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Supervised Moderate-Intensity Combined Aerobic and Resistance Exercise Versus Conventional Physiotherapy for Statin-Associated Muscle Symptoms: An Experimental Study

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ABSTRACT:

Background: Statin-associated muscle symptoms (SAMS) frequently lead to treatment discontinuation and residual cardiovascular risk. Although moderate-intensity exercise is considered safe in statin users, controlled evidence comparing progressive combined aerobic–resistance training with conventional physiotherapy remains limited.

Methods: Sixty adults (aged 40–75 years) with confirmed SAMS were allocated to Group A (supervised moderate-intensity combined aerobic and resistance exercise, n = 30) or Group B (conventional physiotherapy: light aerobic activity, static stretching and education, n = 30) in a double-group pre-post experimental design. Interventions were delivered three times weekly for eight weeks under physiotherapist supervision. Outcomes assessed at baseline and post-intervention by a blinded assessor included Visual Analogue Scale (VAS) pain, hand-held dynamometry muscle strength, Statin-Associated Muscle Symptoms Clinical Index (SAMS-CI), and SF-36 Physical and Mental Component Summary scores.

Results: Both groups improved significantly ($p < 0.001$). Group A showed substantially greater mean changes than Group B in VAS (−3.00 vs −0.90), muscle strength (+5.59 kg vs +1.74 kg), SAMS-CI (−3.77 vs −1.53), SF-36 PCS (+8.70 vs +3.40) and SF-36 MCS (+5.93 vs +1.70), with large between-group effect sizes (Cohen's $d = 2.45–4.03$; all $p < 0.001$). No intervention-related adverse events occurred.

Conclusion: An eight-week supervised moderate-intensity combined aerobic and resistance exercise programme is significantly more effective than conventional

physiotherapy in reducing pain and SAMS severity, improving muscle strength and enhancing quality of life in patients with SAMS.

1. INTRODUCTION

Cardiovascular disease remains the leading cause of morbidity and mortality worldwide. Statins are the cornerstone of pharmacological therapy for primary and secondary prevention of atherosclerotic cardiovascular disease because of their proven efficacy in lowering low-density lipoprotein cholesterol and reducing major adverse cardiovascular events [1,2].

Despite these benefits, long-term adherence is frequently suboptimal. Statin-associated muscle symptoms (SAMS) are the most common reason for dose reduction, temporary interruption or permanent discontinuation of treatment [3,4]. Reported prevalence in observational studies ranges from approximately 5% to 25%, whereas the true pharmacological prevalence is estimated at 1–2% [4,5]. Even when symptoms are not directly caused by the pharmacological action of the statin, they frequently lead patients to stop therapy, thereby increasing residual cardiovascular risk [3,6].

SAMS encompass myalgia, stiffness, cramps, weakness and, less commonly, myopathy or rhabdomyolysis. Symptoms are typically bilateral and proximal and usually appear within weeks to months after initiation or dose escalation [4,7]. Pathophysiology is multifactorial and involves mitochondrial dysfunction, coenzyme Q10 depletion, altered calcium homeostasis, oxidative stress and genetic susceptibility [7,8].

Physical activity and structured exercise are independently recommended for cardiovascular risk reduction. However, many patients and clinicians remain concerned that exercise may provoke or aggravate SAMS. High-quality evidence has challenged this concern. Allard et al. demonstrated that a 12-week moderate-intensity combined endurance and resistance training programme improved muscle strength, fatigue resistance, capillarisation and quality of life in both symptomatic and asymptomatic statin users without increasing muscle symptoms [9]. A subsequent study showed that prolonged moderate-intensity walking did not elevate muscle-injury markers or worsen symptoms more in symptomatic statin users than in asymptomatic users or non-users [10].

Despite emerging evidence supporting the safety and benefits of moderate-intensity exercise in patients with SAMS, clinical physiotherapy practice continues to rely predominantly on conventional approaches that emphasise stretching, light aerobic activity and patient education. There is a clear paucity of controlled comparative studies that specifically evaluate a structured, progressive combined aerobic and resistance exercise protocol against conventional physiotherapy in patients with confirmed SAMS. Few studies have simultaneously assessed pain intensity, objective muscle strength, symptom attribution using the validated SAMS-Clinical Index, and health-related quality of life within a single experimental design.

Therefore, the present study compared the effects of a supervised moderate-intensity combined aerobic and resistance exercise programme with conventional physiotherapy on pain, muscle strength, SAMS severity and quality of life in patients with statin-associated muscle symptoms after an eight-week intervention. The null hypothesis stated that there would be no significant difference in improvement between the two groups; the alternative hypothesis proposed that the combined exercise programme would produce significantly greater improvements.

2. MATERIALS AND METHODS

2.1. Study design

A double-group pre-post experimental design was employed. Participants were randomly allocated into two groups and assessed at baseline and after eight weeks of intervention to evaluate within-group and between-group changes.

2.2. Participants

Sixty participants with SAMS were recruited from the Outpatient Department of Sri Venkateswara College of Physiotherapy, Guntur, and randomly allocated into two equal groups of 30 participants each.

Inclusion criteria were: adults aged 40–75 years; receiving stable statin therapy for a minimum of three months; presence of muscle symptoms (pain, stiffness, cramps or weakness) temporally associated with statin use as defined by the National Lipid Association [5]; ability to understand and follow exercise instructions; and willingness to provide written informed consent.

Exclusion criteria included: history of rhabdomyolysis or creatine kinase levels greater than 10 times the upper limit of normal [5]; uncontrolled cardiac, neurological or severe musculoskeletal disorders; any change in statin dosage within the previous four weeks; participation in a structured exercise programme during the preceding three months; and cognitive impairment that could affect compliance.

2.3. Sample size and group allocation

The total sample size was fixed at 60 participants (30 per group). Participants were randomly assigned to Group A (supervised moderate-intensity combined aerobic and resistance exercise) or Group B (conventional physiotherapy consisting of stretching, light aerobic activity and education).

2.4. Intervention protocols

The intervention period lasted eight weeks with three supervised sessions per week (45–60 minutes each). All sessions were supervised by a qualified physiotherapist. Participants in both groups continued their prescribed statin medication and usual daily activities. Attendance was recorded and adverse events were documented.

Group A – Combined aerobic and resistance exercise programme (adapted from previously published moderate-intensity protocols [9,10]): Warm-up (5–10 min) of low-intensity walking or cycling with dynamic mobility exercises (RPE 7–9); Aerobic training (20–25 min) on treadmill or cycle ergometer at 50–70% of age-predicted maximum heart rate or RPE 11–13; Resistance training (15–20 min) targeting major muscle groups (2–3 sets of 8–12 repetitions with progressive loading); Cool-down (5–10 min) of static stretching and deep-breathing exercises.

Group B – Conventional physiotherapy: Light aerobic activity (10–15 min) at RPE 7–9; Static stretching of major muscle groups (20–25 min); Structured patient education (10–15 min) covering the nature of SAMS, importance of remaining active, activity pacing, energy conservation, recognition of warning symptoms, posture and body mechanics.

2.5. Outcome measures

All outcomes were assessed at baseline and after eight weeks by an assessor blinded to group allocation.

Pain intensity was measured using the Visual Analogue Scale (VAS), ranging from "no pain" (0) to "worst imaginable pain" (10) [11,12]. Muscle strength was evaluated using a hand-held dynamometer for selected major muscle groups (primarily knee extensors and hip abductors) [13,14]. Muscle symptom severity was assessed using the Statin-Associated Muscle Symptoms Clinical Index (SAMS-CI), with total scores categorised as unlikely (≤4), possible (5–8) or probable (9–11) [15,16]. Health-related quality of life was measured using the Short Form-36 (SF-36) questionnaire, yielding Physical and Mental Component Summary scores [17,18].

2.6. Statistical analysis

Data were analysed using statistical software. Descriptive statistics (mean ± standard deviation) were calculated. Normality was assessed with the Shapiro–Wilk test. Within-group comparisons used the paired t-test; between-group comparisons used the independent t-test. Significance was set at $p < 0.05$.

3. RESULTS

3.1. Demographic characteristics and baseline comparability

Sixty participants were included and randomly allocated (Group A mean age 56.0 ± 7.6 years; Group B 54.1 ± 8.2 years; $p = 0.337$). Gender distribution was 20 males/10 females in Group A and 15 males/15 females in Group B. Mean duration of statin therapy was 23.7 ± 14.7 months in Group A and 29.3 ± 12.5 months in Group B (Table 1).

At baseline there were no statistically significant differences between groups in any outcome measure: VAS ($p = 0.400$), muscle strength ($p = 0.258$), SAMS-CI ($p = 0.436$), SF-36 PCS ($p = 0.642$) and SF-36 MCS ($p = 0.421$) (Table 2).

3.2. Within-group comparisons

Both groups showed statistically significant improvement in all outcome measures after the eight-week intervention ($p < 0.001$ for all comparisons).

In Group A, mean VAS decreased from 7.53 ± 1.07 to 4.53 ± 1.28 (mean change −3.00; Cohen's d = −2.55). Muscle strength increased from 23.78 ± 4.16 kg to 29.38 ± 4.34 kg (mean change +5.59 kg; d = 1.32). SAMS-CI reduced from 8.07 ± 1.41 to 4.30 ± 1.44 (mean change −3.77; d = −2.64). SF-36 PCS improved from 42.13 ± 4.13 to 50.83 ± 3.86 (mean change +8.70) and SF-36 MCS from 46.67 ± 5.11 to 52.60 ± 5.26 (mean change +5.93; d = 1.14) (Table 3).

In Group B, mean VAS decreased from 7.30 ± 1.06 to 6.40 ± 1.30 (mean change −0.90; d = −0.76). Muscle strength increased from 25.04 ± 4.38 kg to 26.78 ± 4.37 kg (mean change +1.74 kg; d = 0.40). SAMS-CI reduced from 8.33 ± 1.21 to 6.80 ± 1.40 (mean change −1.53; d = −1.17). SF-36 PCS improved from 42.63 ± 4.16 to 46.03 ± 4.64 (mean change +3.40; d = 0.77) and SF-36 MCS from 47.67 ± 4.42 to 49.37 ± 4.64 (mean change +1.70; d = 0.38) (Table 4).

3.3. Between-group comparisons

Comparison of mean change scores revealed that Group A demonstrated statistically significantly greater improvement than Group B in all outcomes ($p < 0.001$). Between-group effect sizes were large: VAS (d = −2.45), muscle strength (d = 4.03), SAMS-CI (d = −3.17), SF-36 PCS (d = 3.05) and SF-36 MCS (d = 2.69) (Table 5).

Tables

Table 1. Demographic characteristics of participants

Variable	Group A (n=30)	Group B (n=30)	p-value
Age (years), Mean ± SD	56.0 ± 7.6	54.1 ± 8.2	0.337
Male, n (%)	20 (66.7%)	15 (50.0%)	–
Female, n (%)	10 (33.3%)	15 (50.0%)	–
Statin duration (months)	23.7 ± 14.7	29.3 ± 12.5	–

Table 2. Baseline comparison of outcome measures

Outcome	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
VAS (Pain)	7.53 ± 1.07	7.30 ± 1.06	0.400
Muscle Strength (kg)	23.78 ± 4.16	25.04 ± 4.38	0.258
SAMS-CI	8.07 ± 1.41	8.33 ± 1.21	0.436
SF-36 PCS	42.13 ± 4.13	42.63 ± 4.16	0.642
SF-36 MCS	46.67 ± 5.11	47.67 ± 4.42	0.421

Table 3. Within-group comparison – Group A (Combined exercise)

Outcome	Pre-test	Post-test	Mean Change	Cohen's d
VAS	7.53 ± 1.07	4.53 ± 1.28	−3.00	−2.55

Strength (kg)	23.78 ± 4.16	29.38 ± 4.34	+5.59	1.32
SAMS-CI	8.07 ± 1.41	4.30 ± 1.44	−3.77	−2.64
SF-36 PCS	42.13 ± 4.13	50.83 ± 3.86	+8.70	Large
SF-36 MCS	46.67 ± 5.11	52.60 ± 5.26	+5.93	1.14

Table 4. Within-group comparison – Group B (Conventional physiotherapy)

Outcome	Pre-test	Post-test	Mean Change	Cohen's d
VAS	7.30 ± 1.06	6.40 ± 1.30	−0.90	−0.76
Strength (kg)	25.04 ± 4.38	26.78 ± 4.37	+1.74	0.40
SAMS-CI	8.33 ± 1.21	6.80 ± 1.40	−1.53	−1.17
SF-36 PCS	42.63 ± 4.16	46.03 ± 4.64	+3.40	0.77
SF-36 MCS	47.67 ± 4.42	49.37 ± 4.64	+1.70	0.38

Table 5. Between-group comparison of mean change scores

Outcome	Group A Change	Group B Change	p-value	Cohen's d
VAS	−3.00 ± 0.95	−0.90 ± 0.76	<0.001	−2.45
Strength (kg)	+5.59 ± 1.24	+1.74 ± 0.55	<0.001	4.03
SAMS-CI	−3.77 ± 0.86	−1.53 ± 0.51	<0.001	−3.17
SF-36 PCS	+8.70 ± 2.07	+3.40 ± 1.33	<0.001	3.05
SF-36 MCS	+5.93 ± 1.80	+1.70 ± 1.32	<0.001	2.69

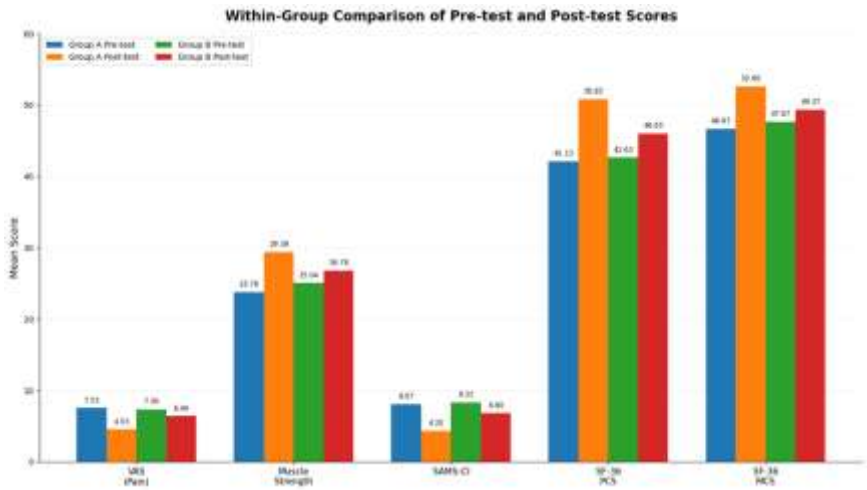


Figure 1: Within-Group Comparison of Mean Change Scores across All Outcome Measures for Group A & Group B

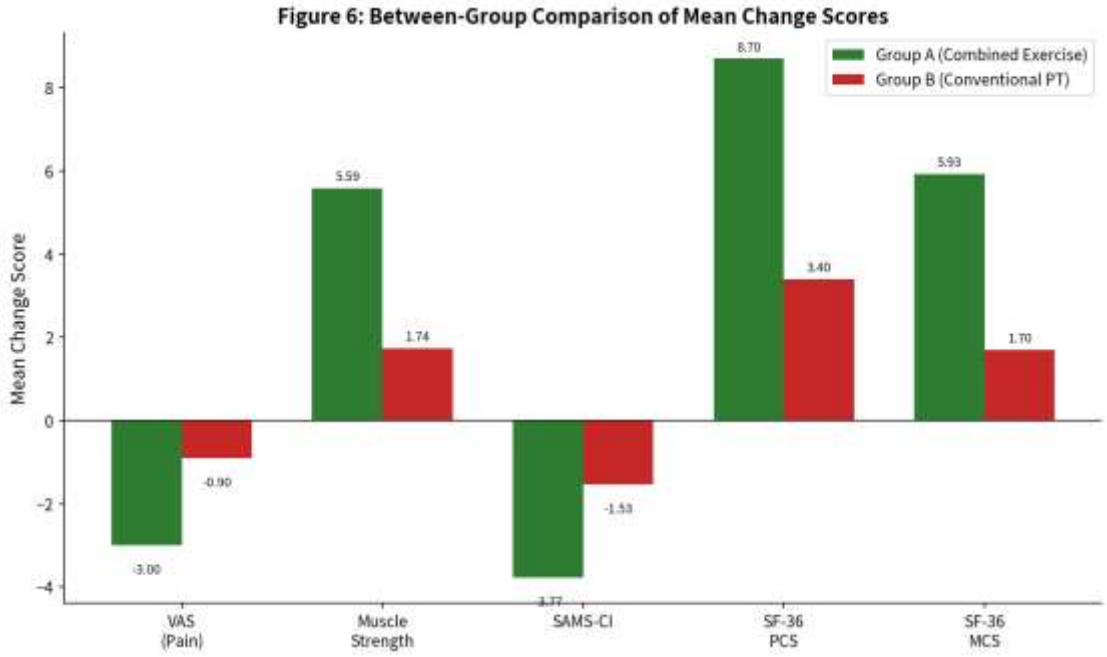


Figure 2: Between-Group Comparison of Mean Change Scores across All Outcome Measures

4. DISCUSSION

The present study demonstrates that both a supervised moderate-intensity combined aerobic and resistance exercise programme and conventional physiotherapy produce statistically significant improvements in pain intensity, muscle strength, SAMS severity and health-related quality of life after eight weeks. However, the combined exercise programme yielded substantially larger improvements across all outcome measures, with between-group effect sizes consistently in the large range (Cohen's d = 2.45–4.03). These findings support the alternative hypothesis and indicate that a structured progressive combined training protocol is clinically superior to conventional physiotherapy approaches that emphasise stretching, low-intensity aerobic activity and education alone.

The magnitude of improvement observed in the combined-exercise group aligns with and extends the work of Allard et al. [9]. In their 12-week moderate-intensity combined endurance and resistance training study, symptomatic and asymptomatic statin users experienced gains in muscle strength, fatigue resistance, capillarisation and quality of life without exacerbation of muscle symptoms. A subsequent investigation showed that prolonged moderate-intensity walking did not elevate muscle-injury markers or worsen symptoms more in symptomatic statin users than in asymptomatic users or non-users [10]. The current results reinforce these observations in a controlled comparative design of shorter duration and further quantify the advantage over conventional physiotherapy.

Several mechanisms may explain the superior outcomes of the combined protocol. Moderate-intensity aerobic exercise improves mitochondrial function, enhances capillarisation and may mitigate oxidative stress—pathophysiological processes implicated in SAMS [7,8]. Concurrent resistance training provides the mechanical stimulus necessary for muscle hypertrophy and strength gains, which can reduce relative loading during daily activities and thereby decrease symptom perception. The progressive nature of the programme likely optimised these adaptations while remaining within a tolerable intensity range.

The concurrent improvements in both physical and mental component summary scores of the SF-36 further underscore the clinical relevance of the combined approach. Patients with SAMS frequently experience reduced physical function and, secondarily, diminished mental well-being because of activity limitation and fear of symptom provocation.

Strengths of the study include random allocation, blinded outcome assessment, use of validated and clinically relevant measures, and high adherence under supervised conditions. Limitations include the modest single-centre sample size, eight-week intervention duration (longer-term retention of benefits and effects on statin adherence remain unknown), assessment of selected lower-limb muscle groups only, and absence of creatine kinase or other biomarkers of muscle injury.

These results provide physiotherapists with evidence that a carefully progressed, supervised moderate-intensity combined aerobic and resistance programme can be safely and effectively prescribed for patients with SAMS. Conventional approaches remain useful as an entry-level or complementary strategy, particularly for highly symptomatic or deconditioned individuals, but appear insufficient as a sole intervention when the therapeutic goal is maximal recovery of strength and reduction of symptom attribution.

Future research should examine longer intervention and follow-up periods, include biomarkers of muscle integrity, explore home-based or hybrid delivery models, and evaluate effects on long-term statin adherence and cardiovascular event rates.

5. CONCLUSIONS

An eight-week supervised moderate-intensity combined aerobic and resistance exercise programme produced significantly greater improvements in pain intensity, muscle strength, SAMS-Clinical Index scores, and both physical and mental components of health-related quality of life than conventional physiotherapy in patients with statin-associated muscle symptoms. The findings support the superior clinical benefit of a structured moderate-intensity combined aerobic and resistance training programme in the management of SAMS.

DECLARATIONS

Consent for publication

Not applicable.

Conflict of Interest:

The authors declare no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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