

Running Head: Aquatic exercise and multiple sclerosis

A randomized controlled trial to establish the impact of aquatic exercise training on functional capacity, balance, and perceptions of fatigue in female patients with multiple sclerosis

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1 **ABSTRACT**

2 **Objective:** To assess the effects of 8-weeks aquatic exercise training on functional capacity, balance,
3 and perceptions of fatigue in women with multiple sclerosis (MS).

4 **Design:** A randomized controlled design.

5 **Setting:** Referral center of a multiple sclerosis society.

6 **Participants:** Women (age:36.4 ±8.2; BMI:24.5 ±1.9) diagnosed with RR-type (relapsing-remitting)
7 MS. After undergoing baseline testing, participants were allocated to either an intervention (aquatic
8 training programme) or a control group.

9 **Interventions:** The intervention consisted of an 8-week aquatic training programme (3 supervised
10 training sessions per week; session duration; 45-60 min; 50-75% heart rate reserve).

11 **Main measures:** Six-minute walk test (6-MWT); balance (Berg Balance Scale; BBS), and
12 perceptions of fatigue (Modified Fatigue Impact Scale; MFIS), at baseline and after an 8 week
13 intervention. Differences over time between the experimental and control groups were assessed by a
14 2x2 (group by time) repeated measures analysis of variance (ANOVA).

15 **Results:** 32 women (age:36.4 ±8.2; BMI:24.5 ±1.9) completed the 8-week aquatic training
16 intervention (experimental group, n=17; controls, n = 15). All outcome measures improved in the
17 experimental group; 6-MWT performance (451±58 m to 503±57 m; $P<0.001$); BBS (pre-test mean,
18 53.59±1.70; post-test mean, 55.18±1.18; $P<0.001$), and in the MFIS (pre-test mean, 43.1±14.6, post-
19 test mean, 32.8 ±5.9; $P<0.01$). A significant group-by-time interaction was evident between the
20 experimental and controls groups for 6-MWT: $P<0.001$, $\eta^2=0.551$; BBS: $P<0.001$, $\eta^2=0.423$; and
21 MFIS: $P<0.001$, $\eta^2=0.679$.

22 **Conclusions:** Aquatic exercise training improves functional capacity, balance, and perceptions of
23 fatigue in women with MS.

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26 **Key Words:** Aquatic; Exercise training; Functional capacity; Fatigue; Multiple sclerosis

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34 INTRODUCTION

35 Multiple sclerosis (MS) is a neurodegenerative condition influencing the central nervous system,¹
36 and is the third largest cause of adult neurological disabilities affecting an estimated 2.5 million
37 adults worldwide.² Approximately 400,000 young people in the US³ suffer from the condition, and
38 prevalence rates increase by approximately 10,000 people every year.⁴ In recent years, studies in the
39 Middle East and Iran indicate a relatively high prevalence of MS. In Iran, the average age of
40 developing MS is 27 years, and >40,000 patients suffer from the condition.⁵

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42 MS affects all aspects of a patient's life and causes a wide range of health, cognitive, and emotional
43 problems.⁷ A number of associated symptoms including double vision, muscle weakness, fatigue
44 and paralysis can all contribute to prolonged disability and a reduced quality of life.^{7,8} However,
45 symptoms are highly variable; mobility problems, poor balance, and sensitivity to heat, are
46 commonly experienced by patients.⁹ Mobility problems and poor balance are caused by a reduction
47 in muscle strength, exercise tolerance, co-ordination, and reaction time which may increase the risk
48 of falls and accidents.¹⁰ To curb the debilitating effects of MS, chronic exercise training is
49 recommended to help control and improve symptoms.¹¹ Patients with MS can improve their walking
50 performance by improving their muscular strength and aerobic capacity.^{6,12,13} Indeed, exercise
51 training benefits patients with MS in many ways, including improvements in cognitive skills and
52 aerobic fitness, gradual improvement in depressive symptoms and physical exhaustion, and reduced
53 risk of developing other significant ailments.^{14,15} Adaptations in muscular strength as a consequence
54 of exercise training may lead to improved walking performance in people with MS.⁶ In a recent
55 systematic review, aquatic exercise improved quality of life in affected patients with MS. The study
56 showed as a consequence of aquatic training, >60% of patients reported a very good or good quality
57 of life, while in <40% of patients, quality of life was reported to be fair/weak. However, there were
58 no reports of any negative effects of water-based exercise.²

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61 The role of aquatic exercise training has been championed by the American Physical Therapy
62 Association (APTA) for a number of clinical conditions.¹⁶ Benefits include toning of muscles,
63 improved aerobic capacity, improved flexibility, and improved anxiety levels.¹⁷ The natural
64 buoyancy and viscosity of water can potentially provide a safe and protective environment for
65 patients with MS to undertake exercise¹⁸ by making it feel easier to move their extremities without
66 the fear of losing balance or falling over¹⁹ and often, these activities do not require a highly
67 competent swimming technique to reap the benefits.²⁰ Previous studies are yet to examine the impact
68 of chronic aquatic exercise training on both physical and psychological well-being including
69 functional capacity, balance, and perceptions of fatigue in participants with MS.

70 Females are an under-represented group in many exercise training studies, and little has been
71 published regarding the impact of exercise training in females with MS. Likewise, MS data from
72 previous studies has relied heavily on Caucasian populations. Hence the novelty of this project is in
73 the population being investigated with mild MS (EDSS <3.5) focusing on outcome measures
74 including functional capacity, balance, and perceptions of fatigue. The location of the study is also
75 important; Isfahan, one of the major cities in Iran, has a soaring upward incidence and prevalence of
76 MS which is the highest in Asia and Oceania⁵. Therefore, the aim of the study was to assess the
77 effects of 8-weeks aquatic exercise training on functional capacity, balance, and perceptions of
78 fatigue in Iranian women with MS. We hypothesized that 8-week of aquatic exercise training will
79 significantly improve functional capacity, balance, and perceptions of fatigue in women with MS.

80

81 **METHODS**

82 The study was approved by the Ethics Committee of the University of Isfahan and the Isfahan
83 University of Medical Sciences, Isfahan, Iran. All participants had been diagnosed with RR-type
84 (relapsing-remitting) MS by Isfahan Multiple Sclerosis Society (IMSS) (a community-based group),
85 and were screened from a rehabilitation program waiting list by a qualified neurologist. After
86 screening, participants were randomly assigned based on age, distance walked during the 6-min walk
87 test, and EDSS score to an intervention or control group. We used the Expanded Disability Status
88 Scales (EDSS) questionnaire to measure the magnitude of neurological impairment and disability. The
89 EDSS questionnaire ranges from a score of 0 (normal neuro status) to a score of 10 (death from MS).
90 Participants with mild MS symptoms with a score ≤ 3.5 were recruited to the study (Appendix 1).
91 Participants were excluded if they had a relapse during the intervention and/or had developed any
92 comorbidities during the intervention (Fig 1).

93

94 **Measurement of Outcomes**

95 Six-minute walk test (6-MWT); balance (Berg Balance Scale; BBS), and perceptions of fatigue
96 (Modified Fatigue Impact Scale; MFIS), were assessed at baseline and after 8 weeks in both groups
97 (Appendix 2). Testing was carried out by research assistants who were independent to the
98 randomization process.

99 **Aquatic exercise training protocol**

100 The experimental group completed a program of physical training in water that included 8
101 consecutive weeks of 3 weekly sessions; each session consisted of 60 minutes of training between an
102 intensity of 50-75% of individual heart rate reserve. The session included a warm-up for 10 minutes,

103 followed by 40 minutes of conditioning exercise, and the final 10 minutes acted as a cool-down
104 (Appendix 3).

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107 **Statistical analysis**

108 Data normality was checked for all variables by the Kolmogorov-Smirnov test. On inspection, all
109 variables were normally distributed. Baseline characteristics between groups were compared using an
110 independent t-test. The homogeneity of the variances were tested using the Levene's test (Appendix
111 4). Differences over time between the experimental and control groups were assessed by a 2x2 (group
112 by time) repeated measures analysis of variance (ANOVA). Bonferroni post hoc adjustments were
113 carried out where necessary, and partial η^2 (η_p^2) effect sizes were also calculated with 0.01, 0.06 and
114 0.14 representing small, medium, and large effect sizes, respectively.²² We also performed an
115 intention to treat analysis (ITTA) using an imputation method, "last observation carried forward"
116 (LOCF) in order to deal with any missing data at follow up.²³ Statistical analysis was performed using
117 SPSS v19 for Windows (IBM, New York, USA). An alpha level <0.05 was used as a threshold for
118 statistical significance. Values are presented as mean \pm standard deviation or 95% confidence
119 intervals (CI), unless otherwise specified.

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122 **RESULTS**

123 Initially, 76 female participants with MS were eligible for the study, of which 40 agreed to
124 participate following an explanation of the study details. In the study, 40 patients with MS were
125 randomly assigned to either the experimental or control groups (20 participants per group).
126 However, 3 participants were excluded from the experimental group, and 5 participants were
127 excluded from the controls for non-medical reasons. Following exclusions, 32 female participants
128 (age: 36.4 ± 8.2 ; BMI: 24.5 ± 1.9) completed the study (experimental group, $n=17$; controls, $n = 15$).
129 All participants in the experimental group completed all of the training sessions. Physical
130 characteristics of both groups are reported in Table 1.

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TABLE 1 ABOUT HERE

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133 Participants in the intervention group (pre-test mean, 24.46 ± 1.85 $\text{kg}\cdot\text{m}^{-2}$; post-test mean, 23.63 ± 1.97
134 $\text{kg}\cdot\text{m}^{-2}$) decreased their BMI by 3.3%, whilst controls (pre-test mean, 24.64 ± 1.92 $\text{kg}\cdot\text{m}^{-2}$; post-test
135 mean, 26.07 ± 2.42 $\text{kg}\cdot\text{m}^{-2}$) increased their BMI by 5.7%. A significant group-by-time interaction
136 ($F_{1,30}=34.539$, $P<0.001$, $\eta_p^2=0.535$) was evident between experimental and controls groups (Table 2).

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TABLE 2 ABOUT HERE

140 **Six-minute walk test (6-MWT)**

141 The 6-MWT performance showed a significant increase from 451 ± 58 m to 503 ± 57 m ($P < 0.001$) in
142 the experimental group (12.2% increase) after eight weeks of the aquatic exercise intervention.
143 Conversely, the mean distance for the 6-MWT decreased significantly from 447 ± 30 m to 418 ± 29 m
144 ($P < 0.01$) in the controls (6.3% decrease; Table 2). A significant group-by-time interaction
145 ($F_{1,30} = 36.779$, $P = .001$, $\eta^2 = 0.551$) was evident between experimental and controls groups.

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147 **Sit to stand test**

148 A -19.2% improvement in time to complete the sit-to-stand test was detected in the experimental
149 group (pre-test mean, 20.99 ± 5.67 seconds; post-test mean, 16.82 ± 5.10 seconds), whereas the control
150 group (pre-test mean, 21.35 ± 4.70 ; post-test mean, 27.34 ± 4.75) worsened by 30.4%. A significant
151 group-by-time interaction ($F_{1,30} = 80.094$, $P = .001$, $\eta^2 = .728$) was evident between experimental and
152 controls groups (Table 2).

153

154 **Push up test**

155 An improvement in performance in the push-up test was found in the experimental group (pre-test
156 mean, 16.94 ± 9.13 ; post-test mean, 25.70 ± 10.53 ; $P < 0.001$); whereas the control group (pre-test
157 mean, 18.07 ± 7.13 ; post-test mean, 10.20 ± 5.03 ; $P < 0.001$) worsened. A significant group-by-time
158 interaction ($F_{1,30} = 39.816$, $P = 0.001$, $\eta^2 = 0.570$) was evident between experimental and controls
159 groups (Table 2).

160

161 **Berg balance scale (BBS)**

162 In the experimental group, BBS score improved by 3.0% (pre-test mean, 53.6 ± 1.7 ; post-test mean,
163 55.2 ± 1.2), whereas performance in the controls deteriorated (pre-test mean, 52.3 ± 3.3 ; post-test
164 mean, 50.2 ± 4.6). A significant group-by-time interaction ($F_{1,30} = 22.0$, $P = .001$, $\eta^2 = 0.42$) in BBS
165 performance was evident between experimental and controls groups (Table 2).

166

167 **Total MFIS score**

168 In the experimental group, MFIS score improved by 20% (pre-test mean, 43.1 ± 14.6 , post-test mean,
169 32.8 ± 5.9 ; $p < 0.01$), whereas performance in the controls deteriorated (pre-test mean, 44.5 ± 9.3 ; post-
170 test mean, 61.00 ± 8.23 ; $p < 0.001$). A significant group-by-time interaction ($F_{1,30} = 63.461$, $p = 0.001$,
171 $\eta^2 = 0.679$) in total MFIS score was evident between experimental and controls groups (Table

172 2).Furthermore, similar trends were also noted for the sub-scales of the MFIS. A significant group-by-
173 time interaction ($F_{1,30} = 62.090$, $p = 0.001$, $\eta^2=0.674$) was evident between experimental and
174 controls groups (Table 2) for the MFIS (physical) sub-scale, for the MFIS (cognitive) sub-scale ($F_{1,30}$
175 $= 11.371$, $p = 0.002$, $\eta^2=0.274$), and for the MFIS (psychosocial) sub-scale ($F_{1,30} = 14.954$, $p =$
176 $0.002, \eta^2=0.333$).

177

178 Differences over time between the experimental and control groups, at baseline and after 8 weeks
179 intervention, are shown in fig 2.

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FIGURE 2 ABOUT HERE

181 **DISCUSSION**

182 Our study examined the impact of an 8-week aquatic exercise training programme in 32 women with
183 MS in Isfahan, Iran. Lifestyle factors; diet; exposure to risk factors of cardiovascular disease; and
184 symptoms and signs of MS, including muscle weakness, fatigue, falls risk, cognitive dysfunction, and
185 paralysis can be different in developing nations.²⁴ Impairment in neuromuscular function limits
186 functional and physiological ability, thereby leading to a progressive decrease in everyday activities
187 and a reduction in quality of life.²⁵ The personal and economic costs of neurological disorders pose a
188 significant burden on public health in these regions.²⁶

189 In MS, aquatic exercise improves muscle strength.²⁷ Musculoskeletal conditions including
190 osteoarthritis are frequently encountered problems in patients with MS. The effects of water
191 buoyancy reduce the loading on joints which can have a positive impact on symptoms. Swimming is
192 a non-weight-bearing activity associated with an increase in lean body mass but does not increase
193 bone mineral density (BMD).²⁸ This is unsurprising given that BMD responds over time to the
194 stress that it is placed under. In addition to the therapeutic effects of water buoyancy, the thermal
195 properties of water may also be key for improving symptoms in patients with MS.¹⁸

196 We found that there were significant improvements in functional capacity, balance, and perceptions
197 of fatigue compared to participants randomized to the control group. We believe that, this study has
198 novelty because it focuses specifically on an under-represented sub-group of clinical research,
199 women. In participants with MS, loss of balance is a significant issue due to poor judgment as well
200 as reduced power and motion control.¹²⁻¹³ Thus, risk of fractures from falls in participants with MS
201 is 2 to 3.5 times higher than in age-matched healthy controls.²⁹ Therefore, interventions which can
202 help improve balance are fundamental in participants with MS. In our study, a significant
203 improvement in BBS score (balance) was found in the experimental group. These results are
204 supported by Salem et al. (2011) who showed an improvement in BBS score following aquatic
205 exercise training.³⁰ No studies beyond 5 weeks are available, so our findings over a longer period (8

206 weeks) are an original contribution to the knowledge base. A limitation of the BBS is that ceiling
207 effects have been identified in higher performing individuals,^{31,32} limiting its applicability for all
208 groups. Further, it does not evaluate verticality or cognitive factors affecting balance,³³ which both
209 influence risk of falling.

210 Smedal and colleagues (2006) conducted a study based on the Bobath concept which led to a
211 significant improved in balance in participants with MS.³⁴ Unfortunately, the study did not include a
212 control group and included different outcome measures making study comparisons difficult with our
213 own. Other studies have focused on participants with a wide range of symptoms (EDSS 1-6.6) but
214 have not necessarily focused on the changes to balance in response to aquatic training.³⁵ However, not
215 all studies investigating improvements in balance in participants with MS have been positive. Debolt
216 and co-workers (2004) assessed the effects of 8 weeks (24 sessions) of strength training on balance
217 measures.³⁶ They reported no change in balance over the intervention period.³⁶ However, some
218 participants demonstrated normal levels of balance at the start of the intervention period, therefore, it
219 may be unsurprising that further improvements were not elicited. Clearly, though the type and mode
220 of training stimulus will also be important for invoking positive physical adaptations.

221

222 We found that functional capacity measured by the 6-MWT significantly improved in participants
223 with MS following the 8-week aquatic training intervention compared to controls. Previous
224 studies^{6,37,38} have evaluated the effects of aerobic exercise training in participants with MS; and have
225 shown significant improvements in functional capacity. Rampello and colleagues (2007) measured
226 the impact of 8 weeks of aerobic exercise training on walking performance and maximal exercise
227 capacity in 19 patients (14 female, 5 male) with mild to moderate MS.³⁸ The aerobic training
228 program consisted of 3 training sessions per week on a cycle ergometer. Each training session
229 consisted of 30 minutes at 60% of maximum work rate. They found that aerobic exercise training
230 was more effective than standardized neuro-rehabilitation (NR) therapy for improving walking
231 performance and maximal exercise capacity. The favorable effects of exercise training in aquatic
232 conditions for improving aerobic capacity has been established previously in apparently healthy
233 older women^{39,40} but not women with MS and EDSS less than 3.5. Takeshima et al (2002) measured
234 aerobic fitness in women aged 60-75 years pre- and following 12 weeks of water based exercise
235 training.³⁹ Women who completed 3 d·wk⁻¹ of a combination of resistance and endurance-type
236 exercise (walking and dancing) achieved significant improvements in total cholesterol, exercise
237 capacity, muscular strength, and percentage body fat.

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239 Our findings add new insights. We have demonstrated that individualized aquatic exercise training
240 can improve functional capacity, balance, and perceptions of fatigue in female participants with mild
241 symptoms of MS (EDSS < 3.5). It should be noted that a previous study in 2015 in Iran showed a

242 decrease in fatigue among women with MS is response to 8-week aquatic training, but used an EDSS
243 score of less than 6 as their inclusion criteria.⁴¹ Bayraktar et al. (2013) showed that comparing
244 aquatic Tai-Chi exercises with home-based exercise showed a significant improvement in functional
245 mobility during the 6-minute walk test and the Timed Up and Go Test ($P < 0.05$); no significant
246 differences were observed in the home-based exercise group ($P > 0.05$). Aquatic exercises also
247 provided statistically significant increases in gait speed.⁴² For aquatic-based programmes, water
248 creates a buoyant, low-impact environment allowing participants to perform therapeutic exercise with
249 less fear of falling.⁴³ In addition, hydrostatic tension provides different proprioceptive and sensory
250 feedback from that experienced on land.⁴⁴

251

252 There are several limitations to our study. Firstly, the study was based on a relatively small number
253 of participants who completed the aquatic exercise intervention. However, future studies with larger
254 sample sizes, over a longer period of time, are needed to support or refute our findings. Secondly,
255 the participants were limited to women, and only patients with EDSS less than or equal to 3.5. The
256 clinicians' preference was not to include participants with more overt symptoms. Given the premise
257 that heat sensitivity may limit exercise in patients with MS, it seems plausible that aquatic exercise
258 training may be appropriate for patients with more pronounced progression of symptoms. It is
259 unclear whether male participants would receive similar benefits to aquatic training, and further
260 research needs to be conducted in this participant cohort. Further, randomized controlled trials
261 comparing aquatic exercise training versus land-based aerobic training interventions versus mixed
262 training regimes should be encouraged to determine the cumulative or additive benefits of these
263 different environments on the physical and psychological well-being of participants with MS. We
264 noted that the performance of our control group deteriorated significantly over the 8-week period.
265 The control group did not perform any structured physical activity during the 8-week intervention
266 which may have contributed to their deterioration. Furthermore, it is possible that the control group
267 were less motivated during the post testing phase, hence contributing to their worsening
268 performance at this time-point. However, we did try to somewhat mitigate for this eventuality by
269 offering them potential involvement in future training studies.

270

271 In conclusion, regular aquatic exercise training improves functional capacity, balance, and perceptions
272 of fatigue in women with mild MS. In supervised conditions, the intervention is safe, and, based on
273 our findings, should be investigated further in a larger cohort of patients, and in a wider spectrum of
274 disease progression.

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392