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Original article

Determinants of change in insulin resistance response to Nordic walking in community-dwelling elderly women

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ABSTRACT

Introduction: Nordic walking, characterized by the use of two walking poles, is becoming increasingly popular. The aim of this study was to analyze the effects produced by a 12-week Nordic walking training program on functional abilities and metabolic profiles, specifically walk distance and insulin resistance, among elderly women.

Methods: The present study included 74 women (68 ± 7 years). The Nordic walking training program of 120 minutes per week was performed for 12 weeks. Before and at the end of the 12-week intervention, 6-minute walking distance (6MWD) and the homeostasis of the model assessment of insulin resistance (HOMA-IR) were measured.

Results and conclusions: After the 12-week Nordic walking training program, 6MWD increased significantly ($p < 0.001$). HOMA-IR improved significantly from a median (interquartile range) of 2.01 (1.31–2.59) to 1.32 (0.86–2.08) after intervention. Stepwise multiple linear regression analyses for changes in HOMA-IR showed that changes in the body mass index (BMI; $\beta = 0.255$, $p = 0.019$), triglycerides (TG; $\beta = 0.266$, $p = 0.015$), and uric acid ($\beta = 0.279$, $p = 0.009$) were independently and significantly associated with changes in HOMA-IR. The increased 6MWD correlated significantly with improved HOMA-IR in participants with baseline gamma-glutamyl transferase (GGT) ≥ 26 IU/L ($r = -0.682$, $p = 0.005$), but not in those with baseline GGT < 26 IU/L ($r = -0.127$, $p = 0.338$). Analysis of covariance showed that two regression lines in each graph were significantly different ($F = 5.64$, $p = 0.020$). These results suggest that increased 6MWD predicts improvement in insulin resistance after a 12-week Nordic walking training program in participants with elevated GGT.

1. Introduction

Nordic walking is characterized by walking with poles to increase the use of the upper body muscles compared with standard walking, and is becoming a popular activity in Northern Europe. Several studies have demonstrated that compared to standard walking, Nordic walking may lead to greater adaptations in the cardiovascular and respiratory systems, as well as greater energy expenditure on both acute and long-term effects of Nordic walking.[1–3] Nordic walking also has positive effects on aerobic performance, body composition, and the metabolic markers of the risk for cardiovascular disease (CVD). Morgulec-Adamowicz and colleagues[4] advocated in a recent review of scientific literature available on Nordic walking, that there are few literatures examining the benefits of Nordic walking as a potential health intervention in elderly adults.

Insulin resistance plays an important role in the pathogenesis of incident diabetes, hypertension, dyslipidemia, and CVD.[5–7] Alternatives have been sought to simplify the measurement of insulin resistance and one of them includes a homeostatic model assessment of insulin resistance (HOMA-IR), which uses fasting insulin and glucose levels to calculate insulin resistance.[8] In addition, serum

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gamma-glutamyl transferase (GGT) is also a clinical marker of glucose levels,[9,10] insulin resistance, and metabolic syndrome.[11,12] Thus, we hypothesized that the 12-week Nordic walking training program might improve functional abilities and metabolic profiles, specifically walking distance, GGT, and insulin resistance assessed by HOMA-IR.

The purpose of this study was to evaluate whether a 12-week Nordic walking training intervention had positive effects on the metabolic state and physical performance of community-dwelling elderly people.

2. Methods

2.1. Participants

The present study was designed as part of the Nomura study.[9] Participants were selected through a community-based annual check-up process in a rural town located in Ehime Prefecture, Japan. The physical activity level of participants, medical history information, present conditions, and medications taken were obtained through the interviewing process. Candidates with CVDs, or any other major illnesses that could affect the laboratory test results, were excluded. The participants were 74 women (aged, 68 ± 7 years). This study was approved by the Ethics Committee of Ehime University Graduate School of Medicine, Ehime, Japan and written informed consent was obtained from each participant.

2.2. Evaluation of risk factors

Information on demographic characteristics and risk factors were collected using the participant's clinical files, at the baseline level and at the completion of the 12 weeks training. Body mass index (BMI) was calculated by dividing weight (kg) by the square of the height (m). We measured blood pressure from the right upper arm of participants in the sedentary position using an automatic oscillometric blood pressure recorder, after having the participants rest for at least 5 minutes. Total cholesterol (T-C), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), high sensitivity C-reactive protein (hsCRP), GGT, uric acid, fasting plasma glucose (FPG), immunoreactive insulin (IRI), hemoglobin A1c (HbA1c), and hemoglobin (Hb) were measured during an overnight fast of > 11 hours. Plasma hsCRP concentration was measured using a Behring BN II nephelometer (Dade Behring Inc., Marburg, Germany), and the inter- and intra-assay coefficient variations were 3.2% and 6.7%, respectively. Serum GGT concentration was assayed with an automatic analyzer (TBA-c6000, Toshiba, Tokyo, Japan) and this intraassay-coefficient of variation was 0.87–2.11%. HOMA-IR was calculated from FPG and IRI levels using the following the formula[8]:

$$\{FPG(mg/dL) \times IRI(\mu U/mL)\}/405 \quad (1)$$

2.3. Intervention

Participants were required to take part in three instructor-led sessions lasting 120 minutes per week for 12 weeks. Participants were issued poles and tutored on the correct technique for using the equipment during the 1st week, dedicating 120-minute sessions to the Nordic walking technique (Fig. 1). The pole length used for the Nordic walk was selected and adjusted to permit a smooth arm motion, based on the International Nordic Walking Federation (INWA) formula (0.68 × body height cm),[13] and to induce a near right-angle elbow flexion upon pole landing.[14] The Nordic walking program was designed so that the performers could be in the aerobic work zone throughout the exercise sessions. Assessment of post intervention dependent variables occurred within 1 week of the final walking session. Two participants dropped out as they were unable to commit to the study, and 18 participants did not report for the postintervention testing due to personal reasons. Seventy-four participants were included in the final analysis. The study consisted of 74 participants who were on antihypertensive medications (28.4%), lipid-lowering medications (20.3%), and antidiabetic medications (13.5%). Treatments remained unchanged during the intervention. No instructions on eating habits or nutrition were provided, and no dietary intervention was administered. Before and at the end of the 12-week intervention, functional tests and metabolic profiles were measured.

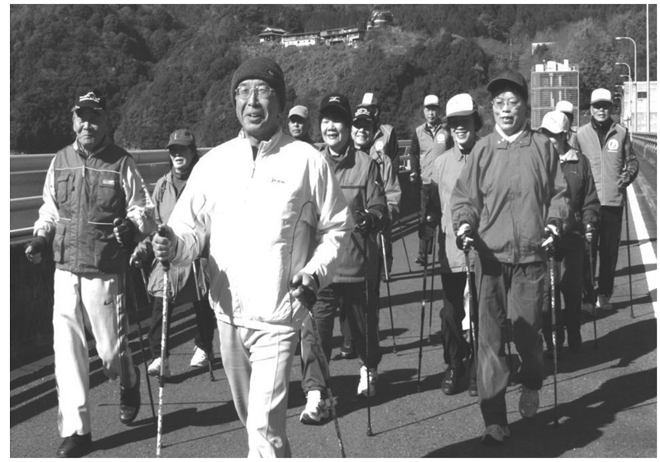

Fig. 1. Nordic walking.

2.4. Six-minute walking distance

The 6-minute walking test (6MWT) measures the distance an individual is able to walk over a total of 6 minutes on a hard, flat surface, at baseline and at 12 weeks. The goal is for the individual to walk as far as possible in 6 minutes. The individual is allowed to self-pace and rest as needed, as they traverse back and forth along a marked walkway.[15]

2.5. Statistical analysis

Data are presented as the mean ± standard deviation (SD) unless otherwise specified, and in the cases of parameters with non-normal distributions (TG, FPG, hsCRP, IRI, and HOMA-IR), the data are shown as median (interquartile range) values. In all analyses, parameters with non-normal distributions were used after log-transformation. Statistical analysis was performed using IBM SPSS Statistics Version 21 (Statistical Package for Social Science Japan, Inc., Tokyo, Japan). Twelve-week changes in various factors and 6-minute walking distance (6MWD) were calculated by subtracting the 12-week values from the baseline values. Differences among pre- and post-training were analyzed by paired *t* test. Pearson's correlation and multiple linear regression analysis were used to estimate baseline factors on HOMA-IR, and changes in their variables on HOMA-IR. The synergistic effect of baseline factors and changes in 6MWD on changes in HOMA-IR was evaluated using a general linear model. A p value < 0.05 was considered significant.

3. Results

Baseline characteristics for participants are shown in Table 1. Participants had a mean age of 68 years (SD, 7 years; range, 53–86 years) and a mean BMI of 24.0 kg/m^2 (3.0 kg/m^2; range,

Table 1
Characteristics of participants.

Characteristics $N = 74$	Pre-data	Post-data	p*
Body mass index[a] (kg/m^2)	24.0 ± 3.0	23.1 ± 2.7	<0.001
Waist circumference (cm)	84.9 ± 8.9	82.5 ± 7.6	<0.001
Systolic blood pressure (mmHg)	144 ± 26	134 ± 19	<0.001
Diastolic blood pressure (mmHg)	77 ± 12	74 ± 13	0.013
Triglycerides (mg/dL)	90 (68–117)	96 (66–116)	0.792
HDL cholesterol (mg/dL)	69 ± 13	67 ± 14	0.026
LDL cholesterol (mg/dL)	132 ± 29	130 ± 31	0.510
High sensitivity CRP (mg/dL)	0.040 (0.020–0.090)	0.030 (0.020–0.073)	0.026
Gamma-glutamyl transferase (IU/L)	16 (12–22)	16 (12–23)	0.337
Uric acid (mg/dL)	4.8 ± 1.0	4.8 ± 1.0	0.775
Hemoglobin A1c (%)	5.7 ± 0.7	5.6 ± 0.5	0.062
Hemoglobin (g/dL)	12.9 ± 0.8	12.6 ± 0.8	<0.001
Fasting plasma glucose (mg/dL)	102 (95–112)	103 (95–107)	0.129
Immunoreactive insulin (μU/mL)	4.40 (3.40-6.85)	4.00 (2.95–5.65)	0.027
6-min walk distance (m)	552 ± 67	573 ± 84	<0.001

Data are presented as mean ± standard deviation or median (interquartile range), and are log-transformed for analysis.
CRP = C-reactive protein; HDL = high-density lipoprotein; HOMA-IR = homeostasis of model assessment of insulin resistance; LDL = low-density lipoprotein.
[a] Body mass index was calculated using weight (kg) divided by the square of the height (m).
* Paired t test.

18.7–33.4 kg/m^2). Participants had several cardiovascular risk factors, and baseline BMI, waist circumference, systolic blood pressure (SBP), LDL-C, HbA1c, and FPG were all at the high end of the normal range.

After the 12-week Nordic walk training program, the 6MWD improved significantly ($p < 0.001$), and BMI, waist circumference, SBP, and diastolic blood pressure (DBP), HDL-C, hsCRP, hemoglobin, and IRI also decreased significantly, while TG, LDL-C, GGT, uric acid, HbA1c, and FPG were unchanged (Table 1).

As shown in Table 2, baseline BMI (r = 0.548, $p < 0.001$), waist circumference (r = 0.485, $p < 0.001$), DBP (r = 0.322, $p = 0.005$), TG (r = 0.320, $p = 0.006$), HDL-C (r = −0.295, $p = 0.011$), GGT (r = 0.475, $p < 0.001$), and Hb (r = 0.230, $p = 0.049$) correlated significantly with the measurements of the baseline HOMA-IR. Stepwise multiple linear regression analyses for HOMA-IR showed that the baseline BMI (β = 0.467, $p < 0.001$), hsCRP (β = −0.279, $p = 0.004$), and GGT (β = 0.414, $p < 0.001$) were independently and significantly associated with the baseline HOMA-IR, and their factors explained 44.3% of the variance in the predicted HOMA-IR.

As shown in Fig. 2, baseline HOMA-IR improved significantly from a median (interquartile range) of 2.01 (1.31–2.59) to 1.32 (0.86–2.08) after the 12-week Nordic walk training program. Relationships between changes in various factors and HOMA-IR after intervention are shown in Table 3. Changes in BMI (r = 0.300, $p = 0.009$), TG (r = 0.338, $p = 0.003$), hsCRP (r = 0.236, $p = 0.043$), GGT (r = 0.285, $p = 0.014$), uric acid (r = 0.284, $p = 0.014$), HbA1c

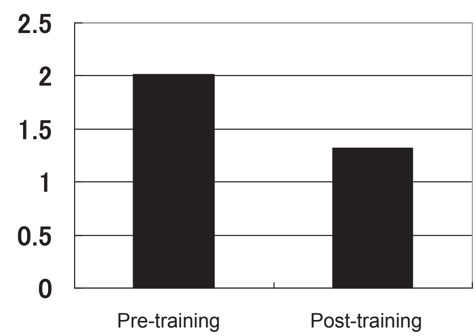

Fig. 2. HOMA-IR (homeostasis of minimal assessment of insulin resistance) before and after the 12-week Nordic walking training program. Values represent the median (interquartile range) values for 74 participants. Post-training data {2.01 (1.31–2.59)} showed significant reductions compared with the pretraining data {1.32 (0.86–2.08)} ($p = 0.022$).

Table 2
Relationship between baseline characteristics and HOMA-IR.

Characteristics $N = 74$	r (p)	Forced β (p)	Stepwise β (p)
Age (y)	−0.195 (0.096)	−0.063 (0.603)	—
Body mass index	0.548 (<0.001)	0.289 (0.090)	0.467 (<0.001)
Waist circumference	0.485 (<0.001)	0.050 (0.749)	—
Systolic blood pressure	0.152 (0.196)	0.057 (0.693)	—
Diastolic blood pressure	0.322 (0.005)	0.077 (0.575)	—
Triglycerides	0.320 (0.006)	0.035 (0.761)	—
HDL cholesterol	−0.295 (0.011)	−0.167 (0.154)	—
LDL cholesterol	0.040 (0.734)	0.018 (0.853)	—
High sensitivity CRP	−0.004 (0.974)	−0.305 (0.004)	−0.279 (0.004)
Gamma- glutamyl transferase	0.475 (<0.001)	0.397 (0.001)	0.414 (<0.001)
Uric acid	0.228 (0.050)	0.138 (0.177)	—
Hemoglobin A1c	0.044 (0.710)	0.060 (0.546)	—
Hemoglobin	0.230 (0.049)	−0.005 (0.965)	—
6-minute walk distance	−0.114 (0.334)	−0.007 (0.946)	—
R^2	—	0.507 (<0.001)	0.443 (<0.001)

β = standardized coefficient; r = Pearson's correlation coefficient; CRP = C-reactive protein; HDL = high-density lipoprotein; HOMA-IR = homeostasis of model assessment of insulin resistance; LDL = low-density lipoprotein.
Data for HOMA-IR, triglycerides, high sensitivity CRP, and γ-glutamyltransferase were skewed, and were log-transformed for analysis. Pearson's correlation coefficient and stepwise multiple linear regression analysis were used to estimate baseline variables on HOMA-IR.

Table 3
Relationship between changes in characteristics and changes in HOMA-IR by the 12-week Nordic walking training program.

Change in characteristics (N = 74)	r (p)	Forced β (p)	Stepwise β (p)
Body mass index	0.300 (0.009)	0.184 (0.136)	0.255 (0.019)
Waist circumference	0.206 (0.078)	0.081 (0.473)	—
Systolic blood pressure	−0.080 (0.497)	−0.122 (0.339)	—
Diastolic blood pressure	0.036 (0.762)	0.113 (0.399)	—
Triglycerides	0.338 (0.003)	0.269 (0.035)	0.266 (0.015)
HDL cholesterol	0.074 (0.534)	0.091 (0.489)	—
LDL cholesterol	0.080 (0.496)	0.021 (0.870)	—
High sensitivity CRP	0.236 (0.043)	0.142 (0.237)	—
Gamma-glutamyl transferase	0.285 (0.014)	0.150 (0.176)	—
Uric acid	0.284 (0.014)	0.186 (0.130)	0.279 (0.009)
Hemoglobin A1c	0.251 (0.031)	0.080 (0.516)	—
Hemoglobin	0.293 (0.011)	0.058 (0.654)	—
6-min walk distance	−0.238 (0.041)	−0.023 (0.851)	—
R^2	—	0.356 (0.007)	0.246 (<0.001)

β = standardized coefficient; r = Pearson's correlation coefficient.
Pearson's correlation coefficient and multiple linear regression analysis were used to estimate change in characteristics on change in HOMA-IR. Change = post-data − pre-data.

(r = 0.251, p = 0.031), Hb (r = 0.293, p = 0.011), and 6MWD (r = −0.238, p = 0.014) correlated significantly with the changes in HOMA-IR. In addition, stepwise multiple linear regression analyses for the changes in HOMA-IR showed that the changes in BMI (β = 0.255, p = 0.019), TG (β = 0.266, p = 0.015), and uric acid (β = 0.279, p = 0.009) were independently and significantly associated with changes in HOMA-IR, and these factors accounted for 24.6% of the variance.

Next, to control potential confounding variables by baseline BMI and GGT which were strongly and significantly associated with the baseline HOMA-IR, the data was further stratified by baseline BMI and GGT using the index of the insulin resistance acquired from previous research, which were performed by residents of the same town (Table 4).[16,17] Changes in 6MWD were significantly associated with changes in HOMA-IR in the GGT ≥ 26 IU/L groups, and there was a significant interaction only between the two groups for GGT (p = 0.014). However, there was no interaction between the two groups regarding BMI.

Fig. 3 shows the relationships between the changes in 6MWD and HOMA-IR of two groups categorized by baseline GGT. In participants with baseline GGT ≥26 IU/L, increased 6MWD correlated significantly with changes in the HOMA-IR (r = −0.682, p = 0.005), but not with those participants with baseline GGT < 26 IU/L (r = −0.127, p = 0.338). Analysis of covariance showed that two regression lines in each graph were significantly different (F = 5.64, p = 0.020).

4. Discussion

The Nordic walk training program is a low cost, safe, and effective form of exercise suitable for the elderly.[18] This study demonstrated that a 12-week structured training program had positive effects on the metabolic state and physical performance of the participants. After the 12-week intervention, HOMA-IR and 6MWD improved significantly. Changes in BMI, as well as changes in TG and serum uric acid, were independently and significantly associated with changes in HOMA-IR. We further suggested that changes in 6MWD also strongly predicted improved HOMA-IR in participants with baseline GGT ≥ 26 IU/L.

Endurance and strength training have well-known cardiovascular adaptations and lead to hypertrophy and increased capillary density in muscles.[19] At a given walking speed, Nordic walking involves more muscles in various body segments and induces greater exercise intensity than level walking.[20] In addition, the use of poles in Nordic walking attenuates muscle activity in the lower extremities during the stance and push-off phases, and decreases that of the lower extremities and increases energy expenditure of the upper body and respiratory system at certain walking speeds.[21] Compared with regular walking, Nordic walking required as much as 67% greater energy expenditure.[22] Nordic walking, examined in the field, results in a significant increase in oxygen use and caloric expenditure compared to regular walking, without significantly increasing perceived exertion.[1] Thus, in our study we conducted Nordic walking as a training program to determine the effects of a 12-week exercise training intervention on insulin resistance in elderly persons.

The 6MWT is a commonly used test to estimate functional exercise capacity and the changes resulting from therapeutic intervention in patients with chronic respiratory disease[23] and heart failure.[24] The test has since been used as a performance–based measurement of functional exercise capacity in healthy elderly persons. The 6MWD in healthy adults has been reported to range from 400 m to 700 m.[25] In our study, the mean value (± SD) of 6MWD was 552 m (±67 m) before training, and it increased significantly after training intervention. The changes in 6MWD caused improvements in HOMA-IR, independent of the change in confounding factors in participants with baseline GGT ≥ 26 IU/L.

The mechanisms of improvement in insulin resistance predicted by the increased 6MWD as well as the decreased BMI and GGT after training intervention, remains to be clarified. However, both elevated BMI and GGT reflect inflammation, which impairs insulin signaling in the liver, muscle, and adipose tissues,[26] and systemic inflammation is closely involved in the pathogenesis of insulin resistance.[11] Moreover, recent data has suggested that serum GGT can also be considered as a marker of oxidative stress.[27] Nordic walking improves chronic inflammation caused by excess body weight, and can also prevent fatty liver in patients whose lipid and

Table 4
Association between changes in 6-minute walk distance and changes in HOMA-IR, within selected subgroups.

Baseline characteristics	n (N = 74)	β (p*)	p-interaction
Body mass index (kg/m^2)			
< 23	32	−0.134 (0.501)	0.978
≥ 23	42	−0.072 (0.582)	
Gamma-glutamyl transferase (IU/L)			
< 26	59	−0.006 (0.962)	0.014
≥ 26	15	−0.586 (0.042)	

β = standardized coefficient.
* Adjusted for change in body mass index, triglycerides, and uric acid.

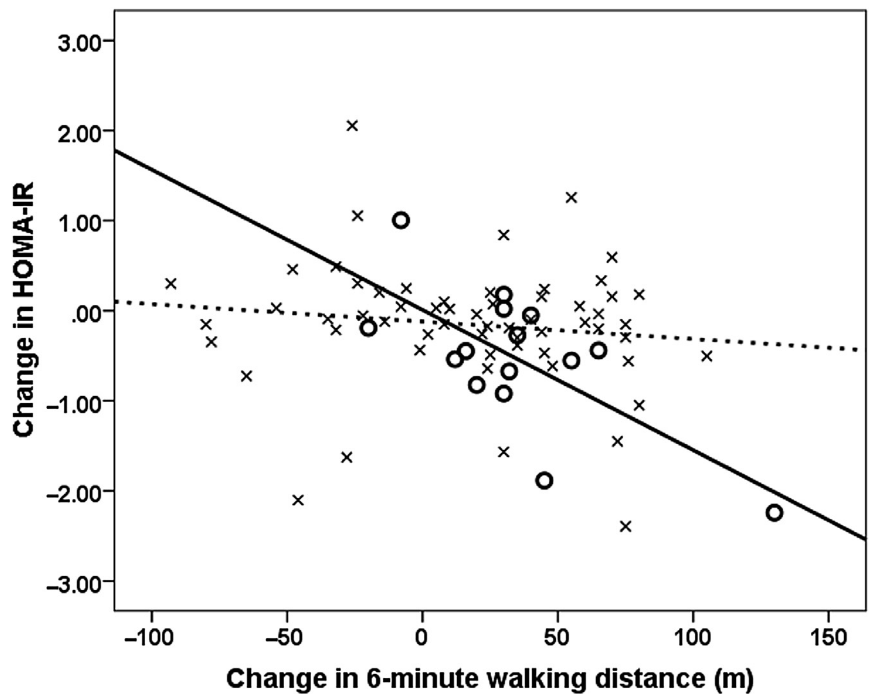

Fig. 3. Relationship between changes in 6-minute walk distance (6MWD) and HOMA-IR (homeostasis of minimal assessment of insulin resistance) after the 12-week Nordic walking training program of participants categorized by baseline gamma-glutamyl transferase (GGT). The increased 6MWD correlated significantly with decreased HOMA-IR in participants with baseline GGT ≥26 IU/L (solid line, $r = -0.682$, $p = 0.005$), but not in those with baseline GGT < 26 IU/L (broken line, $r = -0.127$, $p = 0.338$). Analysis of covariance showed that two regression lines in each graph were significantly different ($F = 5.64$, $p = 0.020$).

glucose metabolisms are already impaired. In our study, HOMA-IR was significantly improved after Nordic walk training. Furthermore, one should note that a correlation of −0.7 can be reached between increased 6MWD and improvements in HOMA-IR, especially in participants with baseline GGT ≥ 26 IU/L, which suggests the existence of oxidative stress.[28,29]

Some limitations of this study must be considered. First, a 12-week intervention may potentially be too brief for measuring the effects of Nordic walk training. Long-term studies of similar exercise intensity and frequency are warranted to elucidate whether Nordic walking may be a sustainable mode of exercise. Secondly, the daily physical activity of participants in our study, prior to entry and during the study, was not controlled or matched. Thirdly, although we have comprehensively adjusted for such confounders as gender, age, markers of inflammation (e.g., hsCRP), GGT, and uric acid, in the association of 6MWD and insulin resistance, other important measures such as cognitive ability, symptoms of depression, or markers of endothelial dysfunction were absent. Therefore the demographics and referral source may limit generalizing.

In conclusion, the present study showed that the increased 6MWD induced by Nordic walk training in participants with mildly elevated GGT may predict improvements in their insulin resistance.

Conflicts of interest

The authors declare that they have no competing interests.

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