy, drugs, and infectious agents<sup>4</sup>. In an initial classification, they were subdivided into juvenile DM or PM, associated with neoplasia and other connective tissue disease<sup>5,6</sup>. Later, in 1996, the amyopathic form was added to the subtypes of dermatomyositis<sup>7</sup>. The incidence of these diseases is estimated at less than 10 new cases per million people, and the prevalence of 10 to 60 cases per million. Dermatomyositis presents two peaks of onset of symptoms, between five and 15 years-old, and 45 and 65 years-old, with females being the most affected in a ratio of  $2:1^3$ .

DM and PM are characterized by systemic manifestations, such as proximal, symmetric, and progressive muscle weakness, usually starting from the cervical spine and scapular, and pelvic girdles. Dysphagia, arthralgia, pulmonary and cardiac involvement, and weight loss are symptoms that affected individuals can present. Dermatomyositis differs from polymyositis because it presents cutaneous involvement, vasculitis, and calcinosis. Gottron's papules and/or Gottron's sign, heliotrope, and poikiloderma in a V-shaped distribution, flaking, fissures, keratosis, and symmetrical hyperpigmentation on palmoplantar regions, commonly aggravated in photoexposed areas, are exclusive manifestations of DM<sup>1,4</sup>.

The diagnosis of both diseases is based on the clinical picture, laboratory tests, and muscle biopsy<sup>8</sup>. Magnetic resonance imaging and electroneuromyography can be used as complementary tests<sup>9,10</sup>. Accurate identification and early multi-professional intervention result in a better prognosis and decrease the probability of progression. Drug treatment consists of the administration of corticosteroids and different types of immunosuppressive therapies, however, the deficit in functional capacity remains.

Thus, analyzing the physical capacity of patients and the types and effects of recommended physical exercises is necessary<sup>3,8,11</sup>.

For a long time, physical exercise was contraindicated and even prohibited for these patients because physical activity was thought to increase the inflammatory process in the affected muscles and aggravate the disease<sup>2,12</sup>. In 1993, the first report of the benefits of physical exercise in this population emerged. Since then, several studies showed the efficacy and safety of physical exercise, which can generate anti-inflammatory effects, in addition to improve muscle performance and aerobic capacity, thus optimizing the health and reducing the inability of patients and the risk of side effects caused by glucocorticoid treatment<sup>1,13,14</sup>.

Pieces of evidence indicate that physical training is essential at all stages of the disease because it improves muscles strength, joint stiffness, grip strength, hypotrophy, loss of resistance, postural deviations, quality of life, and reduces pain and cognitive impact<sup>14,15</sup>. Therefore, our systematic review and meta-analysis aimed to evaluate the impact of physical training on physical performance in patients with dermatomyositis and polymyositis.

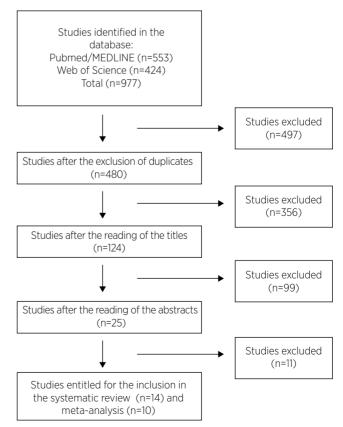
## METHODOLOGY

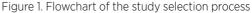
#### **Research Strategy**

In this study, systematic review and meta-analysis were performed based on bibliographic research in the databases available in PubMed/MEDLINE and Web of Science, using combinations of the following keywords in English: dermatomyositis OR polymyositis OR myositis AND exercise OR physical exercise OR physical therapy OR aerobic exercise OR endurance exercise OR exercise OR resistance exercise. Also, a manual search in the references of the studies included in our study was performed. The bibliographic research was conducted in November 2020, with no restrictions regarding the language or year of publication. The systematic review and meta-analysis were conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines <sup>16</sup>.

#### Selection of the studies

The selection of studies was performed by two independent researchers, according to the following steps: (1) exclusion of duplicates; (2) reading of titles; (3) reading of abstracts; and (4) reading of full-text studies. Different evaluations were solved through discussion with a third researcher. Studies that met the following criteria were included in the systematic review: (1) participants diagnosed with dermatomyositis or polymyositis; (2) patients that undergone a physical training protocol; (3) physical performance measured before and after the physical training protocol. Reviews, expert opinions, and case studies were not included. Based on these inclusion/exclusion criteria, a total of 14 studies were selected for inclusion in the systematic review (Figure 1) (one of which performed the rehabilitation process at two different times, therefore, 15 trials are presented). Studies that did not present their data in mean ± standard deviation were excluded from the meta-analysis. Thus, 10 articles were included in the meta-analysis (Figure 1). Several studies analyzed more than one variable of physical performance, therefore, the number of trials (34) was higher than the number of studies (10) in the meta-analysis. A grouping of variables was performed to evaluate the effect of physical training, specifically on variables of aerobic physical performance (15 trials) and resistance (19 trials).





# **Data collection**

The following information was extracted from the studies: author and year of the study; n sample; average age; physical training protocol (type of exercise, duration of the protocol, weekly frequency, session time); the test used to assess the performance; the performance variables measured; and the outcomes.

# Evaluation of methodological quality

The methodological quality of the studies was evaluated by two independent researchers using a scale adapted from the grading of recommendations assessment, development, and evaluation (GRADE)<sup>17</sup>. Different evaluations were solved through discussion with a third researcher. The domains evaluated were: absence of allocation secrecy; absence of masking; incomplete follow-up; selective reporting of outcomes; and other limitations. After this evaluation, the quality of the studies was classified according to the number of negative responses: high quality (5 no); moderate quality (4 no); low quality (3 no); and very low quality (1 or 2 no).

## Statistical analysis

The mean and standard deviation values of the performance variables were obtained from the data provided in the selected studies. Data heterogeneity was evaluated using the  $\chi 2$  test for homogeneity and statistics i<sup>2</sup>. For the meta-analysis, the effect size was estimated for all physical

performance variables. A weighted average estimate of the effect size was calculated to consider differences in the sample size. The size of the non-weighted average effect was also estimated and associated with a 95% confidence interval. Cohen's classification was used to evaluate the magnitude of the effect size, where d<0.20 indicates negligible effect; d=0.20-0.49, small effect; d=0.50-0.79, moderate effect; and d>0.8, large effect<sup>18</sup>.

# RESULTS

## Systematic review

A total of 977 studies were identified in the consulted databases. After excluding duplicates and studies that were not in accordance with the eligibility criteria, we read the titles, abstracts, and full-text studies, resulting in 14 studies (145 patients) selected for inclusion in the systematic review and 10 studies (34 trials, 100 patients) selected for inclusion in the meta-analysis (Figure 1).

Table 1 shows the characteristics of the sample, the physical training protocol, the performed test, the variables analyzed, and the outcomes. We highlight that 57.1% (8/14) of the studies used concurrent physical training (aerobic exercise associated with resistance training); 21.4% (3/14), aerobic training; and 21.4% (3/14), resistance training. Most studies (69.2%) performed 12-weeks of physical training, with weekly training frequency ranging from 2 to 5 days and session duration ranging from 40 to 60 minutes (Table 1).

Table 1. Characterization of the studies included in the systematic review

			Physical training						
Reference	n	Age	Type of exercise	Duration (weeks)	Weekly frequency (×/week)	Session time (min)	Test	Characteristic	Outcome
Alemo- Munters et al., 2013 <sup>19</sup>	9	60 (48-72)	5-min warm-up (cycling at 50% of VO <sub>2max</sub> ) 30-min cycling (70% of	12	3	60	Cycling test until exhaustion	Exercise duration (min)	Pre: 15.4+5.1 Post: 33.7+13.3
			VO <sub>2max</sub> ) 20-min resistance exercise (30-40% 1 RM) Relaxation and stretching				Submaximal cycling until exhaustion – 65% of VO <sub>2max</sub>	VO <sub>2max</sub> (1.min <sup>-1</sup> )	Pre: 1.63±0.30 Post: 1.91±0.30*
Alemo- Munters et al., 2013 <sup>20</sup>	11	62	30-min cycling (70% of VO <sub>2max</sub> ) 20-min resistance exercise (30-40% 1 RM)	12	3	60	Cycling test until exhaustion	VO <sub>2max</sub> (I.min <sup>-1</sup> )	Pre: 1.41±0.47 Post: 1.59±0.55
							5 max repetitions	Knee extensors – load (kg)	Pre: 9.5±7.6 Post: 13.2±8.7
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(continues)

# Table 1. Continuation

		Phy	sical trainin	g					
Reference	n	Age	Type of exercise	Duration (weeks)	Weekly frequency (×/week)	Session time (min)	Test	Characteristic	Outcome
Alemo- Munters et al., 2016 <sup>21</sup>	7		30-min cycling (70% of VO <sub>2max</sub> ) 20-min resistance exercise (30-40% 1 RM)	12	3	60	Cycling test until exhaustion	VO <sub>2max</sub> (I.min <sup>-1</sup> )	Pre: 1.54±0.43 Post: 1.69±0.46
							Submaximal cycling until exhaustion – 65% of VO <sub>2max</sub>	Exercise duration (min)	Pre: 14.6±7.3 Post: 32.6±15.4
Alexanderson, Stenstrom, Lundberg, 1999 <sup>22</sup>	10	53	Warm-up 15-min resistance exercise 15-min walking	12	5	30	7-min submaximal walking	Distance (m)	Pre: 312 Post: 404*
Alexanderson et al., 2007 <sup>23</sup>	8	53	10-min warm-up – cycling (50% of FC <sub>max</sub> ) 45-min resistance	7	3	45	10-15 max repetitions	Right deltoid muscle – load (kg)	Pre: 4.7±3.1 Post: 6.9±4.0*
			exercise (10 RM) 5-min stretching					Right quadriceps muscle – load (kg)	Pre:13.1±2.9 Post: 18.9±5.7*
								Latissimus dorsi muscle – load (kg)	Pre:53.1±16.0 Post: 57.5±30.6
								Gastrocnemius muscle – load (kg)	Pre: 103.8±19.8 Post: 138.7±26.7
								Abdominal muscles – load (kg)	Pre: 0.6±1.7 Post: 1.2±1.6
Habers et al., 2016 <sup>24</sup>	14	12.6 (8.7-17.6)	Interval exercise – treadmill running (65- 90% FC <sub>peak)</sub>	12	3	40-60	Progressive test on the treadmill until exhaustion	VO <sub>2max</sub> (ml.kg <sup>-1</sup> . min <sup>-1</sup> )	Pre: 38.6 Post: 38.6
			Resistance exercise				Progressive test on the treadmill until exhaustion	Exercise duration (min)	Pre: 11.9 Post: 11.8
							6-min walking test	Distance (m)	Pre: 559 Post: 561
							Dynamometry	lsometric force – Knee extensors D (N)	Pre: 255 Post: 286
							Dynamometry	Isometric force – hip extensors D (N)	Pre: 225 Post: 221
Mattar et al., 2014 <sup>25</sup>	13	45.6±8.8	Low-intensity resistance exercise combined	12	2	25-30	1 RM	Leg press – load	Increase of 19.6% *
			with partial blood flow restriction (30% 1 RM)				1 RM	Knee extenders - Load	Increase of 25.2% <sup>*</sup>
							Sit-to-stand test	Repetitions	Increase of 15%*
							Timed get up and go test	Duration (sec)	Reduction of 4.5%*
Nader et al., 2010 <sup>26</sup>	8	51 (44-61)	Resistance exercise (10 RM)	7	3		Progressive test until exhaustion	VO <sub>2max</sub> (ml.min <sup>-1.</sup> kg <sup>-1</sup> )	Pre: 26±3 Post: 31±3*

(continues)

#### Table 1. Continuation

		Phy	sical trainin	ig					
Reference	n	Age	Type of exercise	Duration (weeks)	Weekly frequency (×/week)	Session time (min)	Test	Characteristic	Outcome
Oliveira et al., 2019 <sup>27</sup>	9	46.7±7.8	Resistance exercise 5-min warm-up 30-50-min walking/	12	2	Not reported	Progressive test on the treadmill until exhaustion	VO <sub>2max</sub> (ml.min <sup>-1.</sup> kg <sup>-1</sup> )	Pre: 18.5±4.1 Post: 20.9±5.2
			running 5-min relaxation				Progressive test on the treadmill until exhaustion	Time until exhaustion (min)	Pre: 10.6±2.1 Post: 13.2±1.8
							Timed get up and go test	Duration (sec)	Pre: 7.3±1.1 Post: 6.7±1.1
							30-sec sit-to- stand test	Repetitions	Pre: 13.9±2.8 Post: 16.0±3.7
							1 RM	Leg-press – Load (kg)	Pre: 71.7±14.8 Post: 82.9±14.0
							1 RM	Supine – Load (kg)	Pre: 28.6±9.6 Post: 32.3±10.5
Omori et al., 2012 <sup>28</sup>	10	12±3.2	5-min warm-up on the treadmill 20-min resistance	12	2	60	Progressive test on the treadmill until exhaustion	$VO_{2peak}$	Increase of 13.3%*
			exercise 30-min treadmill running.				Progressive test on the treadmill until exhaustion	Exercise duration	Increase of 18.2%*
		5-min stretching				Timed get up and go test	Duration (sec)	Reduction of 10.3%*	
							1 RM	Leg-press – Load (kg)	Increase of 22%*
							1 RM	Supine – Load (kg)	Increase of 17.4%*
							1 RM	Handgrip – Load (kg)	Increase of 15.3%*
Riisager et al., 2013 <sup>29</sup>	10	16-42	Cycl ergometer (65% of VO <sub>2max</sub> )	12	3-4	40	Progressive test until exhaustion – cycling	VO <sub>2max</sub> (ml.kg <sup>-1</sup> . min <sup>-1</sup> )	Pre: 22.7 ± 4.1 Post: 28.6±6,3
							Progressive test until exhaustion – cycling	Maximum work (W)	Pre: 125±37.9 Post: 162±50.5
							6-min walking test	Distance (m)	Pre: 622±107 Post: 657±110
Varjú et al., 2003 (1) <sup>30</sup>	10	50.6±14.2	Early recovery Resistance exercise Isotonic muscle training	3	5	40-60	Dynamometry	Knee extensors – Muscular strength (N)	Pre: 168±47 Post: 179±52
			Respiratory training					Shoulder abductors - Muscular strength (N)	Pre: 48±31 Post: 61±34*
								Elbow flexors - Muscular strength (N)	Pre: 85±56 Post: 99±43
								Hand flexors - Muscular strength (N)	Pre: 144±45 Post: 181±64

(continues)

			Phy	sical trainin	g					
Reference	n	Age	Type of exercise	Duration (weeks)	Weekly frequency (×/week)	Session time (min)	Test	Characteristic	Outcome	
Varjú et al., 11 44.1±14.6 2003 (2) <sup>30</sup>	11	44.1±14.6	Chronic recovery Resistance exercise Isotonic muscle training	3	5	40-60	Dynamometry	Knee extensors – Muscular strength (N)	Pre: 141±48 Post: 188±41*	
			Respiratory training					Shoulder abductors - Muscular strength (N)	Pre: 53±26 Post: 81±30*	
							Elbow flexors – Muscular strength (N)	Pre: 77±20 Post: 118±44		
							Hand flexors - Muscular strength (N)	Pre: 142±62 Post: 169±75*		
Wiesinger et al., 1998 <sup>31</sup>	8	8 47	47 Warm-up Cycling and step (60% of FC) Relaxation and stretching Indoor Walking (3h/ week)	24	1-4	60	Progressive test on cycle ergometer	VO <sub>2peak</sub> (ml/min/kg)	Pre: 17.5±3.3 Post: 22.3±6*	
							Progressive test on cycle ergometer	Exercise duration (min)	Pre: 377±130* Post: 536±152*	
							lsokinetic dynamometry	lsometric torque peak (Nm)	Pre: 530.2±295.1 Post: 712.1±364.2*	
Wiesinger et al., 1998 <sup>32</sup>	7	56 (44-68)	Warm-up Cycling and step (60% of FC)	6	2-3	60	Progressive test on cycle ergometer	VO <sub>2max</sub> (ml/min/kg)	Pre: 17.4±2.6* Post: 22,5±2.6*	
			Relaxation and stretching				lsokinetic dynamometry	lsometric torque peak (Nm)	Pre: 633.1±260 Post: 819.2±277.9*	

#### Table 1. Continuation

\*: It indicates statistical difference between post vs. pre exercise.

#### **Meta-analysis**

A total of 10 studies (34 trials and 100 patients) were included in the meta-analysis.

After gathering data from the 34 trials (100 patients), the average effect size was 0.72 (95% CI 0.55; 0.89), indicating that physical training had a moderate and significant beneficial effect on the physical performance of patients with dermatomyositis and polymyositis (p<0.05). We did not observe heterogeneity among the studies ( $i^2=6.9\%$ ; Q=35.43, df=33; p=0.354) (Figure 2).

Performing the grouping of aerobic performance variables (15 trials, 69 individuals) the mean effect size

was 0.88 (95% CI 0.54; 1.21), indicating that physical training had a large and significant beneficial effect on the aerobic physical performance of patients with dermatomyositis and polymyositis (p<0.05). We did not observe heterogeneity among the studies (i<sup>2</sup>=38.2%; Q=22.64, df=14; p=0.066) (Figure 3).

Performing the grouping of the variables of resistance performance (19 trials, 66 patients), the mean effect size was 0.64 (95% CI 0.43; 0.85), indicating that physical training presented a moderate and significant beneficial effect on the physical resistance performance of patients with dermatomyositis and polymyositis (p<0.05). We did not observe heterogeneity among the studies ( $i^2=0.0\%$ ; Q=11.47, df=18; p=0.873) (Figure 4).

Study		SMD (95% CI)	Weight %
Alemo-Munters, 2013a (1)	•	1.82 (0.70; 2.93)	2.19
Alemo-Munters, 2013a (2)		0.93 ( -0.05; 1.91)	2.81
Alemo-Munters, 2013b (1)		0.35 ( -0.49; 1.19)	3.71
Alemo-Munters, 2013b (2)		0.45 ( -0.39; 1.30)	3.67
Alemo-Munters, 2016 (1)		0.34 (-0.72; 1.39)	2.44
Alemo-Munters, 2016 (2)		1.49 (0.29; 2.70)	1.89
Alexanderson, 2007 (1)		0.61 ( -0.28; 1.51)	3.29
Alexanderson, 2007 (2)		1.28 (0.31; 2.25)	2.85
Alexanderson, 2007 (3)		0.18 ( -0.70; 1.60)	3.43
Alexanderson, 2007 (4)		1.48 (0.48; 2.49)	2.69
Alexanderson, 2007 (5)		0.36 ( -0.52; 1.25)	3.39
Nader, 2010		1.67 (0.51; 2.82)	2.05
Oliveira, 2019 (1)		0.51 (-0.43; 1.45)	3.03
Oliveira, 2019 (2)		1.33 (0.30; 2.36)	2.54
Oliveira, 2019 (3)		-0.54 ( -1.49; 0.40)	3.01
Oliveira, 2019 (4)		0.64 (-0.31; 1.59)	2.97
Oliveira, 2019 (5)		0.78 (-0.18; 1.74)	2.9
Oliveira, 2019 (6)		0.37 (-0.56; 1.30)	3.07
Riisager, 2013 (1)		1.11 (0.16; 2.06)	2.98
Riisager, 2013 (2)		0.83 (-0.09; 1.75)	3.17
Riisager, 2013 (3)		0.32 (-0.56; 1.20)	3.4
Varjú, 2003 (1)		0.22 (-0.66; 1.10)	3.43
Varjú, 2003 (2)		0.40 (-0.49; 1.29)	3.38
Varjú, 2003 (4)		0.28 (-0.60; 1.16)	3.41
Varjú, 2003 (4)		0.67 (-0.23; 1.57)	3.26
Varjú, 2003 (5)		- 1.05 (0.16; 1.95)	3.3
Varjú, 2003 (6)		1.00 (0.11; 1.89)	3.35
Varjú, 2003 (7)		1.20 (0.28; 2.11)	3.19
Varjú, 2003 (8)		0.39 (-0.45; 1.24)	3.69
Wiesinger, 1998a (1)		- 0.99 (-0.05; 2.04)	2.48
Wiesinger, 1998a (2)		1.12 (0.06; 2.19)	2.4
Wiesinger, 1998a (3)		0.55 (-0.45; 1.55)	2.7
Wiesinger, 1998b (1)		1.96 (0.65; 3.27)	1.62
		0.69 (-0.39; 1.77)	2.32
Wiesinger, 1998b (2)			

Figure 2. Forest plot of the effect of physical training on physical performance in patients with dermatomyositis and polymyositis SMD: standardized mean difference.

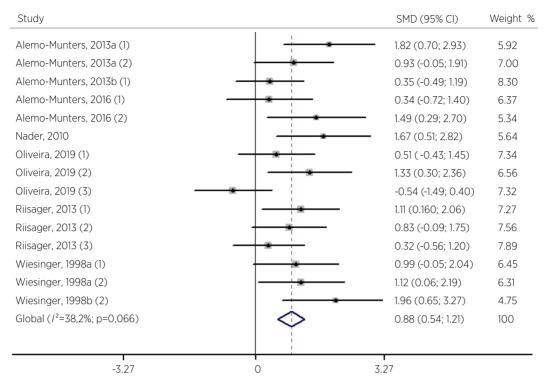


Figure 3. Forest plot of the effect of physical training on physical performance in patients with dermatomyositis and polymyositis SMD: standardized mean difference.

Study		SMD (95% CI)	Weight %
Alemo-Munters, 2013b (2)		0.45 (-0.39; 1.30)	6.15
Alexanderson, 2007 (1)		0.61 (-0.28; 1.51)	5.47
Alexanderson, 2007 (2)		1.28 (0.31; 2.25)	4.68
Alexanderson, 2007 (3)	<b>_</b>	0.18 (-0.70; 1.06)	5.73
Alexanderson, 2007 (4)		1.48 (0.48; 2.49)	4.40
Alexanderson, 2007 (5)		0.36 (-0.52; 1.25)	5.65
Oliveira, 2019 (4)		0.64 (-0.31; 1.59)	4.90
Oliveira, 2019 (5)		0.78 (-0.18; 1.74)	4.77
Oliveira, 2019 (6)		0.37 (-0.56 1.30)	5.08
Varjú, 2003 (1)	<b>_</b>	0.22 (-0.66; 1.10)	5.71
Varjú, 2003 (2)		0.40 (-0.49; 1.29)	5.63
Varjú, 2003 (3)		0.28 (-0.60; 1.16)	5.69
Varjú, 2003 (4)		0.67 (-0.23; 1.57)	5.42
Varjú, 2003 (5)		- 1.05 (0.16; 1.95)	5.49
Varjú, 2003 (6)		- 0.10 (0.11; 1.89)	5.57
Varjú, 2003 (7)		1.20 (0.28; 2.11)	5.28
Varjú, 2003 (8)		0.39 (-0.45; 1.24)	6.20
Wiesinger, 1998a (3)		0.55 (-0.45; 1.55)	4.41
Wiesinger, 1998b (2)		- 0.69 (-0.39; 1.77)	3.76
Overall (l <sup>2</sup> =0.0%; p=0.873)		0.64 (0.43; 0.85)	100
-2.49	0	2.49	

Figure 4. Forest plot of the effect of physical training on physical performance in patients with dermatomyositis and polymyositis SMD: standardized mean difference.

# Evaluation of methodological quality

The evaluation of methodological quality presented 42.8% (6) of the studies with high methodological quality. Whereas another 42.8% (6) studies were

classified as low quality and 14.3% (2) as very low quality. The quality of the studies was mainly affected by the absence of confidentiality of allocation (randomization) and the absence of masking (doubleblind) (Supplementary Table 1).

C	. Evaluation of the methodological	and a lite of a fiber of the	

Reference	Absence of allocation secrecy	Absence of masking	Incomplete follow-up	Selective reporting of outcomes	Other limitation	Quality
Alemo-Munters et al., 2013 <sup>19</sup>	No	No	No	No	No	High
Alemo-Munters, 2013 <sup>20</sup>	No	No	No	No	No	High
Alemo-Munters et al., 2016 <sup>21</sup>	No	No	No	No	No	High
Alexanderson, 1999 <sup>22</sup>	Yes	Yes	Yes	No	No	Very low
Alexanderson, 2007 <sup>23</sup>	Yes	Yes	No	No	No	Low
Habers, 2016 <sup>24</sup>	No	No	No	No	No	Low
Mattar et al., 2014 <sup>25</sup>	Yes	Yes	No	No	No	Low
Nader et al., 2010 <sup>26</sup>	No	No	No	No	No	High
Oliveira, 2019 <sup>27</sup>	Yes	Yes	No	No	No	Low
Omori et al., 2012 <sup>28</sup>	Yes	Yes	No	No	No	Low
Riisager et al., 2013 <sup>29</sup>	Yes	Yes	Yes	No	No	Very low
Varjú et al., 2003 (1) <sup>30</sup>	Yes	Yes	No	No	No	Low
Wiesinger et al., 1998 <sup>31</sup>	No	No	No	No	No	High
Wiesinger et al., 1998 <sup>32</sup>	No	No	No	No	No	High

#### DISCUSSION

This systematic review and meta-analysis aimed to evaluate the effect of physical training on physical performance in patients with dermatomyositis and polymyositis. Our study demonstrated that physical training is effective to increase overall physical performance in these patients (effect size: 0.72 Moreover, it also demonstrated that both aerobic performance variables (effect size: 0.88) and resistance performance variables (effect size: 0.64) benefit from patients' physical training. These outcomes corroborate the pieces of evidence that recommend physical training to patients as an essential component for the treatment program, reinforcing, with scientific evidence, that regular and structured physical exercise results in functional benefits for health promotion and non-drug treatment of rheumatologic diseases<sup>1,19,22</sup>.

Patients with dermatomyositis and polymyositis present inflammatory signs in the skeletal muscle, reduction of maximum oxygen consumption, high levels of blood lactate, and reduction in the proportion of type I muscle fibers, which may result in impairments in oxidative muscle metabolism and be related to the reduction of aerobic capacity and generation of muscle strength<sup>19,31</sup>. Several pieces of evidence indicate that the prescription of physical training (aerobic training, resistance training, or combined resistance-aerobic training) for patients with dermatomyositis and polymyositis is safe and effective in maximizing aerobic capacity, muscle strength, and quality of life. Thus, we suggest the use of physical training in order to complement pharmacological treatment in all stages of diseases<sup>1,25,30,33</sup>. The outcomes of our study corroborate and reinforce the indication of combined physical training (aerobic exercise associated with resistance exercise) for patients with dermatomyositis and polymyositis. In this systematic review, we found several benefits of physical training on physical performance in patients with dermatomyositis and polymyositis, such as an increase in exercise time, maximum oxygen consumption, travelled distance in a time trial running protocol, of the load in resistance exercises, and isometric strength<sup>13,14,19,20,25,29-31</sup>.

Pieces of evidence show that 12 weeks of resistance training caused a general clinical improvement in patients, in addition to greatly improving resistance exercise

performance, and aerobic capacity<sup>19</sup>. Wiesinger et al.<sup>32</sup>, after performing a 6-week program of strength exercises and 1-hour of stationary cycling in fourteen patients (treatment and control groups), reported, in addition to the improvement of aerobic capacity, an increase in strength measured by the isometric torque peak. Some hypotheses for the observed improvement of resistance and aerobic capacity are decrease in lactate levels, increase in VO<sub>2max</sub>, power in VO<sub>2max</sub>, and the activity of mitochondrial enzymes, such as citrate synthase, and 3-hydroxyacyl CoA dehydrogenase measured in biopsies to evaluate skeletal muscle mitochondrial function<sup>19,20</sup>. Similarly, Nader et al.<sup>26</sup> observed an increase in VO<sub>2max</sub> associated with exercise and, when analyzing the molecular profile, they found a subset of transcripts that were associated with a change towards oxidative metabolism.

Other pieces of evidence show that physical training can improve respiratory function and indicate safety and usefulness in starting it 2 to 3 weeks after an acute exacerbation of the disease, without the danger of exacerbation of it<sup>30</sup>. Several studies also showed improvements in muscle strength and the prevention of muscle atrophy due to inactivity, which reduces the level of disability<sup>25,28,30</sup>. In addition, a study demonstrated the influence of physical training on metabolic alterations since it led to an attenuation of insulin resistance and improvements in the parameters of  $\beta$  pancreatic cells<sup>27</sup>.

Since dermatomyositis and polymyositis diseases are characterized by weakness, infiltrations by mononuclear inflammatory cells, and fibrosis, another important fact observed was the reduction of inflammatory and fibrotic activity through marked reductions in the expression of pro-inflammatory and profibrotic genes, in addition to a reduction in tissue fibrosis<sup>22,26</sup>. Nader et al.<sup>26</sup>, when performing a molecular analysis, they found a reduction in the expression of genes that are involved in the activation and regulation of T cells, or those involved in the activation of macrophages/ monocytes. Moreover, some anti-inflammatory genes were positively regulated, as well as the FOXP3, a regulatory T cell marker. Similarly, Alemo-Munters et al.<sup>21</sup> demonstrated a molecular profile of suppression of the inflammatory response.

Despite the benefits demonstrated by physical training in patients with dermatomyositis and polymyositis, our study presents some limitations, such as: reduced number of randomized controlled studies with a large and diversified sample, great variability of training protocols and performance variables analyzed, and approximately 60% of the studies presented low and very low methodological quality, absence of confidentiality of allocation, and masking. We also mention the small sample number, due to the low prevalence of the disease. Thus, to improve the level of evidence in this field, we suggest that randomized controlled studies with double-blind evaluation, an application of standardized protocols, and a larger sample number be performed.

#### CONCLUSION

Considering the outcomes of this systematic review and meta-analysis, we can prove that physical training presented a significant beneficial effect on the resistance, aerobic and general physical performance of patients with dermatomyositis and polymyositis. Most studies performed 12 weeks of physical training, combining aerobic exercises with resistance exercises, being effective in several aspects of the patients' treatment. We considered important to implement a physical exercise program as a form of non-pharmacological treatment due to the preventive and treatment potential for this population, always paying attention to the appropriate recommendations.

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