

## Original Article

# Efficacy of exercise and electromagnetic field therapy on cardiovascular disease risk in patients with type 2 diabetes mellitus. Randomized controlled trial

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**Abstract:** Type 2 diabetes mellitus predisposes patients to abnormally increased atherosclerotic cardiovascular disease risk and deteriorated lower extremity functional status. Objective: To evaluate the effect of combined application of moderate to high intensity interval training and low frequency pulsed electromagnetic therapy on atherosclerotic cardiovascular disease risk and lower extremity function in older adults with type 2 diabetes mellitus. Fifty-four patients (age 45-60 years) with type 2 diabetes mellitus were randomly allocated into four groups: group A underwent moderate to high intensity interval training plus low frequency pulsed electromagnetic therapy for 8 weeks (n=13), group B received low frequency pulsed electromagnetic therapy (n=14), group C underwent moderate to high intensity interval training (n=13), and group D were the controls (n=14). The 10-year atherosclerotic cardiovascular disease risk was evaluated using the Atherosclerotic Cardiovascular Disease Risk Estimator Plus tool, while lower extremity function was assessed using the Short Physical Performance Battery. Statistical comparisons were conducted within and between groups using SPSS 20. A *P*-value <0.05 was considered statistically significant. After 8 weeks, the atherosclerotic cardiovascular disease risk significantly decreased by -10.91% (*P*<0.001) and -6.66% (*P*<0.001) in groups A and C, respectively, non-significantly decreased by -0.16% (*P*=0.43) in group B, and non-significantly increased by 1.35% (*P*=0.24) in group D. The lower extremity function significantly increased by 64.62% (*P*<0.001), 27.48% (*P*=0.001), and 48.49% (*P*<0.001) in groups A, B, and C, respectively. There was a non-significant increase of 0.5% (*P*=0.73) in group D. In conclusion, the combined application of moderate-to-high-intensity interval training and low-frequency pulsed electromagnetic therapy programmes was effective in improving atherosclerotic cardiovascular disease risk and lower extremity function in older adults with type 2 diabetes mellitus. Furthermore, the moderate-to-high-intensity interval training programme is more effective than low-frequency pulsed electromagnetic therapy in improving atherosclerotic cardiovascular disease risk and lower extremity function in patients with type 2 diabetes mellitus.

**Keywords:** Exercise therapy, magnetic field, cardiovascular condition, lower extremity, diabetes

## Introduction

Diabetes mellitus (DM) is a global epidemic [1, 2]. Atherosclerotic Cardiovascular disease (ACVD) is the primary cause of death in patients with DM worldwide [3, 4]. The strong positive correlation between DM and ACVD risk is proportionally correlated with the hyperglycemia status, even before diabetes diagnosis [5]. The presence of DM, in addition to ageing, magnifies the ACVD risk [6]. These facts highlight the importance of considering the ACVD risk-reduction strategies during DM management

[7]. The presence of DM is closely correlated with peripheral circulatory disturbances and lower extremity (LE) ischemia [8], so early and proper management of diabetes-related LE dysfunction is crucial for minimising complications [9, 10].

Exercise therapy is an essential component in DM management to enhance glycaemic control and insulin action [11]. Studies have demonstrated favourable effects of interval training on cardiovascular and metabolic parameters in patients with DM [12, 13]. Exercise training can

improve cardiopulmonary and metabolic variables, which, in turn, can ameliorate the progression of complications and disease prognosis [14]. Engagement in regular physical training has positive effects on cardiovascular, musculoskeletal, metabolic, and psychosocial function in patients with DM, resulting in a lower mortality rate [15]. An increase of weekly activity hours by 11.25 metabolic equivalents can reduce the ACVD mortality by 23% [16]. Interval training includes reciprocal periods of high- and low-intensity training intervals that can improve cardiopulmonary fitness and glycemic control in individuals with type 2 diabetes mellitus (T2DM) [17]. High-intensity interval training (HIIT) in walking mode is a recommended training approach to improve cardiopulmonary fitness, glycaemic control, body composition [18], and control exercise-induced hypoglycaemic attacks in T2DM [22].

Low-frequency pulsed electromagnetic therapy (LFPEMT) is a noninvasive modality that emits therapeutic electromagnetic fields and has beneficial effects on the metabolic profile in patients with T2DM [19], due to its favourable vasoactive, neurostimulatory, and analgesic effects [20]. Studies have clarified the favourable effects of LFPEMT on various musculoskeletal, cardiovascular, metabolic, and functional variables in patients with T2DM [21, 22]. A recent study demonstrated significant effects of crossover application of the LFPEMT and interval exercise training on balance and peripheral vascular status in patients with DM [23].

To the best of our knowledge, the effect of the combined application of moderate-to-high-intensity interval training (M-HIIT) and LFPEMT on ACVD risk and LE function in patients with T2DM has not yet been investigated. This study aimed to explore the effects of combined M-HIIT and LFPEMT on 10-year ACVD risk and LE function in patients with T2DM.

## Materials and methods

### Research design

This study used a randomised, controlled, prospective, single-blind design. Full blinding was not feasible due to the nature of the study; the therapist could not be fully blinded to the treatment procedures. Participants were blinded to the treatment parameters, and assessors were completely unaware of the study design, group allocations, or treatment procedures.

### Participants and randomisation

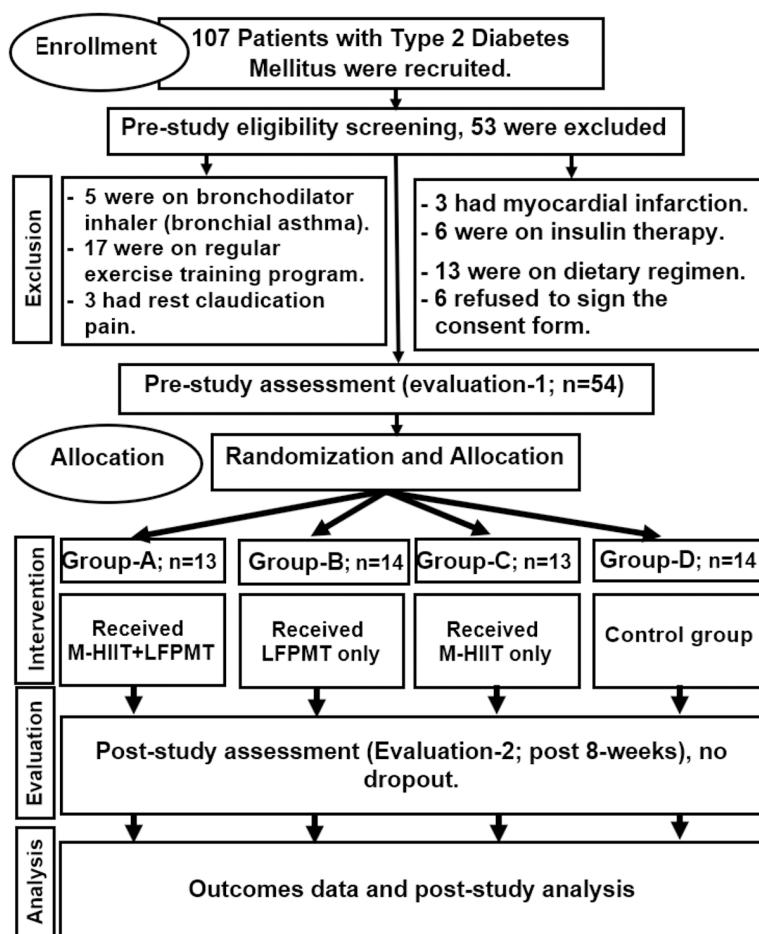
The sample size was estimated using the G-power application, with an effect size of 0.6, alpha error probability of 0.05, power of 0.95, and 4 groups, yielding a sample size of 52 participants, which was deemed suitable to test the study assumptions and clarify the 'between-group' differences. A total of 107 patients were recruited from Saudi Western area governmental hospitals through web-based invitations and face-to-face interviews, and underwent the eligibility screening test battery. Of them, 53 were excluded for various reasons, while 54 participants (39 men and 15 women) were eligible and completed the 8-week study (no drop-outs) (Figure 1). The participants were initially randomised using the randomiser website (<https://www.randomizer.org/>) by an independent statistician into four groups: group A underwent LFPEMT and M-HIIT (n=13), group B received LFPEMT (n=14), group C underwent M-HIIT (n=13), and group D was the control (n=14) (Figure 1). The inclusion criteria were: medically controlled T2DM ( $6.5 < \text{glycated haemoglobin (HbA1c)} \leq 11$ ), T2DM duration  $\geq 5$  years, T2DM treated with oral medications only (no insulin administration), cognitively competent subjects who understood and could follow instructions, and aged 45-60 years. Exclusion criteria were aged younger than 45 or older than 60 years old, treatment with insulin, active infections or recent serious cardiovascular/neuromusculoskeletal health conditions, participation in dietary or exercise programmes during the last 6 months, or refusal to consent to participation and agreement of publication of the study results.

### Ethical considerations

This study adhered to the Helsinki Declaration (1975, revised in 2000). It was approved by the Umm Al-Qura University Local Committee for Biological and Medical Ethics (Approval No. HAPO-02-K-012-2025-06-2823) and registered on ClinicalTrials.gov (ID: NCT06974435). All participants provided written informed consent before study entry. The study was conducted from March to September 2025.

### Demographic data

The demographic data collected included age, weight, height, body mass index, diabetes duration, fasting blood glucose (FBG), nutritional



**Figure 1.** Patients' flow chart. M-HIIT, Moderate to high intensity interval training; LFPMT, Low frequency pulsed electromagnetic therapy.

status, resting heart rate, systolic brachial blood pressure (SBP), diastolic blood pressure (DBP) and smoking status. The individualised maximum heart rate (HRmax) was calculated according to the Tanaka et al. formula, in which the participant's age (in years) is multiplied by 0.7, and the resultant value is then subtracted from 208 [24] (Table 1).

#### Cardiovascular disease risk

The ACVD risk was calculated using the methods of Stone et al. and Nuwanthika et al. The ACVD risk was estimated using the 'ACVD risk-estimator plus' tool (<https://tools.acc.org/ascvd-risk-estimator-plus/#/calculate/estimate/>) developed by the American Heart Association and the American College of Cardiology using the following variables: age in years, sex (male or female), race (white/African American/ or other), systolic and diastolic blood pressure in mmHg, high and low-density-lipoprotein cho-

lesterol in mg/dl, total cholesterol in mg/dl. Blood lipid variables were quantified using a previously described procedure by Nuwanthika et al. in fasting venous blood samples collected in EDTA and plain blood collection tubes. The glycerol phosphate oxidase-peroxidase and the cholesterol oxidase-peroxidase 4-aminoantipyrine methods were used to estimate triglycerides and total cholesterol, respectively [25]. Data regarding the existence of treatments for hypertension, use of statins, and aspirin therapies were also recorded in the form of 'yes or no'. The higher the ACVD risk score, the higher the CVD risk; ACVD risk values below 5% indicate low ACVD risk, while those above or equal to 20 indicate high ACVD risk [25, 26].

#### Lower extremities functional status

The LE function was evaluated using the 20-item Lower Extremity Functional Scale (<https://academic.oup.com/ptj/article/79/4/371/2857730?login=true>), which assesses the patient's ability to perform daily functional activities. Each participant was asked about the level of difficulty encountered during each task, and a score from 0 to 4 was used to represent the level of difficulty. Scoring for each of the 20 items ranges from 0 (extreme difficulty) to 4 (no difficulty), with 1 indicating relative difficulty in performing daily tasks, 2 indicating moderate difficulty, 3 indicating little difficulty, and 4 indicating no difficulty. The tasks include housework, hobbies, sporting activities, getting in and out of the bath, walking, squatting, standing, setting, running, and hopping. The total scale score ranges from 0 to 80; the lower the score, the greater the difficulty and the greater the disability encountered during daily activi-

**Table 1.** The basic characteristics of participants in all groups (Mean  $\pm$  SD)

	M-HIIT+ LFPMT Group (Group-A; n=13)	LFPMT Group (Group-B; n=14)	M-HIIT Group (Group-C; n=13)	Control Group (Group-D; n=14)	P-value <sup>◊</sup>
Age (year)	57.85 $\pm$ 1.07	57.79 $\pm$ 1.05	57.77 $\pm$ 1.09	57.86 $\pm$ 1.29	0.99**
Height (m)	1.62 $\pm$ 0.03	1.61 $\pm$ 0.02	1.60 $\pm$ 0.021	1.61 $\pm$ 0.01	0.6**
Weight (kg)	71 $\pm$ 3.42	70.79 $\pm$ 4.39	70.92 $\pm$ 3.88	70.79 $\pm$ 6.28	0.99**
BMI (Kg/m <sup>2</sup> )	27.29 $\pm$ 2.06	27.301 $\pm$ 1.88	27.65 $\pm$ 1.84	27.24 $\pm$ 2.50	0.96**
Diabetes Duration (year)	13.38 $\pm$ 1.56	13.5 $\pm$ 1.65	13.46 $\pm$ 1.05	13.43 $\pm$ 0.85	0.99**
FBG (Pre; mg/dl)	170.77 $\pm$ 7.0	170.5 $\pm$ 7.4	170.46 $\pm$ 7.26	170.64 $\pm$ 9.75	1.00**
RHR (beat/min)	76.08 $\pm$ 3.33	75.79 $\pm$ 3.19	75.69 $\pm$ 1.97	75.79 $\pm$ 3.19	0.99**
HRmax (beat/min)	164.15 $\pm$ 5.05	164.5 $\pm$ 3.08	164.31 $\pm$ 4.11	164.21 $\pm$ 3.6	0.99**
SBP (Pre; mmHg)	144.08 $\pm$ 3.25	143.43 $\pm$ 2.90	143.85 $\pm$ 1.77	143.5 $\pm$ 1.61	0.9**
DBP (Pre; mmHg)	84.46 $\pm$ 1.27	84.64 $\pm$ 0.93	84.39 $\pm$ 1.2	84.21 $\pm$ 1.42	0.83**
TC (Pre; mmol)	6.33 $\pm$ 0.25	6.33 $\pm$ 0.23	6.31 $\pm$ 0.27	6.29 $\pm$ 0.32	0.94**
HDL (Pre; mmol)	1.07 $\pm$ 0.06	1.07 $\pm$ 0.07	1.07 $\pm$ 0.07	1.06 $\pm$ 0.07	0.85**
LDL (Pre; mmol)	4.41 $\pm$ 0.08	4.46 $\pm$ 0.19	4.43 $\pm$ 0.14	4.45 $\pm$ 0.13	0.8**
Gender (Male: Female)	3 (76.9%): 10 (23.1%)	12 (85.7%): 2 (14.3%)	11 (84.6%): 2 (15.4%)	5 (64.3%): 9 (35.7%)	0.51**
On Hypertension medication	11 (84.6%)	12 (85.7%)	12 (92.3%)	13 (92.9%)	0.86**
On Statins	10 (76.9%)	12 (85.7%)	10 (76.9%)	11 (78.57%)	0.9**
On Aspirin	7 (53.8%)	9 (64.3%)	8 (61.54%)	8 (57.14%)	0.5**
Smoking status (Current smoker: Nonsmoker)	11 (84.6%): 2 (15.4%)	11 (78.6%): 3 (21.4%)	11 (84.6%): 2 (15.4%)	12 (85.7%): 2 (14.3%)	0.96**

<sup>◊</sup>Level of significance at P<0.05; \*\* non-significant; M-HIIT, Moderate to high intensity interval training; LFPMT, Low frequency pulsed electromagnetic field; BMI, body mass index; FBG, fasting blood glucose; RHR, Resting heart rate; HRmax, maximum heart rate; Pre, pre-study; Post, post-study; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

ties. A 9-point difference between two successive evaluations is required to represent a detectable change in LE functional performance [27].

#### *Interventions*

Registered therapists with more than 10 years' experience provided the treatment programmes for groups A, B, and C; one therapist per group. Intervention groups A, B and C received three sessions per week, for 8 weeks. Contributing factors, such as dietary and pharmacological elements, were stabilised as much as possible in all participants during the study through patient education, regular checks and monitoring by the therapist, and by relatives/caregivers at home.

#### *The moderate to high intensity interval training programme*

A supervised M-HIIT program on a treadmill (COSMED T150LC, Italy) was provided three times per week for 8 weeks (day-after-day sessions, total 24 sessions), following the previously reported procedure [28]. The M-HIIT intensity was established based on the calculated HRmax according to Tanaka et al. [24]. The training session started and ended with 10 minutes of warm-up and cool-down, respectively (at 30-50% of HRmax). The training phase included alternating training intervals on 70-85% of HRmax for 4 minutes (4-intervals; moderate-high intensity) and recovery cycles on 40%-50% of HRmax for 3 minutes (3-intervals; low intensity). Treadmill speed and training heart rate were continuously monitored and controlled to maintain the required training intensity between 15-17 on the Borg's scale for rate of perceived exertion during high-intensity interval training phases and between 9-11 during low-intensity training intervals [29].

#### *The low-frequency pulsed electromagnetic therapy programme*

A closely supervised LFPMT program was provided day after day, for 8 weeks, following the previously reported procedure [23]. Following a 10-minute rest, resting vital signs were initially evaluated, with the participant sitting with each foot resting flat on a 36 cm width x 21 cm depth x 2 cm height plate (Flexa applicator) connected to the LFPMT apparatus (Easy Qs, ASA srl,

Italia) that provided LFPMT with a 20 Gauss intensity, 15 Hz frequency, for 30 minutes.

#### *Statistical analysis*

The data are presented as mean  $\pm$  SD. Homogeneity of variances was tested using Levine's test. Data distribution was assessed using the Shapiro-Wilk test. Within- and between-group statistical comparisons were performed using the paired-samples t-test and one-way ANOVA, respectively, in SPSS version 20.0 (SPSS Inc., USA). A *p*-value of  $<0.05$  was considered significant.

## **Results**

#### *Participants' baseline characteristics*

Fifty-four patients with T2DM completed this study; no serious events were reported. There were non-significant differences in baseline characteristics between groups (**Table 1**).

#### *Cardiovascular disease risk*

At baseline, there were no significant differences in ACVD risk mean values ( $P=1.00$ ), but significant differences emerged after 8 weeks ( $P=0.04$ ). There were significant differences between groups in the ACVD risk percentages of change ( $P<0.001$ ), with the highest percentage reduction observed in group A (-10.91%,  $P=0.001$ ), followed by group C (-6.66%,  $P=0.001$ ) and group B (-0.16%,  $P=0.43$ ) (**Table 2**). Significant differences exist pre-study between the ACVD risk and the optimal ACVD risk in all groups ( $P<0.001$ ). Post-study, despite changes in ACVD risk, values did not reach the optimal ACVD risk, and significant differences exist between post-study and optimal ACVD risks in all groups ( $P<0.001$ ).

Regarding the ACVD risk estimation components, between-groups statistical comparisons (pre-study) revealed non-significant differences in mean values for FBG ( $P=1.00$ ), SBP ( $P=0.9$ ), diastolic BP ( $P=0.83$ ), total cholesterol ( $P=0.94$ ), high-density lipoprotein ( $P=0.85$ ), and low-density lipoprotein ( $P=0.8$ ). Post-study results clarified significant differences between groups in mean values of FBG ( $P=0.03$ ), SBP ( $P=0.002$ ), diastolic BP ( $P<0.001$ ), total cholesterol ( $P=0.04$ ), high-density lipoprotein ( $P=0.03$ ), and low-density lipoprotein ( $P=0.01$ ).

## Exercise, electromagnetic therapy, cardiovascular disease risk, diabetes

**Table 2.** Between and within groups comparison of the cardiovascular disease risk and lower extremity function mean values (Mean  $\pm$  SD)

Variables	M-HIIT+ LFPMT Group (Group-A; n=13)	LFPMT Group (Group-B; n=14)	M-HIIT Group (Group-C; n=13)	Control Group (Group-D; n=14)	P-value <sup>‡</sup>
Current 10-Year ASCVD Risk (Pre-study)	36.26 $\pm$ 8.67	36.29 $\pm$ 7.39	36.02 $\pm$ 6.57	36.23 $\pm$ 7.9	1.00**
Current 10-Year ASCVD Risk (Post-study)	31.37 $\pm$ 7.50	36.22 $\pm$ 7.4	32.31 $\pm$ 5.6	38.21 $\pm$ 6.6	0.04*
T, P	13.19, <0.001*	1.01, 0.33**	8.70, <0.001*	-2.90, 0.01*	
LEF (Pre-study)	39.92 $\pm$ 2.22	40 $\pm$ 2.08	39.85 $\pm$ 2.23	38.86 $\pm$ 2.48	0.51**
LEF (Post-study)	65.54 $\pm$ 1.85	50.93 $\pm$ 2.46	59 $\pm$ 2.94	39 $\pm$ 2.04	<0.001*
T, P	-31.51, <0.001*	-18.89, <0.001*	-18.47, <0.001*	-0.25, 0.73**	
FBG (Pre-study)	170.77 $\pm$ 7.00	170.5 $\pm$ 7.4	170.46 $\pm$ 7.26	170.64 $\pm$ 9.75	1.00**
FBG (Post-study)	163.00 $\pm$ 5.85	167.93 $\pm$ 7.13	165.08 $\pm$ 5.95	170.71 $\pm$ 8.58	0.03*
T, P	17.63, <0.001*	6.19, <0.001*	12.06, <0.001*	-0.16, 0.87**	

<sup>‡</sup>Level of significance at P<0.05; \*significant; \*\*non-significant; M-HIIT, Moderate to high intensity interval training; LFPMT, Low frequency pulsed electromagnetic field therapy; ASCVD, Atherosclerotic cardiovascular disease risk; LEF, lower extremity function; FBG, Fasting blood glucose level.

#### Lower extremity function

Pre-study, there were no significant differences in the LE function between groups ( $P=0.51$ ); post-study, significant differences exist ( $P<0.001$ ). Significant differences exist between groups in the LE function percentages of change ( $P<0.001$ ), with the highest percentage increase obtained in group A (64.62%,  $P<0.001$ ), followed by group C (48%,  $P<0.001$ ) and group B (27.48%,  $P<0.001$ ) (**Table 2**).

#### Discussion

After 8 weeks of study duration, results indicated higher and more significant effects of the combined application of M-HIIT and LFPMT on ASCVD risk and LEF in patients with T2DM compared to either alone. Patients with T2DM suffer a variety of cardiovascular dysfunctions [1].

The current study clarified the beneficial role of combining exercise therapy and electromagnetic therapy in patients with T2DM. Combined application of the AET and PEMFT can significantly control blood pressure, even in patients with hypertension [30]. The improvement in CVD risk in response to the combined effects of M-HIIT and PEMFT can, in part, be due to reductions in SBP and DBP secondary to arterial vasodilation produced by enhanced endothelial function and increased nitric oxide production [31]. The LFPMT proved effective in augmenting cardiovascular function through enhancing microcirculation, capillary perfusion and cutaneous blood flow in diabetic patients with peripheral circulatory disturbances [32].

Regarding exercise training, beneficial effects were observed with moderate-intensity aerobic exercise. Still, higher-intensity interval training can provide greater improvements in patients with T2DM [33], and progressively increased training intensity over several weeks is recommended to prevent acute hyperglycemic attacks that can accompany suddenly implemented high training intensities [34, 35]. Regular physical activity can significantly improve blood pressure [36], enhance peripheral vascular health and glycaemic control [28], improve peripheral circulation, and significantly ameliorate the progression of the ischemic tissue pathway in patients with long-standing T2DM [37]. Wormgoor et al. reported that interval training is a suitable therapeutic option for con-

trolling various T2DM-related disturbances, including hyperglycemia, abnormally elevated blood pressure, and abnormal lipid profiles [13]. Previous studies reported significant increases in the peripheral vascular flow-mediated dilation in response to LFPMT. They related this response to the improved endothelial vascular health [31], improved peripheral vascular resistance [38-40], and LFPMT-induced nitric oxide bioavailability [41, 42], in response to vasodilation effects produced by increased calcitonin gene expression as well as adenosine A2A receptors [43], in response to LFPMT.

The LEPMT can effectively produce arteriolar vasodilation [44], enhance distal microcirculation and microvascular recruitment [45], eliminate tissue hypoxemia, and improve neural function [46, 47]. The present study results are consistent with previously published findings, showing that the LFPMT is effective in improving physical performance and peripheral vascular function [23, 48]. The LFPMT can significantly reduce systemic blood pressure, augment peripheral vascular endothelial function in patients with elevated blood pressure [31, 38], and improve transneuronal blood flow in the elderly population [38, 39].

The current study showed that M-HIIT alone or in combination with LFPMT effectively modulates cardiovascular and functional variables. This agrees with previous reports, which clarify that only 2 hours per week of brisk walking (equivalent to 10 METs) can significantly reduce cardiovascular mortality and morbidity in patients with T2DM [49]. Increased physical activity can favourably modulate modifiable cardiovascular disease risk factors, such as hyperglycemic indices and high-density lipoprotein cholesterol [50, 51]. Aerobic exercise training can also minimise the diabetes-related systemic low-grade inflammation [52], reduce triglycerides, decrease low-density lipoprotein cholesterol and increase high-density lipoprotein levels [53, 54], reducing the blood pressure [55, 56], which in turn can significantly reduce the cardiovascular disease risk [34, 35, 57].

Increased activity level is directly correlated with improved physical performance and cardiovascular function. Exercise therapy, particularly interval training, is associated with reduced CVD [58, 59] and all-cause mortality in

patients with diabetes, as well as in normal counterparts without CVD risk factors [60, 61]. Increasing physical activity level is directly related to improved cardiopulmonary fitness. Training at 50-75% of maximal exercise capacity can increase cardiopulmonary fitness by 12% in patients with T2DM [34, 62]. Exercise training can produce its anti-atherosclerotic effects by improving endothelial function [63, 64], reducing angiotensin II levels, increasing myokines' anti-inflammatory activity [65], and increasing flow-mediated dilation in patients with T2DM [66, 67].

The present study clarified the enhanced LE functional status in response to M-HIIT alone or to the combined application of M-HIIT and LFPMT. These improvements can be justified based on the peripheral vascular health improvements in response to M-HIIT and LFPMT [23], since exercise-induced improvements in peripheral vascular function are commonly translated into improved peripheral circulation [68] and increased physical performance [69]. Exercise-related improvements in peripheral vascular health (and hence controlled vascular disorders) can be attributed to increased capillary density in the extremity muscles, increased regional perfusion [70], altered inflammatory markers, and improved endothelial function [71].

The present study documented the positive effect of LFPEMT on LE function, in line with previous studies. Abdelaal and Abdelgalil reported that twice-weekly sessions for 12 weeks of LFPEMT significantly improved functional capacity by 15.73% in patients with diabetic peripheral polyneuropathy [72]. The LFPEMT can effectively enhance regional cellular metabolic activities [73, 74], neural pulse propagation velocity, and motor unit recruitment and action potential amplitude [75, 76], all of which can improve LE function in response to LFPEMT application.

The exercise-induced improvements in lower extremity function can also be attributed to intracellular increases in mitochondrial oxidative capacity and skeletal muscle metabolic activity [77, 78]. Improved physical function following exercise training can be attributed to enhanced glucose utilisation and insulin sensitivity [14]. An increase in exercise-induced glucose uptake in skeletal muscle may explain

improved physical function and performance. Taguchi et al. reported increased bradykinin concentration in response to exercise training, which may contribute to enhancing insulin signalling and GLUT-4 translocation [79], leading to exercise-induced increases in glucose transport and utilisation in diabetic patients [80, 81]. The significant increase in the lower extremity function can also be explained based on the training-related downregulation of the muscular proteins' catabolic mechanisms, and enhancing the PGC-1 alpha signalling activities and improving the muscle-to-fat ratio [82, 83], thereby improving muscle strength and mass in trained patients with T2DM.

#### *Limitations*

Although the clinical importance of the current study's findings is significant, certain points limit its generalisability, including a relatively short study duration and the inclusion of patients with T2DM receiving only oral hypoglycemic agents. Future studies are warranted to uncover further responses and adaptations to short- and long-term combined M-HIIT and LFPMT programmes, and to include comparisons with other treatment programmes and with patients with type 1 diabetes.

#### **Conclusion**

Combined application of M-HIIT and LFPMT is more effective than either alone in controlling ACVD risk and increasing LEF in patients with T2DM. Given the need for precautions and safety measures, M-HIIT and LFPMT should be included in any rehabilitation programme designed to improve ACVD and LEF in patients with T2DM.

#### *Practical message*

Implementation of properly selected therapeutic procedures is essential to achieve target goals during the rehabilitation of patients with T2DM, who are at an increased risk for ACVD. Combined application of M-HIIT and LFPMT is safe and effective in improving the commonly attenuated ACVD risk and LEF in patients with T2DM. The combined application of both procedures is more effective than either alone. Patients with T2DM and an increased ACVD risk will greatly benefit from a well-structured rehabilitation program that includes the combined application of M-HIIT and LFPMT.

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## Disclosure of conflict of interest

None.

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