Uphill and Downhill Walking in Multiple Sclerosis
A Randomized Controlled Trial

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Background: Various exercise protocols have been recommended for patients with multiple sclerosis (MS). We investigated the effects of uphill and downhill walking exercise on mobility, functional activities, and muscle strength in MS patients.

Methods: Thirty-four MS patients were randomly allocated to either the downhill or uphill treadmill walking group for 12 sessions (3 times/week) of 30 minutes’ walking on a 10% negative slope (n = 17) or a 10% positive slope (n = 17), respectively. Measurements were taken before and after the intervention and after 4-week follow-up and included fatigue by Modified Fatigue Impact Scale; mobility by Modified Rivermead Mobility Index; disability by Guy’s Neurological Disability Scale; functional activities by 2-Minute Walk Test, Timed 25-Foot Walk test, and Timed Up and Go test; balance indices by Biodex Balance System; and quadriceps and hamstring isometric muscles by torque of left and right knee joints. Analysis of variance with repeated measures was used to investigate the intervention effects on the measurements.

Results: After the intervention, significant improvement was found in the downhill group versus the uphill group in terms of fatigue, mobility, and disability indices; functional activities; balance indices; and quadriceps isometric torque (P < .05). The results were stable at 4-week follow-up.

Conclusions: Downhill walking on a treadmill may improve muscle performance, functional activity, and balance control in MS patients. These findings support the idea of using eccentric exercise training in MS rehabilitation protocols. Int J MS Care. 2016;18:34–41.

Multiple sclerosis (MS) is a degenerative and demyelinating disease of the central nervous system, causing a variety of dysfunctions in sensory and muscle function. Due to the variety of functional disability in patients with MS, rehabilitation intervention, especially exercise therapy, is a necessary part of their treatment protocol.

In general, different types of exercise therapy are used to enhance functional activity, muscle strength, and mobility in patients with MS. The results of these studies showed not only that aerobic exercises can cause physiologic changes and improve ambulatory function and fatigue but also that strength training exercise can increase muscle fiber size and muscle strength and improve functional activities and balance in patients with MS. In a systematic review study, the authors suggested that “resistance training of moderate intensity seems to be well tolerated and to have beneficial effects on patients with MS.”

Endurance and resistance training sessions have been designed based on concentric contraction (contraction accompanied by shortening of muscle length, eg, uphill walking) of the involved muscles, which causes muscular hypertrophy and improves functional activity. It must be pointed out that these types of exercises are generally considered high-intensity training (60%–80% of the maximum voluntary contraction force), which may tire out patients with MS. However, some research has shown that eccentric exercise training (contraction accompanied by elongation of muscle length, eg, downhill walking), compared with concentric exercise, may...
improve balance in elderly people\textsuperscript{11} and increase muscle strength in patients with Parkinson disease\textsuperscript{12} and MS.\textsuperscript{13} This is due to its potential for high muscle force production at a uniquely low energy cost\textsuperscript{14} so that downhill walking (as a model of eccentric exercise) requires less energy cost than uphill walking (as a model of concentric exercise).\textsuperscript{15} However, eccentric activity of muscles is necessary to control human body movement against gravity.\textsuperscript{16}

Conflicting results have been reported regarding the effects of eccentric exercises for patients with MS.\textsuperscript{4,13,17} Ponichtera and colleagues\textsuperscript{17} showed greater muscle performance as a result of concentric exercise and concluded that strengthening concentric exercise training may be most effective in treating the strength deficit in patients with MS. However, Robineau and colleagues\textsuperscript{13} showed that eccentric training exercise may improve quadriceps and hamstring muscle strength and also the quality of walking in patients with MS. In a more recent study, Hayes and colleagues\textsuperscript{4} also showed no additional beneficial effect of eccentric training on lower-extremity muscle strength gains compared with standard exercise in patients with MS. However, the varying intensities of the training exercises may be the reason for the reported contradictory findings.

These study results plus reported delayed-onset muscle soreness after eccentric activity of muscles\textsuperscript{18} may cause therapists not to consider eccentric exercise training as a therapeutic protocol for patients with MS. Considering the reported beneficial effects of eccentric exercises in individuals with Parkinson disease,\textsuperscript{12} patients with MS,\textsuperscript{13} elderly people,\textsuperscript{11} and patients with other neurologic disorders,\textsuperscript{19} we aimed to find the possible beneficial effect from low-intensity eccentric and concentric exercise in patients with MS. This study was designed to compare the effects of low-intensity eccentric training (downhill walking) and low-intensity concentric training (uphill walking) on fatigue severity, disability, and mobility indices and also functional activity, muscle strength, and balance performance in individuals with MS. The results of this study may be used to determine the clinical importance of using eccentric or concentric exercise training and to establish a rehabilitation training protocol for patients with MS.

**Materials and Methods**

This study was approved by the Ethical Committee of Semnan University of Medical Sciences (Semnan, Iran) and included patients with a diagnosis of relapsing-remitting MS who were able to walk with or without aid. A neurologist in the university’s outpatient clinics referred the patients to the Neuromuscular Rehabilitation Research Center at Semnan University of Medical Sciences by considering inclusion and exclusion criteria. The inclusion criteria were age 18 to 50 years, MS diagnosis, difficulty in walking, the ability to walk a 10-m distance in less than 10 minutes (with or without a cane), and the ability to walk on a treadmill with or without hand supports. The exclusion criteria were confirmed severe disability during the past year, pregnancy, corticosteroid treatment during the past month, severe mental disorder (a score ≥3 on the mental section of Guy’s Neurological Disability Scale [GNDS]), inability to perform mild-to-moderate sport activities (a score ≥3 on the upper- or lower-limb section of the GNDS), any regular exercise activities (at least twice a week and >20 minutes per session), and reporting diseases that may interfere with fulfillment of the intervention protocol, such as arthritis in the lower-limb joints, diabetes, or unstable cardiovascular disease.

In the first session, all the participants signed the consent form and completed the demographic information sheet. Then they completed the Modified Fatigue Impact Scale, the Modified Rivermead Mobility Index, and the GNDS. At the first session of evaluation, the participants were familiarized with the test procedures. The patients were then randomly allocated by prepared sealed envelope to one of the two experimental groups: eccentric or concentric exercise. All the measurements were repeated after 4 weeks’ intervention and also after a 4-week follow-up period. All the evaluation sessions were conducted by an assessor (FM) masked to the study groups. Figure 1 shows the flow diagram of the study.

**Outcome Measurements**

Primary outcomes included functional activity, muscle strength, and balance control; and disability, mobility, and fatigue were considered to be secondary outcomes. Considering the fatigability of patients, each of the muscle strength, functional activity, and balance tests were performed in three different sessions with a 24-hour rest time. All the evaluations were performed before and after the treatment. All the primary and secondary outcomes were measured after a 4-week follow-up period to investigate the stability of possible changes.

**Functional Activity Evaluation**

Three functional tests were performed to evaluate patients’ functionality: the 2-Minute Walk Test (2MWT), the Timed 25-Foot Walk test (T25FW), and the Timed Up and Go (TUG) test.
Muscle Strength Evaluation

The muscle torque of the left and right hamstrings and the quadriceps was isometrically measured using the System 4 Pro dynamometer (Biodex Medical Systems, Shirley, NY) at 30°, 60°, and 90° of knee flexion. Each test was repeated three times, with 2-minute rest intervals.22 Because of the large amount of data, the maximum isometric torque values of the quadriceps and hamstring muscles in the aforementioned angles of the left and right knees were summed and considered as the muscle strength of the quadriceps and hamstrings.

Balance Evaluation

A Biodex Balance System (BBS; Biodex Medical Systems) was used to evaluate the dynamic and static balance indices. Its reliability for evaluating dynamic and static postural balance has been reported in previous studies.23 The reliability of its measurements was indicated by $r = 0.94$ (Overall Stability Index [OSI]), $r = 0.95$ (Anterior/Posterior Stability Index [APSI]), and $r = 0.93$ (Medial/Lateral Stability Index [MLSI]). The BBS allows for up to 20° of foot platform tilt and calculates three separate measurements: the MLSI, the APSI, and the OSI, indicating the postural sway in the anteroposterior and mediolateral directions as well as overall.

To measure the OSI, APSI, and MLSI scores, the participants were asked to step onto the BBS platform with bare feet and assume a comfortable position. The position of the feet on the platform was different among the participants. The exact position of the feet was detected by the graded surface of the platform and was recorded in the software for further correction. The participants were asked to maintain their foot positions on the platform throughout the test session. Before starting the test procedure, participants were trained for 1 minute to adapt to the test procedure. Then, all the participants performed two different test conditions in a systematic order: 1) static and 2) dynamic conditions, with eyes open and eyes closed. During the static balance test, the platform was locked under the patient’s feet; during the dynamic test, the platform was unlocked under the patient’s feet, with stability levels ranging progressively from 6 (most stable) to 1 (least stable). At all stages of the balance test, the assessor instructed the individuals to maintain their center of pressure (COP) in the smallest of the concentric rings (balance zones) on the BBS monitor, named the A zone. Each test condition was repeated three times, with 20-second rest intervals. The OSI, APSI, and MLSI were calculated from the mean of the COP displacement during the three test tri-
als. The machine calculated the OSI by taking the COP displacement in the anteroposterior (sagittal plane) and mediolateral (frontal plane) directions into account, and the APSI and MLSI were calculated from the platform displacement in the sagittal and frontal planes, respectively. Because of the large amount of information, the sum of the COP displacements was calculated by adding the OSI, APSI, and MLSI and was considered as the balance index during the eyes-open and eyes-closed situations. Note that a higher score indicates poorer balance.\textsuperscript{24} To investigate the effect of the intervention, the mean changes in the sum of the OSI, APSI, and MLSI in each group were calculated from baseline during both situations (eyes open and eyes closed) of the static and dynamic test conditions.

**Disability Evaluation**

The patients were asked to fill out the GNDS to evaluate the extent of their disability. This questionnaire has been acknowledged as a reliable ($r = 0.636–0.757$) and valid ($r = 0.557–0.910$) tool for disability evaluation in patients with MS.\textsuperscript{25}

**Mobility Evaluation**

The Modified Rivermead Mobility Index was used to evaluate the mobility level in neurologic conditions. The reliability and validity of this index has been confirmed for mobility evaluation in patients with neurologic disorders.\textsuperscript{26}

**Fatigue Severity Evaluation**

Fatigue during the final week was evaluated by the Modified Fatigue Impact Scale questionnaire, which has previously been confirmed as reliable and valid for the Persian population.\textsuperscript{27}

**Interventions**

The treatment interventions consisted of 30 minutes of walking on a 10% positively or 10% negatively sloped treadmill 3 days a week for 4 weeks under the supervision of a qualified therapist (familiar with the test procedure) who watched the performance and controlled the heart rate using a heart rate monitoring system (Polar Electro Inc, Lake Success, NY). A 10% negative slope (a model of downhill running) was used for the eccentric training, and a 10% positive slope (a model of uphill running) was used for the concentric training.\textsuperscript{28} The intensity of the training was defined by measuring the patient’s heartbeat during the training using the Polar device. In the first session, the volunteers were asked to walk at a speed at which their heartbeat reached 55% of maximum heart rate (MHR), which was calculated using the following formulas: $202 - (0.55 \times \text{Age})$ for males and $216 - (1.09 \times \text{Age})$ for females.\textsuperscript{29} The walking speed was gradually increased to reach 85% of MHR during the final week of the training sessions.\textsuperscript{30}

**Data Analysis Method**

To compare the possible treatment effects, an intention-to-treat analysis was used involving all patients who were randomly assigned to their groups. A statistical software program (IBM SPSS Statistics for Windows, version 20; IBM Corp., Armonk, NY) was used to apply the analysis of variance statistical method, with repeated measurement to analyze three time measurements and determine possible significant mean changes between experimental groups after the intervention (times 1 to 2) and also after a 4-week follow-up period (times 1 to 3). In the case of observed statistical differences, the post hoc Tukey test, with $\alpha < .05$ and a confidence level of 95%, was used to specify the differences between the groups. To adjust for baseline differences, an analysis of covariance was performed using the Leven test.

**Results**

As the flow diagram in Figure 1 shows, 34 patients with MS were block randomized on a sex variable to the eccentric or concentric training groups (14 females and 3 males in each). One patient from the eccentric group and two from the concentric group left the training protocol for personal reasons. Table 1 shows the mean values of the demographic characteristics, with no statistically significant differences between the groups. Analysis of covariance on the primary and secondary outcomes confirmed the homogeneity of variances between the uphill and downhill groups at baseline (Tables 2–4).

**Changes in Functional Activities and Muscle Torque**

Table 2 shows the data at baseline, after the intervention, and after 4-week follow-up for the 2MWT, the...
T25FW, the TUG test, and maximum isometric torque of the quadriceps and hamstring muscles. The downhill and uphill walking groups showed significantly better functional activity performance after the intervention, but the downhill group demonstrated better results in terms of functional activity and isometric torque of the quadriceps muscles compared with the uphill group, even after 4 weeks of follow-up (Table 2).

**Discussion**

The aim of this study was to investigate the effects of downhill and uphill walking on the functional activity, muscle strength, and quality of balance control in patients with MS. These findings revealed that aerobic downhill walking on a treadmill is more effective in reducing the fatigue intensity and disability indices and improving mobility compared with aerobic uphill walking on a treadmill. These results are in agreement with those of a study performed by Robineau et al., who showed that strengthening eccentric exercises may improve walking by increasing muscle strength. In contrast to the present study, Hayes et al. reported that applying resistance eccentric exercise has no beneficial effects in patients with MS, and standard exercise training may have better functional results. This opinion has also been verified by Broekmans et al., who conclude that light and moderate exercises are appropriate to improve muscle strength in patients with MS.

In the present study, we used walking on a treadmill with a 10% positive or negative slope as the intervention. The gradual increase in the exercise intensity training, from 55% of MHR in the first session to 85% of MHR in the final session, may have prevented extreme fatigue in the patients with MS.

**Balance Control**

Table 3 shows the sum of COP sway in all directions, in the static and dynamic conditions, with eyes open and eyes closed, before and after the intervention and after a 4-week follow-up period. Analysis showed significantly lower COP sway after the intervention in both groups. However, a comparison between the mean changes in the sum of COP sway during the static and dynamic balance tests showed that the downhill group experienced a significant reduction in COP sway (increased balance control) compared with the uphill group (Table 3). All the findings remained unchanged after the 4-week follow-up (Table 3).

**Changes in the Disability, Mobility, and Fatigue Indices**

After the 4-week intervention, significant improvement was seen in both experimental groups in terms of disability, fatigue, and mobility, and the downhill group demonstrated a larger reduction in the disability indices and fatigue intensity and a significant increase in the mobility index compared with the uphill group.

The mean changes were seen to be stable in the downhill group after the 4-week follow-up (Table 4).

**Table 2. Comparison of functional activities and sum of quadriceps and hamstring isometric muscle torques in patients with multiple sclerosis at baseline, after the intervention, and after 4-week follow-up between the downhill and uphill treadmill walking groups**

<table>
<thead>
<tr>
<th>Test</th>
<th>Experimental group</th>
<th>Baseline, mean (SD)</th>
<th>After 4-wk intervention</th>
<th>After 4-wk follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td>Downhill</td>
<td>Uphill</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>2MWT, m</td>
<td>120.1 (23.6)</td>
<td>160.1 (35.7)</td>
<td>.001 .0001</td>
<td>157.9 (29.2)</td>
</tr>
<tr>
<td>T25FW, s</td>
<td>8.7 (2.4)</td>
<td>6.1 (1.8)</td>
<td>.002 .001</td>
<td>6.2 (1.4)</td>
</tr>
<tr>
<td>TUG test, s</td>
<td>9.8 (1.7)</td>
<td>7.5 (1.3)</td>
<td>.008 .041</td>
<td>8.1 (1.4)</td>
</tr>
<tr>
<td>Sum of MIQT, Nm</td>
<td>496.6 (71.7)</td>
<td>651.7 (112.5)</td>
<td>.001 .011</td>
<td>606.2 (79.4)</td>
</tr>
<tr>
<td>Sum of MIHT, Nm</td>
<td>507.1 (98.6)</td>
<td>571.2 (93.8)</td>
<td>.016 .016</td>
<td>275.6 (47.1)</td>
</tr>
</tbody>
</table>

Abbreviations: 2MWT, 2-Minute Walk Test; MIHT, maximum isometric hamstring torque; MIQT, maximum isometric quadriceps torque; SD, standard deviation; T25FW, Timed 25-Foot Walk test; TUG, Timed Up and Go.

The post hoc Tukey test was used to examine significant differences within and between groups.
Uphill and Downhill Walking in MS

energy demand during downhill walking, which is easier to perform for fatigued patients with MS.

Another effect of the current downhill walking was an improvement in quadriceps muscle function, which was not seen in the hamstring muscles. When walking on a treadmill with a 10% negative slope, the quadriceps muscles are the main knee muscles that control the bending of the knee with their negative work or eccentric contraction. Some studies have pointed out that this type of exercise can be used to help increase muscle strength in elderly patients and those with neurologic conditions, although they applied strengthening exercises instead of aerobic exercises. It seems that the increase in muscle strength due to eccentric contractions may be a result of the increased load acting on have reduced fatigue and improved mobility. These results are in agreement with findings that 20 minutes of aerobic walking on a treadmill not only may increase the distance and speed of walking but also may reduce oxygen consumption owing to an improvement in the gait pattern. This can be due to neuromuscular adaptation in the downhill group, which may cause more prominent muscle fatigue resistance and mobilization of different muscle activation strategies during eccentric exercise. It seems that during an eccentric exercise, different muscle activation strategies may prevent early fatigue in the downhill group. However, it has been shown that the concentration of heat shock protein may be increased significantly during uphill exercise compared with downhill exercise, and this may indicate less

**Table 3. Comparison of the sum of COP sway during static and dynamic balance tests in the eyes-open and eyes-closed conditions in patients with multiple sclerosis at baseline, after the intervention, and after 4-week follow-up between the downhill and uphill treadmill walking groups**

<table>
<thead>
<tr>
<th>Sum of COP sway condition</th>
<th>Experimental group</th>
<th>Baseline, mean (SD)</th>
<th>After 4-wk intervention</th>
<th>After 4-wk follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Downhill</td>
<td>Uphill</td>
<td>Within-group <em>P</em> value</td>
<td>Between-group <em>P</em> value</td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td><em>P</em> value</td>
<td><em>P</em> value</td>
</tr>
<tr>
<td>EOSB</td>
<td>1.49 (0.38)</td>
<td>1.01 (0.21)</td>
<td>.001</td>
<td>.002</td>
</tr>
<tr>
<td>ECSB</td>
<td>3.14 (0.79)</td>
<td>2.31 (0.28)</td>
<td>.003</td>
<td>.003</td>
</tr>
<tr>
<td>EODB</td>
<td>4.11 (0.41)</td>
<td>3.07 (0.31)</td>
<td>.006</td>
<td>.026</td>
</tr>
<tr>
<td>ECDB</td>
<td>5.43 (1.19)</td>
<td>4.25 (0.45)</td>
<td>.024</td>
<td>.015</td>
</tr>
</tbody>
</table>

Abbreviations: COP, center of pressure; ECDB, eyes-closed dynamic balance; ECSB, eyes-closed static balance; EODB, eyes-open dynamic balance; EOSB, eyes-open static balance; SD, standard deviation.

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</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td><em>P</em> value</td>
<td><em>P</em> value</td>
</tr>
<tr>
<td>Disability (GNDS)</td>
<td>35.4 (9.1)</td>
<td>21.8 (5.3)</td>
<td>.006</td>
<td>.012</td>
</tr>
<tr>
<td>Mobility (MRMI)</td>
<td>10.6 (3.1)</td>
<td>14.3 (2.7)</td>
<td>.090</td>
<td>.005</td>
</tr>
<tr>
<td>Fatigue (MFIS)</td>
<td>28.6 (9.7)</td>
<td>21.9 (5.3)</td>
<td>.004</td>
<td>.037</td>
</tr>
</tbody>
</table>

Abbreviations: GNDS, Guy’s Neurological Disability Scale; MFIS, Modified Fatigue Impact Scale; MRMI, Modified Rivermead Mobility Index; SD, standard deviation.

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<tr>
<td></td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td><em>P</em> value</td>
<td><em>P</em> value</td>
</tr>
<tr>
<td>Disability (GNDS)</td>
<td>24.6 (6.6)</td>
<td>31.1 (8.2)</td>
<td>.01</td>
<td>.018</td>
</tr>
<tr>
<td>Mobility (MRMI)</td>
<td>13.4 (2.8)</td>
<td>11.5 (2.3)</td>
<td>.011</td>
<td>.009</td>
</tr>
<tr>
<td>Fatigue (MFIS)</td>
<td>23.3 (4.9)</td>
<td>26.1 (5.1)</td>
<td>.009</td>
<td>.028</td>
</tr>
</tbody>
</table>

Abbreviations: GNDS, Guy’s Neurological Disability Scale; MFIS, Modified Fatigue Impact Scale; MRMI, Modified Rivermead Mobility Index; SD, standard deviation.

The post hoc Tukey test was used to examine significant differences within and between groups.
the muscle filaments in the contracting muscle. This improvement in muscle strength and performance has been reported in patients with MS and also in elderly people after performing eccentric exercises, which have low energy cost and high force production. It has been shown that downhill running does not impair the acid-base balance of the body and may significantly decrease the levels of physiological indicators compared with uphill and even level-ground running. This finding may indicate that downhill walking exercise may result in more energy-efficient performance.

The increased quadriceps muscle strength was accompanied by better functional activities in patients with MS. This was reflected in the downhill treadmill walking exercise group’s ability to walk longer distances in the 2MWT compared with the uphill walking exercise group. These results were also confirmed by the T25FW and the TUG test, in which the downhill walking group required less time to complete the tasks. Different findings have been reported regarding the effects of training protocols on the functional activity of patients with MS. Although Collett et al. did not find any considerable changes in the distance traveled during the 2MWT after 12 weeks of concentric strengthening training, some studies have pointed out the positive effects of treadmill training. These findings are in agreement with the present results, which show that walking on a treadmill with a negative slope has better effects on the time required to walk a 25-foot distance and complete the TUG test compared with walking on a positively sloped treadmill. However, it seems that the higher load developed during the eccentric exercise may explain the increased muscle strength and improved performance observed in the downhill group.

One of the other problems in patients with MS during the activities of daily living is the difficulty in controlling balance and posture, which may increase their risk of falling. Many studies have investigated the effects of various exercise protocols on balance control in these patients. Although some of these reports have confirmed that strengthening exercises at home may not increase the balance control index of patients with MS, another showed that rehabilitation exercises may improve the balance control indices and, thus, lower the risk of falling. On the other hand, some researchers have concluded that training with treadmill walking may improve balance performance and functional mobility in patients with MS. These reports are in agreement with the present findings that showed that aerobic downhill treadmill training protocols may reduce COP sway as a balance index.

**Conclusion**

The findings of the present study show that a negatively sloped treadmill training protocol not only is beneficial to the mobility and disability indices and reduces fatigue in patients with MS but also may improve functional activities by increasing the strength of the antigravity muscles and provide better balance control compared with the positively sloped treadmill training protocol. However, considering that the lower total load during downhill treadmill walking required less energy compared with uphill treadmill walking, an alternative study might be recommended. This study would assess whether a balanced muscle training protocol that would include both uphill and downhill walking exercises is equally or more beneficial. Because both interventions had positive effects on the outcomes, with downhill walking being more effective, there may not be additive gains, but potentially further gains in stability and endurance could be achieved. A study of the efficacy of the combination of uphill and downhill walking for patients with MS could be of increasing value. Nevertheless, the positive gains shown here offer a positive approach.

This study was performed on patients with mild-to-moderate MS who were able to walk and were younger than 50 years. However, nonambulatory patients with MS were not involved, which may limit the transferability of the results to these severe patients. Because only patients with a diagnosis of relapsing-remitting MS participated in the study, we cannot also recommend application of the downhill walking protocol to other types of MS.

Another limitation of this study was that the technique used to measure exercise intensity (age-adjusted MHR) has not been validated, particularly in people...
with neurologic disease. In addition, due to the presence of dysautonomia in MS, heart rate may not be a reliable marker of exercise intensity. It also should be considered that there was no control group without treadmill exercise to present the net effect of uphill and downhill walking exercise.

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**References**


