Resistive Home Exercise in Patients with Recent-onset Polymyositis and Dermatomyositis — A Randomized Controlled Single-blinded Study with a 2-year Followup

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ABSTRACT. ***Objective.*** To evaluate the outcome of resistive home exercise and its possible longterm influence on health, disability, and disease activity in patients with active polymyositis (PM) or dermatomyositis (DM).

Methods. Nineteen patients with recent-onset PM/DM were included after introduction of high-dose prednisolone. They were assessed by independent assessors as to perceived health, muscle performance, aerobic capacity, and serum creatine phosphokinase (CPK) at baseline and after 24 weeks, including repeated muscle biopsies at 24 weeks (single-blinded randomized controlled study), and in an open-label followup at 52, 78, and 104 weeks. Patients were randomized to 12 weeks, 5 days/week resistive home exercise with telephone support and encouragement for another 12 weeks of twice-a-week home or gym exercise (EG, n = 10) or to 24 weeks, 5 days/week range of motion exercise (CG, n = 9). Patients in the CG group without inflammatory infiltrates in muscle biopsies at 24 weeks were invited to the 12-week resistive home exercises.

Results. At baseline, the EG had poorer perceived health, but otherwise the groups were comparable. At 24 weeks, both groups improved in muscle performance and aerobic capacity ($p < 0.001$ to < 0.05) with no signs of increased inflammation assessed by CPK levels or muscle biopsies. Both groups improved in muscle performance and aerobic capacity up to 52 weeks ($p < 0.05$) lasting to 104 weeks in the EG ($p < 0.05$) and presented minor improvements in perceived health.

Conclusion. Our study supports the safety of resistive exercise in patients with active PM/DM but did not reveal any between-group differences in exercise effects. An individually adapted physical therapist–supervised home exercise program might be recommended in early active PM/DM, with regular evaluation of muscle performance and health. (First Release May 1 2014; J Rheumatol 2014;41:1124–32; doi:10.3899/jrheum.131145)

Key Indexing Terms:
POLYMYOSITIS DERMATOMYOSITIS EXERCISE
MUSCLE PERFORMANCE AEROBIC CAPACITY

Polymyositis (PM) and dermatomyositis (DM) are rare, chronic conditions characterized by low muscle performance and fatigue[1]. Although a majority of patients respond favorably to immunosuppressive treatment, many develop sustained disability[2,3] and report poorer subjective health than the general population, suggesting the need for additional interventions[4]. One such intervention is physical exercise.

Different exercise regimens have been reported to improve muscle strength and endurance, aerobic capacity,

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and subjective health in established PM and DM, but still resulting in lower performance levels than in healthy individuals[5,6,7,8,9,10]. Experience of exercise in patients with recent-onset or flaring PM or DM is more limited. Resistive submaximal exercise was well tolerated in 2 small open studies including altogether 16 patients[11,12]. A 5-day/week resistive home exercise program in combination with conventional immunosuppressive treatment was well tolerated in an open pilot study including 11 patients with recent-onset, active PM or DM[13]. Although these studies suggest that resistive exercise is safe in patients with recent onset and active disease, no randomized controlled study has evaluated effects of early resistive exercise in these patients. Our hypothesis was that early introduction of exercise in combination with immunosuppressive agents would be more effective to improve muscle performance assessed by the primary outcome myositis-specific Functional Index (FI) than immunosuppressive treatment alone, both in a short-term and a longterm perspective.

The aim of our study was to evaluate the outcome of a 12-week resistive home exercise program followed by gym-based or home-based exercise in combination with immunosuppressive treatment on perceived health, muscle performance, aerobic capacity, and disease activity in patients with recent-onset PM or DM in a randomized controlled trial (RCT) setting. Further, we aimed to evaluate possible longterm influence of this exercise program on disability, disease activity, and exercise/physical activity habits in an 80-week open-label extension of the study.

MATERIALS AND METHODS

All patients with recent-onset PM or DM registered at the Solna and Huddinge sites of the Karolinska University Hospital, Stockholm, and at the University Hospital, Malmö, Sweden, during 1998-2002 were consecutively invited to participate. Inclusion criteria: (a) diagnosis of definite or probable PM or DM according to Bohan and Peter criteria[14], (b) diagnosis duration < 3 months, (c) age 18–70 years, (d) clinical signs of improvement with conventional immunosuppressive treatment, and (e) ability to perform the exercise program. Exclusion criteria: (a) severe osteoporosis, (b) concomitant malignancy, or (c) cardiovascular disease contraindicating exercise. Twenty-three patients were screened and 3 were excluded because of severe osteoporosis and 1 for heart involvement. Demographic data of the 19 included patients are presented in Table 1. All patients were treated with prednisolone, starting at 0.75 mg/kg/day and another immunosuppressive agent according to the treating physician's choice, mainly azathioprine or methotrexate.

The study was approved by the Regional Ethical Review Board at Karolinska Institutet and patients signed informed consent forms.

Clinical assessments. The disease-specific FI was used as primary outcome to assess muscle performance[15]. The FI includes testing of correctly performed repetitions in 11 muscle groups; elbow flexion, shoulder flexion and abduction, hip flexion and abduction, step test, heel and toe lifts, neck flexion and trunk flexion, with additional tests of ability to transfer from side to side lying down, transfer up to sitting, and peak expiratory flow. Total score varies from 0 to 64 (64 = full capacity).

Aerobic capacity, a secondary outcome, was measured using an 8-min submaximal treadmill test[16]. Patients' estimated maximal heart rate was calculated using the formula 220 minus age in years, and 50% and 70% of their estimated maximal heart rate was then calculated and recorded. During the first 4 min of the test, the treadmill was set on 0° elevation and the patients were instructed to find a brisk walking speed allowing 4 additional min of walking at an elevation of 5°. During the last 4 min of the test the walking speed was kept stable. Subjective central and peripheral exertion, using the Borg RPE-scale 6-20[17], was rated at 4 and 8 min. Estimated maximal oxygen uptake in ml/kg × min was calculated according to the formula:

$$15.1 + (13.55 \times \text{km/h}) - (0.327 - \text{work heart rate}) - (0.16 \times \text{km/h} \times \text{age}) + (0.00504 \times \text{work heart rate} \times \text{age}) + (5.98 \times \text{sex [female = 0, male = 1]})$$[16].

To measure perceived health, the Swedish version of the Nottingham Health Profile (NHP) was used, consisting of 45 items divided into 5 categories: Physical function, Pain, Sleep, Energy, and Social, each scored 0–100 (100 = poor health)[18].

Disease activity was measured by analysis of creatine phosphokinase (CPK) levels and degree of muscle inflammation was assessed in repeated muscle biopsies. A first biopsy was taken for diagnostic purposes and a repeat biopsy was performed at 24 weeks. The biopsies were taken under local anesthesia from the vastus lateralis using a semiopen technique, and the second biopsy was taken from the contralateral side[19,20]. Muscle inflammation was scored as presence or absence of inflammatory infiltrates using routine stainings by an experienced neuropathologist.

Study design. This is a 24-week single-blinded randomized controlled study with an 80-week open-label followup. An initial muscle biopsy was taken for diagnostic purposes. Within 3 months after starting immunosuppressive treatment with perceived clinical improvement, patients were enrolled by any of 2 rheumatologists (MD, IEL) and randomized into an exercise group (EG) or a control group (CG) using a randomization table. An independent nurse was responsible for the randomization, which was concealed to the blinded assessors and the 2 rheumatologists responsible for patient enrollment throughout the data collection. She informed the exercise supervisors about group allocation. Three well-trained physical therapists blinded to group allocation, 1 at each participating center, assessed patients recruited from their own center and supervised the exercise for patients from any of the other centers. Exercise supervisors and assessors met before study start and at least once a year for discussions and training of tests procedures and the exercise program. At the time of randomization, baseline assessments of muscle performance, aerobic capacity, perceived health, and serum levels of CPK were taken. Study participants were not blinded to group allocation.

The EG performed a resistive home exercise program and brisk walking for 12 weeks with weekly telephone support and were then encouraged to continue with twice-a-week home/gym exercise for another 12 weeks. Exercise at a gym was given as an alternative to a home exercise to improve compliance based on experience from an open-exercise study using the same home exercise program[13]. The CG was instructed to perform only a 15-min range of motion (ROM) exercise program 5 days a week and to only perform activities of daily living and ordinary walks for 24 weeks without any telephone support. At 24 weeks a followup muscle biopsy and all clinical assessments were repeated. Patients were then followed up at 52, 78, and 104 weeks in an open-label extension of the study. The EG was encouraged to keep on exercising at home or in a gym throughout the 104-week study period. If the 24-week muscle biopsy did not display inflammatory infiltrates, the CG was, according to suggestions from the Regional Ethical Review Board, invited to the same 12-week resistive home exercise program that the EG used, and then encouraged to continue twice-a-week exercise at home or in a gym until the 2-year followup. In case of remaining inflammation in the biopsy, patients in the CG were instructed to continue with ROM exercise only. Both groups kept an exercise diary recording frequency of home/gym exercise or ROM exercise and walks as well as any encountered problems with exercise up to 24 weeks, and then reported their exercise and physical activity levels at each followup visit throughout the rest of the study.

Table 1. Demographic data of 19 patients with polymyositis and dermatomyositis.

Characteristics	All Patients, n = 19, Median (Q1–Q3)	Exercise Group, n = 10, Median (Q1–Q3)	Control Group, n = 9, Median (Q1–Q3)
Age, yrs	60.0 (52.0–67.0)	56.5 (44.0–62.0)	62.0 (54.0–70.0)
Diagnosis, PM/DM	10/9	5/5	5/4
Sex, female/male, n	14/5	9/1	5/4
Diagnosis duration, mo	3.0 (2.0–3.0)	2.0 (1.5–3.0)	3.0 (2.5–3.0)
Serum CPK at diagnosis, μcat/l	23 (15.0–60.0)	27.4 (15.0– > 76.8)	21.9 (15.1–42.4)
Serum CPK at baseline, μcat/l	1.9 (0.6–5.7)	2.1 (0.5–4.7)	1.9 (0.8–5.7)
Prednisolone dose at diagnosis, mg/day	60 (45.0–60.0)	50.0 (50.0–60.0)	60.0 (40.5–60.0)
Prednisolone dose at baseline, mg/day	40 (30.0–60.0)	40.0 (25.0–40.0)	40.0 (40.0–50.0)
DMARD			
AZA/MTX/CYC, n	13/3/2	9/1/10	4/2/2
Muscle function at baseline			
FI, 0–64	42 (30.0–48.5)	39.8 (24.0–48.5)	46.5 (40.0–48.0)
Aerobic capacity, ml × kg × min	25.01 (18.51–26.57)[2]	23.59 (18.51–25.06)[1]	26.47 (21.73–28.43)[1]
Perceived health at baseline			
NHP Energy, 0–100	24.0 (0.0–100.0)[4]	80.4 (30.4–100.0)[2]	0.0 (0.0–24.0)[2]
NHP Pain, 0–100	9.0 (0.0–20.2)[4]	19.8 (14.2–28.6)[2]	0.0 (0.0–9.0)[2]
NHP Sleep, 0–100	21.7 (12.6–39.8)[4]	34.6 (18.9–42.3)[2]	12.6 (0.0–34.3)[2]
NHP Social, 0–100	0.0 (0.0–22.0)[4]	0.0 (0.0–32.1)[2]	0.0 (0.0–16.0)[2]
NHP Emotional, 0–100	33.9 (7.2–61.0)[4]	50.5 (39.0–72.7)[2]	7.22 (0.0–16.2)[2]
NHP Physical, 0–100	10.6 (0.0–21.4)[4]	16.5 (10.7–33.7)[2]	0.0 (0.0–10.6)[2]

Q1–Q3: lower to upper quartile; PM: polymyositis; DM: dermatomyositis; CPK: creatine phosphokinase; DMARD: disease-modifying antirheumatic drug; AZA: azathioprine; MTX: methotrexate; CYC: cyclophosphamide; FI: Functional Index; NHP: Nottingham Health Profile; [1] = 1 missing case; [2] = 2 missing cases; [4] = 4 missing cases.

Exercise program. The EG was introduced to a 5-day/week resistive home exercise program for the first 12 weeks with weekly telephone support from the physical therapist. The home exercise program contained step-up exercise for warmup, shoulder flexion and knee extension in a sitting position, hip flexion and abduction, as well as pelvic lifts and situps lying down. Each exercise was performed in 10 repetitions bilaterally and the program ended with stretching[13]. Exercise intensity was prescribed individually. Thus, patients with severe muscle impairment (performing < 20% maximal FI total score) exercised only against gravity while patients with less severe impairments received additional weight cuffs of 0.25–2.0 kg. In addition, patients also took a 15-min walk at an intensity level of 50–70% of their estimated maximal heart rate 5 days a week.

Statistical analysis. Because the study included a limited number of patients and most assessments produced ordinal data, descriptive data are presented as median values with upper and lower quartiles (Q1-Q3). Data were analyzed with StatSoft Statistica 10. Mann-Whitney U test and Fisher's exact test were used to analyze between-group differences at baseline. The Kruskal-Wallis ANOVA and the Friedman's ANOVA were used to analyze between-group and within-group differences at followup because the primary outcome, FI, produced ordinal data. Differences between specific timepoints within a group according to hypothesis based on visual interpretation of box-plot graphs were analyzed with the Wilcoxon signed-rank test. Significance level was set to $p < 0.05$. No power analysis was performed and owing to the relatively large number of dropouts at 104 weeks, both per protocol analysis and intention-to-treat analysis (ITT) were used, with the last value carried forward from 78-week assessments. Patients were also analyzed individually according to criteria for minimal clinically relevant change. To be a responder, patients had to improve > 20% in the FI score or aerobic capacity compared to baseline. A clinically relevant deterioration was defined as > 20% worsening in these variables[21].

RESULTS

Compliance in the 24-week exercise plan. Ten patients were randomized to the EG. They started exercising a median of 2 months (1.5–3.0) after introduction of glucocorticoids, and the resistive home exercise program was well tolerated overall. Study compliance is presented in Figure 1. Two patients in the EG divided the program into 2 parts with a rest in-between because of low initial muscle performance. One patient recovered very well in muscle performance before 12 weeks and described the home exercise program as being too easy. Therefore, he only performed about 30% of the home exercise sessions and instead replaced the exercise program with brisk walks. During the first 12 weeks the EG performed a mean of 79% (± SD 22%) of the 60 possible resistive home exercise sessions and performed a mean 81% (± SD 31%) of the 60 possible walks. Two patients in the EG died during the following 12 weeks, 1 from malignant ovarian cancer and 1 from fast progressive alveolitis. Between 12 and 24 weeks, the remaining 8 patients exercised at home or at a gym 1–3 times per week and took walks several days per week (Table 2). Patients did not report side effects of exercise, other than short-term muscle soreness, especially in the beginning, and shortly after increasing the exercise loads. In the CG, 1 patient did not perform the ROM-exercise owing to poor eyesight, while 8 patients completed all ROM home exercise sessions and did not perform other kinds of exercise programs during the first 24 weeks of the study (Table 3).

Effects after 24 weeks on perceived health and disability. At baseline there were no statistically significant differences in the disability measures between the 2 groups. The EG rated poorer health in 4 NHP domains compared to the CG (Table

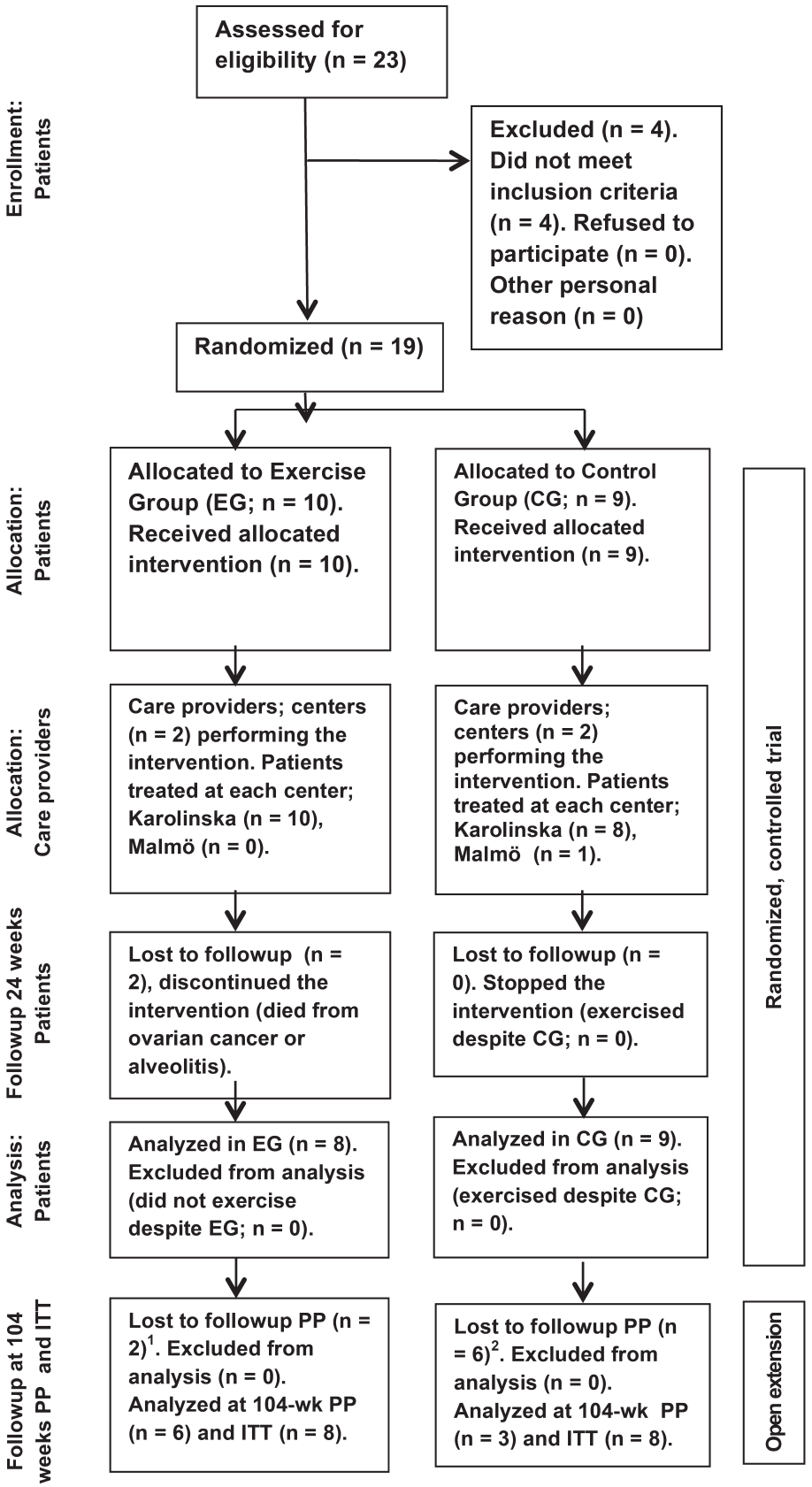

Figure 1. Flow diagram for patients according to the CONSORT randomized controlled trials of nonpharmacologic treatment[25] and through the 2-year open-extension part. One patient dropped out because of osteoporosis and pain and one for unknown reasons. Six patients were lost to followup of the Functional Index (FI) and aerobic capacity test for unknown reasons, but completed all assessments of disease activity measures and the Nottingham Health Profile. PP: per protocol; ITT: intention-to-treat analysis with 78-week assessments carried forward.

Table 2. Compliance to exercise during the 2-year followup in the exercise group.

Case	Sex, F/M, (age), yrs	DX, PM/DM	DX, Duration, mos	0–12 Wks Home Exercise, % of 60	0–12 Wks, Walks, % of 60	12–24 Wks, Exercise/Walks per Wk, n	24–104 Wks, Exercise/Walks per Wk, n
1	F (53)	PM	4[#]	73[a,c,d]	87	1/3	0/4
2	M (61)	PM	1	30[b]	100	2/3	0/4
3	F (44)	DM	3	100[b]	100	2/7	2/7
4[e]	F (41)	DM	5[#]	66[a,c]	0	0/0	—
5	F (74)	PM	2	92[a]	90	3/5	3/7
6	F (65)	DM	2	75[a]	67	1–2/5	2/5
7	F (50)	DM	2	100[b]	100	1/7	0/7[f]
8[g]	F (62)	DM	3	70[a,c,h]	65	0/0	—
9	F (23)	PM	1.5	100[b]	100	2/6	2/6
10	F (60)	PM	1	87[b]	98	1/7	1/7

[a] = performed the easy-intensity home exercise program. [b] = performed the moderate-intensity home exercise program. [c] = divided each home exercise session in 2 halves. [d] = could not exercise for the first 2 weeks because of nausea, vomiting, and muscle pain; [e] = died before 24-week followup from fast-progressing alveolitis; [f] = had a mild relapse with slightly increased disease activity at 36 weeks; [g] = died before 24-week followup from ovarian cancer; [h] = did not exercise for about 2 weeks because of hospitalization for severe skin rash infection. [#] = Slow response to glucocorticoid treatment with no clinical signs of improvement during the first 3 months. Patients were included when they perceived clinical improvement. DX: diagnosis; PM: polymyositis; DM: dermatomyositis; % of 60: % of maximal 60 sessions during 12 weeks

Table 3. Compliance to exercise during the 2-year follow up in the control group.

Case	Sex, F/M, (age), yrs	DX	DX, Duration, mos	0–24 Wks ROM Home Exercise, % of 120	24–36 Wks, Home Exercise, % of 60	24–36 Wks, Walks, Times/ Wk, % of 60	36–104 Wks, Exercise/Walks/ Wk, n
11	F (71)	PM	3	100	0	100	0/7
12	M (60)	PM	1.5	100[a]	0	100	0/7
13	F (54)	DM	3	100	6[b]	100	0/7
14	M (52)	PM	3	100	100	100	0–2/7
15	F (88)	PM	3	100	0	0	0/0[c]
16	M (67)	DM	2	100	0	0	0/4
17	F (53)	DM	2.5	40–100[d]	77	92	1/7
18	M (62)	DM	3	0	15	0	0/1[e]
19	F (70)	PM	3	100[f]			

PM: polymyositis; DM: dermatomyositis; % of 120: % of maximal 120 sessions during the 24-week ROM period; ROM: range of motion. [a] = additional daily physical activity with farm work. [b] = sepsis infection and increasing shortness of breath and was diagnosed with interstitial lung disease, lung fibrosis after 24 weeks. [c] = poor eyesight due to cataract and developing herpes zoster with severe pain during the second year of followup prevented exercise. [d] = additional physical activity daily at work as a nurse. [e] = playing golf once a week. [f] = no information about exercise or physical activity from 24–104 weeks.

1). After 24 weeks, both groups had improved muscle performance and aerobic capacity compared to baseline (Figures 2A, 2B). Five patients in the EG were responders with > 20% improvement in FI and aerobic capacity at 24 weeks (Figures 3A, 3C). Four patients in the CG were responders in FI and 3 in aerobic capacity at the same timepoints (Figures 3B, 3D). There were no statistically significant between-group differences in any of the variables. The EG improved in the NHP domain Energy with 60.8 (37.2–63.3) compared to baseline values of 80.4 (30.4–100.0; $p < 0.05$) while the CG had improved in the domain Sleep with median 0.0 (6.1–12.6) compared to baseline values of 12.6 (0.0–34.3; $p < 0.05$).

Effects on disease activity after 24 weeks. At baseline, the median CPK levels were 2.05 (0.5–4.7) and 1.9 (0.8–5.7) μcat/l in the EG and the CG, respectively, significantly lower compared to time of diagnosis, when the EG had a median of 27.4 μcat/l (15.0 to > 76.8; $p < 0.01$) and the CG had 21.9 μcat/l (15.1–42.3; $p < 0.01$). At 24 weeks, both groups had similar CPK levels, with median of 0.9 (0.5–1.2; EG) and 1.3 (1.1–3.3; CG). The EG had a median dose of prednisolone of 9.5 (7.5–12.5) mg/day compared to 10.0 (7.5–12.5) mg/day in the CG. The number of patients taking immunosuppressive treatment remained unchanged. Initial and repeated muscle biopsies were obtained from 8 of 10 patients in the EG, showing presence of inflammatory infiltrates in 6 and absence in 2. At 24 weeks no patient in the EG had inflammatory infiltrates. In the CG, biopsies were available from 7 patients at time of diagnosis and at 24 weeks. Five showed presence and 2 absences of inflam-

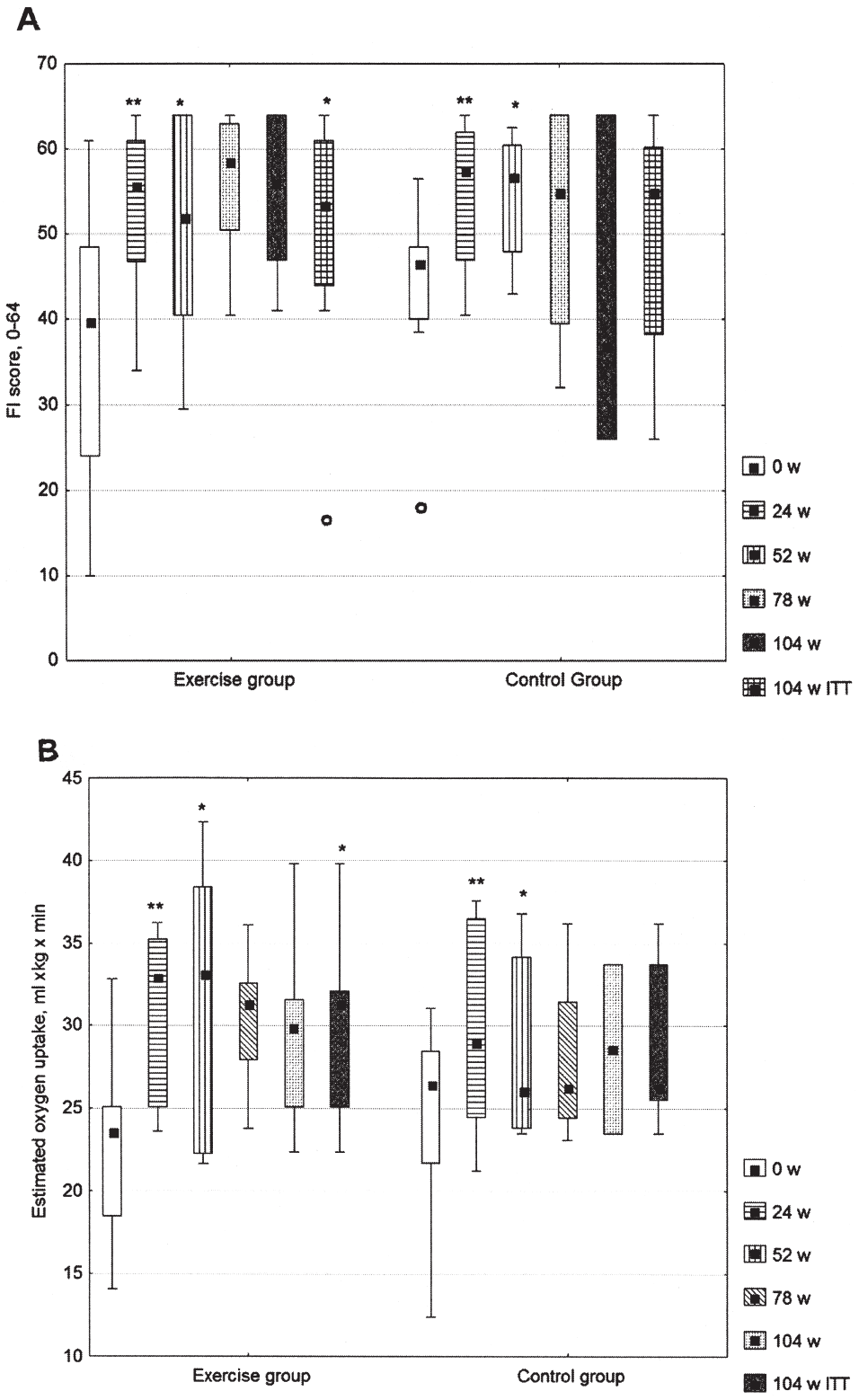

Figure 2. A. Muscle performance assessed by the Functional Index (FI)[16] in the exercise group and the control group. Maximal score = 64 (high performance). * $p < 0.05$, ** $p < 0.01$. B. Aerobic capacity (estimated oxygen uptake) assessed by a treadmill test[17] in the exercise group and control group. * $p < 0.05$, ** $p < 0.01$. ITT: intention-to-treat analysis.

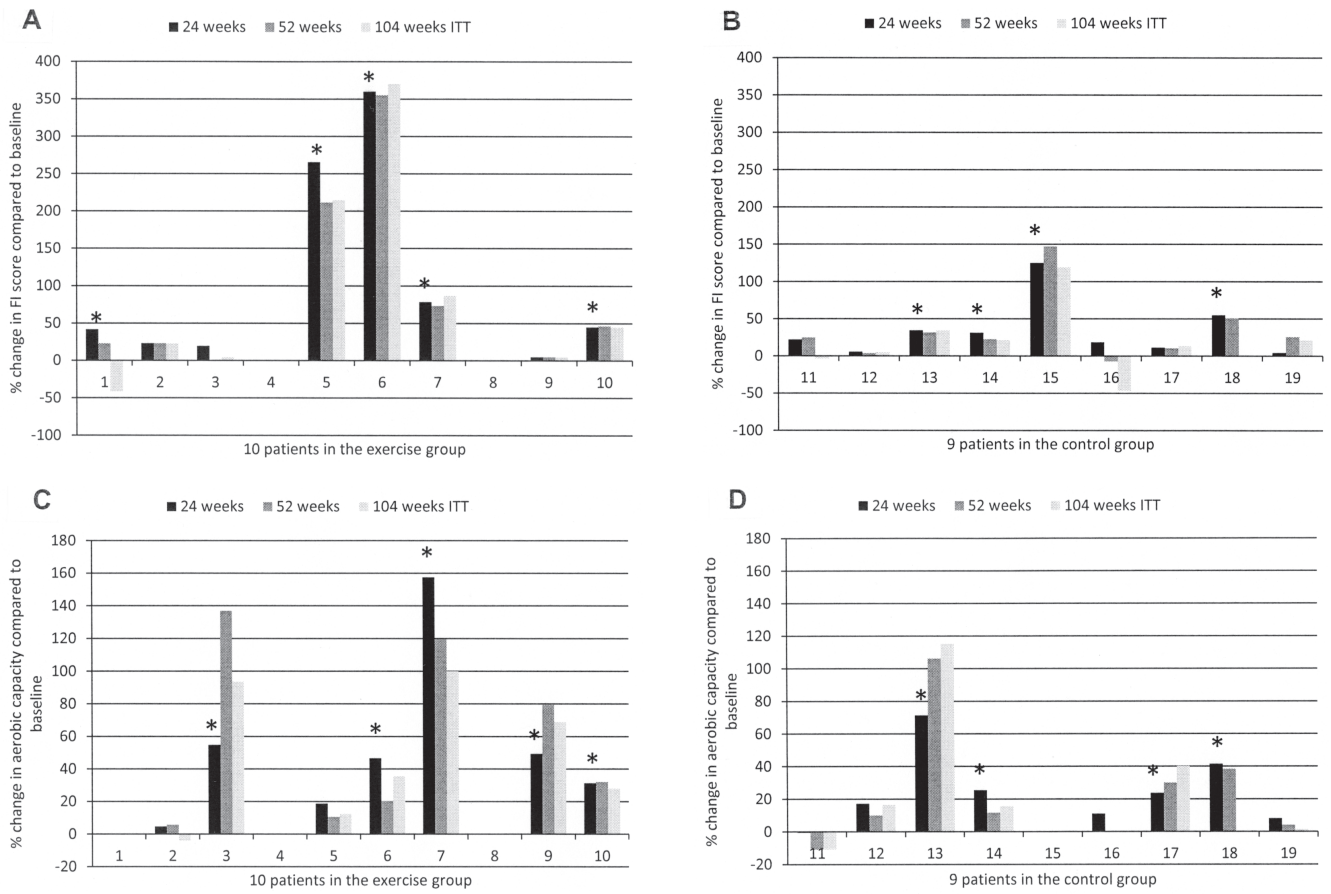

Figure 3. A. Responders (improving ≥ 20%) and nonresponders in muscle performance assessed by the Functional Index (FI)[16] at followup in the exercise group. ITT = intention-to-treat, carrying the 78-week value forward. * ≥ 20% improvement at 24 weeks compared to baseline. Patients 5, 6, 7, and 10 were responders also at 104 weeks ITT. B. Responders (improving ≥ 20%) and nonresponders in muscle performance assessed by the FI[16] at followup in the control group. * ≥ 20% improvement at 24 weeks compared to baseline. Patients 13, 14, and 15 were responders also at 104 weeks ITT. C. Responders (improving > 20%) and nonresponders in aerobic capacity assessed by a treadmill test[17] in the exercise group. * ≥ 20% improvement at 24 weeks compared to baseline. Patients 3, 6, 7, 9, and 10 were responders also at 104 weeks ITT. D. Responders (improving > 20%) and nonresponders in aerobic capacity assessed by a treadmill test[17] in the control group. * 20% improvement at 24 weeks compared to baseline. Patients 13 and 17 were responders also at 104 weeks ITT.

matory infiltrates. At 24 weeks only 1 patient still had inflammatory infiltrates, however small, and the patient was cleared to start the resistive home exercise program. All cases with missing initial biopsies had been diagnosed with DM based on clinical symptoms.

Exercise compliance at 52–104 weeks. Five patients in the EG (n = 8) kept exercising 1–3 times per week throughout the rest of the study, while 2 patients did not exercise. However, all patients kept their frequent walking habits (Table 2). All patients in the CG (n = 9) were invited to start the 12-week resistive home exercise at 24 weeks. Four patients chose to enter and performed a mean of 22% (± SD 27%) of the possible 60 home exercise sessions, which was statistically less than what the EG performed ($p < 0.001$). The CG performed a mean of 55% (± SD 51%) of the 60 possible walks, which was not different from the EG. Two patients in the CG continued to exercise once or twice a week after completing the 12-week supervised resistive home exercise program. These 2 and 3 additional CG members also continued to take regular walks (Table 3). The factors most limiting exercise and walks for both groups were common colds or icy winter conditions.

Possible longterm influence on disability and disease activity at 52–104 weeks. At 52 weeks both groups had improved muscle performance (FI) and aerobic capacity compared to baseline (Figures 2A, 2B). Only the EG was also statistically significantly improved in muscle performance and aerobic capacity at 104 weeks (ITT analyses) compared to baseline (Figures 2A, 2B). Four patients in each of the groups were responders, improving > 20% in FI at 52 and 104 (ITT) weeks (Figures 3A, 3B), while 5 patients in the EG and 3 in the CG were responders for aerobic capacity (Figure 3C, 3D). The EG improved in the NHP domain Energy at 52 and 104 weeks (ITT) compared to baseline, with median 30.4 (0–60.8) and 32.6 (0–62.0), respectively ($p < 0.05$), while the CG remained unchanged.

The CPK levels remained unchanged throughout the longterm followup. At the last followup, both groups had similar doses of prednisolone of median 2.5 (1.25–5.0) mg/day (EG) and median 2.8 (2.5–5.0) mg/day (CG).

DISCUSSION

In this 24-week randomized controlled study followed by an 80-week open-label extension, we could confirm the safety of a resistive home exercise program in combination with immunosuppressive treatment in patients with recent-onset PM and DM, both in a short-term and longterm perspective. The hypothesis that early exercise in combination with medical treatment is more effective to reduce disability than medical treatment alone could not be confirmed. However, the low number of patients and frequent dropouts during the open-label extension hampered the analysis.

There were no between-group differences at baseline regarding sex and diagnosis distribution, muscle performance, aerobic capacity, or disease activity; however, the EG had lower perceived health compared to the CG. Such random differences may occur in small samples such as ours where a few individuals may influence the group median and would be hard to avoid by use of block randomization because all sociodemographics and outcome measures could not be balanced in this small sample. The fact that 6 patients in the EG and 5 in the CG had inflammatory infiltrates and similar CPK levels at diagnosis indicate that there probably were no baseline between-group differences in disease activity.

There was overall good compliance with the resistive home exercise program by the EG. All patients in the CG were invited to the telephone-supervised resistive home exercise program, but only 4 accepted. Some declined because they had started to work fulltime or part-time and lacked the energy to perform the resistive home exercise. This might also have been the reason for poorer compliance with exercise and physical activity in the CG. Thus, early exercise and regular telephone support might help patients with PM and DM to adopt and maintain a physically active lifestyle, although this hypothesis cannot be confirmed by our study design.

During the first 24-week RCT, both groups improved muscle performance and aerobic capacity. The improvement during these 24 weeks, when the 2 groups were given immunosuppressive treatment in a similar manner, is therefore likely to mainly reflect effects of the immunosuppressive treatment. The hypothesis that physical exercise introduced early has additional favorable effects on muscle performance or aerobic capacity in a 2-year perspective compared to exercise introduced after 6 months of immunosuppressive treatment was not confirmed. The within-EG improvements in muscle performance and aerobic capacity lasting up to the 104-week (ITT) followup might support the benefit of early supervised exercise in terms of sustained exercise and physical activity levels that were not seen in the CG. The EG improvement in NHP domain Energy at 104 weeks (ITT), which was not seen in the CG, could support a positive effect of exercise, but most likely reflects a regression to the mean because the EG had significantly lower scores than the CG at baseline. The frequent dropouts at the 104 week followup in both groups make conclusions more uncertain.

The lack of within-group improvement in the domain NHP Physical function is surprising because we have previously reported significant improvements in Medical Outcomes Study Short Form-36 (SF-36) questionnaire domains Physical functioning, Bodily pain, and Vitality following the same resistive home exercise program and medical treatment in patients with recent-onset PM and DM in a 12-week small open study[13]. One reason for this lack of improvement might be that the SF-36 is more sensitive to detecting changes in perceived health than is the NHP. This possibility is in line with one previous study of patients with PM and DM following the same resistive home exercise program using the NHP without revealing significant changes[22].

Serum levels of CPK were used as a proxy for disease activity. The rapid reduction of CPK levels from time of diagnosis to enrollment in the exercise study confirmed that both groups had responded to medical treatment, and the stable levels throughout the study support the safety of early exercise. A limitation is the absence of clinical disease activity scores; we started our study before the International Myositis Assessment and Clinical Studies disease activity core set was published[23]. However, there were no or minor inflammatory infiltrates in the repeated muscle biopsies in the EG at 24 weeks, further supporting the safety of exercise introduced early.

Our results concerning safety of early resistive exercise in patients with recently diagnosed onset PM and DM are in line with earlier studies[8,11,12,13]. Patients with high disease activity in the study by Heikkillä, *et al*[8] improved by a mean 3.7% in FI scores after a 3-week exercise period, while patients in our EG improved by a mean 44% after 24 weeks. This difference is likely because 3 weeks is too short a time to achieve improvement[24].

Our study was a multicenter study including 3 large rheumatology clinics in Sweden. The fact that only 23 patients fit the study inclusion criteria during the 5-year inclusion period reflects the rarity of the disease. An important limitation is the lack of power analysis and the low number of patients, conditions that may explain lack of significant between-group differences, with frequent dropouts further hampering the analyses and conclusions. Therefore we used ITT analysis for the 2-year followup. Nonparametrical statistics are usually less effective than parametric tests, but were nevertheless used because the primary outcome, FI, produces ordinal data and neither of the variables were normally distributed in our small groups. The exercise intensity level was defined only for the aerobic

walks, but not for the resistive home exercise program, which is another limitation to our study. Training resistance was prescribed individually and loads were gradually adapted by telephone support depending on how patients described their exercise experience. The program was likely more strength training-oriented for patients with very low FI scores, in which cases the FI also likely assessed muscle strength rather than muscle endurance. The inclusion of systematic self-reported perceived exertion would have been one way to establish exercise intensity in this home-based setting. In addition, objective assessment of physical activity and exercise level such as the use of heart rate watches or a pedometer would have been a useful complement to the exercise diaries to ensure compliance. Because exercise might reduce the risk of glucocorticoid-related side effects and enhance the adoption and maintenance of a physically active lifestyle, we suggest resistive exercise in addition to medical treatment for patients with active PM or DM within 3 months after starting immunosuppressive treatment or as soon as they are able to do some kind of low-intensity exercises. Level of disability varies among patients, therefore we recommend that baseline disability assessments be performed before introducing exercise to enable individual adaption of starting exercise loads and intensity and to allow regular followup after 3, 6, and 12 months. As muscle performance and health improves, exercise loads/intensity should be increased by support of a physical therapist and according to patients' individual goals and interests.

Our study supports the safety of early resistive home exercise in combination with immunosuppressive treatment in patients with recently diagnosed PM/DM. But we could not draw conclusions on the effects of early exercise in combination with medical treatment versus medical treatment alone, indicating the need for larger multicenter trials.

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