ORIGINAL ARTICLE

Effect of Aquatic Exercise Training on Fatigue and Health-Related Quality of Life in Patients With Multiple Sclerosis

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Objective: To examine the effectiveness of aquatic exercise training on fatigue and health-related quality of life (HRQOL) in women with multiple sclerosis (MS).

Design: Randomized controlled trial, 4-week and 8-week follow-up.

Setting: Referral center of a multiple sclerosis society.

Participants: Women (N=32) diagnosed with relapsing-remitting MS (mean age ± SD, 32.6±8.0y) were recruited into this study. After undergoing baseline testing by a neurologist, participants were randomly assigned to either an intervention (aquatic exercise) or a control group.

Interventions: The intervention consisted of 8 weeks supervised aquatic exercise in a swimming pool (3 times a week, each session lasting 60min).

Main Outcome Measures: At baseline, 4 weeks, and 8 weeks, fatigue and HRQOL were assessed by a blind assessor using the Modified Fatigue Impact Scale and the Multiple Sclerosis Quality of Life-54 questionnaire, respectively. A mixed-model approach to repeated-measures analysis of variance was used to detect within- and between-subject effects.

Results: Findings are based on 21 patients (10 from the exercise group and 11 from the control group) who had data available on outcomes. There was no significant difference between the 2 groups at the baseline. Patients in the aquatic exercise group showed significant improvements in fatigue and subscores of HRQOL after 4 and 8 weeks compared with the control group. Results obtained from the intention-to-treat analysis were consistent with those of per-protocol analysis.

Conclusions: The findings suggest that aquatic exercise training can effectively improve fatigue and HRQOL of patients with MS and should be considered in the management of this relatively common public health problem.

Key Words: Fatigue; Multiple sclerosis; Quality of life; Rehabilitation.

MULTIPLE SCLEROSIS (MS) is a relapsing-remitting and chronic progressive disease that affects the brain and spinal cord, resulting in loss of muscle control, vision, balance, and sensation. Usually, a person is diagnosed with MS between 20 and 50 years of age, with women being twice as likely as men to be affected earlier in life.[1] Fatigue is one of the most common disabling complaints in patients with MS.[2,3] It causes people with MS to lose their job,[4] limits their social relationships,[5] affects their mental health,[6] and generally impairs a person's ability to perform routine daily tasks.[7] Further, research has indicated that patients with MS are disproportionally likely to exhibit depressive symptoms[3,8] and manifest low levels of quality of life compared with a healthy population and with those with other chronic illnesses.[9]

MS currently has no cure and available treatments are offered to slow the progression of the disease, reduce relapses, or improve symptoms.[2] Therefore, the symptomatic and supportive interventions that aim to improve daily functioning of patients with MS are important.[10] Exercise training is considered a significant behavioral strategy with implications for slowing disease progression in MS.[11] A review of several studies based on 600 participants has suggested that exercise training programs are associated with small, but clinically meaningful, improvements in walking mobility among MS patients.[12] Despite benefits of physical exercise for patients with MS, recent studies suggest that individuals with MS are physically less active than the average, healthy population.[13]

Randomized controlled trials have indicated that exercise training is associated with increased fitness,[14] reduced motor fatigue,[15] improved quality of life,[16] and psychological conditions[17] in MS patients. The American Physical Therapy Association has established preferred practice patterns that provide a basis for the exercise therapy of patients, including those with MS.[18] One specific type of physical therapy that is recommended by the American Physical Therapy Association is

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List of Abbreviations

ANOVA	analysis of variance
BMI	body mass index
EDSS	Expanded Disability Status Scale
HRQOL	health-related quality of life
IMSS	Isfahan Multiple Sclerosis Society
ITT	intention-to-treat
MFIS	Modified Fatigue Impact Scale
MS	multiple sclerosis
MSQOL-54	Multiple Sclerosis Quality of Life-54
RRMS	relapsing-remitting multiple sclerosis

aquatic exercise. Notwithstanding, there is limited information about the modes of physical activity performed by MS patients.[13,19] A recent study by Weikert et al[19] has found walking to be the most common type of self-reported physical activity among people with MS, followed by gardening and weight training.

The buoyant nature and viscosity of water facilitate physical activities for individuals with a physical weakness. In addition, as patients with MS may experience exacerbating symptoms in exposure to heat, aquatic exercise can help to reduce weakness and other neurologic symptoms.[20] However, there is little known about the effectiveness of aquatic exercises on the level of fatigue and quality of life in patients with MS. Further, there is a lack of knowledge about the impact of duration of aquatic exercise on fatigue and quality of life of MS patients. The available evidence about the impact of aquatic exercise is based on weak study designs. Case reports and case series have suggested benefits of pool exercise in improved fitness and movements of patients with MS.[21,22] Their findings have been supported by quasi-experimental[23-25] and noncontrolled[26] trials.

In a noncontrolled trial, Salem et al[26] found improved motor function after a 5-week aquatic exercise program among 11 patients with MS. Salem's study[26] did not examine the effect of aquatic exercise on patients' quality of life. To date, there is a lack of evidence based on randomized controlled trials examining the effect of an aquatic exercise program on fatigue and quality of life of MS patients. The present study aims to examine changes in fatigue and health-related quality of life (HRQOL) in patients with relapsing-remitting multiple sclerosis (RRMS) after 4 and 8 weeks of aquatic exercise training. The following is hypothesized: (1) MS patients who undergo aquatic exercise achieve significant improvement in fatigue and HRQOL; and (2) the impact of 8 weeks of aquatic exercise is greater than that of 4 weeks of aquatic exercise.

METHODS

Participants

The present study was approved by the Ethics Committee of the University of Isfahan and the Isfahan Multiple Sclerosis Society (IMSS). One hundred seventy-eight patients diagnosed with MS were referred to the IMSS by public and private neurology clinics (fig 1). Participants included in this study were all women diagnosed with RRMS referred to the IMSS by public and private neurologists in 2009. In order to prevent extreme fatigue in patients with more severe disability, the referring neurologists requested to include patients with the Expanded Disability Status Scale (EDSS) scores[27] of $\leq$3.5. The inclusion criteria were as follows: diagnosis of clinically or laboratory-supported MS, a minimum time of 2 years since the diagnosis was made, no relapse within the 4 weeks preceding baseline, and ability to participate in regular exercise sessions. Patients were excluded from the study if they had a relapse during the intervention period and/or had a disease preventing their participation (eg, cardiovascular, respiratory, or skeletal diseases). After explaining the purpose of the study to the patients and obtaining informed consent, 32 patients were recognized eligible and recruited into the study. They were randomly allocated into 2 groups: exercise and control. Randomization was completed by someone who had no other study responsibilities using shuffled, sealed envelopes with group allocations inside.

All patients in both the exercise and control groups were instructed to refrain from use of medication (except their routine treatment), use of supplementary nutrition, consumption of tea and coffee, smoking cigarettes, and any rigorous physical activity within 48 hours before the baseline tests. During the 8-week program, 6 patients from the exercise group and 5 patients from the controls were excluded from continuing the study. The reasons for exclusion were experience of relapse, personal circumstances, being unable to regularly participate in exercise training, and refusing to participate in measurement of outcomes at both 4-week and 8-week measurements. As a result, 21 patients (10 in the exercise and 11 in the control groups) remained in the study.

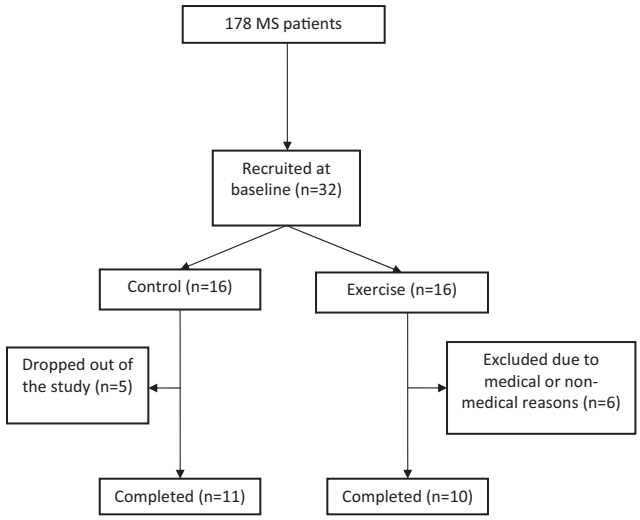

Fig 1. Sampling frame of the study.

Design

One week before the start of the intervention period, all patients in the exercise and control groups were asked to fill out a questionnaire comprising information about sociodemographic, clinical, and anthropometric characteristics. The intervention group was administered an 8-week aquatic exercise training, while the participants in the control group were asked to maintain their current treatment and behavior throughout the 8-week study period. The patients in the 2 groups were treated similarly except for the exercise training. Outcome measures were assessed by research assistants who were blind to the patients' groups.

Aquatic Exercise Training

All participants in the exercise group took part in an aquatic exercise program for a period of 8 weeks. It consisted of 3 sessions per week, each session lasting 60 minutes (including 10 minutes of warm-up, 40 minutes of exercise, and 10 minutes of cool-down). The aquatic exercise training was led and supervised by a certified aquatic instructor who had experience in conducting aquatic exercise programs for persons with physical disabilities. Lifeguards and pool safety equipment were available during the training sessions. Intensity was prescribed at 50% to 75% maximal heart rate reserve. The aquatic exercise was undertaken in Isfahan University's swimming pool, with water temperature maintained between 28°C and 30°C. The patients were advised to report to the trainer or the research supervisor if they encountered any difficulty, extreme fatigue, or disability during and between exercise sessions.

During the first training session, participants were familiarized with the exercise training in water. They were instructed

about target training intensity and palpating and measuring their 15-second radial pulse. They also completed an assessment of their competency in measuring pulse. The patients were encouraged to maintain their target heart rate throughout the 40 minutes of aquatic exercise. Heart rate was measured at the start and end of the warm-up, 3 times during the 40-minute exercise (at 10, 25, and 35min), and again at the end of the cool-down.

The warm-up and cool-down periods were performed in the pool and included low-intensity aerobic exercises such as breathing exercises, flexibility, walking, and neck, arm, and leg movements. The aquatic exercises included activities focused on joint mobility, flexor and extensor muscle strength, balance movements, posture, functional activities, and intermittent walking. Throughout the training session, quality of movements was emphasized and neutral spinal position was encouraged. For security, patients were allowed to hold onto a noodle or foam hand bars while performing exercises. At the end of each session of exercise training, patients were encouraged to participate in 5 minutes of entertaining and playful activities. Incorporation of such activities helped to make the program enjoyable and promote exercise adherence.

Measurement of Outcomes

For both the exercise and control groups, fatigue and HRQOL were assessed at the baseline, as well as at the end of week 4 and week 8 of the study.

Fatigue

The patients' fatigue was measured using the Modified Fatigue Impact Scale (MFIS). The MFIS is a modified form of the Fatigue Impact Scale,[7] based on items derived from interviews with MS patients concerning how fatigue impacts their lives. It has been recommended as an outcome measure for use in MS[28] and is commonly used to generate an overall score of fatigue.[29] This instrument provides an assessment of the effects of fatigue in terms of physical, psychosocial, and cognitive functioning. Research has indicated that the MFIS is a multidimensional scale and should not be used as a single overall score of fatigue.[30] For the purpose of this study, the overall scale, as well as physical, psychosocial, and cognitive subscales of the MFIS, were used as outcome measures. The full-length MFIS consists of 21 items, with options scored between 0 and 4. Each patient's sum of scores for the 21 items ranges between 0 and 84, with a higher score representing more fatigue. Reliability and validity of the MFIS have been established in patients with MS.[6,7,31]

Health-Related Quality of Life

Measurement of HRQOL can serve as a screening tool for patients reporting changes in disease-related symptoms and functional ability. The HRQOL was assessed by the disease-specific Multiple Sclerosis Quality of Life-54 (MSQOL-54) questionnaire[32] at baseline, 4 weeks, and 8 weeks. Unlike some quality of life measures, the MSQOL-54 questionnaire does not provide a single number to summarize quality of life. It consists of 54 items divided into 12 multi-item scales, 2 single-item scales, and 2 composite scores (physical and mental health). The subscales are physical function, role limitation–physical, role limitation–emotional, pain, emotional well-being, energy, health perceptions, social function, cognitive function, health distress, overall quality of life, and sexual function. The summary scores are the physical health composite summary and the mental health composite summary. The MSQOL-54 questionnaire has been widely used in different cultures and languages[33] and has shown good reliability and validity within the MS population.[34] The Persian translation of the MSQOL-54 questionnaire has been used for patients with MS and proved good reliability and validity.[35] Scores for each dimension can range from 0 to 100 (full health). Scale scores were created by averaging the items within scales and transforming the mean scores linearly from 0 to 100 possible scores, with higher scores indicating a better HRQOL.

Table 1: Baseline Characteristics of MS Patients

Characteristics	Exercise (n=10)	Control (n=11)	P*
Age (y)	33.7±8.6	31.6±7.7	.57
Weight (kg)	59.1±9.1	59.5±7.1	.89
BMI (kg/h^2)	23.9±4.0	24.0±3.0	.98
Disease duration	4.9±2.3	4.6±1.9	.70
Age at diagnosis	28.8±7.6	27.1±6.8	.59
EDSS	2.9±0.9	3.0±0.7	.67
MFIS–overall	42.1±14.1	45.6±8.9	.51
MSQOL-54–physical	43.9±6.8	43.5±5.8	.87
MSQOL-54–mental	44.4±9.3	42.5±10.5	.33

NOTE. Values are mean ± SD or as otherwise indicated.
*Derived from independent samples *t* tests.

Statistical Analysis

The per-protocol analysis included all patients who had data available at baseline, 4 weeks, and 8 weeks. Initially, independent samples *t* tests were used to compare the baseline characteristics of exercise and control groups (table 1). Then, we conducted a series of repeated-measures analysis of variance (ANOVA), which were performed for each outcomes measure to assess differences across time (4 and 8wk) and between study groups, and for the interaction between time and study group. For these analyses the assumptions of sphericity and homogeneity of the variances were tested using Mauchly and Levene tests (appendix 1). The Huynh-Feldt correction was applied if there was violation to the sphericity assumption.

The efficacy of the repeated-measures ANOVA model was assessed by comparison with a more comprehensive mixed-model longitudinal data analysis approach. Employing diagonal, autoregressive (1), or unstructured covariances had no effect on the results. As expected, the repeated-measures ANOVAs and mixed-model approaches yielded identical conclusions for all outcome variables.

In the present analyses, we have examined 17 outcomes at 2 time points (weeks 4 and 8). This increases the possibility that the type I error is inflated by chance, which is known as the problem of multiplicity.[36] A Bonferroni procedure could be used to control the family-wise error rate from going above the conventional level of .05. This method is a very conservative procedure because of the high level of correlation between the different outcomes and therefore is not used here.[37,38] Under Bonferroni correction, a P value $< .003$ (.05/17) would be deemed significant. Even for the conservative threshold of $P<.003$, it is clear from table 2 that the study group-by-time interaction would still be significant for 10 scores. Statistical analyses were performed using IBM SPSS (version 20).[a] Statistical significance was set at $P<.05$. Values are presented as mean ± SD, unless otherwise specified.

Sensitivity Analysis

To investigate sensitivity to potential intention-to-treat (ITT) bias, a sensitivity analysis was performed whereby the last values

Table 2: Comparison of Fatigue and Quality of Life in Exercise and Control Groups at 4 and 8 Weeks

Characteristics	Control			Exercise			Group Effect	Group-Time Interaction
	Baseline	4wk	8wk	Baseline	4wk	8wk	*P**	*P**
MFIS–overall	45.6±8.9	53.8±13.9	60.8±9.0	42.1±14.1	39.9±11.4	32.3±6.4	.002	<.001
MFIS–physical	20.7±8.2	24.8±8.6	29.5±5.8	19.2±6.6	16.2±4.1	14.0±3.3	.003	<.001
MFIS–psychosocial	18.6±7.7	22.9±6.6	24.5±5.7	17.1±7.6	18.3±7.0	14.4±3.0	.027	.018
MFIS–cognitive	6.2±1.5	6.1±1.1	6.7±1.5	5.8±1.8	5.4±1.2	3.9±1.7	.009	.008
MSQOL-54–physical	43.5±5.8	44.0±6.1	44.2±4.4	43.9±6.8	54.3±5.3	65.4±6.6	<.001	<.001
MSQOL-54–mental	42.5±10.5	42.5±9.9	43.6±8.9	44.4±9.3	56.9±4.6	70.2±5.7	<.001	<.001
Physical health	46.4±10.5	48.2±5.6	44.5±9.9	45.5±10.5	50.5±7.6	62.5±7.9	.019	.001
Mental health	45.1±18.7	43.3±19.4	40.7±16.6	49.6±19.2	60.0±19.9	70.8±18.8	.036	<.001
Health perception	57.7±12.5	55.0±10.7	54.5±7.2	59.5±17.7	62.5±11.1	76.0±10.7	.030	.002
Energy	35.3±8.5	41.1±11.0	40.7±10.5	34.0±11.0	50.8±9.6	60.4±8.9	.021	<.001
Role limitation–physical	38.6±13.1	36.4±20.5	36.4±17.2	40.0±12.9	50.0±20.4	67.5±20.6	.036	<.001
Role limitation–emotional	33.3±29.8	36.4±23.3	39.4±20.1	36.7±39.9	53.3±39.1	66.7±27.2	.217	.026
Bodily pain	36.1±15.1	37.9±16.6	41.8±14.1	33.7±15.5	57.7±12.4	71.7±15.0	.014	<.001
Health distress	49.5±14.9	45.4±11.3	50.4±11.9	48.5±12.0	62.5±16.5	71.0±21.4	.034	.005
Social functioning	45.4±11.9	49.2±5.8	47.7±8.4	47.5±11.8	59.2±9.9	66.7±15.2	.014	.009
Cognitive function	50.9±9.4	49.1±12.4	52.7±9.8	52.0±15.5	55.5±13.8	61.5±12.0	.296	.059
Sexual function	40.5±16.3	41.7±11.8	44.0±10.5	44.0±21.4	47.6±20.3	50.0±19.3	.566	.757

NOTE. Data are expressed as mean ± SD.
*Obtained with repeated-measures ANOVA. *P* values obtained for the study group-by-time interaction were nearly identical to those from the repeated-measures ANOVA presented here and the sensitivity analysis for either a mixed-model longitudinal analysis or ITT analysis. The results of statistical significance of study group and study group-by-time interactions were the same whether ITT or complete data were employed. The only exception was role limitation–emotional, where the ITT had *P*=.07 while the complete data had *P*=.03, and therefore an ITT analysis would conclude that role limitation–emotional is nonsignificant.

were carried forward for those subjects who left the study. Thus, data were employed for 32 subjects as opposed to the 21 subjects who completed the study. As expected, differences at the end of the study were marginally smaller for the ITT dataset. Although *P* values for ITT were generally slightly larger, conclusions drawn for the study group-by-time interaction were the same except for the role limitation–emotional score, which had *P*=.07 for ITT and *P*=.03 for the complete data.

RESULTS

Baseline Characteristics

Of the 32 RRMS patients (all women) who were eligible to participate in the study, 21 patients (10 exercise and 11 control) were present at both the 4-week and 8-week follow-up and were included in the analysis. Six patients in the exercise group and 5 controls were excluded from the analyses because they had no data at 4 or 8 weeks. There was no significant difference in the baseline characteristics of those who dropped out of the study compared with those who completed the study. At baseline, patients were aged 32.6±8.0 years and had a height of 157.5±6.5cm, weight of 59.3±8.2kg, and body mass index (BMI) of 23.9±3.4kg/m^2. The EDSS scores ranged from 1.5 to 3.5 (mean, 2.9) in the exercise group and from 1.5 to 3.5 (mean, 3.0) in the control group and were not statistically different from one another. Table 1 compares the characteristics of the patients between the 2 groups at baseline. In general the 2 groups were comparable in relation to age, weight, BMI, disease duration, age at diagnosis, EDSS, MFIS, and MSQOL-54.

Comparison of Exercise and Control Groups at 4 and 8 Weeks

A series of repeated-measures ANOVAs was used to compare fatigue and HRQOL of MS patients at both 4 and 8 weeks between the exercise and control groups (see table 2). The test statistics were adjusted by Huynh-Feldt correction if the data did not meet the sphericity assumption. The data in table 2 show that for the MFIS–overall and its subscales, patients in the exercise group had lower scores than controls at both 4 weeks and 8 weeks. Both physical and mental health composite scores of HRQOL, as well as health perception, energy, role limitation (physical and emotional), bodily pain, health distress, and social functioning subscales, were significantly different between the 2 groups at both 4 and 8 weeks to the favor of the exercise group (fig 2). In addition, there was a significant intervention-by-time interaction for all outcome measures except MFIS–cognitive, MFIS–psychosocial, and sexual functioning of HRQOL. The results of Levene tests showed that the assumption of homogeneity of variances was not violated.

In a series of sensitivity analyses we examined the robustness of findings using ITT analysis. The new findings based on ITT were not materially different from those presented in table 2. The only exception was role limitation–emotional, where the ITT had *P*=.07, while the complete data (per-protocol) had *P*=.03, and therefore an ITT analysis would conclude that the difference in role limitation–emotional is nonsignificant.

Fatigue and HRQOL in the Exercise Group

Table 3 shows the change of fatigue and HRQOL in both the control and exercise groups between baseline, 4 weeks, and 8 weeks. In the control group, the MFIS–overall and MFIS–physical significantly deteriorated from baseline to 8 weeks. There was no significant difference in the composite scores and subscales of HRQOL among MS patients in the control group over the course of the study. For the patients in the exercise group, the MFIS–overall and MFIS–physical and –cognitive subscales significantly improved from baseline to 8 weeks. However, the similar changes were not statistically significant from baseline to 4 weeks. It is also noted that measures of HRQOL of MS patients in the exercise group improved significantly during the 4- and 8-week aquatic training. Except for mental health and sexual function, the

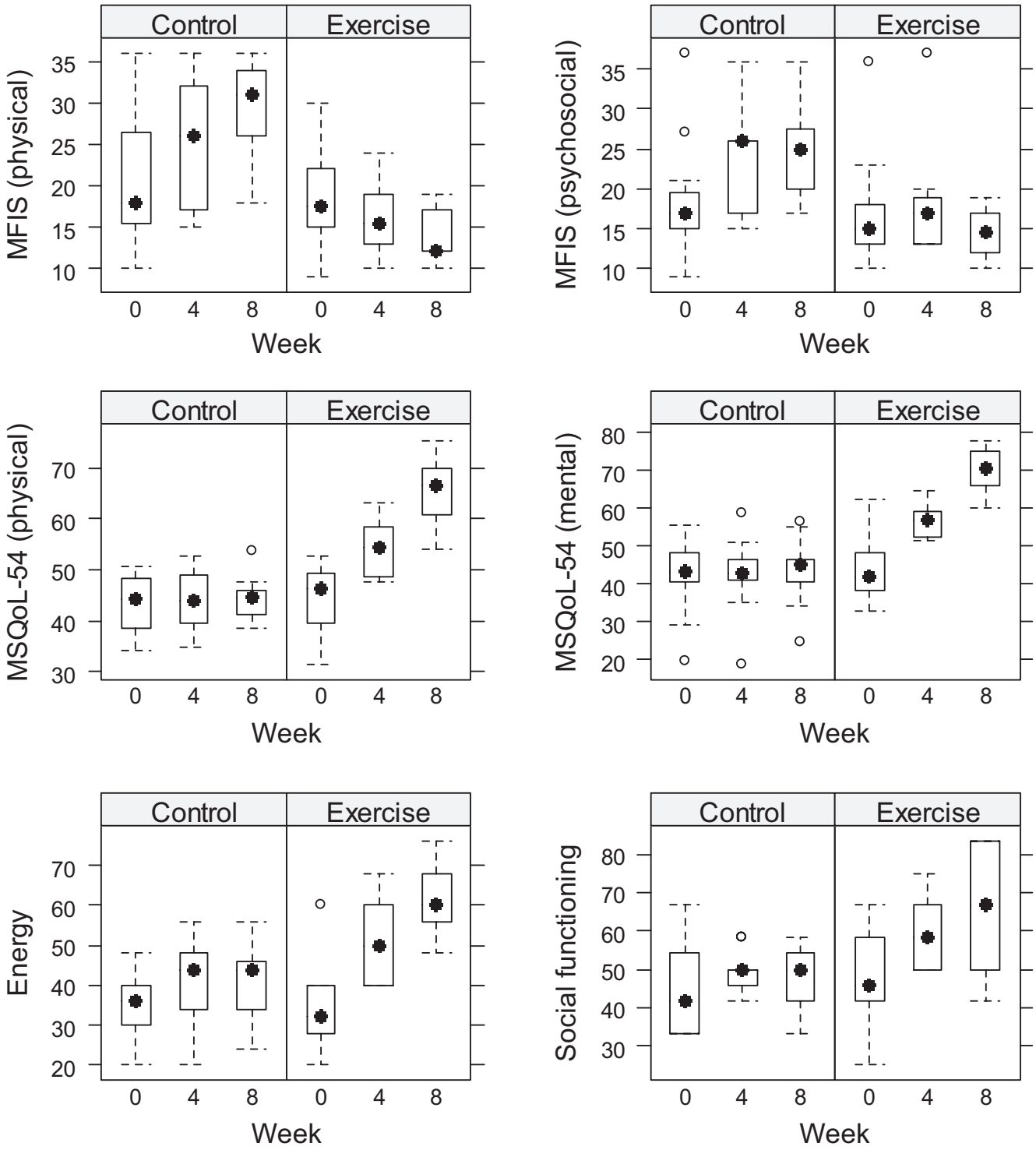

Fig 2. Boxplots of MFIS–physical, MFIS–psychosocial, MSQOL-54–physical, MSQOL-54–mental, energy, and social functioning for control and exercise groups over time. Clear differences in trends are evident between control and exercise groups for all variables except the MFIS–psychosocial. All study group-by-time interactions were significant (all *P*<.001 except MFIS–psychosocial with *P*<.05).

other subscales of the MSQOL-54 questionnaire showed a remarkable improvement from baseline to 4 and 8 weeks. Further, the improvement in physical and mental health composite scores, energy, role limitation (both physical and emotional), pain, health distress, and social function between 4 weeks and 8 weeks was statistically significant. There was no report of accident, increased fatigue, or adverse effects related to the aquatic exercise.

Table 3: Pairwise Comparisons Examining Fatigue and Quality of Life at Baseline, 4 Weeks, and 8 Weeks

	Control			Exercise		
Characteristics	Difference Between Baseline and 4wk	Difference Between 4wk and 8wk	Difference Between Baseline and 8wk	Difference Between Baseline and 4wk	Difference Between 4wk and 8wk	Difference Between Baseline and 8wk
MFIS–overall	8.3±3.1	7.0±3.1	15.3±2.4‡	−2.2±2.1	−7.6±2.8	−9.8±3.2*
MFIS–physical	4.1±1.1*	4.7±1.9	8.8±1.4‡	−3.0±1.4	−2.2±1.2	−5.2±1.7*
MFIS–psychosocial	4.3±2.5	1.6±1.5	5.9±2.5	1.2±0.9	−3.9±1.9	−2.7±2.2
MFIS–cognitive	−0.1±0.6	0.6±0.4	0.5±0.6	−0.4±0.7	−1.5±0.5	−1.9±0.6*
MSQOL-54–physical	0.5±0.9	0.2±0.9	0.7±1.0	10.4±1.5‡	11.1±1.7‡	21.5±1.7‡
MSQOL-54–mental	0.1±1.8	1.1±1.0	1.1±1.6	12.5±2.4†	13.2±1.8‡	25.8±3.1‡
Physical health	1.8±38.0	−3.6±3.4	−1.8±3.5	5.0±4.1	12.0±2.1†	17.0±3.5†
Mental health	−1.8±1.9	−2.5±1.6	−4.4±1.6	10.4±5.1	10.8±5.2	21.2±6.1*
Health perception	−2.7±1.4	−0.5±2.4	−3.2±3.1	3.0±3.7	13.5±4.1*	16.5±5.5*
Energy	5.8±2.7	−0.4±0.8	5.4±2.7	16.8±3.7†	9.6±2.1†	26.4±3.9‡
Role limitation–physical	−2.3±4.1	0.0±3.4	−2.3±4.1	10.0±4.1	17.5±5.3*	27.5±5.8†
Role limitation–emotional	3.0±5.4	3.0±3.0	6.1±6.1	16.7±5.5*	13.3±7.4	30.0±7.8*
Bodily pain	1.8±4.6	3.9±2.2	5.8±4.5	24.0±2.3‡	14.0±1.7‡	38.0±2.1‡
Health distress	−4.1±2.7	5.0±4.5	0.9±4.5	14.0±4.9	8.5±4.4	22.5±6.4*
Social functioning	3.8±3.6	−1.5±1.9	2.3±4.6	11.7±3.1*	7.5±2.9	19.2±3.7†
Cognitive function	−1.8±1.7	3.6±2.1	1.8±1.9	3.5±2.4	6.0±1.4†	9.5±3.4
Sexual function	1.2±3.4	2.4±1.5	3.6±3.5	3.6±2.5	2.4±2.4	5.9±4.7

NOTE. Data are expressed as mean differences ± SE. The level of statistical significance for the pairwise comparisons obtained with Bonferroni post hoc tests adjusted for multiple comparisons: *$P<.05$; †$P<.01$; ‡$P<.001$.

DISCUSSION

In the present study, it was hypothesized that aquatic exercise improves fatigue and HRQOL of MS patients. This randomized controlled trial is one of the few available studies that examined the efficacy of an 8-week aquatic exercise program for patients with RRMS. The findings of this study demonstrate that the aquatic program for individuals with MS is feasible and can improve their fatigue and HRQOL. RRMS patients in the exercise group showed significant improvement in fatigue and HRQOL after both 4 and 8 weeks of aquatic exercise. The contribution of our findings to the available evidence is twofold. First, they strongly support the clinical recommendation to consider an aquatic exercise program for patients with MS.[18] Second, our data suggest that the effect size of improvement in fatigue and HRQOL is significantly greater after 8 weeks of aquatic exercise compared with 4 weeks.

Previous research has shown significant benefits for the aerobic rehabilitation in MS patients.[11,14-16] To date, there is shortage of evidence from randomized controlled studies on the effectiveness of aquatic exercise in patients with MS. Case series and noncontrolled trials have suggested improved physical and mental health, improved quality of life, and reduced fatigue in individuals with MS after aquatic rehabilitation programs.[21,22,24-26] The 2 available studies by Roehrs and Karst[24] and Salem and colleagues[26] found that the quality of life of patients with MS improves after aquatic exercise training. However, Salem's study[26] did not report significant improvement in fatigue after 5 weeks of aquatic exercise. In agreement with Salem,[26] our data do not suggest significant change in patients' fatigue after 4 weeks. However, remarkable improvement in fatigue from baseline to week 8 supports Roehrs and Karst's study[24] that suggests that a longer period of aquatic exercise is associated with less fatigue in MS patients.

The findings of this study, based on a randomized controlled design, along with previous research suggest that aquatic exercise improves both physical and mental health and may be recommended in the management of MS patients. Research has shown that in patients with MS, self-perception of quality of life is more influenced by their general health, mental health, and energy than actual physical ability.[39,40] It is also known that fatigue is a common symptom of patients with MS that can affect other aspects of quality of life. Therefore, it is plausible that interventions that improve mental health, physical health, and energy in MS patients can lead to better quality of life.

The impact of aquatic exercise on fatigue and HRQOL of MS patients can be explained by 2 possible mechanisms. First, because individuals with MS are sensitive to heat and their symptoms worsen in warm temperature, pool water can reduce the body temperature and increase exercise tolerance compared with land-based exercise training. Second, the buoyant effect of water can decrease gravity and resistance against body movements and assist MS patients in enduring longer periods of physical activity with less fatigue.

Study Limitations

There are several limitations to this study. First, the study was based on a relatively small number of participants who completed the aquatic exercise intervention. Although the small sample size may lower the statistical power, the effect size of the differences in outcome measures between the exercise and control groups suggests that the findings are less likely to be affected by sample size. However, a larger sample size could produce more accurate findings and improve the generalizability of the data. Second, a large number of significance tests were conducted, and the interpretations are based on a multiple statistical procedure not controlling for the overall type I error rate. However, employing a family-wise error rate adjustment via Bonferroni correction would have been very conservative and would not have materially altered the conclusions presented here. Third, the participants were limited to women and patients with an EDSS score of ≤3.5. It can be argued that restriction of MS patients to those with low EDSS scores affects the generalizability of the observed findings to the broader MS population. It was the clinicians' preference

not to include MS patients with higher EDSS scores. Given the rationale that sensitivity to heat may constrain MS patients from exercising, it seems plausible that aquatic exercise is ideal for those with higher EDSS scores and may even result in better outcomes. Although there is no reason to limit the findings of this study to women[10] and those with lower EDSS scores, there remains a need for future studies with larger sample sizes that include MS patients with more severe disability as well as progressive cases. Further, randomized controlled trials comparing aquatic exercise versus land-based aerobic rehabilitation can help identify the relative effectiveness of these 2 types of exercise in MS patients.

CONCLUSIONS

Existing evidence indicates that aquatic exercise is not among the common modes of physical activity in MS patients. Notwithstanding the limitations of this study, the findings suggest that aquatic exercise therapy can effectively improve fatigue and physical and mental HRQOL in patients with RRMS. The 8-week aquatic exercise training had no harmful effects for patients with MS. Based on the findings of this study and previous research, it seems reasonable to promote exercise therapy to patients with MS. Clinicians and service providers are recommended to consider aquatic exercise as an effective intervention in the management of patients with MS. However, there remains a need for a randomized controlled trial with a larger sample size in order to investigate the effectiveness of aquatic exercise in patients with more severe disability and also to compare the effect of aquatic exercise with that of land-based aerobic rehabilitation programs.

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APPENDIX 1: TEST OF ASSUMPTIONS OF SPHERICITY AND HOMOGENEITY OF VARIANCES

Characteristics	Mauchly Test* (*P*)	Levene Test† (*P*)		
		Baseline	4wk	8wk
MFIS–overall	.93	.36	.24	.59
MFIS–physical	.51	.39	.09	.11
MFIS–psychosocial	.28	.95	.49	.12
MFIS–cognitive	.45	.47	.91	.90
MSQOL-54–physical	.81	.57	.63	.18
MSQOL-54–mental	.08	.94	.33	.48
Physical health	.35	.95	.39	.66
Mental health	.66	.92	.85	.79
Health perception	.03	.23	.44	.33
Energy	.01	.73	.57	.49
Role limitation–physical	.61	.65	.71	.47
Role limitation–emotional	.35	.20	.07	.44
Bodily pain	.02	.97	.55	.79
Health distress	.21	.13	.21	.09
Social functioning	.02	.71	.09	.14
Cognitive function	.11	.13	.52	.26
Sexual function	.01	.18	.08	.07

*Sphericity assumption test.
†Homogeneity of variances assumption test.

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a. SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.