UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

What Physical Training Intensity And Volume Is Most Optimal To Improve Physical Fitness In T2DM Patients?

Alexandre Caenen
Ward Melotte

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

PROMOTOR :
Prof. dr. Dominique HANSEN

BEGELEIDER :
De heer Tin GOJEVIC

COPROMOTOR :
dr. Felipe VILACA CAVALLARI MACHADO

2024
2025

UHASSELT
KNOWLEDGE IN ACTION

www.uhasselt.be
Universiteit Hasselt
Campus Hasselt:
Martelarenlaan 42 | 3500 Hasselt
Campus Diepenbeek:
Agoralaan Gebouw D | 3590 Diepenbeek

UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

What Physical Training Intensity And Volume Is Most Optimal To Improve Physical Fitness In T2DM Patients?

Alexandre Caenen
Ward Melotte

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

PROMOTOR :
Prof. dr. Dominique HANSEN

COPROMOTOR :
dr. Felipe VILACA CAVALLARI MACHADO

BEGELEIDER :
De heer Tin GOJEVIC

Table of contents

Thesis Overview and Acknowledgments

This thesis, written by Alexandre Caenen and Ward Melotte, focuses on the influence of specific types of exercise on physical fitness capacity in patients with type 2 diabetes mellitus (T2DM). Physical activity plays a vital role in improving health and quality of life for individuals with T2DM by positively impacting metabolic health, cardiovascular risk factors, and mental well-being. While both moderate aerobic exercise and high-intensity interval training have been shown to improve physical fitness, the optimal training intensity and volume for this population remain unclear. Addressing this gap is essential to develop effective exercise prescriptions and enhance health outcomes.

Our research question aims to determine the most effective intensity and volume of physical training to improve physical fitness in patients with T2DM. This master's thesis is a sub-analysis of a prospective single-blind, randomized controlled trial conducted at the REVAL campus of Hasselt University in Diepenbeek and Jessa Hospital. The main trial investigates the independent effects of exercise volume and intensity during a six-month intervention on global longitudinal strain in T2DM patients.

Data collection was performed by drs. Tin Gojevic, Meike Peeters, Noor Wouters and ourselves (Alexandre Caenen and Ward Melotte) who were both responsible for drafting the introduction, methods, results, discussion and conclusion.

Through this thesis, we aim to provide insights that can help physical therapists recommend the most suitable exercise interventions to optimize the health of patients with T2DM.

We want to sincerely thank everyone who helped us along the way while working on this thesis. In particular, we are grateful to Prof. Dr. Dominique Hansen, Dr. Felipe Machado and Tin Gojevic for their guidance, support and advice throughout the project. We also want to thank all the participants for their time, flexibility, and commitment, without whom, this study would not have been possible. Finally, we'd like to thank REVAL (Hasselt University) and Jessa Hospital (Hasselt) for giving us the opportunity to carry out our measurements at their facilities.

Abstract

Background: T2DM is a high-prevalent disease found in all regions worldwide. These patients have a high risk of long-term complications and comorbidities, which can be reduced by increasing their exercise capacity.

Objectives: The aim of this study is to find the most optimal training intensity and volume for T2DM patients to improve their exercise capacity.

Methods: A sub-analysis of a prospective, single-blind, randomized controlled trial was conducted in 66 T2DM patients. Participants were randomized into one of three intervention groups (LVMI, HVMI, LVHI) or a control group. Intervention groups followed a 72-session training program, three times per week. Physical fitness parameters (VO_2@VT1, VO_2@VT2, absolute VO_{2peak}, relative VO_{2peak}, Load@VT1, Load@VT2, and $Load_{peak}$) were assessed at baseline, three months, and six months using the CPET.

Results: After six months, all exercise capacity parameters improved significantly in the LVHI group. The LVMI group also showed significant improvements in most parameters, while the HVMI group improved in five out of the seven parameters. Except for $Load_{peak}$ no significant p-values were found for interaction between time and group.

Conclusions: All intervention types show advantages compared to no intervention. This means there is no optimal training intensity and volume, which suggests that, for people with T2DM, engaging in any kind of physical activity (LVMI, HVMI, or LVHI) is better than staying inactive.

Keywords: type 2 diabetes mellitus, physical fitness, intensity, volume, randomized controlled trial

Introduction

Diabetes is a disease which, according to World Health Organization (2020), is found in every population in the world and in all regions. The World Health Organization (2020) states that the prevalence in adults rose from 4.7% in 1980 to 8.5% in 2014. “Diabetes mellitus, commonly known as diabetes, is a group of metabolic disorders characterized by the presence of hyperglycaemia in the absence of treatment” (World Health Organization, 2020). According to Nisha (2016) there are 3 main types of diabetes: type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM) and gestational diabetes.

Other names for T2DM are “Non-Insulin-Dependent Diabetes Mellitus” or “adult-onset diabetes” (Batra & Singh, 2016 in Nisha, 2016). According to Galicia-Garcia et al. (2020) T2DM primarily results from impaired insulin secretion combined with reduced sensitivity of insulin-responsive tissues.

Holman et al. (2015) states that 90.4% of people in the UK, diagnosed with diabetes mellitus, have T2DM. Most people with the condition may be unaware of their illness in the early stages, as there are often no noticeable symptoms (Nishimura et al., 2016 in Nisha 2016). In many early cases of T2DM, managing the condition may be possible through a healthy diet and regular monitoring of blood glucose levels (Nisha, 2016). However, since T2DM is a progressive condition, medication may eventually become necessary (Nisha, 2016).

Diabetes is associated with long-term complications such as retinopathy, nephropathy, and neuropathy, alongside a higher risk of conditions like cardiovascular, peripheral arterial, cerebrovascular diseases, cataracts, erectile dysfunction, nonalcoholic fatty liver disease, certain infections like tuberculosis, and generally worse health outcomes (World Health Organization, 2020). Conditions that are commonly associated with T2DM, such as hypertension and dyslipidemia, are well-established risk factors for atherosclerotic cardiovascular disease (ASCVD), and diabetes itself poses an independent risk (American Diabetes Association Professional Practice, 2024).

Physical activity is important to improve health outcomes and quality of life (National Center for Chronic Disease Prevention and Health Promotion (U.S.), Division of Diabetes Translation, 2009). It also has a positive impact on glycemic control and insulin action (Consentino et al. 2020), lipid levels (Johnson et al. 2009), blood pressure (Cauza et al. 2005), cardiovascular

events (Blair et al. 1995, in Colberg et al. 2010) mortality (Blair et al. 1995, in Colberg et al. 2010), and quality of life (Williamson et al. 2009) and depression (Williamson et al. 2009). The majority of adults should participate a minimum of 150 minutes of moderate- to high-intensity aerobic exercise per week, ideally distributed over at least three days (World Health Organization, 2020).

It is proven that high intensity interval training (HIIT) also improves physical fitness in adults with T2DM by aerobic training, done between 65-90% of the peak oxygen consumption (VO_{2peak}) or 75-95% of the heart rate peak (HR_{peak}) for ten seconds to four minutes, followed by twelve seconds to five minutes of active or passive recovery (Kanaley et al., 2022). Gildea et al. (2021), also mentions that moderate intense continuous training leads to increased VO_{2peak} responses.

As previously stated, both moderate aerobic exercise and HIIT are effective to improve VO_{2peak} in T2DM patients. However, it is still unclear which intensity and volume is most effective. This is important information to provide people with T2DM the best possible health outcomes. Therefore our research question aims to find out what physical training intensity and volume is most optimal to improve physical fitness in T2DM patients. We distinguish low-volume moderate-intensity (LVMI), high-volume moderate-intensity (HVMI), low-volume high-intensity (LVHI) and a control group. We hypothesize that HVMI will be more effective for improving submaximal exercise parameters due to the higher volume. We also expect LVHI to be most effective for improving peak exercise parameters. We also expect LVMI to improve these parameters compared to the control group, but not as much as they might improve in the other groups.

Methods

Study design and participants

This master thesis is a sub-analysis of a prospective single-blind, randomized-controlled trial, performed at REVAL campus in University of Hasselt Diepenbeek and Jessa hospital, which aims to examine the independent impact of exercise volume and intensity during a 6-month exercise intervention on global longitudinal strain in T2DM patients. Patients with T2DM were recruited through the endocrinology services of Jessa Hospital and via general practitioners and randomly sorted by a computer-generated randomization schedule in one of four groups. Participants were stratified according to age, glycated haemoglobin (HbA1c), sex and body mass index (BMI). Inclusion criteria for these participants were physical inactivity (structured physical activity was not allowed, as in Mitranun et al., (2014), age 30-75 years, HbA1c of 6-9% (if they took blood glucose lowering medication) or 6.5-9% (without taking blood glucose lowering medication), and/or a two-hour plasma glucose ≥11.1 mmol/L or ≥200 mg/dL following a 75g oral glucose load during an oral glucose tolerance test (OGTT). Participants were excluded if they followed exogenous insulin therapy, suffered from any disease which could significantly impact participation of the exercise intervention (such as chronic heart disease, significant arrhythmias, cardiac events, clinical heart failure, percutaneous coronary intervention, chronic obstructive pulmonary, cerebrovascular or peripheral vascular disease, severe hypertension, ongoing cancer, severe neuropathy, renal disease), as in Van Ryckeghem et al. (2020), or were unable to regularly participate in the exercise intervention.

This trial has been prospectively registered at ClinicalTrials.gov: (NCT05023538) on the 10th of June 2021. Ethical approval has been obtained from the Ethics Committee of UZ/KU Leuven; Ethics Committee of UZA; Ethics Committee of Jessa Hospital and Ethics Committee of UHasselt.

Procedure

Measurements

At screen visit, participants were examined for inclusion and exclusion criteria. They received an explanation about the research and were invited to sign an informed consent. During the entirety of the study, participants were monitored for adverse events. An adverse event is any

unexpected medical incident occurring in a patient during the technical examination or intervention, which does not necessarily have a direct causal relationship with the procedure.

At baseline, participants were assessed for fasted (>8 hours) blood samples, as explained in Mitranun et al. (2014). Blood parameters included glucose, HbA1c, and lipid profile (as in Liu et al., 2016), and insulin (as in Van Ryckeghem et al., 2020). Systolic and diastolic blood pressure were measured using an OMRON Automatic Blood Pressure Monitor (Model: M6 AC). Anthropometric measures included body height, body mass, BMI (calculated as described in Liu et al., 2016), waist and hip circumference, and waist-to-hip ratio. Body composition (fat mass and fat percentage) was assessed via bioelectrical impedance using the Bodystat 1500, as in Mitranun et al. (2014). Muscle strength was measured as mean right-hand grip strength using a JAMAR Hydraulic Hand Dynamometer (Sammons Preston Rolyan, Samons Court 4, Bolingbrook, IL 60440). Finally, physical fitness and cardiac function were evaluated during maximal exercise testing, and perceived dyspnea and leg fatigue were rated using the BORG scale (1–10) (Appendix A, image A4). The same assessments at baseline (T0) were conducted at 3 months (T1) and 6 months (T2). More details about the cardiopulmonary exercise testing and muscle force and endurance testings are mentioned below.

Cardiopulmonary exercise testing

Physical fitness was assessed by maximal cardiopulmonary exercise tests (CPET) using a specific computer program (Blue Cherry). During these tests, electrocardiograms (ECGs) were continuously monitored to monitor potential (serious) adverse events. CPETs were executed on a cycle ergometer, the same as Nytrøen et al. (2019), to which workload increased based on age, sex and peak respiratory gas exchange ratio (RER) >1.9, until volitional fatigue. Oxygen consumption (VO_2), expiratory volume (VE), and RER were collected by the use of a metabolic cart (Jaeger Oxycon). Participants were seated on a cycle ergometer and connected to a 12-lead ECG. They wore a mask and performed at least three lung function tests. Afterwards, a resting ECG was monitored for 10 seconds. Following the resting ECG, the CPET began with one minute of inactivity, during which the examiner provided instructions on what would happen during the CPET. After this minute, the participants cycled at a speed of 60-65 rates per minute (rpm), as in Van Ryckeghem et al. (2020), until reaching volitional fatigue. Participants generally cycled for about 10 minutes. To ensure consistency in this duration, an intensity protocol was selected to match the expected maximal load, estimated by Blue Cherry,

which the patient should be able to handle for 10 minutes. Once the patient was unable to cycle at a speed of 60-65 rpm or in case of adverse events, the examiner stopped the test. When the patient was unable to continue due to dyspnea or leg fatigue, they had the option to stop the test independently. After stopping the test, the patient was immediately asked what the reason for stopping was (shortness of breath, leg fatigue or both) and to give a score on a BORG for dyspnea and leg fatigue (1-10). Participants were instructed to keep the mask on for another 3 minutes to collect data of their recovery.

We quantify physical fitness by the following parameters: VO_2 at Ventilatory Threshold 1 (VT1), VO_2 at Ventilatory Threshold 2 (VT2), absolute VO_{2peak}, relative VO_{2peak}, Load at VT1, Load at VT2 and $Load_{peak}$, which are the primary parameters of this study, while all previously mentioned parameters are the secondary parameters.

Muscle force

Maximal handgrip strength of the right hand was measured by a hand-held dynamometer. Participants were instructed to squeeze the dynamometer three times as hard as they could. After each time the grip strength was measured, participants rested for a minute before measuring again. Throughout the testing, participants received consistent verbal instructions and encouragement.

Other investigations

Fasted (>8 hours) blood samples are collected to investigate glycaemic control and lipid profiles. Systolic and diastolic blood pressure are measured, as Van Ryckeghem et al. (2020), at the left arm. Anthropometrics for a body height was only measured at baseline. Afterwards, the same height was used for calculation of BMI. Body weight was measured again at every assessment moment. Waist circumference was measured just above the umbilical, while the hip circumference was measured at the height of the greater trochanter. Using these parameters, waist-to-hip ratio was calculated. The BORG for dyspnea and leg fatigue was asked immediately after finishing cycling, during the final 3 minutes of recuperation.

Exercise training programme

After baseline testing, participants were randomized into one of four groups: LVMI, HVMI, LVHI, control intervention. Table 1 represents a summary of these exercise modalities.

Table 1

Summary of Exercise Modalities

	Phase 1 (First week)	Phase 2 (2-6 weeks)	Phase 3 (7-26 weeks)	
Low-volume moderate intense Group 1	3	3		frequency (sessions/week)
	5 min	5 min		warming-up
	20 min	30 min		duration of training part
	50% VO_{2peak}	60% VO_{2peak}		intensity of training part
	5 min	5 min		cooling-down
High-volume moderate intense Group 2	3	3	3	frequency (sessions/week)
	5 min	5 min	5 min	warming-up
	20 min	40 min	50 min	duration of training part
	50% VO_{2peak}	60% VO_{2peak}	60% VO_{2peak}	intensity of training part
	5 min	5 min	5 min	cooling-down
Low-volume high-intense Group 3	3	3		frequency (sessions/week)
	5 min	5 min		warming-up
	20 min	6 * 1 min bouts		duration and intensity of
	50% VO_{2peak}	(85% VO_{2peak}), interspersed by 4 min bouts (50% VO_{2peak})		training part
	5 min	5 min		cooling-down
Control (usual care) Group 4	x	x	x	

Within all intervention groups, the training load was progressively increased based on the BORG scale (6-20) (Appendix A, image A5), and previously recorded wattages, aiming for a perceived exertion between 12 and 14. This gradual progression continued throughout the 6-month training period for a duration of 72 sessions. In the first week of phase 2, we inserted a transition period for the HVMI participants where they cycled for 30 minutes at 60% of their VO_{2peak} to prepare them for the continuous 40 minutes the following training sessions. The control group did not participate in the structured cycling interventions. However, they were encouraged to maintain their usual daily activities and avoid engaging in new structured exercise programs during the study period.

Statistical analysis

All statistical analyses were conducted using SPSS STATISTICS (29.0.2.0).

Descriptive statistics were used to determine the mean and standard deviations (SD) of the normally distributed patient characteristics and median and interquartile range for the non-normally distributed variables to give an overview of the baseline characteristics. Initially, the Shapiro-Wilk test was used to assess normality ($p \geq 0.05$). Due to the strict nature of this test, the quantile-quantile plot (Q-Q plot) was examined if the p-value was less than 0.05 to evaluate whether the data should still be considered normally or non-normally distributed.

To check for measurement errors, outliers were examined within a 95% confidence interval. If outliers were present, it was assessed whether they were actual errors or if they could be logically explained through clinical reasoning. If no logical explanations for the measurement errors were found, the original values were reviewed to verify whether the data had been correctly recorded from the measurements.

To check if there were significant differences between the groups at baseline, one-way ANOVA was performed for each normally distributed exercise variable. If not normally distributed, Kruskall-Wallis test was used.

To test the hypotheses (i.e.: we hypothesize that HVMI will be more effective for improving submaximal exercise parameters due to the higher volume), two-way mixed ANOVA was used. To conduct the two-way mixed ANOVA, three F-tests were used to determine if there were significant main (F-test for within-group and F-test for between-group) and interaction effects. Significance was set at $p < .05$. Afterwards, Tukey HSD was conducted as a post-hoc test to identify which specific groups exhibited significant differences while controlling for multiple comparisons. The homogeneity of variance was checked using the Levene's test. If $p \geq 0.05$, homogeneity was assumed. Mauchly's test was used to evaluate sphericity. To compensate for violations of sphericity, Huynh-Feldt corrections were applied.

Paired t-test for normally distributed data and Wilcoxon signed-rank test for non-normally distributed data were used to look for differences between pre and post intervention within the same groups.

Results

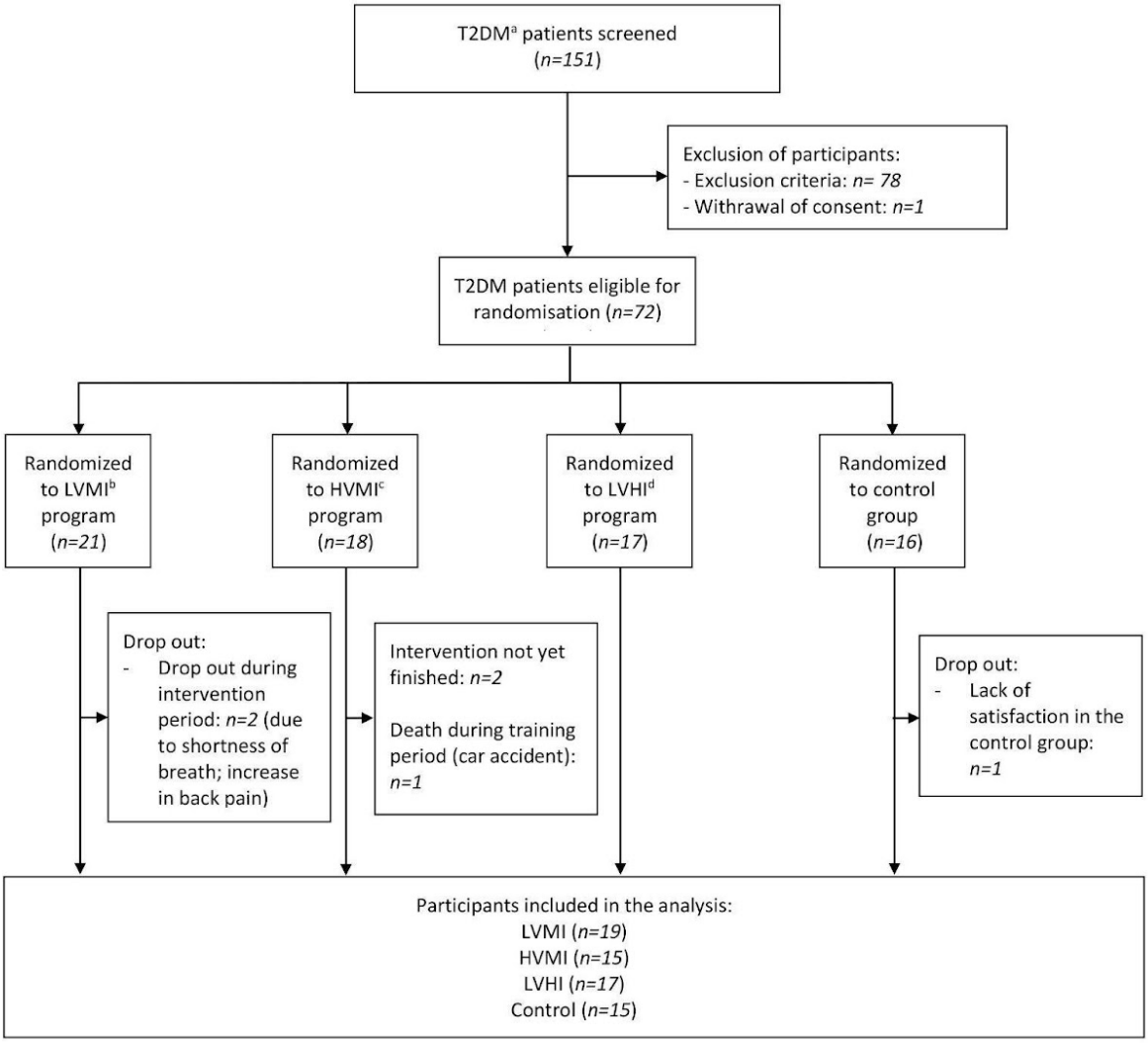
Participant selection and characteristics

In 'flowchart' (Figure 1), the inclusion of participants was illustrated schematically. 151 T2DM Participants were screened for inclusion and exclusion criteria. Afterwards, 72 participants were randomly distributed in one of four groups. Following the exclusion of drop-outs, the interventions were completed by 19 (LVMI), 15 (HVMI), 17 (LVHI), and 15 (control) participants.

The characteristics of the participants were presented in 'table 2'. The sample size consisted mostly out of male participants. Participants had a mean age between 62 and 64 years. According to the BMI, most participants were overweight or obese. Blood pressure values (SBP and DBP) were in general pre-hypertense and hypertense. Waist-to-hip ratios were elevated in most groups. Participants showed rather poor glycaemic control when looked at their HbA1c values. Regarding lipid profiles, all total cholesterol, HDL-cholesterol and LDL-cholesterol were overall well controlled. Based on the Borg-scores, participants perceived the CPET's generally to be hard for both shortness of breath and leg fatigue at baseline. For the exercise parameters, one-way ANOVA and Kruskall-Wallis were conducted. This test found that, at baseline, all patients were evenly distributed across the four different groups for each exercise capacity parameter (VO_2@rest: p = .532; VO_2@VT1: p = .522; VO_2@VT2: p = .558 ; absolute VO_{2peak}: p = .717; relative VO_{2peak}: p = .398; Load@VT1: p = .557 ; Load@VT2: p = .842; $Load_{peak}$: p = .714) as well as for all other parameters. Only the Kruskal-Wallis test was used for hip circumference, SBP, VO_2@rest, relative VO_{2peak}, plasma insulin, HDL-cholesterol, and triglycerides due to non-normally distributed data.

Figure 1

Flowchart of the Study.



Note. Visual representation of the participant selection process, starting from all registered individuals to those who ultimately completed the study.

[a]T2DM = type 2 diabetes mellitus; [b]LVMI = low-volume moderate-intense group; [c]HVMI = high-volume moderate-intense group; [d]LVHI = low-volume high-intense group.

Table 2

Baseline Characteristics of Patients Across All Groups: Anthropometrics, Cardiometabolic, and Fitness Measures

	LVMI[a] (*n*=19)	HVMI[b] (*n*=15)	LVHI[c] (*n*=17)	Control (*n*=15)
Age				
Age	64.06 ± 5.23	62.38 ± 7.40	62.83 ± 7.39	63.01 ± 7.92
Antropometrics				
Body mass (kg)	84.53 ± 14.17	86.07 ± 9.71	86.59 ± 20.00	87.07 ± 18.95
Body height (cm)	171.82 ± 10.26	172.63 ± 8.25	172.57 ± 9.87	170.73 ± 9.61
BMI[d] (kg/m²)	28.86 ± 5.76	28.94 ± 3.30	29.01 ± 6.04	29.87 ± 5.89
Waist circumference (cm)	103.38 ± 10.27	101.80 ± 8.53	102.13 ± 14.43	105.45 ± 15.43
Hip circumference (cm)	100.63 [99.23-106.67]	105.07 [98.67-107.37]	103.32 [99.17-111.40]	107.60 [97.00-114.33]
Waist-to-hip ratio	1.00 ± 0.06	0.98 ± 0.06	0.99 ± 0.07	0.99 ± 0.09
Body composition				
Fat mass (%)	32.17 ± 8.94	31.62 ± 9.76	30.82 ± 8.37	34.16 ± 8.90
Fat mass (kg)	27.44 ± 9.95	27.18 ± 8.81	26.73 ± 9.73	30.15 ± 10.99
Blood pressure				
SBP[e] (mmHg)	141.00 [121.00-152.00]	137.33 [119.67-148.33]	135.53 [119.00-138.50]	132.00 [122.33-147.00]
DBP[f] (mmHg)	85.33 ± 6.87	82.67 ± 10.63	82.02 ± 8.53	82.07 ± 10.24
Muscle force				
Right handgrip strength (kg)	37.84 ± 10.05	39.16 ± 10.94	42.73 ± 14.82	39.10 ± 8.17
Physical fitness				
VO_2@rest[g] (l/min)	0.31 ± 0.08	0.33 ± 0.05	0.33 ± 0.12	0.30 ± 0.07
VO_2@VT1[h] (l/min)	0.92 ± 0.21	1.02 ± 0.35	0.89 ± 0.26	0.90 ± 0.27
VO_2@VT2[i] (l/min)	1.40 ± 0.35	1.55 ± 0.37	1.54 ± 0.36	1.38 ± 0.35
Absolute VO_{2peak}[j] (l/min)	1.70 ± 0.44	1.81 ± 0.38	1.83 ± 0.46	1.72 ± 0.38
Relative VO_{2peak}[k] (ml/min.kg)	20.13 ± 4.64	21.11 ± 3.80	21.52 ± 4.86	19.39 ± 5.29
Load@VT1[l] (Watt)	61.58 ± 19.35	72.87 ± 36.15	61.53 ± 24.55	62.80 ± 22.34
Load@VT2[m] (Watt)	114.47 ± 31.93	124.80 ± 41.92	118.94 ± 32.03	115.60 ± 35.39
$Load_{peak}$ (Watt)	148.79 ± 42.14	166.20 ± 51.50	158.65 ± 46.65	152.47 ± 42.79
BORG				
BORG breathing (1-10)	5.78 ± 1.93	5.60 ± 2.35	6.38 ± 1.78	5.87 ± 2.42
BORG legs (1-10)	6.24 ± 2.46	5.33 ± 1.92	5.94 ± 2.49	6.20 ± 1.90
Blood profile				
HbA1c[n]	6.82 ± 0.90	6.77 ± 0.85	6.82 ± 0.78	6.71 ± 0.61
Plasma insulin (pmol/l)	77.00 [47.00-110.00]	79.00 [58.00-120.00]	73.00 [56.00-140.00]	77.00 [51.00-180.00]
Total cholesterol (mmol/l)	170.63 ± 42.87	164.00 ± 38.17	152.47 ± 34.48	158.53 ± 41.92
HDL-cholesterol[o] (mmol/l)	51.00 [44.00-55.00]	45.00 [35.00-64.00]	50.00 [40.00-68.00]	48.00 [41.00-59.00]
LDL-cholesterol[p] (mmol/l)	92.26 ± 31.82	78.27 ± 27.77	76.24 ± 24.57	84.73 ± 35.67
Triglycerides (mmol/l)	132.00 [70.00-196.00]	124.00 [98.00-206.00]	87.00 [63.50-154.00]	94.00 [78.00-132.00]
Gender				
Male	14	10	11	10
Female	5	5	6	5

Note. Mean values are presented before the ± sign, with standard deviations following for the normally distributed groups. For non-normally distributed groups, the median and interquartile range (IQR) are reported instead.

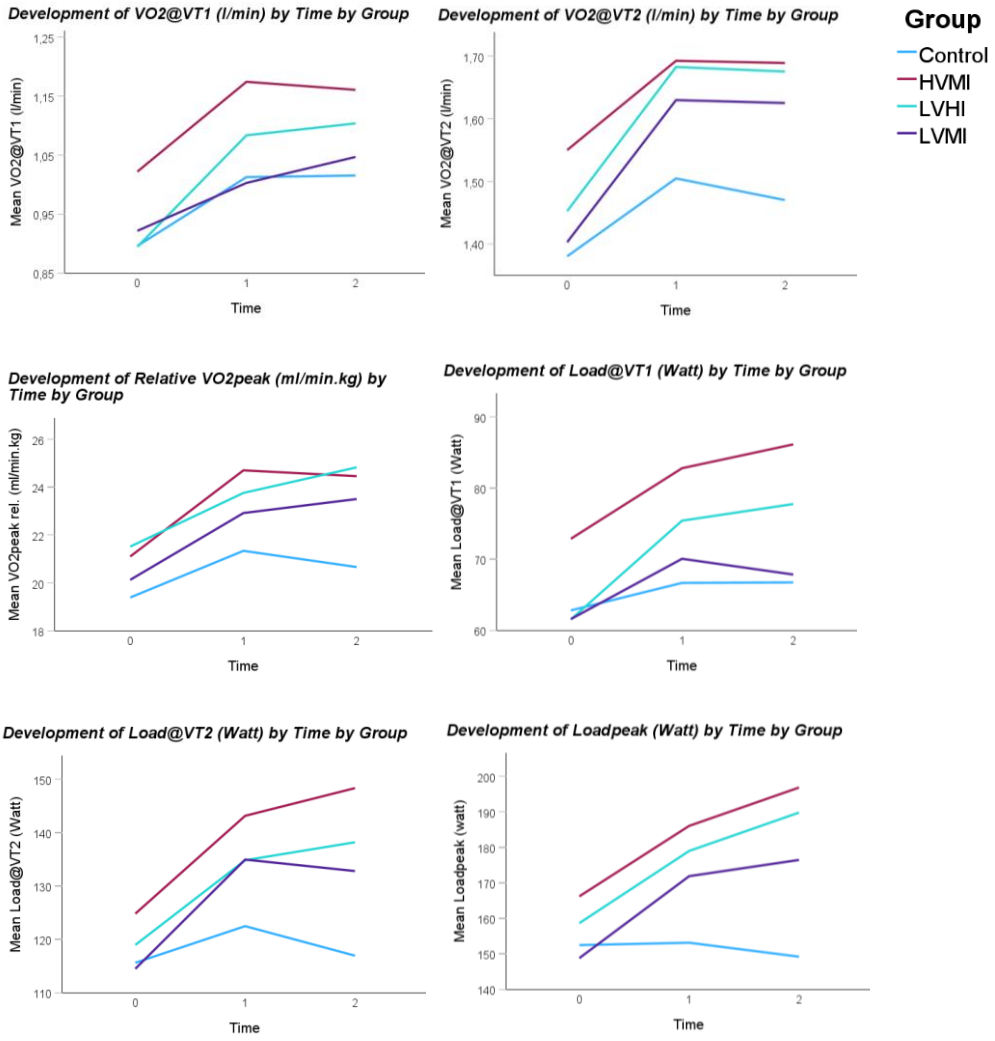
[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]BMI = body mass index; [e]SBP = systolic blood pressure; [f]DBP = diastolic blood pressure; [g]VO_2@rest = volume of oxygen consumption per minute at rest; [h]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [i]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [j]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [k]Relative VO_{2peak}= maximal volume of oxygen consumption per minute divided by the body weight; [l]Load@VT1 = Load at ventilatory threshold 1; [m]Load@VT2 = Load at ventilatory threshold 2; [n]HbA1c = Glycated hemoglobin A1c; [o]HDL cholesterol = high-density lipoprotein cholesterol; [p]LDL cholesterol = low-density lipoprotein cholesterol.

Evaluation of group, time and interaction effects

The two-way mixed ANOVA was performed by conducting three F-tests (Table 3). The F-test for the within group concludes there is a significant improvement of all exercise parameters over time (VO_2@VT1: $p < .001$; VO_2@VT2: $p < .001$; absolute VO_{2peak}: $p < .001$; relative VO_{2peak}: $p < .001$; Load@VT1: $p = .001$; Load@VT2: $p < .001$; $Load_{peak}$: $p < .001$). The F-test for between groups shows there is no significant difference in all exercise parameters between all groups, without taking time into account. Lastly, the F-test for the interaction between within- and between-subjects effects indicated that the evolution over time was influenced by groups only for $Load_{peak}$ ($p < .001$) (Figure 2). Of all measured variables, only $Load_{peak}$ was subjected to further analysis using a one-way ANOVA to evaluate group differences after six months. The interaction p-value was significant, while the between group comparison at T2 showed no significant p-value ($p = .069$). Nonetheless, this p-value is relatively close to .05.

Figure 2

Development of All Parameters over Time per Group



Note. This figure represents the development of VO_2@VT1, VO_2@VT2, relative VO_{2peak}, Load@VT1, Load@VT2 and $Load_{peak}$. Mean values are presented for four distinct groups across three measurement time points (T1, T2, T3). Each line represents one group.

Table 3

Exercise Capacity Following a 72-Sessions Exercise Training Intervention

	LVMI[a] (n=19)			HVMI[b] (n=15)			LVHI[c] (n=17)			Control (n=15)			p_{Time}[g]	p_{Group}[h]	$p_{Time*Group}$[i]
	T0[d]	T1[e]	T2[f]	T0	T1	T2	T0	T1	T2	T0	T1	T2			
VO_2@rest[j] (l/min)	0.31 ± 0.08	0.31 ± 0.07	0.33 ± 0.08	0.33 ± 0.05	0.33 ± 0.06	0.32 ± 0.10	0.33 ± 0.12	0.31 ± 0.07	0.33 ± 0.07	0.30 ± 0.07	0.34 ± 0.06	0.33 ± 0.05	.817	.928	.426
VO_2@VT1[k] (l/min)	0.92 ± 0.21	1.00 ± 0.25	1.05 ± 0.30	1.02 ± 0.35	1.17 ± 0.41	1.16 ± 0.31	0.89 ± 0.26	1.08 ± 0.42	1.10 ± 0.27	0.90 ± 0.27	1.01 ± 0.28	1.01 ± 0.28	<.001*	.470	.822
VO_2@VT2[l] (l/min)	1.40 ± 0.35	1.63 ± 0.43	1.63 ± 0.43	1.55 ± 0.37	1.69 ± 0.38	1.69 ± 0.36	1.54 ± 0.36	1.68 ± 0.48	1.68 ± 0.50	1.38 ± 0.35	1.50 ± 0.47	1.47 ± 0.35	<.001*	.561	.628
Absolute VO_{2peak}[m] (l/min)	1.70 ± 0.44	1.90 ± 0.49	1.95 ± 0.53	1.81 ± 0.38	2.03 ± 0.52	2.05 ± 0.57	1.83 ± 0.46	2.02 ± 0.57	2.11 ± 0.58	1.72 ± 0.38	1.81 ± 0.51	1.77 ± 0.38	<.001*	.514	.212
Relative VO_{2peak}[n] (ml/min.kg)	20.13 ± 4.64	22.92 ± 5.01	23.50 ± 5.83	21.11 ± 3.80	24.70 ± 5.48	24.46 ± 5.71	21.52 ± 4.86	23.76 ± 5.10	24.83 ± 4.99	19.39 ± 5.29	21.34 ± 6.06	20.67 ± 5.23	<.001*	.302	.320
Load@VT1[o] (Watt)	61.58 ± 19.35	70.06 ± 21.61	67.84 ± 27.80	72.87 ± 36.15	82.79 ± 37,52	86.13 ± 30.99	61.53 ± 24.55	75.41 ± 33.92	77.75 ± 25.45	62.80 ± 22.34	66.67 ± 26.34	66.73 ± 25.06	.001*	.338	.689
Load@VT2[p] (Watt)	114.47 ± 31.93	134.94 ± 42.15	132.79 ± 43.16	124.80 ± 41.92	143.14 ± 45.33	148.33 ± 38.58	118.94 ± 32.03	134.82 ± 41.60	138.19 ± 45.49	115.60 ± 35.39	122.47 ± 47.29	116.93 ± 39.91	<.001*	.564	.230
$Load_{peak}$ (Watt)	148.79 ± 42.14	171.89 ± 48.68	176.47 ± 52.92	166.20 ± 51.50	186.07 ± 53.64	196.87 ± 57.09	158.65 ± 46.65	179.00 ± 58.01	189.81 ± 53.51	152.47 ± 42.79	153.13 ± 45.86	149.20 ±42.34	<.001*	.306	<.001*

Note. Mean values are presented before the ± sign, with standard deviations following, for the normally distributed groups. For non-normally distributed groups, the median and IQR are reported instead. This was done for all measuring moments. P-values were presented for the within subjects (Time), between-subjects (Group), and the interaction (Time*Group) for all parameters.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]T0 = baseline measurement; [e]T1 = measurement after 3 months; [f]T2 = measurement at the end of the exercise programme; [g]p_{Time} = p-value for the within-subjects (Time); [h]p_{Group} = p-value for the between-subjects (Group); [i]$p_{Time*Group}$ = p-value for the interaction of within- and between-subjects; [j]VO_2@rest = volume of oxygen consumption per minute at rest; [k]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [l]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [m]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [n]Relative VO_{2peak} = maximal volume of oxygen consumption per minute divided by the body weight; [o]Load@VT1 = Load at ventilatory threshold 1; [p]Load@VT2 = Load at ventilatory threshold 2.

* $p < .05$

Evaluation of improvements over time per group

After Two-Way Mixed ANOVA and associated post-hoc tests were conducted, paired T-test, for normally distributed parameters (VO_2@VT1, VO_2@VT2, absolute VO_{2peak}, Load@VT1, Load@VT2, $Load_{peak}$) or Wilcoxon Signed Rank test, for non-normally distributed parameters (VO_2@rest, relative VO_{2peak}), were performed to get an overview of the evolution of the parameters over time (T2-T0) within the same group (Table 5).

Table 5

Paired t-Test and Wilcoxon Signed-Rank test of the Difference Between T0 and T2

Group	Exercise parameter	Change in six months ($T2^k$-$T0^l$)	One-Sided p-value	Two-Sided p-value
LVMI[a]	VO_2@rest[d] (l/min)	0.03 [0.00-0.08]		.158
	VO_2@VT1[e] (l/min)	0.13 ± 0.21	.009*	.018*
	VO_2@VT2[f] (l/min)	0.22 ± 0.22	<.001*	<.001*
	Absolute VO_{2peak}[g] (l/min)	0.25 ± 0.22	<.001*	<.001*
	Relative VO_{2peak}[h] (ml/min.kg)	3.21 [2.33-5.23]	<.001*	<.001*
	Load@VT1[i] (Watt)	6.26 ± 19.17	.086	.171
	Load@VT2[j] (Watt)	18.32 ± 21.83	<.001*	.002*
	$Load_{peak}$ (Watt)	27.68 ± 20.94	<.001*	<.001*
HVMI[b]	VO_2@rest (l/min)	-0.01 [-0.07-0.03]		.463
	VO_2@VT2 (l/min)	0.14 ± 0.30	.048*	.097
	Absolute VO_{2peak} (l/min)	0.24 ± 0.32	.006*	.011*
	Relative VO_{2peak} (ml/min.kg)	4.15 [1.93-5.26]	.005*	.009*
	Load@VT1 (Watt)	13.27 ± 32.71	.069	.138
	Load@VT2 (Watt)	23.53 ± 30.37	.005*	.010*
	$Load_{peak}$ (Watt)	30.67 ± 20.17	<.001*	<.001*
LVHI[c]	VO_2@rest (l/min)	0.02 [-0.05-0.05]		.756
	VO_2@VT1 (l/min)	0.21 ± 0.18	<.001*	<.001*
	VO_2@VT2 (l/min)	0.21 ± 0.24	.001*	.003*
	Absolute VO_{2peak} (l/min)	0.25 ± 0.17	<.001*	<.001*
	Relative VO_{2peak} (ml/min.kg)	3.69 [2.15-4.14]	<.001*	<.001*
	Load@VT1 (Watt)	15.69 ± 15.66	<.001*	.001*
	Load@VT2 (Watt)	17.94 ± 23.05	.004*	.007*
	$Load_{peak}$ (Watt)	28.56 ± 17.18	<.001*	<.001*
Control	VO_2@rest (l/min)	0.05 [0.03-0.07]	.019*	.037*
	VO_2@VT2 (l/min)	0.09 ± 0.24	.082	.165
	Absolute VO_{2peak} (l/min)	0.05 ± 0.19	.155	.310
	Relative VO_{2peak} (ml/min.kg)	0.95 [-0.48-2.84]		.100
	Load@VT1 (Watt)	3.93 ± 24.33	.271	.541
	Load@VT2 (Watt)	1.33 ± 14.23	.361	.722
	$Load_{peak}$ (Watt)	-3.27 ± 14.39	.197	.394

Note. Two-Sided p-values are presented for each exercise parameter for each group. If this was significant, one-sided p-value can be taken into account. Means and standard deviations (after the ± sign) of the difference between T0 and T2 are also presented in the table for normally distributed variables, while median and IQR were presented for normally-distributed variables.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]VO2@rest = volume of oxygen consumption per minute at rest; [e]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [f]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [g]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [h]Relative VO2peak = maximal volume of oxygen consumption per minute divided by the body weight; [i]Load@VT1

= Load at ventilatory threshold 1; [j]Load@VT2 = Load at ventilatory threshold 2; [k]T2 = measurement at the end of the exercise programme; [l]T0 = baseline measurement.

* $p < .05$

Discussion

Importance of the study and main findings

All intervention groups showed a significant improvement in most of the exercise parameters over time, while the control group did not improve significantly in any parameter. This emphasizes the positive effects of these interventions. More specifically, the LVHI group shows improvements in all exercise parameters, while the HVMI and LVMI groups show improvements in almost all exercise parameters. This indicates that all three types of intervention can be used to improve physical fitness, while no intervention is not recommended. However, none of the intervention groups were superior compared to each other.

Comparison with other studies

For this section, comparisons were made with other studies involving patients with non-insulin-dependent type 2 diabetes. These studies included an exercise intervention and, ideally, a control group receiving standard care only. Additionally, we focused on studies that assessed improvements in exercise-related outcomes, such as relative VO_{2peak} or workload capacity.

In addition, a systematic review (Pfeifer et al. 2022) about the improvement of relative VO2peak in patients with T2DM was published. This article states that structured physical exercise interventions resulted in an increase of 2.41 ml/min.kg in relative VO_{2peak} as compared with control. Our study also found increases in relative VO_{2peak} within the intervention groups, but in general, shows greater improvements.

According to Støa et al. (2017), HIIT was shown to be more effective, or at least equally effective, for improvements in relative VO_{2peak} as moderate-intensity, continuous exercise (equivalent with the HVMI intervention). In our study, HIIT was not superior to other intervention groups for improvement in VO_{2peak}. However, relative VO_{2peak} improved in all intervention groups.

Also, other types of interventions were used in some studies. For example, Hansen et al. (2009) found no differences in changes in relative VO2peak between low-to-moderate intensity and

moderate-to-high intensity training following long-term exercise. The results of this study were generally in line with our study.

Another study (Moura et al. 2014) showed that moderate intense continuous training also resulted in an improvement of relative VO_{2peak}, which is consistent with our findings.

Duennwald et al. (2014) found that HIIT was more effective for improving relative VO_{2peak} than continuous exercise at a moderate intensity. They also indicated that HIIT does have the advantage of being less time-consuming, while yielding equally good or even better results.

Gentil et al. (2023) also compared two different types of HIIT training, which are called short interval high-intensity training group (S-HIIT) and long interval high-intensity training (L-HIIT). A moderate-intensity continuous training group was also included. In contrast to our study, HIIT training was most effective in improving relative VO_{2peak}. Furthermore, L-HIIT appeared to be the most effective in Gentil et al. (2023). In contrast to our study, Gentil et al. (2023) did not find an increase in VO_{2peak} for the MICT group, which was also considered a strange result in their study. However, all training sessions and testing in this study were conducted on a treadmill, unlike the other studies.

Strengths and limitations

While interpreting the findings, it is important to consider both the strengths and limitations of the current study. The strengths are discussed first, followed by the limitations.

The study had a good homogeneity at baseline among patients. The patients were randomized into four groups, which reduces selection bias and improves the internal validity. The risk for measurement bias is rather low, due to this study using a standardized approach. The study also did measurements on multiple time points (baseline, after three months, after six months), so both short-term and long-term changes can be analysed. Also, a control group was added, allowing for a distinction to be made between intervention effects and natural changes over time. The three intervention groups all had a different volume and intensity, so the most optimal combination could be found. For measuring physical fitness (VO_2 and Load), the CPET was used, which is the gold standard. During training, the patients were supervised and monitored throughout all training sessions. Also, a consistent frequency of 3 training sessions per week was maintained as much as possible.

Unfortunately, there are some limitations to this study. Differences over time within the same group were only compared between T2 and T0. Another limitation is the small sample size. Moreover, blinding was not always possible, as the training sessions had to be adapted by the researcher. T2DM patients are likely to take medication which may have an influence on the results. Medication intake was however not recorded. Due to this being a clinical study, some patients did not reach the wanted intensity, which can influence the results. It can also create attrition bias. Some people wanted to participate in the study, because they wanted to train. When they heard they were classified into the control group, they stopped the study. Sometimes this could also happen in the opposite way. Self-selection bias may also have influenced the results of this study, due to higher participant motivation or greater interest in sports, potentially making the results appear more positive than they actually are. The sample size may not fully represent the general T2DM population, which may lead to a sampling bias. Participants were encouraged and motivated to do their best during both the training sessions and the tests. This, combined with supervision, may have led to the Hawthorne effect, potentially enabling them to achieve better results.

Implications for clinical practice and recommendations for future research

The lack of significant differences between the three intervention groups indicates that neither training at moderate versus high intensity, nor exercising at lower versus higher volume, makes a meaningful difference in this regard. What seems to matter most is that aerobic exercise is undertaken; the precise intensity or volume appears to be of less importance. Despite this, significant improvements were present in all intervention groups, which indicates the importance of aerobic training in T2DM patients. To strengthen this statement, further research with larger sample sizes will be needed to produce more useful results. Additionally, a long-term follow-up is recommended for future studies to enable more reliable conclusions.

Conclusion

This prospective, single-blind, randomized controlled trial aimed to investigate which type of training (LVMI, HVMI or LVHI) is most effective for T2DM patients with respect to their physical fitness.

All intervention programs are equally superior to no intervention. Therefore, it is better for T2DM patients to engage in any form of exercise (LVMI, HVMI or LVHI) than to remain inactive.

However, further research with larger sample sizes is needed to obtain more reliable results.

References

American Diabetes Association. (2018). 4. Lifestyle Management: Standards of Medical Care in Diabetes-2018. *Diabetes care, 41*(Supplement_1), S38–S50. https://doi.org/10.2337/dc18-S004

American Diabetes Association Professional Practice Committee. (2024). 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2024. *Diabetes Care*, *47* (Supplement_1), S179-S218. https://doi.org/10.2337/dc24-S010

Blair, S., Kohl, H., Barlow, C., Paffenbarger, R., Gibbons, L., & Macera, C. (1995). Changes in physical fitness and all-cause mortality. A prospective study of healthy and unhealthy men. *JAMA, 273*(14), 1093–1098. https://pubmed.ncbi.nlm.nih.gov/7707596/

Cauza, E., Hanusch-Enserer, U., Strasser, B., Ludvik, B., Metz-Schimmerl, S., Pacini, G., Wagner, O., Georg, P., Prager, R., Kostner, K., Dunky, A., & Haber, P. (2005). The relative benefits of endurance and strength training on the metabolic factors and muscle function of people with type 2 diabetes mellitus. *Archives of physical medicine and rehabilitation, 86*(8), 1527–1533. https://doi.org/10.1016/j.apmr.2005.01.007

Colberg, S., Sigal, R., Fernhall, B., Regensteiner, J., Blissmer, B., Rubin, R., Chasan-Taber, L., Albright, A., & Braun, B.(2010). Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care*, *33*(12), e147-167. https://doi.org/10.2337/dc10-9990

Cosentino, F., Grant, P., Aboyans, V., Bailey, C., Ceriello, A., Delgado, V., Federici, M., Filippatos, G., Grobbee, D., Hansen, T., Huikuri, H., Johansson, I., Jüni, P., Lettino, M., Marx, N., Mellbin, L., Östgren, C., Rocca, B., Roffi, M., Sattar, N., . . . ESC Scientific Document Group. (2020). 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD). *European heart journal, 41*(2), 255–323. https://doi.org/10.1093/eurheartj/ehz486

Duennwald, T., Gatterer, H., Wille, M., Pocecco, E., Phillippe, M., Kruesmann, P., Dzien, A., Bernardi, L., & Burtscher, M. (2014). Effects of Supervised Short-Term Exercise

Training On Cardiorespiratory Control and Exercise Capacity in Type 2 Diabetes Patients. *Journal Of Diabetes And Metabolism*, *5*. https://doi.org/10.4172/2155-6156.1000418

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. *International journal of molecular sciences, 21*(17), 6275. https://doi.org/10.3390/ijms21176275

Gentil, P., Silva, L., Antunes, D., Carneiro, L., De Lira, C., Batista, G., De Oliveira, J., Cardoso, J., Souza, D., & Rebelo, A. (2023). The effects of three different low-volume aerobic training protocols on cardiometabolic parameters of type 2 diabetes patients: A randomized clinical trial. *Frontiers in Endocrinology*, *14*. https://doi.org/10.3389/fendo.2023.985404

Gildea, N., McDermott, A., Rocha, J., O'Shea, D., Green, S., & Egaña, M. (2021). Time-course of V̇o2 kinetics responses during moderate-intensity exercise subsequent to HIIT versus moderate-intensity continuous training in type 2 diabetes. *Journal of applied physiology (Bethesda, Md. : 1985), 130*(6), 1646–1659. https://doi.org/10.1152/japplphysiol.00952.2020

Hansen, D., Dendale, P., Jonkers, R., Beelen, M., Manders, R., Corluy, L., Mullens, A., Berger, J., Meeusen, R., & Van Loon, L. (2009). Continuous low- to moderate-intensity exercise training is as effective as moderate- to high-intensity exercise training at lowering blood HbA1c in obese type 2 diabetes patients. *Diabetologia*, *52*(9), 1789–1797. https://doi.org/10.1007/s00125-009-1354-3

Holman, N., Young, B., & Gadsby, R. (2015). Current prevalence of Type 1 and Type 2 diabetes in adults and children in the UK. *Diabetic medicine : a journal of the British Diabetic Association*, *32*(9), 1119–1120. https://pubmed.ncbi.nlm.nih.gov/25962518/

IBM (2023). SPSS STATISTICS (29.0.2.0) [Windows]. https://www.uhasselt.be/en/info-for/current-students/facilities-and-services/software-student

Johnson, N., Sachinwalla, T., Walton, D., Smith, K., Armstrong, A., Thompson, M., & George, J. (2009). Aerobic exercise training reduces hepatic and visceral lipids in obese

individuals without weight loss. *Hepatology (Baltimore, Md.), 50*(4), 1105–1112. https://doi.org/10.1002/hep.23129

Kanaley, J., Colberg, S., Corcoran, M., Malin, S., Rodriguez, N., Crespo, C., Kirwan, J., & Zierath, J. (2022). Exercise/Physical Activity in Individuals with Type 2 Diabetes: A Consensus Statement from the American College of Sports Medicine. *Med Sci Sports & Exercise*, *54*(2), 353-368. https://doi.org/10.1249/MSS.0000000000002800

Liu, J., Chen, Y., Yuen, M., Zhen, Z., Chan, C., Lam, K., Tse, H., & Yiu, K. (2016). Incremental prognostic value of global longitudinal strain in patients with type 2 diabetes mellitus. *Cardiovascular diabetology, 15*, 22. https://doi.org/10.1186/s12933-016-0333-5

Lund Research Ltd. (2018). *Mixed ANOVA using SPSS Statistics*. Retrieved on 12 October 2024. https://statistics.laerd.com/spss-tutorials/mixed-anova-using-spss-statistics.php

Meesen, R., & Nysen, R. (2022). Wetenschappelijke vorming (WV2) (p. 223). Acco.

Mitranun, W., Deerochanawong, C., Tanaka, H., & Suksom, D. (2014). Continuous vs interval training on glycemic control and macro- and microvascular reactivity in type 2 diabetic patients. *Scandinavian journal of medicine & science in sports, 24*(2), e69–e76. https://doi.org/10.1111/sms.12112

Moura, B., O'Neill, H., & Amorim, P. (2015). Can an Aerobic Exercise Program Influence Sedentary Behavior and Moderate-Vigorous Physical Activity in Patients with Type 2 Diabetes? *Annals of Sports Medicine and Research , 2*(1), [1014]. https://doi.org/10.47739/2379-0571/1014

National Center for Chronic Disease Prevention and Health Promotion (U.S.), Division of Diabetes Translation. (2009). National Diabetes Fact Sheet, 2007. *Centers for Disease Control and Prevention.* https://stacks.cdc.gov/view/cdc/5613

Nisha, K. (2016). Diabetes Mellitus: Classification, Symptoms and Management: A Review. *Research & Reviews: Journal of Biology*, *4*, 1-16. https://www.rroij.com/open-access/diabetes-mellitus-classification-symptoms-and-management-a-review-.pdf

Nytrøen, K., Rolid, K., Andreassen, A., Yardley, M., Gude, E., Dahle, D., Bjørkelund, E., Relbo Authen, A., Grov, I., Philip Wigh, J., Have Dall, C., Gustafsson, F., Karason, K., &

Gullestad, L. (2019). Effect of High-Intensity Interval Training in De Novo Heart Transplant Recipients in Scandinavia: One-Year Follow-Up of the HITTS Randomized, Controlled Study. *Circulation, 139*(19), 2198–2211. https://doi.org/10.1161/CIRCULATIONAHA.118.036747

Palomares Carrascosa, I. (2024, 7 october). *Choosing the Right Statistical Test: A Decision Tree Approach*. Retrieved on 26 March 2025. https://www.statology.org/choosing-the-right-statistical-test-a-decision-tree-approach/

Pfeifer, L., De Nardi, A., Da Silva, L., Botton, C., Nascimento, D., Teodoro, J., Schaan, B., & Umpierre, D. (2022). Association Between Physical Exercise Interventions Participation and Functional Capacity in Individuals with Type 2 Diabetes: A Systematic Review and Meta-Analysis of Controlled Trials. *Sports Medicine - Open*, *8*(1). https://doi.org/10.1186/s40798-022-00422-1

Portney, L. (2020). Foundations of Clinical Research: Applications to Evidence-Based Practice (Fourth Edition) [Pdf]. *F. A. Davis Company*. Retrieved on 4 November 2024. https://www.scribd.com/document/816170464/Foundations-of-Clinical-Research-Applications-to-Evidence-Based-Practice-4th-Edition-Leslie-G-Portney-all-chapter-instant-download

Støa, E., Meling, S., Nyhus, L., Strømstad, G., Mangerud, K., Helgerud, J., Bratland-Sanda, S., & Støren, Ø. (2017). High-intensity aerobic interval training improves aerobic fitness and HbA1c among persons diagnosed with type 2 diabetes. *European journal of applied physiology, 117*(3), 455–467. https://doi.org/10.1007/s00421-017-3540-1

Van Ryckeghem, L., Keytsman, C., Verboven, K., Verbaanderd, E., Frederix, I., Bakelants, E., Petit, T., Jogani, S., Stroobants, S., Dendale, P., Bito, V., Verwerft, J., & Hansen, D. (2020). Exercise capacity is related to attenuated responses in oxygen extraction and left ventricular longitudinal strain in asymptomatic type 2 diabetes patients. *European journal of preventive cardiology, 28*(16), 1756–1766. https://doi.org/10.1093/eurjpc/zwaa007

VoedingenBeweging. (2025). *Borg RPE schaal*. Retrieved on May 26, 2025, from https://voedingenbeweging.nu/borg-schaal/

Wewege, M., Ahn, D., Yu, J., Liou, K., & Keech, A. (2018). High-Intensity Interval Training for Patients With Cardiovascular Disease-Is It Safe? A Systematic Review. *Journal of the American Heart Association, 7*(21), e009305. https://doi.org/10.1161/JAHA.118.009305

Williamson, D., Rejeski, J., Lang, W., Van Dorsten, B., Fabricatore, A., Toledo, K., & Look AHEAD Research Group (2009). Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. *Archives of internal medicine, 169*(2), 163–171. https://doi.org/10.1001/archinternmed.2008.544

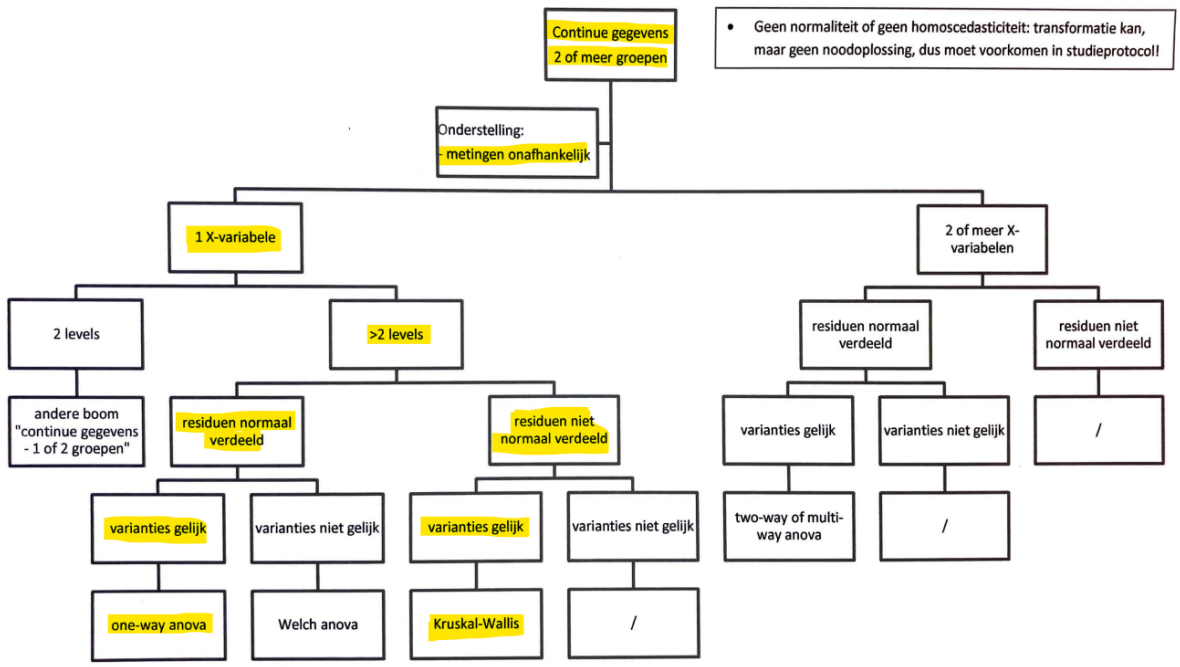
World Health Organization. (2020). HEARTS-D: Diagnosis and management of type 2 diabetes. https://iris.who.int/bitstream/handle/10665/331710/WHO-UCN-NCD-20.1-eng.pdf

Yerramalla, M., Fayosse, A., Dugravot, A., Tabak, A., Kivimäki, M., Singh-Manoux, A., & Sabia, S. (2020). Association of moderate and vigorous physical activity with incidence of type 2 diabetes and subsequent mortality: 27 year follow-up of the Whitehall II study. *Diabetologia, 63*(3), 537–548. https://doi.org/10.1007/s00125-019-05050-1

Appendix A

Image A1

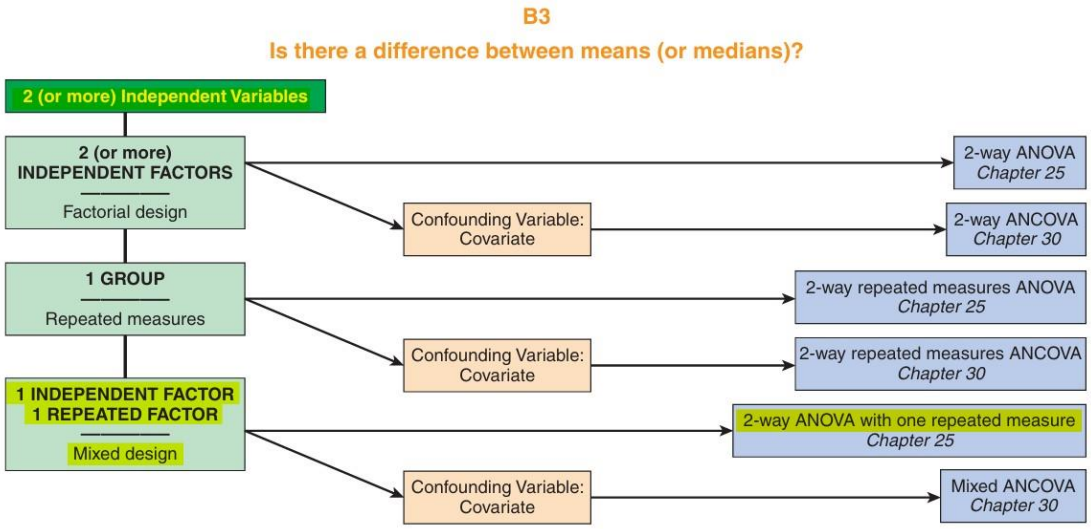
Decision Tree One-Way ANOVA and Kruskal-Wallis



Note. This image gives a visual representation of the pathway that was followed in the search of an appropriate test. Reprinted from Wetenschappelijke vorming (WV2) (p.223), by R. Meesen and R. Nysen, 2022, Acco.

Image A2

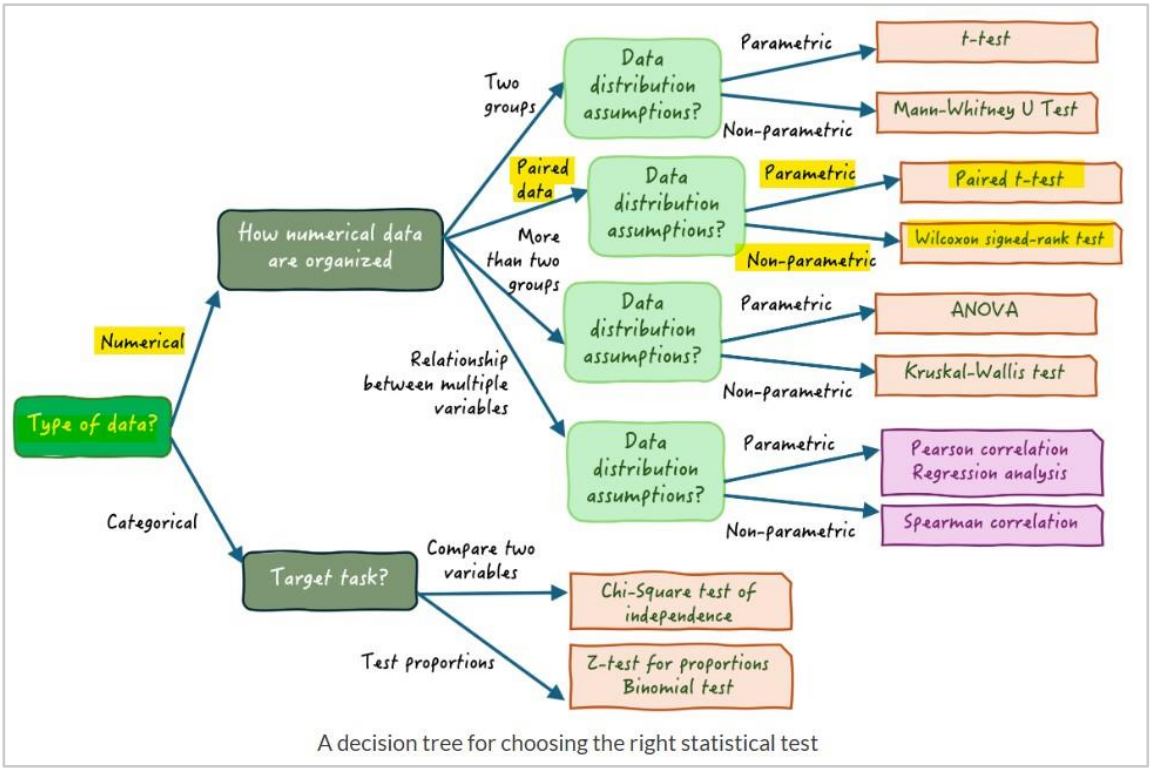
Decision Tree 2-Way Mixed ANOVA



Note. Visual representation of the pathway followed in the search for an appropriate test. Based on Foundations of clinical research: Applications to evidence-based practice (4th ed.) (Portney, 2020, p. 625).

Image A3

Decision Tree Paired t-test and Wilcoxon signed-rank test



Note. This image provides a visual representation of the pathway followed in the search for an appropriate test. From Choosing the Right Statistical Test: A Decision Tree Approach (retrieved March 26, 2025, from [https://www.statology.org/choosing-the-right-statistical-test-a-decision-tree-approach/]).

Image A4

Borg-Scale (0-10)

Note. This image shows the Borg Rating of Perceived Exertion scale (0-10), used to assess perceived dyspnea and leg fatigue. From Borg RPE schaal (retrieved May 26, 2025, from https://voedingenbeweging.nu/borg-schaal/).

Image A5

Borg-Scale (6-20)

Note. This image shows the Borg Rating of Perceived Exertion scale (6-20), used to assess perceived dyspnea and leg fatigue. From Borg RPE schaal (retrieved May 26, 2025, from https://voedingenbeweging.nu/borg-schaal/).

Appendix B

Table B1

Differences between groups at baseline

	p-value
Age	
Age	.908
Antropometrics Body mass (kg)	.970
Body height (cm)	.942
BMI[a] (kg/m²)	.949
Waist circumference (cm)	.847
Hip circumference (cm)	.778
Waist-to-hip ratio	.889
Body composition Fat mass (%)	.760
Fat mass (kg)	.771
Blood pressure SBP[b] (mmHg)	.196
DBP[c] (mmHg)	.654
Muscle force	
Right handgrip strength (kg)	.620
Physical fitness	
VO_2@rest[d] (l/min)	.532
VO_2@VT1[e] (l/min)	.522
VO_2@VT2[f] (l/min)	.558
Absolute VO_{2peak}[g] (l/min)	.717
Relative VO_{2peak}[h] (ml/min.kg)	.398
Load@VT1[i] (Watt)	.557
Load@VT2[j] (Watt)	.842
$Load_{peak}$ (Watt)	.714
BORG	
BORG breathing (1-10)	.762
BORG legs (1-10)	.656
Blood profile	
HbA1c[k]	.977
Plasma insulin (pmol/l)	.882
Total cholesterol (mmol/l)	.568
HDL-cholesterol[l] (mmol/l)	.897
LDL-cholesterol[m] (mmol/l)	.390
Triglycerides (mmol/l)	.222

Note. Table 1 represents the significance of differences between groups at baseline for each parameter. For non-normally distributed parameters (hip circumference, SBP, VO_2@rest, relative VO_{2peak}, plasma insulin, HDL-

cholesterol, and triglycerides) Kruskal-Wallis analysis was conducted, while for the normally distributed data the One-Way ANOVA was used.

[a]BMI = body mass index; [b]SBP = systolic blood pressure; [c]DBP = diastolic blood pressure; [d]VO_2@rest = volume of oxygen consumption per minute at rest; [e]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [f]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [g]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [h]Relative VO_{2peak}= maximal volume of oxygen consumption per minute divided by the body weight; [i]Load@VT1 = Load at ventilatory threshold 1; [j]Load@VT2 = Load at ventilatory threshold 2; [k]HbA1c = Glycated hemoglobin A1c; [l]HDL cholesterol = high-density lipoprotein cholesterol; [m]LDL cholesterol = low-density lipoprotein cholesterol.

* $p < .05$

Evaluation of group, time and interaction effects

Outliers were firstly identified. Following this assessment, it was determined that significant outliers were found in the control group for relative VO_{2peak} (3) (Appendix B, Table B3). Nonetheless, outliers were still included in the data-analysis.

After checking for normality, only VO_2@rest and relative VO_{2peak} were interpreted as nonnormally distributed data (Appendix B, Table B5).

All of the exercise parameters were significantly equally distributed, when checked for homogeneity.

The assumption of sphericity was also assumed (VO_2@rest: $p = .60$; VO_2@VT1: $p = .518$; VO_2@VT2: $p = .932$; absolute VO_{2peak}: $p =. 692$; relative VO_{2peak}: $p = .743$; Load@VT1: $p = .725$; Load@VT2: $p = .409$).

Table B2

Overview of Outliers for the Non-Exercise Parameters

	LVMI[a]	HVMI[b]	LVHI[c]	Control
Antropometrics Body mass (kg)	-	-	-	-
Body height (cm)	-	-	-	-
BMI[d] (kg/m²)	-	-	-	-
Waist circumference (cm)	-	-	-	-
Hip circumference (cm)	3	-	-	-
Waist-to-hip ratio	10	6	6	5
Body composition Fat mass (%)	-	-	-	-
Fat mass (kg)	-	-	-	-
Blood pressure SBP[e] (mmHg)	-	-	-	-
DBP[f] (mmHg)	-	-	-	-
Muscle force Right handgrippower (kg)	-	-	-	-
BORG BORG breathing (1-10)	-	-	-	-
BORG legs (1-10)	-	-	-	-
Blood profile Hba1c[g]	-	2	-	-
Plasma insulin (pmol/l)	3	-	-	-
Total cholesterol (mmol/l)	-	-	-	-
HDL-cholesterol[h] (mmol/l)	-	-	-	-
LDL-cholesterol[i] (mmol/l)	-	-	-	-
Triglycerides (mmol/l)	1	4	2	3

Note. Only extreme outliers are reported for the non-exercise parameters in this table, as identified by SPSS boxplot analysis. Extreme outliers are defined as values exceeding ±3 times the interquartile range (IQR) from the first or third quartile. Mild outliers were not included.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]BMI = body mass index; [e]SBP = systolic blood pressure; [f]DBP = diastolic blood

pressure; [g]HbA1c = Glycated hemoglobin A1c; [h]HDL cholesterol = high-density lipoprotein cholesterol; [i]LDL cholesterol = low-density lipoprotein cholesterol.

Table B3

Overview of Outliers for the Exercise Parameters

	LVMI[a]	HVMI[b]	LVHI[c]	Control
VO_2@rest[d] (l/min)	-	1	-	-
VO_2@VT1[e] (l/min)	-	-	-	-
VO_2@VT2[f] (l/min)	-	-	-	-
Absolute VO_{2peak}[g] (l/min)	-	-	-	-
Relative VO_{2peak}[h] (ml/min.kg)	-	-	-	3
Load@VT1[i] (Watt)	-	-	-	-
Load@VT2[j] (Watt)	-	-	-	-
Load peak (Watt)	-	-	-	-

Note. Only extreme outliers are reported for the exercise parameters in this table, as identified by SPSS boxplot analysis. Extreme outliers are defined as values exceeding ±3 times the interquartile range (IQR) from the first or third quartile. Mild outliers were not included.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]VO_2@rest = volume of oxygen consumption per minute at rest; [e]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [f]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [g]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [h]Relative VO_{2peak}= maximal volume of oxygen consumption per minute divided by the body weight; [i]Load@VT1 = Load at ventilatory threshold 1; [j]Load@VT2 = Load at ventilatory threshold 2

Table B4

Significance of Shapiro-Wilk at T0 and Their Associated Q-Q plot

	Shapiro Wilk				Q-Q plot
	LVMI[a]	HVMI[b]	LVHI[c]	Control	
Antropometrics Body mass (kg)	.104	.446	.867	.396	
Body height (cm)	.879	.965	.363	.590	
BMI[d] (kg/m²)	.100	.867	.349	.978	
Waist circumference (cm)	.745	.712	.657	.220	
Hip circumference (cm)	.002	.079	.753	.437	Q- Q plot interpreted as nonnormally distributed data
Waist-to-hip ratio	.945	.485	.278	.210	
Body composition					
Fat mass (%)	.303	.384	.292	.072	
Fat mass (kg)	.063	.940	.027	.080	Q- Q plot interpreted as normally distributed data
Blood pressure SBP[e] (mmHg)	.230	.244	.008	.341	Q- Q plot interpreted as nonnormally distributed data
DBP[f] (mmHg)	.279	.284	.066	.347	
Muscle force					
Right handgrippower (kg)	.508	.511	.275	.318	
BORG		.041	.220	.309	
BORG breathing (1-10)	.233				Q- Q plot interpreted as normally distributed data
BORG legs (1-10)	.498	.237	.451	.037	Q- Q plot interpreted as normally distributed data
Blood profile HbA1c[g]	.045	.411	.044	.746	Q- Q plot interpreted as normally distributed data
Plasma insulin (pmol/l)	<.001	.004	.002	.115	Q- Q plot interpreted as nonnormally distributed data
Total cholesterol (mmol/l)	.175	.356	.058	.093	
HDL-cholesterol[h] (mmol/l)	.983	.190	.005	.189	Q- Q plot interpreted as nonnormally distributed data
LDL-cholesterol[i] (mmol/l)	.108	.195	.142	.169	
Triglycerides (mmol/l)	<.001	<.001	.007	.002	Q- Q plot interpreted as nonnormally distributed data

Note. This table presents the significance of non-exercise parameters across the study sample. When the Shapiro–Wilk test indicated a significant deviation from normality, a Q–Q plot was used for further interpretation.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]BMI = body mass index; [e]SBP = systolic blood pressure; [f]DBP = diastolic blood pressure; [g]HbA1c = Glycated hemoglobin A1c; [h]HDL cholesterol = high-density lipoprotein cholesterol; [i]LDL cholesterol = low-density lipoprotein cholesterol.

* $p < .05$

Table B5

Significance of Shapiro-Wilk at T0, T1 and T2 and Their Associated Q-Q plot

	Shapiro-Wilk												Q- Q plot
	LVMI[a]			HVMI[b]			LVHI[c]			Control			
	T0[d]	T1[e]	T2[f]	T0	T1	T2	T0	T1	T2	T0	T1	T2	
VO_2@rest[g] (l/min)	.207	.130	.881	.382	.223	.010	.098	.002	.823	.282	.550	.349	Q- Q plot interpreted as non-normally distributed data
VO_2@VT[h] (l/min)	.540	.788	.241	.047	.026	.858	.753	.068	.895	.223	.165	.170	Q- Q plot interpreted as normally distributed data
VO_2@VT2[i] (l/min)	.040	.076	.148	.756	.015	.467	.133	.265	.326	.096	.241	.074	Q- Q plot interpreted as normally distributed data
Absolute VO2peak[j] (l/min)	.172	.591	.868	.853	.111	.741	.278	.094	.103	.986	.550	.802	
Relative VO2peak[k] (ml/min.kg)	.631	.998	.643	.531	.057	.808	.383	.998	.306	.030	.103	.019	Q- Q plot interpreted as non-normally distributed data
Load@VT1[l] (Watt)	.965	.560	.172	.007	.045	.595	.266	.078	.434	.612	.966	.919	Q- Q plot interpreted as normally distributed data
Load@VT2[m] (Watt)	.080	.240	.703	.516	.193	.305	.240	.121	.387	.604	.137	.380	
$Load_{peak}$ (Watt)	.309	.418	.626	.373	.928	.357	.118	.380	.079	.289	.178	.403	

Note. This table presents the significance of non-exercise parameters across the study sample. When the Shapiro–Wilk test indicated a significant deviation from normality, a Q–Q plot was used for further interpretation.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]T0 = baseline measurement; [e]T1 = measurement after 3 months; [f]T2: measurement at the end of the exercise programme; [g]VO_2@rest = volume of oxygen consumption per minute at rest; [h]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [i]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [j]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [k]Relative VO_{2peak} = maximal volume of oxygen consumption per minute divided by the body weight; [l]Load@VT1 = Load at ventilatory threshold 1; [m]Load@VT2 = Load at ventilatory threshold 2.

* $p < .05$

Table B6

Observed Effect Sizes of the Exercise Parameters with their Associated Test

	One-way ANOVA (η^2_p)	Kruskal-Wallis (ε^2)	Two-way mixed ANOVA (η^2_p) - Time	Two-way mixed ANOVA (η^2_p) - Group	Two-way mixed ANOVA (η^2_p) - Time*Group
VO_2@rest[a]	-	-0,013	.003	.008	.049
VO_2@VT1[b]	.035	-	.169	.042	.024
VO_2@VT2[c]	.033	-	.265	.034	.036
Absolute VO_{2peak}[d]	.021	-	.317	.037	.066
Relative VO_{2peak}[e]	-	−.001	.369	.058	.056
Load@VT1[f]	.033	-	.104	.055	.032
Load@VT2[g]	.013	-	.249	.034	.065
Loadpeak	.022	-	.428	.292	.058

Note. For the one-way ANOVA and two-way mixed ANOVA a η^2_p of .01 represents a small, .06 moderate, .14 large effect size. For the Kruskal-Wallis an ε^2 of around .01 represents a small, .06 moderate, .14 large effect size.

[a]VO_2@rest = volume of oxygen consumption per minute at rest; [b]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [c]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [d]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [e]Relative VO_{2peak} = maximal volume of oxygen consumption per minute divided by the body weight; [f]Load@VT1 = Load at ventilatory threshold 1; [g]Load@VT2 = Load at ventilatory threshold 2.

Table B7

Observed Effect Sizes of the Exercise Parameters for the paired t-test

	Paired t-test (d)			
	LVMI[a]	HVMI[b]	LVHI[c]	Control
VO2@VT1[d]	.595	.377	1.155	.429
VO2@VT2[e]	1.023	.460	.892	.378
Absolute VO2peak[f]	1.118	.753	1.508	.272
Load@VT1[g]	.327	.406	1.002	.162
Load@VT2[h]	.839	.775	.778	.094
$Load_{peak}$	1.322	1.520	1.663	-.227

Note. For the paired t-test a d_p of .2 represents a small, .5 moderate, .8 large effect size.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]VO_2@VT1 = volume of oxygen consumption per minute at ventilatory threshold 1; [e]VO_2@VT2 = volume of oxygen consumption per minute at ventilatory threshold 2; [f]Absolute VO_{2peak} = maximal volume of oxygen consumption per minute; [g]Load@VT1 = Load at ventilatory threshold 1; [h]Load@VT2 = Load at ventilatory threshold 2.

Table B8

Observed Effect Sizes of the Exercise Parameters for the Wilcoxon signed-rank test

	Wilcoxon signed-rank test (r)			
	LVMI[a]	HVMI[b]	LVHI[c]	Control
VO_2@rest[d]	-.324	.190	-.078	-.538
Relative VO_{2peak}[e]	.785	.675	.840	.425

Note. For the Wilcoxon signed rank test a r_p of .1 represents a small, .3 moderate, .5 large effect size.

[a]LVMI = low-volume moderate-intense group; [b]HVMI = high-volume moderate-intense group; [c]LVHI = low-volume high-intense group; [d]VO_2@rest = volume of oxygen consumption per minute at rest; [e]Relative VO_{2peak} = maximal volume of oxygen consumption per minute divided by the body weight