





Effects of high-intensity interval walking training on muscle strength, walking ability, and health-related quality of life in people with diabetes accompanied by lower extremity weakness: A randomized controlled trial

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Keywords

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ABSTRACT

Aims/Introduction: This study examined the effects of high-intensity interval walking training (IWT) compared to moderate-intensity continuous walking training (CWT) on muscle strength, walking ability, and health-related quality of life (QOL) in people with diabetes accompanied by lower extremity weakness.

Materials and Methods: People with diabetes accompanied by low isometric knee extensor strength using a simple manual dynamometer ($n = 50$) were screened and randomly divided into 2 groups: CWT ($n = 25$) and IWT ($n = 25$). Both groups were instructed by a physical therapist to perform walking training with the goal of 120 min/week over a 5-month period. The primary outcome, mean change of isometric knee extensor strength, and secondary outcomes, such as gait speed and health-related QOL, were measured at baseline and the end of the intervention.

Results: At the end of the intervention, there was no significant difference in the degree of change in isometric knee extension strength between the two groups. However, there was a significant increase in changes in gait speed and physical QOL in the IWT group (gait speed, $P < 0.01$; physical QOL, $P < 0.05$).

Conclusions: The present study showed that IWT for people with diabetes accompanied by lower extremity weakness did not improve knee extension muscle strength compared to CWT but did improve walking ability and physical QOL.

INTRODUCTION

Muscular strength, physical function, and quality of life (QOL) decline with aging^{1,2}. We previously reported that people with diabetes are highly accompanied by decreased muscular mass and strength and impaired walking ability compared to non-diabetic adults >30 years of age, particularly in terms of significant weakness in knee extension muscles^{3,4}. Obesity and

diabetic neuropathy demonstrated a significantly higher prevalence, while gait speed, physical activity, and the physical QOL were also significantly lower in people with diabetes accompanied by muscle weakness alone with a normal muscle mass, which is so-called dynapenia, than in non-diabetic subjects^{3,4}. Therefore, muscle weakness should be assessed clinically in middle-aged and older people with diabetes.

High-intensity interval walking training (IWT), an intermittent exercise method that combines alternating moderate- and

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high-intensity fast walking, is reportedly effective in managing blood glucose levels and body weight in people with diabetes^{5,6}. In healthy adults, IWT increases the load on the femoral skeletal muscles, such as the quadriceps and biceps femoris, as well as their contractility⁷. In addition, IWT can improve knee extension muscle strength in middle-aged and older community-dwelling individuals after 5 months of intervention⁸.

However, there are few reports on the effects of IWT in people with diabetes accompanied by muscle weakness.

This study examined the effects of IWT compared to moderate-intensity continuous walking training (CWT) on muscle strength, walking ability, and QOL in people with diabetes accompanied by lower extremity weakness.

MATERIALS AND METHODS

Study participants

This study was approved by the Ethics Committee of Tokushima University Hospital (location information: Tokushima City, Japan; approval number: 4213) and registered in the affiliated hospital medical information network (UMIN000040658). Written informed consent was obtained from all study participants for the publication of this report.

A total of 74 people with diabetes being treated at the Tokushima University Hospital were enrolled in this study. Participants were recruited from August 2022 to February 2023. The inclusion and exclusion criteria are shown in Table S1. The eligible participants were people with diabetes, 30–80 years old, who were able to exercise at 70% of their VO_{2peak} . Participants with low isometric knee extension strength per body weight (BW) measured at 90° knee extension using a simple manual dynamometer (μ Tas F-1; ANIMA, Tokyo, Japan) and normal skeletal muscle mass index (SMI) were also included. Sarcopenic participants with low skeletal muscle mass were excluded because this study focused on muscle strength but not skeletal muscle mass. Low SMI was defined according to the criteria proposed by the Asian Working Group for Sarcopenia 2019², and low knee extension strength per BW was defined according to our previous reports^{3,4}.

A stratified randomization strategy based on age and type of diabetes was applied to equally allocate the 50 participants into the CWT or IWT groups. This two-group, stratified, randomized, single-blind, parallel-group trial was conducted over 5 months. The exercise instructor generated a randomization list. Following the order of this list, the research staff randomly assigned eligible participants (1:1, two blocks of size 13) to the IWT or CWT groups. Physicians and research staff who collected the clinical data were blinded to the groupings, whereas the exercise instructor and participants were not. Data from previous trials of middle-aged and older community-dwelling individuals were used to estimate the necessary sample sizes⁸. Calculations were based on an effect size of 0.9 (absolute difference, 11.8 Nm), absolute value of isometric knee extension strength (standard deviation [SD] = 13.1 Nm), α level of 0.05,

and power ($1-\beta$) of 80%. The required sample size for each group was thus determined to be 21 participants. Assuming a dropout rate of 16%, we chose to recruit 25 participants in each group.

Interventions of CWT and IWT

This intervention study was conducted from February to September 2023. The CWT group performed sustained walking at an intensity of 50% VO_{2peak} , whereas the IWT group performed intermittent walking at more than 70% and less than 40% VO_{2peak} in 3-min intervals^{8–10}. The exercise instructors directed both the CWT and IWT groups to practice walking training with a goal of 120 min per week for at least 5 months. In the IWT group, training adherence was defined as 100% when the fast walking (intensity of $VO_{2peak} \geq 70\%$) time was 60 min/week. In the CWT group, training adherence was defined as 100% when the total walking time was 120 min/week. Before the intervention, the exercise instructors instructed the participants regarding practical CWT or IWT exercises. During the intervention period, the instructors provided CWT and IWT exercise instructions and encouragement to the participants during their regular outpatient hospital visits. The exercise instructor was a single physical therapist trained in both the CWT and the IWT. During the intervention, a triaxial accelerometer (JD Mate; Kissei Comtec, Matsumoto, Japan) was attached to each participant's waist to record the training date, exercise intensity, and time. Each participant received exercise instruction on a walking course at the Tokushima University Hospital.

Outcome measurements

The following outcomes were measured by blinded research staff at baseline, during the 3-month intervention, and at the end of the intervention period. However, the VO_{2peak} was measured by an exercise instructor (a non-blinded research staff member) who was fully trained in both the CWT and the IWT. The primary outcome parameter was the change in isometric knee extension strength, measured at a knee angle of 60°. Gait speed, VO_{2peak} , and health-related QOL were the secondary outcome parameters, whereas glycated hemoglobin (HbA1c) level, body mass index (BMI), and SMI represented additional tertiary outcomes.

Clinical data

Data regarding the type of diabetes, duration of diabetes, HbA1c level, estimated glomerular filtration rate (eGFR), urinary albumin to creatinine (Cr) ratio, diabetic neuropathy, diabetic retinopathy, hypertension, dyslipidemia, blood pressure, and medications for diabetes were collected from the medical records of each participant. The eGFR was calculated according to the equation proposed by the Japanese Society of Nephrology¹¹. Diabetic neuropathy, retinopathy, and nephropathy were defined in accordance with the standard criteria of the Japan Diabetes Society¹².

Muscle strength

The left and right isometric knee extension strength at 60° of knee flexion and grip strength were assessed at baseline, 3 months, and at the end of the intervention. The maximum isometric knee extension strength at 60° of knee flexion, which was known to be a stronger isometric knee extension muscle strength than those at 90°, was assessed using a muscle function assessment machine (Biodex System 4; Biodex Medical Systems, New York, USA). To estimate the knee extension strength per BW, knee extension values were calculated as absolute values (Nm) divided by BW (Nm/kg BW). Upper extremity strength was measured in both hands using the maximum isometric grip strength values while standing. The participants were placed in an upright position with a Smedley hand dynamometer (GRIP-D TTK5401; Takei Scientific Instruments, Nigata, Japan) adjusted to 90° at the second joint of the index finger.

Body composition and skeletal muscle mass

BW, BMI, body fat, and upper and lower limb skeletal muscle mass were calculated using a multifrequency bioelectrical impedance analyzer (BIA), a direct segment multiple frequency-based instrument (In Body Japan; Tokyo, Japan). BIA measurements: a strong positive correlation between DXA- and multifrequency BIA-based measurements of skeletal muscle mass has been previously reported, confirming the validity of multifrequency BIA measurements of skeletal muscle mass¹³. SMI was calculated by dividing the sum of each participant's skeletal muscle mass for both the upper and lower extremities by the square of their height². Body composition and skeletal muscle mass data were collected at baseline, 3 months, and at the end of the intervention.

Physical performance

Gait speed tests were performed at baseline, 3 months, and at the end of the intervention. Peak VO₂, resting heart rate, and peak heart rate were assessed at baseline and at the end of the intervention. For the gait speed test, the participants were instructed to walk 10 m at normal speed. The time taken to walk 4 m (3–7 m) was measured twice, and the values were averaged². The estimated VO_{2peak}, resting, and peak heart rates were measured by attaching an accelerometer (JD Mate; Kissei Comtec, Matsumoto, Japan) to the participant's waist. With the encouragement of a trained physiotherapist, the participants gradually increased their speeds (through three subjective levels—slow, medium, and fast—for 3 min each) to finally walk at their fastest walking speed. The energy expenditure within 30 s of the final fast walk was defined as VO_{2peak}. The VO_{2peak} determined using this method was highly correlated with that measured using a bicycle ergometer ($r = 0.91$, $P < 0.0001$)⁹.

Health-related QOL

The participants' health-related QOL, represented as a summary of physical and mental QOL components, was assessed

using the Short-Form 36 Health Survey, a questionnaire consisting of 36 questions measuring both physical and mental health¹⁴. Health-related QOL data were collected by the researchers at baseline and at the end of the intervention.

Total energy and macronutrient intake

The total energy, macronutrient intake, and energy ratios of macronutrient quantities were estimated for the participants using group-based food frequency questionnaires (Eiyoku-kun version 5.0; Kenpakusha, Tokyo, Japan) administered by a registered dietitian at baseline and at the end of the intervention¹⁵.

Physical activities and fall risk survey

The amount of physical activity per week for each participant was estimated using the short version of the International Physical Activity Questionnaire^{16,17}, which was used to calculate metabolic equivalents (METs) per week. The fall risk index was scored using a questionnaire consisting of 21 items¹⁸. Physical activity and fall risk were assessed by the researchers at baseline.

Statistical analyses

Statistical analyses of the main results were performed after excluding participants who withdrew from the study (the full analysis set). The supplementary results of the per-protocol set analysis, including participants who completed the training protocol (training adherence $\geq 100\%$, CWT; $n = 13$, IWT; $n = 6$), are also shown. A two-way repeated-measures analysis of variance was used to assess the effects of the intervention on the primary and secondary outcome measures between the groups. Mean or median changes (Δ) in the measured primary and secondary outcomes from baseline to 3 months (baseline – 3 months = $\Delta 3$ months) and the end of the intervention (baseline – end of intervention = Δ end of intervention) were compared using an unpaired Student's *t*-test or Mann–Whitney *U* test and the χ^2 test or Fisher's exact test.

Baseline differences between the groups in terms of clinical characteristics and primary and secondary outcomes were evaluated using an independent group unpaired Student's *t*-test or Mann–Whitney *U* test and χ^2 tests or Fisher's exact test. During the intervention period, differences in training frequency per week between groups were assessed using the Mann–Whitney *U* test. The relationship between training adherence (total or fast walking times) and change in gait speed or change in the physical QOL component at the end of the intervention was analyzed using Pearson's correlation. Primary and secondary outcome data (baseline to end of intervention) were tested for normality using the Shapiro–Wilk test. All statistical analyses were performed using the IBM SPSS Statistics version 25 software (IBM Corp., Armonk, NY, USA) with a significance level of $\alpha = 0.05$. All statistical tests were 2-tailed, with the significance level set at $P < 0.05$.

RESULTS

Study population

In the IWT group, four participants had to discontinue training within the first month after the intervention (owing to fundus hemorrhage, $n = 1$; steroid therapy, $n = 1$; inability to operate the triaxial accelerometer, $n = 1$; unable to continue fast training, $n = 1$). Therefore, the final full analysis set included 25 and 21 participants in the CWT and IWT groups, respectively (Figure 1). A per-protocol set analysis including participants who completed the training protocol included 13 and 6 participants in the CWT and IWT groups, respectively (Figure 1).

Tables 1 and S2 present the participants' clinical characteristics and outcomes, respectively. There were no significant differences between the two groups in terms of clinical characteristics, primary and secondary outcomes at the baseline. There were also no significant differences in the total energy or macronutrient intake between the groups throughout the intervention period.

Adverse events

One patient in the IWT group developed fundus hemorrhaging, which was considered to be an adverse event associated with the training. During the intervention, three participants in the CWT group and 10 participants in the IWT group complained of either knee or hip joint pain, with a significantly higher rate in the IWT group (CWT: $n = 3$, IWT: $n = 10$, $P = 0.008$). However, these participants were able to continue training until the end of the intervention without having to discontinue training because their symptoms had later subsided.

Training adherence

Regarding the training adherence during the intervention period, the training frequency was 3.8 (1.7, 4.7) days/week for the CWT group and 2.3 (1.3, 3.3) days/week for the IWT group (median [25th, 75th interquartile range], CWT [$n = 25$] vs IWT [$n = 21$]; $P = 0.052$). The total walking adherence rates during the intervention period were 100.1% (39.5%, 148.4%) in

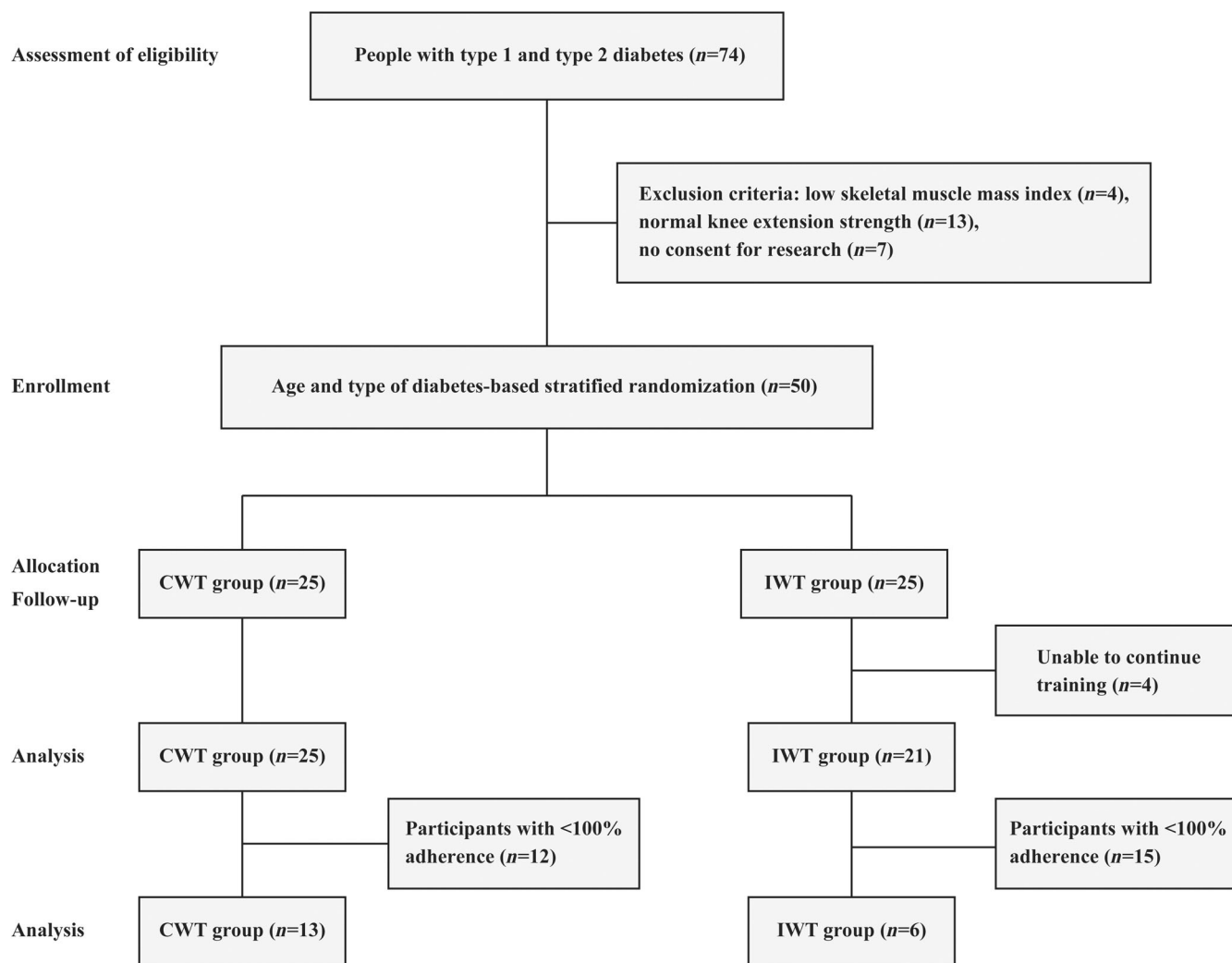


Figure 1 | Flowchart showing the study participants. CWT, continuous moderate-intensity walking training; IWT, interval fast walking training.

Table 1 | Baseline clinical characteristics of 46 participants in the CWT and IWT groups

	CWT group (n = 25)	IWT group (n = 21)	P value
Age (years)	59.4 ± 11.9	59.4 ± 11.7	0.987
Female/male (n)	12/13	16/5	0.072
Type 1/type 2 diabetes (n)	3/22	2/19	0.999
Duration of diabetes (years)	14.7 ± 7.8	13.3 ± 9.5	0.578
BMI (kg/m ²)	27.3 [25.6, 33.1]	31.0 [23.6, 34.1]	0.965
≥25.0 kg/m ² (%)	80.0	66.7	0.305
≥30.0 kg/m ² (%)	40.0	52.4	0.401
HbA1c (%)	6.9 [6.6, 7.8]	7.0 [6.8, 7.7]	0.842
Diabetic neuropathy (n)	14	11	0.806
Skeletal muscle mass index (kg/m ²)	7.48 [6.78, 8.54]	7.38 [6.80, 7.99]	0.310
Right leg, knee extension angle of 60° (Nm)	117.8 ± 46.6	113.3 ± 34.9	0.715
Left leg, knee extension angle of 60° (Nm)	118.4 ± 41.9	120.2 ± 34.4	0.878
Gait speed (m/s)	1.11 ± 0.21	1.13 ± 0.11	0.634
Physical activity (METs min/week)	1,173 [693, 1,485]	1,155 [1,056, 1,419]	0.707
Fall risk index (score)	5.4 ± 3.3	4.8 ± 2.1	0.481
VO _{2peak} /BW (mL/kg BW/min)	19.8 ± 3.5	20.9 ± 3.8	0.333
Physical QOL component summary (score)	41.9 ± 15.1	43.3 ± 14.8	0.746
Mental QOL component summary (score)	53.9 ± 8.5	50.7 ± 8.9	0.222

Data are shown as the number, mean value ± SD, and median [25th percentile, 75th percentile]. BMI, body mass index; BW, body weight; CWT, moderate-intensity continuous walking training; HbA1c, glycated hemoglobin; IWT, high-intensity interval walking training; METs, metabolic equivalents; Nm, Newton meter; QOL, quality of life; s, second; VO_{2peak}, estimated peak aerobic capacity.

the CWT group ($n = 25$, median [25th, 75th]). The adherence rate to the fast walking training during the intervention period was 62.1% (19.4%, 119.7%) in the IWT group ($n = 21$, median [25th, 75th]).

Primary and secondary outcomes

Tables 2 and S3 show the values of the primary and secondary outcomes at 3 months and at the end of the intervention (full analysis set: CWT, $n = 25$; IWT, $n = 21$). The IWT did not interact with the primary outcome, such as isometric knee extension strength (right and left leg, knee extension angle of 60°), at 3 months and at the end of the intervention between the two groups. However, significant interactions were identified for the secondary outcomes, such as gait speed, both at 3 months and at the end of the intervention between the two groups (3 months, $P = 0.007$; end of intervention, $P = 0.011$). There was also a significant interaction between the secondary outcomes of the physical health components at the end of the intervention ($P = 0.017$).

Table 2 | Primary and secondary outcomes at 3 months and at the end of the intervention for 46 participants in the CWT and IWT groups

	CWT group (n = 25)	IWT group (n = 21)	Interaction P value
At 3 months of intervention			
Primary outcome			
Right leg, knee extension angle of 60° (Nm)	113.0 ± 39.9	112.3 ± 41.7	0.831
Left leg, knee extension angle of 60° (Nm)	120.5 ± 46.8	118.4 ± 44.3	0.317
Secondary outcome			
Gait speed (m/s)	1.14 ± 0.23	1.21 ± 0.16	0.007
Other outcomes			
BMI (kg/m ²)	27.1 [25.5, 31.6]	31.0 [24.0, 33.7]	0.571
HbA1c (%)	6.8 [6.3, 7.3]	6.8 [5.9, 7.6]	0.359
Skeletal muscle mass index (kg/m ²)	7.61 [7.11, 8.20]	7.40 [6.84, 8.13]	0.780
At the end of intervention			
Primary outcomes			
Right leg, knee extension angle of 60° (Nm)	116.5 ± 38.7	112.1 ± 40.6	0.630
Left leg, knee extension angle of 60° (Nm)	122.3 ± 38.7	114.6 ± 39.4	0.283
Secondary outcomes			
Gait speed (m/s)	1.14 ± 0.23	1.21 ± 0.16	0.011
VO _{2peak} (mL/kg BW/min)	19.7 ± 3.5	20.6 ± 4.8	0.853
Physical QOL component summary (score)	42.3 ± 14.1	46.3 ± 13.0	0.017
Mental QOL component summary (score)	53.0 ± 9.0	50.1 ± 9.0	0.809
Other outcome			
BMI (kg/m ²)	27.0 [25.2, 32.0]	30.6 [23.6, 33.2]	0.741
HbA1c (%)	6.8 [6.4, 7.5]	7.0 [6.3, 7.4]	0.418
Skeletal muscle mass index (kg/m ²)	7.69 [6.93, 8.43]	7.26 [6.61, 8.17]	0.859

Data are shown as the mean ± SD and median [25th percentile, 75th percentile]. BMI, body mass index; CWT, moderate-intensity continuous walking training; HbA1c, glycated hemoglobin; IWT, high-intensity interval walking training; Nm, Newton meter; QOL, quality of life; s, second; VO_{2peak}, estimated peak aerobic capacity.

Tables 3 and Table S4 show the change from baseline to 3 months or the end of the intervention for the primary or secondary outcomes (full analysis set: CWT, $n = 25$; IWT, $n = 21$). From baseline to 3 months and at the end of the intervention, the change in gait speed was significantly higher in the IWT group (3 months, $P = 0.006$; end of intervention, $P = 0.008$). From baseline to the end of the intervention, the changes in physical QOL component summaries were also significantly higher in the IWT group ($P = 0.016$). From baseline to 3 months and at the end of the intervention, the percentage of participants who increased their gait speed by ≥ 0.1 m/s was

Table 3 | Change from baseline to 3 months and at the end of the intervention for 46 participants in the CWT and IWT groups

	CWT group (n = 25)	IWT group (n = 21)	P value
Change from baseline to 3 months of intervention			
Primary outcomes			
Right leg, knee extension angle of 60° (Nm)	3.48 ± 21.8	1.58 ± 15.6	0.756
Left leg, knee extension angle of 60° (Nm)	7.64 ± 18.5	1.47 ± 18.5	0.301
Secondary outcomes			
Gait speed (m/s)	0.03 ± 0.05	0.08 ± 0.06	0.006
Other outcomes			
BMI (kg/m ²)	−0.12 [−0.76, 0.53]	0.04 [−0.32, 0.20]	0.749
HbA1c (%)	−0.20 [−0.50, −0.20]	−0.20 [−0.40, −0.10]	0.929
Skeletal muscle mass index (kg/m ²)	0.09 [−0.08, 0.25]	0.12 [0.01, 0.24]	0.869
Change from baseline to end of intervention			
Primary outcomes			
Right leg, knee extension angle of 60° (Nm)	−1.30 ± 24.1	2.27 ± 17.0	0.580
Left leg, knee extension angle of 60° (Nm)	3.87 ± 21.3	−3.17 ± 24.8	0.311
Secondary outcomes			
Gait speed (m/s)	0.03 ± 0.05	0.08 ± 0.06	0.008
VO _{2peak} (mL/kg BW/min)	−0.10 ± 2.53	−0.22 ± 2.42	0.860
Physical QOL component summary (score)	0.40 ± 3.43	2.99 ± 3.58	0.016
Mental QOL component summary (score)	−0.83 ± 3.90	−0.54 ± 4.25	0.811
Other outcomes			
BMI (kg/m ²)	−0.45 [−1.02, 0.52]	−0.27 [−0.64, 0.08]	0.766
HbA1c (%)	−0.10 [−0.50, 0.10]	−0.20 [−0.30, 0.10]	0.982
Skeletal muscle mass index (kg/m ²)	0.04 [−0.25, 0.25]	0.05 [−0.08, 0.21]	0.402

Data are shown as the mean ± SD and median [25th percentile, 75th percentile]. BMI, body mass index; CWT, moderate-intensity continuous walking training; HbA1c, glycated hemoglobin; IWT, high-intensity interval walking training; Nm, Newton meter; QOL, quality of life; s, second; VO_{2peak}, estimated peak aerobic capacity.

significantly higher in the IWT group than in the CWT group (full analysis set; 3 months; $P = 0.004$, end of intervention; $P = 0.003$, Figure 2). A per-protocol set analysis is shown in Tables S5–S7 and Figure S1. Similar results were obtained in the full analysis set analysis.

Correlation between training adherence and changes in outcome measures

Table S8 shows the correlation coefficients between training adherence during the intervention period and changes in gait

speed and physical QOL components by the end of the intervention. In the IWT group, changes in the gait speed and physical QOL components were significantly positively correlated with adherence to fast walking ($P < 0.05$). However, there was no significant correlation between changes in gait speed or physical QOL components and training adherence to the total walking time in the CWT group.

DISCUSSION

High-intensity fast walking has been reported to increase the load on the femoral skeletal muscles, such as the quadriceps and biceps femoris, as well as their contractility². In addition, IWT has been found to improve knee extension muscle strength in middle-aged and older community-dwelling individuals during intervention at 5 months⁸. Therefore, based on these studies, we hypothesized that 5 months of IWT but not the CWT could increase the knee extensor strength in people with diabetes accompanied by lower extremity weakness.

For IWT, all participants were instructed to fast walk at an intensity of $\geq 70\%$ of their VO_{2peak} with a wider stride length and higher cadence (steps per minute) than the CWT group. In particular, the participants were instructed to perform IWT with a wider stride length due to an increase in knee extensor strength. However, training adherence in the IWT group failed to achieve the goal in this study (62.1% [19.4%, 119.7%] for fast walking). Such an unexpectedly low adherence rate to fast walking might have contributed to the lack of improvement in knee extensor strength in the IWT group.

In the IWT group, the median BMI was 31.0 (23.6, 34.1) kg/m², and 52.4% of the participants were obese (BMI ≥ 30 kg/m²). Masuki *et al.* reported that IWT adherence decreased over the course of the exercise period, which was attributed to the higher BMI group than the lower BMI group¹⁹. However, it is possible that obese people choose a more secure gait and narrow stride length because of reduced overload on the knee and/or hip joints and other parts of the body. In this study, 3 participants in the CWT group and 10 participants in the IWT group complained of either knee or hip joint pain, with a significantly higher rate in the IWT group. Pataky *et al.* reported that obese people had narrower stride lengths during fast walking than those with a normal body weight²⁰. Excessive fat mass over the abdomen and in the hip region limits the degree of potential hip flexion and might lead to narrowing of stride length²¹. Thus, obesity might decrease adherence to the IWT regimen owing to increased overload of the knee and/or hip joints and other parts of the body. Therefore, exercise counseling should be provided in combination with weight management via other interventions when intervening with IWT in people with diabetes and obesity. People with diabetes who have physical limitations such as obesity or muscle weakness may have difficulty continuing exercise therapy compared to the general population.

In the present study, at 3 months into the intervention period and at the end of the intervention, the secondary

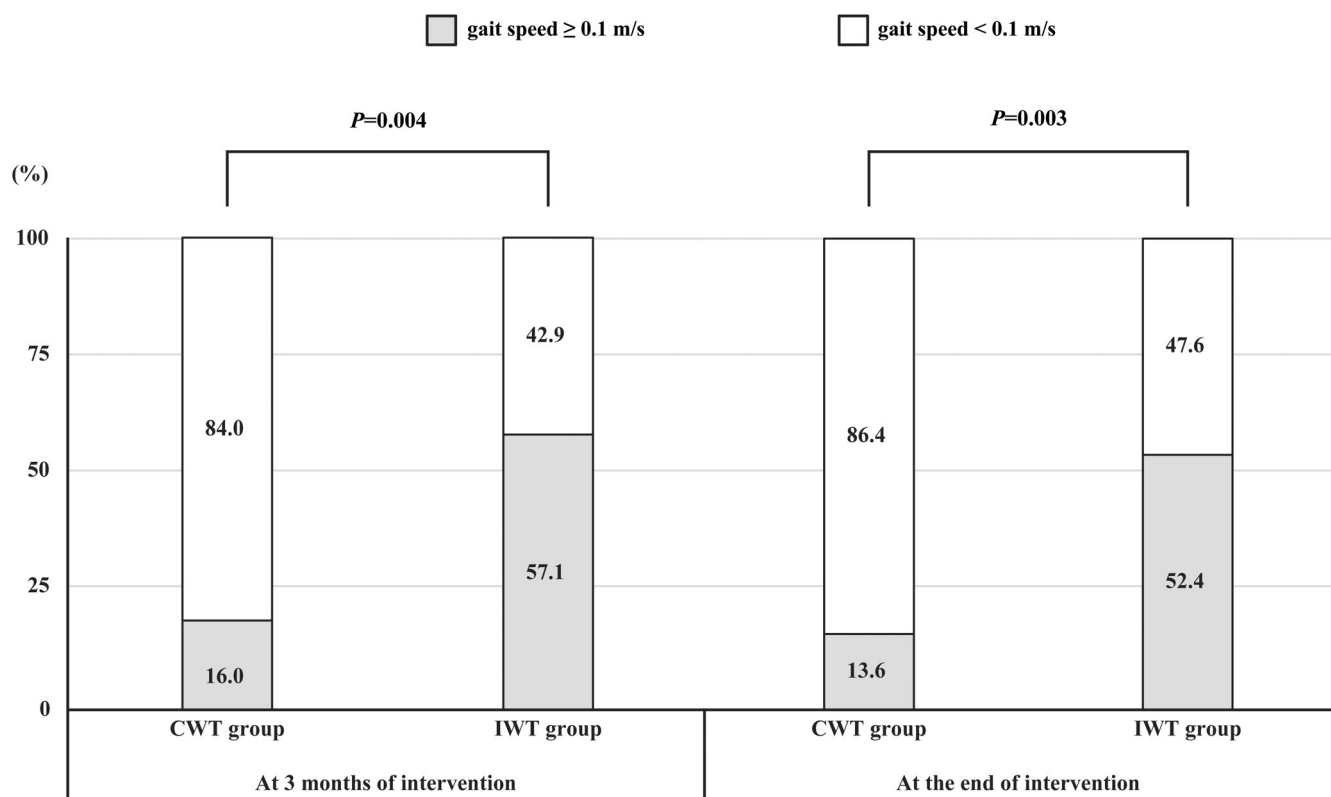


Figure 2 | Percentage of participants with an increase in gait speed of ≥ 0.1 m/s from baseline to 3 months and at the end of the intervention in the CWT and IWT groups. CWT, moderate-intensity continuous walking training; IWT, high-intensity interval walking training; s, second.

outcome of gait speed in the IWT group was significantly increased in the IWT group compared with the CWT group. At the end of the intervention, 52.4% of the IWT group had an increase in gait speed of at least 0.1 m/s, which was significantly higher than that in the CWT group. Our previous study also showed that people with diabetes accompanied by reduced muscle strength had slower gait speeds than healthy individuals⁴. Judge *et al.* reported that a 0.1 m/s decrease in gait speed was associated with a 10% decrease in instrumental activities of daily living (ADL)²². Therefore, walking training may be clinically important for improving walking ability in people with diabetes to maintain ADL.

Apart from muscle strength and stride length, balance, center of gravity, and cadence are also related to improvements in gait speed²³. In this study, these factors might have influenced the gait speed improvement in the IWT group. Of note, the rate of adherence to fast walking in the IWT group was positively correlated with the changes in walking speed. However, there was no significant correlation between the changes in gait speed and training adherence to total walking time in the CWT group. Indeed, in the CWT group, the total walking adherence was 100.1% (39.5%, 148.4%; median [25th, 75th]), but there was no notable increase in gait speed because moderate walking

was performed at 50% $\text{VO}_{2\text{peak}}$ exercise intensity. Low-to-moderate-intensity exercise therapy does not improve the gait function in older adults²⁴. In contrast, moderate-to-high-intensity exercise therapy has been shown to significantly improve the walking ability^{24,25}. Therefore, a combination of fast walking, such as the IWT, may be more effective in improving the walking ability in people with diabetes.

The results of this study showed that the secondary outcome of the physical QOL score was significantly better in the IWT group than in the CWT group. At baseline, the QOL score was 43.3 ± 14.8 points in the IWT group, which was lower than the national Japanese standard score of 50²⁶. Our previous study also showed that people with diabetes accompanied by reduced muscle strength had lower physical activity levels and physical QOL scores than healthy individuals⁴. Eckert *et al.* reported that people with type 2 diabetes and obesity have lower physical activity and QOL scores than those with normal body weights²⁷. Therefore, the improvement in the QOL following IWT seen in people with diabetes with a high BMI, muscle weakness, and a poor QOL observed in this study represents a clinically meaningful effect.

The IWT group showed a significant positive correlation (data not shown, $r = 0.597$, $P = 0.004$) between changes in

physical QOL score and changes in gait speed, which may indicate that improvements in QOL were related to improvements in walking ability. Previous reports have shown that there is a positive correlation between walking ability and QOL in people with type 2 diabetes²⁸. In this study, physical QOL score and gait speed improved even without an increase in knee extension muscle strength. In the IWT group, participants without obesity (BMI < 30 kg/m², *n* = 10) had a significantly higher change in gait speed than the participants with obesity (BMI ≥ 30 kg/m², *n* = 11) at the end of the intervention (data not shown, *P* < 0.05). The increase in stride length and cadence might affect the improved walking ability in participants without obesity of the IWT group. Additionally, gait speed changes in the IWT group were significantly positively correlated with changes in the lower limb muscle mass at the end of the intervention (data not shown, *r* = 0.470, *P* < 0.05). Therefore, it is possible that an increase in muscle strength, such as in the plantar flexors and dorsiflexors of the ankle joint, contributed to improvements in walking ability. In future studies, knee extension and ankle muscle strength should be evaluated before and after the IWT training period.

Several limitations associated with the present study warrant mention. This study was performed in a single-center setting, and the obtained sample sizes for diabetes were small. Therefore, a sub-analysis by type of diabetes and sex was impossible to perform. Further multicenter interventional studies with larger sample sizes are necessary to confirm our results. Exercise instruction and encouragement were provided to the participants once every 6–8 weeks during the intervention period. As previously reported, exercise instruction and encouragement should be provided to participants once every 4 weeks during the intervention period^{8,19}. In this study, there may have been inadequate instruction of participants about IWT. In this study, the effects of IWT were evaluated in people with diabetes who had a decrease in isometric knee extension muscle strength. However, the effects of IWT on people with diabetes who have decreased skeletal muscle mass and strength are unknown in this study.

The results of this study showed that IWT for people with diabetes accompanied by lower extremity weakness did not improve knee extension muscle strength compared to CWT but did improve walking ability and physical QOL. In this study, training adherence in the IWT group failed to achieve the goal.

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DISCLOSURE

The authors declare no conflict of interest.

Approval of the research protocol: This study was approved by the Ethics Committee of Tokushima University Hospital (approval number: 4213, approval date: 25 July 2022).

Informed consent: Written informed consent was obtained from all study participants between August 2022 and February 2023 at Tokushima University Hospital.

Registry and the registration no. of the study/trial: This study was registered in the University Hospital Medical Information Network (approval date: registry 5 June 2020, approval number: UMIN000040658).

Animal studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. The definition of low skeletal muscle mass and low knee extension strength at screening.

Table S2. Baseline clinical characteristics of 46 participants in the CWT and IWT groups.

Table S3. Primary and secondary outcomes at 3 months and the end of the intervention for 46 participants in the CWT and IWT groups.

Table S4. Change from baseline to 3 months and the end of the intervention for 46 participants in the CWT and IWT groups.

Table S5. Baseline clinical characteristics of 19 participants with training adherence $\geq 100\%$ in the CWT and IWT groups.

Table S6. Primary and secondary outcomes at 3 months and at the end of the intervention for 19 participants with training adherence $\geq 100\%$ in the CWT and IWT groups.

Table S7. Change from baseline to the end of the intervention for 19 participants who had training adherence $\geq 100\%$ in the CWT and IWT groups.

Table S8. The correlation coefficient between training adherence during the intervention period and the change amount in Δ Gait speed and Δ Physical QOL component summary.

Figure S1. Percentage of participants with an increase in gait speed of ≥ 0.1 m/s from baseline to 3 months and at the end of the intervention in the CWT ($n = 13$) and IWT ($n = 6$) groups. CWT, moderate-intensity continuous walking training; IWT, high-intensity interval walking training; sec, second.

Data S2. CONSORT 2010 checklist.