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The efficacy of different Aerobic, Pilates and combined therapeutic exercise protocols to functional capacity, fatigue and quality of life in adults with Multiple Sclerosis: controlled experimental intervention

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Abstract

Background: Multiple Sclerosis (MS) is a complex neurodegenerative disease affecting the central nervous system (CNS). It is considered to be an idiopathic disease of possibly autoimmune origin. The immune system attacks myelin, which is the protective layer around nerve fibers leading to demyelination. This causes disturbances in the communication networks within the brain and spinal cord. The participation of a person with MS in a physical exercise program has been debated as bearing positive effect in its fitness, function, disease symptoms and quality of life. The rate of physical activity is substantially lower in persons with multiple sclerosis (MS) than in the general population.
Scope: The purpose of this study was to evaluate the efficacy of different therapeutic exercise protocols to functional capacity, fatigue and quality of life in adults with MS.
Methods: Controlled experimental interventions were developed by forming a group of aerobic exercise (n=6), pilates (n=6), combined exercise (n=6) and a control one (n=18). Berg Balance Scale (BBS), Timed 25-Foot Walk, Fatigue Severity Scale (FSS) and Multiple Sclerosis Quality of Life (MSQOL)-54 were used to assess functional aspects and quality of life in all 36 adults with MS before and after exercise protocols.
Results: At 18 months post interventions all three experimental groups were significantly improved ($p<0.05$) regarding the Mental Health Composite (MHC) while significantly lower scores were found regarding the Mental and Physical Health Composites in the control group ($p<0.05$). Physical Health Composite (PHC) was also improved in all intervention groups but not significantly ($\alpha=0.05$). BBS, Timed 25-Foot Walk and FSS significantly improved over time in the combined and aerobic exercise groups ($p<0.05$). The pilates exercise group showed the less not significant improvement and the control group had negative execution scores in all aforementioned scales assessed ($\alpha=0.05$).
Conclusions: Findings indicated the efficacy of aerobic and combined exercise protocols in people with MS. Various exercise combinations are recommended to select the best rehabilitation regimen for people with MS individually or in groups.

Keywords: Multiple Sclerosis; Physical Exercise; Pilates; Aerobic Exercise; Combination of exercises; Quality of Life.

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1 Introduction

Multiple sclerosis (MS), is a chronic inflammatory demyelinating disorder of the central nervous system (CNS) that predominantly involves the white matter (WM). Pathology studies conducted as early as the 19th century have already recognized that MS affects not only the WM but also the gray matter (GM), which somehow got neglected over the years. MS is characterized by relapses, lesions, and progression of neurological disability because of inflammatory demyelination and transection of axons, along with ongoing neurodegeneration involving loss of neurons. The exact aetiology of MS remains unknown. It is believed that a combination of genetic, infectious, environmental and/or autoimmune factors contribute to disease onset. It has an onset during early adult life (20-40 years) with women having MS almost 2.5 times more often than men. Most common symptoms are fatigue, emotional and cognitive changes, mobility limitations, sleeping problems resulting in a person's poor quality of life and loss of independence (Motl et al., 2011; Motl et al., 2018).

One's participation in a regular physical exercise program results in his physical, cognitive and emotional improvement. Although physical exercise has been previously discouraged for people with MS for fear of possibly increasing fatigue or triggering a disease exacerbation, there is now evidence that participating in a physical exercise program improves MS patients' aerobic and muscular fitness, fatigue, depression, walking, balance, cognition, and the overall quality of life. There also may be additional benefits for CNS structure, sleep quality and cardiovascular/metabolic comorbidity (Motl et al., 2018). Another crucial factor is that participating in regular physical exercise training a person with MS may experience reduced rates of relapses and slowed disability progression.

At the same time, various physical exercise applications have been recommended in the field of MS population. In particular aerobic exercise, is associated with improvements in muscle strength, balance, walking capacity and fatigue (Petajan et al., 1996; Rampello et al., 2007; Sabapathy et al., 2011). Swank et al. (2013) suggested among others a positive effect in mood, sleep and concentration, an improvement in the cognitive function (Motl et al., 2011; Beier et al., 2014; Briken et al., 2014) and the overall quality of life in MS patient's population (Motl & Gosney, 2008).

On the other hand, Pilates exercise is also becoming popular to MS persons. Pilates is a series of exercises based on the whole-body movement emphasizing awareness of body structure, body alignment, and muscle recruitment with a focus on stabilizing core muscles during dynamic movement. Thus, it has been stated as beneficial in MS patients by improving balance and mobility through core muscles activation (Whitney et al., 2018).

In a recent study by Kara et al., (2017), a comparison of aerobic and pilates exercise programs in MS participants found similar moderate changes in cognition, physical performance, balance, depression and fatigue levels in both groups. Pilates exercises was found more effective than aerobic only in cognition. The results though of combined training sessions for MS have not been systematically developed, evaluated and compared with aerobic and pilates in a controlled experimental study (Konecny et al., 2010). Consequently, the aim of this research attempt was to evaluate the efficacy of different aerobic, pilates and combined therapeutic exercise protocols to functional capacity, fatigue and quality of life in adults with Multiple Sclerosis.

2 Method

2.1 Study design

The study was developed locally in a center of Greek MS Society and formed a Randomised Controlled Trial (RCT). Approval was attained by the ethics committee of Medical school, Aristotle University of Thessaloniki. Data collection and interventions were held from April 2017 to October of 2018 (18 months period). Patients were randomly sited to three therapeutic exercise protocols and one control group. Stratified block randomization was applied generating sample sizes and random codes for each participant. The subjects' baseline characteristics used as main covariances for the stratification were age and Kurtzke Expanded Disability Status Scale (EDSS) (Kurtzke, 1983). Administration of the center was involved only in the randomization process while patients, physicians and trainers were blinded. All participants voluntarily filled the informed consent. Baseline scores were recorded within 5 days before the intervention and post-test scores were recorded 72-80 hours after the end of the protocol for each group.

2.2 Participants

A total of 18 participants were included in the three experimental groups having been diagnosed with Relapsing-Remitting MS (RRMS) following sequential convenience sampling in Thessaloniki, center of Greek MS Society, Greece. The control group was formed by the same pooled subjects' site. All participants were identified and checked for compliance before any group assignment was made. The participants' mean age was found 41.7±8.7 years in the compo group, 49±10.2 in the aero group, 46.3±12.4 in the pilates group and 46.1±14 in the control group. The mean of the years since 1st diagnosis of MS was 14±7.2 with a minimum of 2 and maximum of 27 years for all participants in experimental groups and control. Kruskal-Wallis test showed no statistically significant differences between groups at baseline demographic and MS characteristics and particularly in age, BMI, EDSS, number of years since 1st MS diagnosis at a significance level of α=0.05 (see Table 1).

Table 1. Participants' demographic and MS characteristics

		N	Mean	SD	Min	Max	Kruskal-Wallis
Age	combo	6	41.7	8.7	32.0	55.0	H=1.163, df=3 p=0.777
	aero	6	49.0	10.2	37.0	67.0	
	pilates	6	46.3	12.4	29.0	62.0	
	control	18	46.1	14.0	24.0	74.0	
	Total	36	45.9	12.1	24.0	74.0	
BMI	combo	6	25.0	4.4	18.4	31.1	H=0.990, df=3, p=0.813
	aero	6	27.8	5.6	21.0	37.4	
	pilates	6	25.5	3.7	21.1	31.2	
	control	18	25.9	6.1	18.2	42.3	
	Total	36	26.0	5.3	18.2	42.3	
EDSS	combo	6	3.2	1.8	1.0	5.5	H=0.299, df=3, p=0.965
	aero	6	2.8	1.4	1.0	5.0	
	pilates	6	2.8	2.0	0.5	6.0	
	control	18	2.8	1.5	0.0	5.0	

Years since 1st diagnosis	Total	36	2.8	1.6	0.0	6.0	H=1.035, df=3, p=0.801
	combo	6	11.5	7.5	3.0	21.0	
	aero	6	13.0	6.4	5.0	22.0	
	pilates	6	15.0	7.2	6.0	27.0	
	control	18	14.9	7.8	2.0	27.0	
	Total	36	14.0	7.2	2.0	27.0	

Compo: Combined therapeutic exercise protocol, aero: Aerobic therapeutic exercise protocol, pilates: Pilates therapeutic exercise protocol, control: Control group, EDSS: Kurtzke Expanded Disability Status Scale, BMI: Body Mass Index= kg/m^2

Gender was similarly distributed among experimental and control group with a higher frequency of women in all cases. As a total, 77.8% of the sample were females and 22.2% males.

Table 2. Gender and exercise group crosstabulation

	combo (n=6)	**aero** (n=6)	**pilates** (n=6)	**control** (n=6)	**Total** (n=36)
Female	5 (83.3%)	4 (66.7%)	5 (83.3%)	14 (77.8%)	28 (77.8%)
Male	1 (16.7%)	2 (33.3%)	1 (16.7%)	4 (22.2%)	8 (22.2%)

Eligible participants had to be able to walk even by using an assisting mean and have a score equal or less than 6 (≤6) in the EDSS based on McDonald criteria. All included subjects should have followed the complete exercise protocol otherwise they were dropped off.

2.3 Inclusion Criteria

All patients were diagnosed with Relapsing Remitting Multiple Sclerosis (RRMS) and had to comply with the following criteria: be 18 years old and/or more, have the cognitive ability to give written and spoken consent for their participation to the intervention. As mentioned before, they should be adults, right-handed and being diagnosed with definite RRMS according to McDonald criteria by the attended neurologist.

2.4 Exclusion Criteria

Patients excluded were mainly those of the following criteria: history of systemic disease, concomitant neurological disorders, epilepsy, heart diseases, anemia, or severe depression, serious surgery, diabetes, cancer / chemotherapy, pregnancy. Other health status not allowing exercise protocol intervention such as cardiovascular diseases and/or musculoskeletal injuries/diseases. Patients undergoing an MS attack or relapsing period were also excluded.

2.5 Experimental Interventions

All exercise sessions were led by an experienced and certified physical activity instructor with training on adapting exercises for individuals with MS. A detailed curriculum of exercise programs is available from the authors on request. All three experimental therapeutic exercise protocols lasted for 18 months and were developed as follows:

Aerobic therapeutic exercise protocol. Reduction of fatigue in MS patients affected by mild or moderate disability. MS patients can positively adapt to resistance training

which may bring about lower fatigue level and improved ambulation. Numerous studies have demonstrated that exercise training can improve muscle strength in persons with MS. Protocols have included progressive resistance training (PRT), aerobic exercise (AE), combined AE and PRT, and other physical activities (Kjolhede et al., 2012; American College of Sports Medicine, 2007; Learmonth et al., 2012). Participants in the aerobic group performed 3 physical exercise training sessions per week each of 60 minutes total duration. Each session consisted of 10 minutes warm up period (respiration, limb stretching and flexibility exercises) and 45 minutes of exercise at an intensity that was associated with 60% Heart Rate Reserve (HRR). Initially, a moderate intensity of 40% to 60% of HRR was considered and increased to 80% with the main goal to achieve regular exercise patterns. The main program included isotonic exercises, strengthening exercises, machines, elastic bands, stretch and aerobic combined exercises, balance and walking exercises. A 5-minute cooling period was fixed at the end of all sessions. Special consideration and comments were developed considering non-weight-bearing modes if there was joint pain or injury, watching for indications of hyperthermia and providing guidelines on water consumption during exercise.

Pilates therapeutic exercise protocol. The pilates exercise protocol's key elements were developed according to the pilates basic exercise program which consists of breathing, focusing, placement of the rib cage, shoulder, head and the neck (Lessen, 2014; Siler & Turlington, 2000; Pilates & Miller, 1945; Pilates, 1998). When the pilates exercises were appropriately executed by the patients holding on relevant key elements, the level/difficulty was increased.

Participants in the pilates group performed 2 physical exercise training sessions per week each of 60 minutes total duration. Each session consisted of 10 minutes warm up period (respiration, limb stretching and flexibility exercises) and 45 minutes of mat exercise. The main program included: 1st exercise-ARM SCISSORS (2sets x 6 rep), 2nd exercise-ABDOMINAL PREP (2sets x 6 rep), 3rd exercise-SPINAL ROTATION (2sets x 8 rep), 4th exercise-CAT STRETCH (2sets x 6 rep), 5th exercise-HALF ROLL BACK (2sets x 8 rep), 6th exercise-SPINE TWIST (2sets x 8 rep), 7th exercise-HUNDRED (2sets x 10 rep/counting), 8th exercise-BREAST STROKE PREPS - HANDS BY HIPS (2sets x 10 rep/counting), 9th exercise-SHOULDER BRIDGE PREP (2sets x 10 rep), 10th exercise-OBLIQUES ROLL BACK (2sets x 10 rep), 11th exercise-NECK PULL (2sets x 6 rep), 12th exercise-ROLLING LIKE A BALL (2sets x 6 rep). Five minutes cool down SHELL STRETCH and static/proprioceptive or passive stretching at the end of each pilates session was fixed.

Combined therapeutic exercise protocol. Participants in the combined exercise group performed 4 physical exercise training sessions per week each of 60 minutes total duration. Each session consisted of 10 minutes warm up period (respiration, limb stretching and flexibility exercises) and 45 minutes of various combinations of aerobic and resistance exercises with different repetition rates (Dalgas et al., 2008; Konecny et al., 2010; Surakka et al., 2004). The intensity was associated with a moderate intensity of 40% to 60% HRR increased to 80% with the main goal was to achieve regular exercise patterns. Five minutes cool down, static and proprioceptive or passive stretching at the end of each combined exercise session was considered at the end of all sessions.

2.6 Primary Outcomes

Pre- and post-intervention scores of Multiple Sclerosis Quality of Life (MSQOL)-54 instrument, were recorded and analyzed to investigate primary outcomes for all three experimental groups and the control group (Vickrey et al., 1995). The MSQOL-54 questionnaire is well-accepted for its reliability and validity to combine the Quality of Life

(QOL) aspects of the Short Form 36-Item Health Survey Questionnaire (SF-36) (Ware, 1993) with the MS particularities. The 54-items/questions result to 14 subscales analyzing different health related dimensions whereas further scoring formulas lead to the composites of Physical and Mental Health where the higher the score the QOL is better.

2.7 Secondary Outcomes

Pre- and post-intervention scores of FSS, Timed 25-foot walk test and BSS were used to assess functional tasks' performance and fatigue, as secondary outcomes.

Berg balance scale (BBS) as developed and validated by Berg et al. (1989; 1992) was used to measure postural control and balance of the MS study population. The instrument evaluates individual's balance maintenance ability by performing a set of 14 everyday living tasks. The five-point likert scales' (ranging from 0 to 4) sum gives the instrument's total score which may range from 0-56. The lowest is the score (0-20) the higher is the risk to fall whereas higher score (41-56) indicates low fall risk. BBS was adapted into the Greek language in 2015 by Lampropoulou S. even though it is widely used in elderly and other special populations encountering with problems in Activities of Daily Living (ADLs) such as MS (Cattaneo et al., 2006; Fjeldstad et al. 2009).

FSS is widely used with MS and other clinical populations to rate fatigue severity through 9 items scored with a 7-point likert scale from 1 to 7 (Krupp et al. 1989). The mean score of the 9 items' sum gives the final FSS score ranging from 9-63 while higher scores shows worse impact of fatigue in ADLs. FSS has been translated and validated in Greek MS patients (Bakalidou et al., 2013). A score more than 36 indicates serious functional problems in the modality and fatigue to execute physical, mobility and social daily tasks.

The timed 25-foot walk is a quantitative lower limbs function measure. It is the first test of the Multiple Sclerosis Functional Composite Measure (MSFC) tools given at each visit. The patient is placed at one end of a clearly marked 25-feet course and is instructed to walk with safety as fast as possible. Instructions are given once again with the patient walking the same distance backwards. Patients' performance is recorded in seconds with 3 minutes (180 seconds) time limit per trial. Timed 25-foot walk is one of the most used evaluations in MS testing locomotion. In our case test was performed according to the instructions given by authors (Cutter et al., 1999; Fischer et al., 1999).

2.8 Statistics

Descriptive statistical methods were used to summarize biological and demographical characteristics of the sample. Non parametric statistical methods were used since samples were not normally distributed. Kruskal-Wallis non parametric test was used to compare groups at their baseline continuous variables and characteristics such as age, BMI, EDSS and years since 1st MS diagnosis. Wilcoxon Signed Ranks Test (non parametric) was used to compare improvements over time, from baseline to post-rehabilitation values. Monte Carlo simulation at 95% (α=0.05) confidence level was computed from the statistical tests executed. SPSS V25 and excel spreadsheets 365 were combined to perform main statistical analysis and form the results' presentation.

3 Results

All 14 MSQOL-54 subscales' mean scores increased from baseline measurements to the ones made post therapeutic exercise protocols completion in all experimental groups except the Emotional well-Being (EB) that slightly decreased in the case of aerobic and pilates group. On the contrary, the control group had negative results in all MSQOL-54 dimensions' repeated measurements made after the 18 months intervention period (Table 3).

Table 3. Mean changes from baseline to post rehabilitation for all MSQOL-54 subscales

	combo group (N=6)		**aerobic group (N=6)**		**pilates group (N=6)**		**control group (N=18)**	
MSQOL-54 subscale	Mean change	SD	Mean change	SD	Mean change	SD	Mean change	SD
MSQOL (PF)	21.7	38.6	31.8	33.1	29.2	36.6	-25.3	34.1
MSQOL (RP)	8.3	37.6	20.8	29.2	16.7	30.3	-5.6	29.1
MSQOL (RE)	39.0	44.4	50.2	40.7	50.2	35.0	-57.5	25.2
MSQOL (BP)	26.0	16.0	16.8	19.4	15.7	20.3	-10.2	16.8
MSQOL (EB)	3.3	4.7	-1.3	3.3	-2.0	4.2	-22.7	4.6
MSQOL (EN)	22.7	8.6	18.0	17.3	12.7	9.3	-18.2	6.2
MSQOL (HP)	3.3	6.1	2.5	4.2	-1.7	12.1	-5.0	4.2
MSQOL (SF)	12.7	12.9	5.7	13.9	5.8	20.4	-6.4	19.5
MSQOL (CF)	5.8	17.4	7.5	12.9	2.5	12.9	-7.5	7.1
MSQOL (HD)	12.5	7.6	10.0	4.5	7.5	5.2	-7.5	3.9
MSQOL (SX)	25.0	13.9	16.7	15.8	15.3	17.8	-12.0	11.5
MSQOL (CH)	8.3	12.9	8.3	12.9	4.2	10.2	-4.2	9.6
MSQOL (SS)	4.2	10.2	8.3	12.9	4.2	10.2	-4.2	9.6
MSQOL (OQ)	11.4	11.5	3.1	10.2	3.9	11.7	-4.4	8.0

PF: Physical Function, RP: Role limitations-Physical, RE: Role limitations-Emotional, BP: Body Pain, EB: Emotional well-Being, EN: Energy/fatigue, HP: Health Perceptions, SF: Sexual Function, CF: Cognitive Function, HD: Health Distress, SX: Sexual function, CH: Change in Health, SS: Satisfaction with Sexual function, OQ: Overall Quality of life

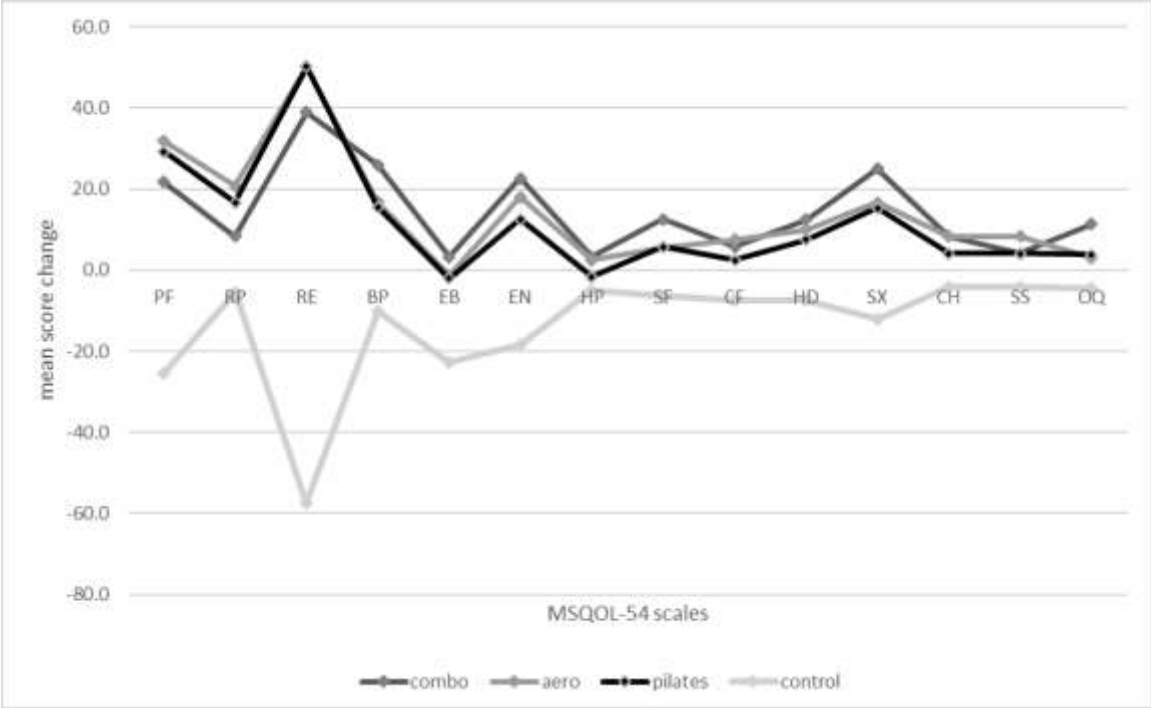

Figure 1. Mean score changes in MSQOL-54 subscales per group

All walking and balance ability scales assessed, meaning Timed 25-Foot Walk test, FSS and Berg Balance Scale scores', had positive results and statistically significantly improved over time ($p<0.05$) for the combined and aerobic experimental exercise groups (see Table 4). Pilates experimental exercise group showed an improvement in all aforementioned scales' scores but relatively lower than the other two intervention groups and not statistically significant ($\alpha=0.05$). Control group had negative execution scores in all tests at the repeated time measurements were made.

MSQOL-54 (PHC) score had a marginally significant improvement in the combined and aerobic experimental exercise groups ($p<0.061$) and a not significant one in the case of the pilates rehabilitation group. MSQOL-54 (MHC) score was found significantly better in all experimental groups post rehabilitation ($p<0.05$). On the contrary, control group had statistically significant lower MSQOL PHC and MHC scores over time ($\alpha=0.05$) (Table 4).

Table 4. Baseline/post rehabilitation data and mean change from baseline for all outcomes within groups

T25-Foot Walk	**Baseline**		**Post-rehabilitation**		**Change**		**Wilcoxon test (baseline-post rehabilitation sec)**
Group	Mean	SD	Mean	SD	Mean	SD	
combo (n=6)	12.4	7.4	9.4	5.6	-3.0	2.2	z=-2.201, p=0.035*
aerobic (n=6)	9.8	3.7	7.9	3.9	-1.9	1.1	z=-2.201, p=0.030*
pilates (n=6)	9.9	5.3	9.4	6.4	-0.4	2.2	z=-0.524, p=0.685
control (n=18)	11.8	6.5	16.6	7.5	4.8	5.3	z=-3.593, p=0.000*

FSS	Baseline		Post-rehabilitation		Change		Wilcoxon test (baseline-post rehabilitation score)
Group	Mean	SD	Mean	SD	Mean	SD	
combo (n=6)	41.3	8.4	30.7	7.1	-10.7	4.1	z=-2.207, p=0.030*
aerobic (n=6)	38.0	6.6	31.7	5.8	-6.3	1.9	z=-2.207, p=0.031*
pilates (n=6)	36.3	8.9	31.8	6.5	-4.5	4.9	z=-1.792, p=0.095
control (n=18)	35.6	9.5	44.9	8.4	9.3	4.7	z=-3.740, p=0.000*
Berg	**Baseline**		**Post-rehabilitation**		**Change**		**Wilcoxon test (baseline-post rehabilitation score)**
Group	Mean	SD	Mean	SD	Mean	SD	
combo (n=6)	47.0	4.7	50.5	4.1	3.5	1.4	z=-2.226, p=0.032*
aerobic (n=6)	47.7	3.4	51.7	2.6	4.0	1.4	z=-2.207, p=0.029*
pilates (n=6)	46.8	4.7	50.7	4.1	3.8	3.0	z=-2.003, p=0.062
control (n=18)	46.3	3.6	42.2	4.7	-4.1	2.3	z=-3.746, p=0.000*
MSQOL-54 (PHC)	**Baseline**		**Post-rehabilitation**		**Change**		**Wilcoxon test (baseline-post rehabilitation score)**
Group	Mean	SD	Mean	SD	Mean	SD	
combo (n=6)	56.7	22.5	72.4	22.1	15.7	11.1	z=-1.992, p=0.061
aerobic (n=6)	49.5	17.8	65.0	20.4	15.5	10.1	z=-1.997, p=0.061
pilates (n=6)	53.6	20.2	66.3	19.4	12.7	14.1	z=-1.572, p=0.151
control (n=18)	55.0	12.9	43.3	4.3	-11.7	11.8	z=-2.812, p=0.003*
MSQOL-54 (MHC)	**Baseline**		**Post-rehabilitation**		**Change**		**Wilcoxon test (baseline-post rehabilitation score)**
Group	Mean	SD	Mean	SD	Mean	SD	
combo (n=6)	53.3	20.8	68.3	13.9	15.0	10.3	z=-2.207, p=0.030*
aerobic (n=6)	49.0	15.7	63.7	13.0	14.7	11.1	z=-2.214, p=0.028*
pilates (n=6)	52.0	15.5	65.6	12.8	13.6	9.3	z=-2.201, p=0.030*
control (n=18)	62.9	11.0	39.6	5.2	-23.3	7.6	z=-3.757, p=0.000*

Note: No statistically significant differences were found between groups at baseline (α=0.05) Abbreviations: SD, Standard Deviation ; PHC, Physical Health Composite ; MHC, Mental Health Composite ; Timed 25-Foot Walk test: subjects' walk time (2 trials' mean) in seconds ; Fatigue Severity Scale (FSS): the score ranges from 9-63 where a total less than 36 indicates not important fatigue and when is higher than 36 further advice is needed ; Berg Balance Scale scores' interpretation: 41-56=low fall risk, 21-40=medium fall risk, 0-20=high fall risk, MSQOL-54 Physical and Mental Health Composites" score: the higher the score the QOL is increased

Among the three experimental groups the combined exercise protocol group had the better mean improvement in the mental and physical composite scale of the MSQOL-54, followed by the aerobic exercise protocol group. The smaller improvement in both MSQOL-54 composite scales showed the pilates exercise group while the control group showed an important decline in both cases (Figure 2).

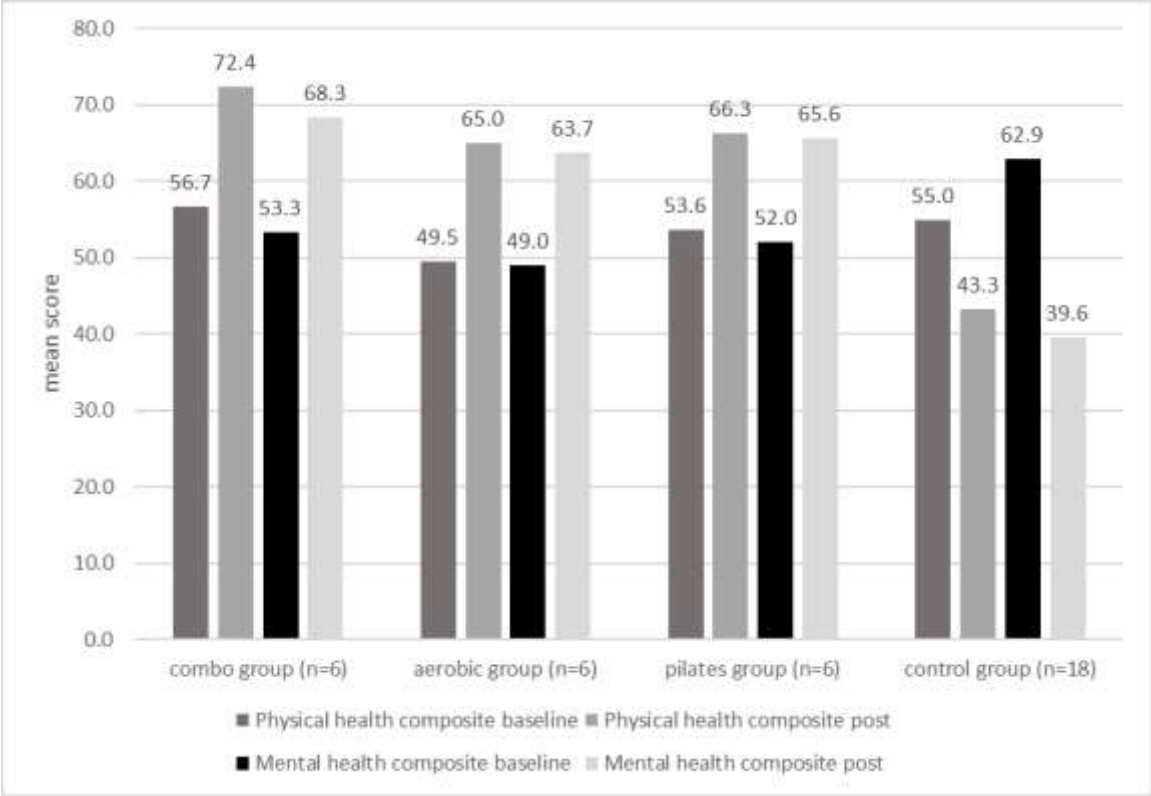

Figure 2. Mean scores in PHC and MHC of MSQOL-54 per group

4 Discussion

Previously, MS patients were advised not to participate in physical exercise. During recent years, it has been increasingly acknowledged that exercise benefits MS patients. Although it is known that physical exercise is beneficial for individuals with MS (Petajan 1996), only a few studies have specifically examined differences among different types of exercise programs so far.

Our results indicated that a combined exercise schedule with a predominant aerobic component was more effective. The greater improvement in functional capacity, fatigue and quality of life was revealed in the combined exercise protocol group followed by the aerobic exercise protocol group with significant positive results after the completion of the relative exercise protocols ($p<0.05$). Pilates experimental group showed the lowest improvement compared with the combined and aerobic groups while there was no significant improvement over time ($\alpha=0.05$). Control group showed a statistically significant decline in all primary and secondary outcomes. It is therefore proposed that a combined exercise protocol may give better results in people with MS leading to improved balance skills, better walking abilities, enhanced muscle strength, quality of life and fatigue. Furthermore, all modalities used in this model were simple, convenient and feasible. Hence, the proper combination of aerobic exercises with smaller portions of resistance exercises may be more suitable and lead to better results in patients with MS (Rietberg et al., 2005; Motl & Pilutti, 2012).

Satisfaction with Sexual function (SS) Health Perceptions (HP) Cognitive Function (CF) Sexual Function (SF) and Role Limitations-Physical (RP) were the subscales among all 14 MSQOL-54 composites having not significant improved results in the experimental groups post-intervention (α=0.05). Still control group had negative results in all MSQOL-54 dimensions' repeated measurements made after the 18 months intervention period.

On the other hand, it was observed a tangible improvement in functional tests' scores and scales after the aerobic and Pilates intervention as well. It can be therefore supported that even lower intensity and frequency (2 or three times per week) exercise rehabilitation can help people with MS after a given period of repetitions (Romberg et al., 2005).

Although current research indicates that MS patients can gain a wide variety of therapeutic and functional benefits from regular activity, the influence of exercise on the progression of MS symptoms remains unclear and additional studies are needed. The requirement for exercise in MS patients is emphasized by their physiological profile, which probably reflects both the effects of the disease per se and the reversible effects of an inactive lifestyle. Finally, various exercise combinations are recommended to select the best rehabilitation regimen for people with MS.

Conflicts of interest

None to report.

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Appendix

Table 5. MSQOL-54 main subscales baseline and post rehabilitation mean scores

	combo group (n=6)		**aerobic group (N=6)**		**pilates group (N=6)**		**control group (N=18)**	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
MSQOL (PF) Physical health baseline	61.7	31.1	49.2	27.5	55.0	31.1	66.2	31.0
MSQOL (PF) Physical health post rehab	83.4	32.0	81.0	29.1	84.2	30.1	40.8	8.1
MSQOL (RP) Role limitations-	45.8	45.9	20.8	40.1	29.2	40.1	30.6	23.6

physical baseline								
MSQOL (RP) Role limitations-physical post rehab	54.2	40.1	41.7	34.2	45.8	33.2	25.0	21.0
MSQOL (RE) Role limitations-emotional baseline	38.8	49.1	27.7	38.9	33.2	36.5	74.0	31.6
MSQOL (RE) Role limitations-emotional post rehab	77.8	40.4	77.8	27.3	83.3	28.0	16.5	17.0
MSQOL (BP) Pain baseline	65.0	25.1	69.8	16.9	71.0	18.3	70.7	16.9
MSQOL (BP) Pain post rehabilitation	91.0	11.0	86.7	17.3	86.7	17.3	60.5	11.8
MSQOL (EB) Emotional well-being baseline	48.0	8.4	49.3	5.5	50.0	6.1	57.3	7.0
MSQOL (EB) Emotional well-being post rehab	51.3	6.9	48.0	7.6	48.0	7.6	34.7	5.7
MSQOL (EN) Energy baseline	39.3	16.5	37.3	12.6	40.0	11.0	50.7	11.0
MSQOL (EN) Energy post rehab	62.0	21.7	55.3	22.4	52.7	16.3	32.4	13.7
MSQOL (HP) Health perceptions baseline	55.8	26.5	47.5	20.9	51.7	21.6	41.7	2.4
MSQOL (HP)	59.2	31.7	50.0	24.5	50.0	24.5	36.7	2.4

Health perceptions post rehab								
MSQOL (SF) Social function baseline	61.0	20.1	55.5	20.3	58.2	23.0	59.1	21.6
MSQOL (SF) Social function post rehab	73.7	21.4	61.2	22.9	64.0	22.3	52.7	10.8
MSQOL (CF) Cognitive function baseline	69.2	24.6	60.0	20.7	65.0	20.0	66.7	6.4
MSQOL (CF) Cognitive function post rehab	75.0	11.0	67.5	8.8	67.5	8.8	59.2	12.4
MSQOL (HD) Health distress baseline	66.7	18.3	62.5	13.7	65.0	13.4	60.0	8.4
MSQOL (HD) Health distress post rehab	79.2	12.4	72.5	11.7	72.5	11.7	52.5	5.8
MSQOL (SX) Sexual function baseline	58.3	9.1	61.1	10.1	65.3	16.2	67.6	9.4
MSQOL (SX) Sexual function post rehab	83.3	14.9	77.8	13.6	80.6	12.5	55.6	10.7
MSQOL (CH) Change in health baseline	41.7	12.9	41.7	12.9	45.8	10.2	50.0	0.0
MSQOL (CH) Change in health post rehab	50.0	0.0	50.0	0.0	50.0	0.0	45.8	9.6

MSQOL (SS) Satisfaction-sexual function baseline	45.8	10.2	41.7	12.9	45.8	10.2	50.0	0.0
MSQOL (SS) Satisfaction-sexual function post rehab	50.0	0.0	50.0	0.0	50.0	0.0	45.8	9.6
MSQOL (OQ) Overall quality of life baseline	57.8	6.6	57.2	5.3	59.4	8.6	56.3	6.2
MSQOL (OQ) Overall quality of life post rehab	69.2	15.3	60.3	15.4	63.3	13.9	51.9	5.6

Table 6. Descriptive statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Time for 25-Foot Walk baseline (sec)	6	12.3650	7.41756	5.80	22.44	5.9125	9.6750	21.0975
Time for 25-Foot Walk post rehabilitation (sec)	6	9.3983	5.62056	4.70	17.12	4.9325	6.7900	16.2650

Ranks

		N	Mean Rank	Sum of Ranks
Time for 25-Foot Walk post rehabilitation (sec) - Time for 25-Foot Walk baseline (sec)	Negative Ranks	6[a]	3.50	21.00
	Positive Ranks	0[b]	0.00	0.00
	Ties	0[c]		
	Total	6		

a. Time for 25-Foot Walk post rehabilitation (sec) < Time for 25-Foot Walk baseline (sec)
b. Time for 25-Foot Walk post rehabilitation (sec) > Time for 25-Foot Walk baseline (sec)
c. Time for 25-Foot Walk post rehabilitation (sec) = Time for 25-Foot Walk baseline (sec)

Table 7. **Descriptive statistics**

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Time for 25-Foot Walk baseline (sec)	6	9.7850	3.66354	6.58	16.36	6.8200	8.7500	12.6175
Time for 25-Foot Walk post rehabilitation (sec)	6	7.8917	3.87851	4.40	15.39	5.6375	6.6550	9.9975

Ranks

		N	Mean Rank	Sum of Ranks
Time for 25-Foot Walk post rehabilitation (sec) - Time for 25-Foot Walk baseline (sec)	Negative Ranks	6[a]	3.50	21.00
	Positive Ranks	0[b]	0.00	0.00
	Ties	0[c]		
	Total	6		

a. Time for 25-Foot Walk post rehabilitation (sec) < Time for 25-Foot Walk baseline (sec)
b. Time for 25-Foot Walk post rehabilitation (sec) > Time for 25-Foot Walk baseline (sec)
c. Time for 25-Foot Walk post rehabilitation (sec) = Time for 25-Foot Walk baseline (sec)

Table 8. Descriptive statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Time for 25-Foot Walk baseline (sec)	6	9.8900	5.25215	5.10	19.03	5.7375	8.5150	13.9300
Time for 25-Foot Walk post rehabilitation (sec)	6	9.4417	6.35482	4.70	21.80	5.8400	6.7050	13.3400

Ranks

		N	Mean Rank	Sum of Ranks
Time for 25-Foot Walk post rehabilitation (sec) - Time for 25-Foot Walk baseline (sec)	Negative Ranks	4[a]	3.25	13.00
	Positive Ranks	2[b]	4.00	8.00
	Ties	0[c]		
	Total	6		

a. Time for 25-Foot Walk post rehabilitation (sec) < Time for 25-Foot Walk baseline (sec)
b. Time for 25-Foot Walk post rehabilitation (sec) > Time for 25-Foot Walk baseline (sec)
c. Time for 25-Foot Walk post rehabilitation (sec) = Time for 25-Foot Walk baseline (sec)

Table 9. Descriptive statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Time for 25-Foot Walk baseline (sec)	18	11.8250	6.45567	4.01	25.20	7.2175	9.6450	14.8500
Time for 25-Foot Walk post rehabilitation (sec)	18	16.5794	7.53655	6.22	28.25	10.4875	15.2200	23.5275

Ranks

		N	Mean Rank	Sum of Ranks
Time for 25-Foot Walk post rehabilitation (sec) - Time for 25-Foot Walk baseline (sec)	Negative Ranks	2a	1.50	3.00
	Positive Ranks	16b	10.50	168.00
	Ties	0c		
	Total	18		

a. Time for 25-Foot Walk post rehabilitation (sec) < Time for 25-Foot Walk baseline (sec)
b. Time for 25-Foot Walk post rehabilitation (sec) > Time for 25-Foot Walk baseline (sec)
c. Time for 25-Foot Walk post rehabilitation (sec) = Time for 25-Foot Walk baseline (sec)

Table 10. Descriptive statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles 25th	50th (Median)	75th
Age	36	45.86	12.128	24	74	37.00	46.00	53.75
BMI	36	25.9789	5.28094	18.16	42.30	21.8425	25.5500	28.6275
EDSS	36	2.819	1.5591	0.0	6.0	1.625	2.500	3.875
Years since 1st diagnosis	36	14.03	7.245	2	27	7.25	13.00	20.00
Rehabilitation exercise protocol	36	3.00	1.171	1	4	2.00	3.50	4.00

Ranks

Rehabilitation exercise protocol		N	Mean Rank
Age	combo	6	14.75

	aero	6	20.92
	pilates	6	19.75
	control	18	18.53
	Total	36	
BMI	combo	6	17.00
	aero	6	22.33
	pilates	6	17.83
	control	18	17.94
	Total	36	
EDSS	combo	6	20.58
	aero	6	18.00
	pilates	6	17.67
	control	18	18.25
	Total	36	
Years since 1st diagnosis	combo	6	15.00
	aero	6	17.33
	pilates	6	19.50
	control	18	19.72
	Total	36	

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