Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effects of high-intensity interval training versus moderate-intensity continuous training on glycemic control and body composition in adult patients with type 2 diabetes mellitus

Annelien Loverix

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie,

afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

PROMOTOR :

dr. Kenneth VERBOVEN

COPROMOTOR :

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Acknowledgement

First of all, I would like to express my very great appreciation to my promotor Dr. Kenneth Verboven and copromotor Dra. Lisa Van Ryckeghem, for the guidance through this master thesis and for their support, patience, valuable feedback and assistance. Without their help, I would not have been able to complete this master thesis. I am very grateful for the opportunity I have been given to be a part of the ongoing research project performed by Dra. Lisa Van Ryckeghem, under supervision of Prof. Dr. Dominique Hansen, at the REVAL Research Centre in Diepenbeek.

In the second place, I would like to thank my partner at KU Leuven, Laurine Gummieny for the smooth and pleasant coöperation during the past two years. As being my partner in crime, we further developed our skills and knowledge in the writing of this master thesis and the conduction of related research.

Furthermore, I would like to thank all participants for their complete involvement for this research project. Without their voluntary efforts, the realization of this master thesis would have been impossible.

Lastly, a grateful mention goes out to the Jessa Hospital, Hasselt University and REVAL Rehabilitation Centre for the accommodation and to everyone who contributed to this research project.

Leopoldsburg, 20/05/2020   A.L.

Research context

This master thesis is situated in the research domain related to 'Rehabilitation of Cardiorespiratory and Internal Diseases', within the faculty of rehabilition sciences at Hasselt University.

Currently, our society is experiencing an increasing prevalence of chronic internal diseases such as obesity, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease and cancer. The increase in prevalence of these conditions is often a direct result of inactivity and an unhealthy lifestyle. These internal syndromes lead to increasing health costs, a shorter lifespan and a lower quality of life. Therefore, research that leads to improvements in the prevention, care and treatment of these internal syndromes is of great importance. Diabetes Mellitus (DM) has become a widespread epidemic, primarily caused by an increase in prevalence and incidence of type 2 diabetes mellitus (T2DM) (American Diabetes Association, 2010). Besides dietary and pharmacological interventions, lifestyle changes including the adoption and maintenance of physical activity are the cornerstones to the prevention and reduction of the incidence of type 2 diabetes (Reyes-Garcia, 2019). To date, several researchers have been investigating the effect of structured exercise interventions on underlying mechanisms in T2DM. However, uncertainty regarding the proper application of exercise characteristics in endurance-type training in this patient population still exists.

In attempt to optimize endurance training strategies for adult patients with T2DM, both a systematic review of available scientific literature and an experimental research project are part of the master thesis, which is part of the master's program 'Rehabilitation Sciences and Physiotherapy' at Hasselt University. In particular, this second part of the master thesis focuses on determining the effects of a high intensity interval training program vs a moderate intensity continuous training program on the regulation of glycemic control in T2DM patients. Additionally, this part of the master thesis is part of an ongoing PhD research project, led by Prof. Dr. Dominique Hansen and Dra. Lisa van Ryckeghem, concerning the effect of high-interval training on cardiac function and regulation of glycemic control in diabetic cardiomyopathy. This project is executed in collaboration with Jessa Hospital, Campus Virga

Jesse Hasselt, and was carried out within the REVAL Rehabilitation Research Center at Hasselt University.

Protocol establishment, approval of the ethical committees, patient recruitment and data acquisation for this master thesis were conducted by Dra. Lisa Van Ryckeghem, since the research design was already set up. Data collection was finished by March 2020, whereafter the data files were checked and completed independently by Laurine Gumienny and Annelien Loverix. The statistical plan was composed by Laurine Gumienny and Annelien Loverix in cooperation with Dr. Kenneth Verboven Dra. Lisa Van Ryckeghem. Data processing was performed independently by Laurine Gumienny and Annelien Loverix. Whenever a discrepancy between results existed, they reflected how they accomplished the results and discussed the possible differences until a consensus was reached. The result of this master thesis is completed by equal contribution of the master students. Academical writing was conducted by Laurine Gumienny and Annelien Loverix under supervision of Dr. Kenneth Verboven and Dra. Lisa Van Ryckeghem. In the termination of this master thesis the following distinction was made: Laurine Gumienny focussed on outcome measures regarding the regulation of glycemic control and exercise capacity. Conversely the aim of this master thesis was to answer the following research question: "In what extent do the effects of a high-intensity interval training program differ from those of a moderate-intensity continuous training program in glycemic control and body composition in adult patients with T2DM?"

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Table of contents

1 Abstract

Background Physical activity is one of the cornerstones in prevention and management of T2DM, but the effects of different exercise intensities on the regulation of glycemic control still remain unclear.

Objectives This randomized clinical trial evaluates if high-intensity interval training (HIIT) can be as clinically effective as moderate intensity continuous training (MICT), matched for energy expenditure, on glycemic control and body composition in T2DM patients.

Participants Twenty-four T2DM patients participated in a 24-week bicycle endurance training program. Three supervised exercise sessions per week were performed consisting of either 35 min cycling at 70-80% peak heart rate (MICT) or six to eight 1 min intervals at 90-100% of peak workload interspersed by 4 min at 70% peak heart rate (HIIT).

Measurements Glycemic control and variables of body composition were evaluated at baseline, after 12 and after 24 weeks of intervention.

Results The intervention program was completed by 20 patients (time since diagnose 10 ± 7 years, age 63 ± 10 years, BMI 30.0 ± 5.7 kg/m², HbA1c 50 ± 8 mmol/mol). HbA1c (12 weeks) and fasting glucose (12 and 24 weeks) only decreased significantly after MICT ($p<0.05$). AUC OGTT decreased significantly in both intervention groups (12 and 24 weeks) ($p<0.05$). Subtotal fat mass (% and kg of subtotal mass) reduced significant in both intervention groups ($p<0.05$). Additionaly, MICT promoted significant improvements in body weight (kg), BMI (kg/m^2) subtotal total mass (kg) after 24 weeks ($p<0.05$). Significant interaction effects (time*group) were detected in subtotal fat mass (kg) and subtotal total mass (kg) after 24 weeks, both variables reduced significantly more after MICT ($p<0.05$).

Conclusion HIIT and MICT did not differ on parameters of insulin sensitivity and glycemic control in well controlled T2DM patients after 24 weeks of intervention. Although subtotal fat mass and subtotal total mass, reduced more with MICT.

2 Introduction

Diabetes mellitus (DM) refers to a general term for a group of metabolic disorders and is a growing worldwide public health problem, affecting 463 million people in 2019. The prevalence is projected to increase to 578 million by 2030 and 700 million by 2045. In 2019, in Belgium, an estimated 561 200 patients in the population aged 20 to 79 years suffered from DM. This number is expected to rise to 624 200 cases by 2030. By accounting for 90-95% of all cases, type 2 diabetes mellitus (T2DM) is the most common type of DM (IDF Diabetes Atlas, 2019). This increasing worldwide prevalence is driven by a complex interaction of socioeconomic, demographic, environmental and genetic factors and is coupled with high rates of diabetes related morbidity and mortality (Wu, Ding, Tanaka & Zhang, 2014).

In DM either an impaired insulin secretion, an impaired insulin efficacy or a combination of both manifests clinically as hyperglycemia. In T2DM the status of hyperglycemia is primarily caused by a decrease of insulin sensitivity of peripheral target tissues, such as skeletal muscles, liver and adipose tissue, coupled with the progressive loss of adequate beta cell insulin production and secretion (Unger & Parkin, 2010). The exact etiology of T2DM is not known. An association of insulin secretory defects related to inflammation and metabolic stress among other contributors, including genetic factors, in T2DM has been reported (American Diabetes Association, 2020).

Of interest, physical and biochemical variables associated with the subsequent development of T2DM have been identified and may include both modifiable and non-modifiable factors. Older age, genetic susceptibility, certain ethnic backgrounds (such as South Asians, Hispanics and Aboriginals) and a history of gestational DM are non-modifiable variables. Obesity (especially abdominal obesity), physical inactivity, high fasting insulin and impaired glucose tolerance can be depicted as modifiable DM related variables. (Ransom, Goldenberg, Mikalachki, Prebtani & Punthakee, 2013). Management of these modifiable associated variables is imperative to prevent long-term complications in these patients (The Action to Control Cardiovascular Risk in Diabetes Study Group, 2008).

The fundamental objective of T2DM treatment is to achieve integral lifestyle changes that lead to optimized long-term metabolic control. Metabolic control should be directed towards reaching and maintaining glycated hemoglobin (HbA1c) levels ≤ 7% without producing risks (hypoglycemia, polypharmacy) that outweigh the benefits, thereby avoiding any adverse

effects and deterioration in quality of life (Davies, D'Alessio, Fradkin, Kernan, Mathieu, & Mingrone, 2018). These integral lifestyle changes should include an individualized plan addressing dietary changes, physical activity, optimal pharmacological treatment, weight loss, smoking cessation and psychological support.

Patients with T2DM and excess weight should follow a dietary program with reduction in caloric intake to reach and retain a Body Mass Index (BMI) of approximately ≤25 kg/m². T2DM patients are recommended to engage in minimal 150 minutes of moderate-to-vigorous intensity aerobic exercise activity, spread over at least three days per week (American Diabetes Association, 2020), as this is associated with a reduction in HbA1c, triglycerides, blood pressure and insulin resistance in these patients (Boule, Haddad, Kenny, Wells, & Sigal, 2001; Snowling, & Hopkins, 2006). Despite the well-documented health benefits, lack of time is a major barrier to participation in, and adherence to regular physical activity in patients with T2DM (Booth, Lowis, Dean, Hunter & McKinley, 2013). In recent years, high-intensity interval training (HIIT) has gained more interest since it is a less time-consuming alternative to moderate- intensity continuous training (MICT). In HIIT, an exercise session consists of brief intermittent bursts of vigorous (or high intense) exercise interspersed by periods of low-intensity exercise or complete rest (De Nardi, Tolves, Lenzi, Signori, & Da Silva, 2018). Literature comparing the effect of these structured endurance exercise interventions with different exercise intensities show controversial results with respect to clinical important outcomes such as glycemic regulation, lipid control and body composition (Liubaoerjijin, Terada, Fletcher, & Boulé, 2016). Due to the use of relatively short training periods, the chronic physiological cardiovascular and musculoskeletal adaptations and may have stayed unrevealed (Da Silva et al., 2019). Therefore, the primary objective of the current clinical trial is to examine the impact of 24 weeks of HIIT (high-intensity interval training) versus MICT (moderate-intensity continuous training) on the regulation of glycemic control and parameters of body composition in well-controlled adult patients with T2DM.

3 Methods

3.1 Participants

This study uses a randomized controlled trial design, to compare the effects of a high-intensity interval training program to a moderate-intensity continuous training program on glycemic control and body composition in patients with T2DM. For this clinical trial, participants were recruited through the outpatient endocrinology department of the Jessa Hospital (Hasselt), via local general practitioners (Diepenbeek) and through the Flemish Diabetes Association. After initial screening by means of a standardized questionnaire, 28 T2DM patients fulfilled the eligibility criteria and were enrolled in this clinical trial. To be included in the trial, participants should I) be diagnosed with T2DM, according to the American Diabetes Association criteria (American Diabetes Association, 2020); II) be aged > 18 years; III) have a stable antidiabetic treatment for at least three months before inclusion and IV) be able to perform a maximal cardiopulmonary exercise test (CPET). Participants were excluded if: their body mass index (BMI) is < 20 kg/m²; iron deficiency anemia was present; they were unstable with regard to weight (change > 5 kg/ 6 months); they suffered from diabetic complications (retinopathy, neuropathy, kidney problems); they demonstrated evidence of renal, liver, lung, cardiovascular, orthopedic, neurological or oncological disease; they demonstrated symptoms of dyspnea during exercise or when they were participating in another clinical trial. Before obtaining their written informed consent, participants were informed about the nature and risks of the experimental procedures.

3.2 Ethical approval

The study protocol was approved by the local Medical Ethics Committee of Jessa Hospital and Hasselt University, Hasselt, Belgium on 25/09/2017 (study registration number B243201733478) and a copy is included in the appendix.

3.3 Study design

A two-group randomized controlled trial was applied. In the run-in period, different measurements (see section 'Baseline assessments') were performed in all participants before

randomization in the study. After these baseline assessments, one participant was excluded due to clinical signs of coronary artery disease. As such, 27 participants were randomly assigned to one of two groups: (1) Moderate Intensity Continuous Training (MICT) (n= 12) or (2) High Intensity Interval Training (HIIT) (n= 15). Randomization was carried out by opaque sealed envelopes.

3.4 Baseline assessments

Baseline assessments were performed on two experimental days. Participants were instructed to refrain from physical exercise for 24 – 48 hours prior to the experimental days. In addition, they were asked to avoid the consumption of alcohol or unhealthy food.

An oral glucose tolerance test (OGTT) and a dual-energy x-ray absorptiometry (DEXA) scan were executed on experimental day A. On experimental day A, participants refrained from their anti-diabetic medication and arrived in a fasting state. A non-fasting venous blood sample collection and a maximal cardiopulmonary exercise test (CPET) were performed on experimental day B, within ten days apart from experimental day A. Assessments executed at different time points are summarized in table 1.

Table 1
Assessments executed at different time points

Baseline	12 weeks	24 weeks
Venous blood sample	Venous blood sample	Venous blood sample
OGTT	OGTT	OGTT
DEXA-scan		DEXA-scan
CPET	CPET	

DEXA, dual-energy x-ray absorptiometry; CPET cardiopulmonary exercise test; OGTT, oral glucose tolerance test

3.4.1 Dual – energy x-ray absorptiometry (DEXA) scan

To evaluate body composition, participants were subjected to a DEXA scan (Hologic Series Delphi-A Fan Beal X-ray Bone Densitometer) at the Rehabilitation Research Center (REVAL) of the Biomedical Research Institute of Hasselt University. A DEXA scan was performed at baseline and within seven to ten days after the last exercise session of the intervention program, in a fasting state, to avoid the influence of the nutritional status. Following measurements were obtained: BMI, body weight, subtotal fat mass (kg), subtotal lean mass

+ bone mineral content (BMC) (kg), subtotal total mass (kg), subtotal percentage fat mass (fat%), and android/gynoid ratio.

3.4.2 Oral glucose tolerance test (OGTT)

Participants were subjected to a two-hour oral glucose tolerance test (OGTT) at REVAL after fasting overnight. Starting with the intake of 75 g glucose, concentrations of glucose were measured at T= 0, 30, 60, 90 and 120 minutes (min). The first venous blood sample (T = 0 min) was used for the assessment of fasting glucose concentration. The following samples (T = 30, 60, 90 and 120 min) were used to assess the regulation of glycemic control. Glucose responses after T = 0 min were calculated using the standard trapezoidal method as glucose area under the curve (AUC) during OGTT as an index of glucose (in)tolerance (Sakaguchi et al., 2016). An OGTT was performed at baseline, after 12 weeks of intervention and within seven to ten days after the last exercise session of the intervention program. Blood samples were analyzed (Roche Cobas 8000, Roche Diagnostics International Ltd, Rotkreuz, Switzerland) in the clincal laboratory of Jessa Hospital (Hasselt, Belgium).

3.4.3 Venous blood sample

A venous blood sample was obtained for assessment of blood glycated hemoglobin concentration (HbA1c) (ion exchange chromatography (Menarini HA-8180 HbA1c auto-analyser, Menarini Diagnostics, Diegem, Belgium). These blood samples were taken at Jessa Hospital, at baseline, after 12 weeks of intervention and within seven to ten days after the last exercise session of the intervention program and were subsequently analyzed in the clinical laboratory of Jessa Hospital.

3.4.4 Cardiopulmonary exercise test (CPET)

A maximal cardiopulmonary exercise test on a cycle ergometer (eBike, GE Medical systems, Milwaukee, Wisconsin, USA) was performed at Jessa Hospital. As a safety measure, we first measured capillary blood glucose through a finger prick by a glucose meter (Accu-Chek Aiva, Roche Diagnostics, Machelen, Belgium). In case of hyperglycemia (blood glucose ≥ 300 mg/dL) the CPET was delayed until normalisation of blood glucose values. In case of hypoglycemia (blood glucose < 100 mg/dL) (Colberg et al., 2010), the patient was offered a carbohydrate

supplementation (250 ml Coca-Cola, when insufficient another 250 ml of Coca-Cola). Thereafter, participants were installed on the stationary cycle ergometer. A 12-lead electrocardiogram (ECG) was used to continuously evaluate the heart rhythm and rate (Cardiosoft 6.6, GE Medical systems, Freiburg, Germany). Both an oxygen saturation meter (Nonin WristOx2 3150, Nonin Medical AB, USA) and a spirometer (Jaeger MasterScreen CPX Metabolic Cart, CareFusion, Germany GmbH, Hoechberg, Germany) were used. A ramp stage protocol was carried out. The protocol started with a three-min rest period, followed by a three-min warming up at a workload of 20 watt (W). Thereafter, the workload increased according to a stepwise protocol: 20 W every minute, until volitional exhaustion. The test was ended when patients were no longer able to maintain cycling frequency of ≥ 60 revolutions per minute (rpm) or when indications were observed to end the test (dizziness, severe desaturation ($SpO_2 < 80\%$) (ATS/ACCP Statement on cardiopulmonary exercise testing, 2003). Peak exercise effort was confirmed when respiratory gas exchange ratio (RER) was ≥1.10. Rest blood pressure (BPrest) was taken prior to the test (Durashock DS54, HILL-Rom, USA) and was thereafter monitored every two minutes with a sphygmomanometer (WelchAllyn, Adult 11, New York, VS) and stethoscope (Littman, 3M science, The Netherlands). Before and immediately after the CPET, a BORG score (between one and ten) on degree of dyspnea and leg and/or general fatigue was asked from every participant. A CPET was performed at baseline and after 12 weeks of intervention. Based on the CPET after 12 weeks of intervention, individual training programs were adapted to guarantee the training intensity (based on heart rate zones or workload, see section "interventions"), if necessary.

3.5 Exercise training interventions

All participants were instructed not to alter their dietary intake habits and medication use throughout the study duration. After randomization, 24 participants started a 24-week bicycle intervention program consisting of three individually supervised exercise sessions per week at REVAL rehabilitation research center. Prior to and immediately after the exercise session, capillary blood glucose was measured by a finger prick and a glucose meter (Accu-Chek Aiva, Roche Diagnostics, Machelen, Belgium) to ensure patient safety. In case of pre-session glucose values > 300 mg/dL or < 100 mg/dL, exercise sessions were delayed and in case of hypoglycemia (blood glucose < 100 mg/dL), the participant was offered carbohydrate

supplementation. Attention was required for the possibility of hyperglycemia occurring in the HIIT group, since activities of high intensity can cause blood glucose to rise (Young-Hyman, De Groot, Hill-Briggs, Gonzalez, Hood, & Peyrot, 2016). The dietary intake of the last meal prior to the exercise session was recorded, this could explain possible abnormal glucose values. Exercise intensity was standardized by continuous heart rate monitoring (Polar, H7, Polar electro oy, Finland). As shown in table 2, patients in the MICT group, cycled at 70-80% of HRpeak achieved during CPET. Workload during intervals in the HIIT group, shown in table 3, was calculated based on Wpeak (%) achieved during CPET.

Each supervised session included a five-min warm-up (60-70% HRmax at 70 rpm) and a five-min cool-down (60-70% HRmax at 50 rpm). After the exercise sessions, data with respect to energy expenditure (calories and distance) were noted. Calorie consumption data was derived from the heart rate monitor (Polar, H7, Polar electro oy, Finland) and distance was monitored by the cycle ergometer (Excite Bike, Technogym, Zaventem, Belgium).

The MICT and HIIT groups were designed to yield the same energy expenditure per exercise session during the entire intervention program, based on the method used in the study of Mitranun, Deerochanawong, Tanaka, & Suksom (2014). The isocaloric aspect was controlled by the energy expenditure calculated by the heart rate monitor. All exercise sessions were individually supervised, and the adherence was monitored by the investigators.

Table 2

MICT intervention program

Warming up	Exercise session	Cooling down	Total session duration
5'	35'	5'	45'
60-70% HRpeak	70-80% HRpeak	60-70% HRpeak	

MICT, moderate intensity continuous training; HR heart rate

In the MICT group, patients warmed up gradually to achieve a 60-70% of HRpeak within five min. After warming up, each exercise session consisted of 35 min exercise at a heart rate corresponding with exercise performed between 70-80% of HRpeak. Thereafter, a five-min cool-down was performed, resulting in a total session duration of 45 min.

Table 3

HIIT intervention program

	Warming up	Exercise session		Cooling down	Total session duration
		Interval phase	Recovery phase		
Phase 1 Week (1-2)	5' 60-70% HRpeak	35' 70-80% HRpeak		5' 60-70% HRpeak	45'
Phase 2 Week (3-6)	5' 60-70% HRpeak	6*1' 90-100% Wpeak	6*4' 70% HRpeak	5' 60-70% HRpeak	40'
Phase 3 Week (7-12)	5' 60-70% HRpeak	7*1' 90-100% Wpeak	7*4' 70% HRpeak	5' 60-70% HRpeak	45'
Phase 4 Week (13-24)	5' 60-70% HRpeak	8*1' 90-100% Wpeak	8*4' 70% HRpeak	5' 60-70% HRpeak	50'

HIIT, high intensity interval training; HR, heart rate; W, workload

The HIIT exercise program is based on the study of Mitranun et al. (2014). This intervention program was divided into three phases: phase one (week 1-2), phase two (week 3-6) and phase three (week 7-12). In the present study, a fourth phase was added (week 13-24). In phase one, the participants performed the identical training program to the one that the MICT group performed to gradually habituate patients to the exercise intervention. In phase two, after warming up to reach 60-70% of HRpeak within five min, the participants performed six one-min high-intensity intervals at 90-100% Wpeak with a four-min low-intensity recovery at 70% HRpeak. The exercise sessions were terminated with a five-min cool-down period, resulting in a total session duration of 40 min.

In phase three, following the same warming up routine to reach the 60-70% HRpeak within five min, the participants performed seven one-min high-intensity intervals at 90-100% Wpeak with a four-min low-intensity recovery at 70% HRpeak. The exercise sessions were terminated with a five-min cool-down period, resulting in a total session duration of 45 min.

In phase four, all participants performed warming up to achieve 60-70% HRpeak within five min, then performed eight one-min high-intensity intervals at 90-100% Wpeak with a four-min low-intensity recovery at 70% HRpeak and a five-min cool-down period, resulting in a total session time of 50 min.

3.6   Outcome measures

3.6.1   Primary outcome measures

The primary outcome measure concerning glycemic control was HbA1c, measured through a venous blood sample analysis. The HbA1c assay is known for close correlation with a complete measure of average glycemia over the preceding eight to twelve weeks (Nathan, Turgeon & Regan, 2007). Therefore, this measurement of chronic glycemia levels is considered as an excellent comparative to the measurement of glucose concentrations which tend to fluctuate within and between days (International Expert Committee, 2009).

3.6.2   Secondary outcome measures

Secondary outcome measures related to glycemic control included fasting glucose, and Area Under the Curve (AUC) derived from the Oral Glucose Tolerance Test (OGTT). BMI and other measures of body composition (body weight, subtotal fat mass, subtotal lean body mass + BMC, subtotal total mass, subtotal % fat mass and android/gynoid ratio), were obtained from a DEXA scan.

3.7   Data-analysis

Data are presented as means ± standard deviations (SD).
To test normality of the different intervention groups, the Normal Quantile Plot and the Shapiro-Wilk test were used. Homoscedasticity was verified using the Brown-Forsythe test.

3.7.1   Between-group comparison

Stepwise details of the between-group statistical analysis are depicted in figure 1. In case both assumptions, namely normality and homoscedasticity were met in both intervention groups, an unpaired, two-sample t-test was performed for between group comparisons (at baseline, after 12 weeks and after 24 weeks of intervention). If the assumption of normality was not met in one of two intervention groups, but the assumption of homoscedasticity was met, the non-parametric Wilcoxon Rank Sum test (n≥ 10 in both groups) or the Wilcoxon Rank Sum Exact test (n< 10 in one of the groups) was performed.
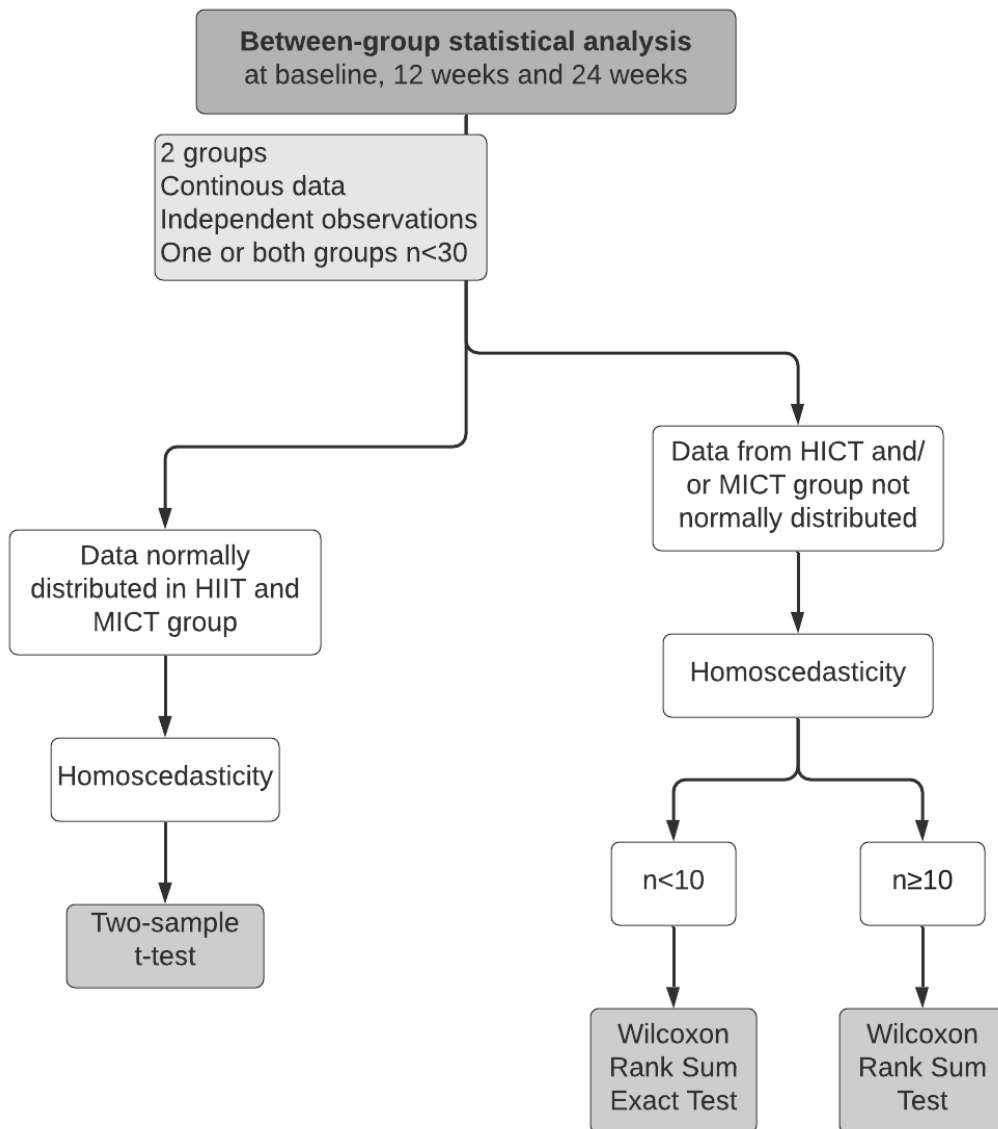
Figure 1. Between-group statistical analysis

3.7.2 Within-group comparison

Stepwise details of the within-group statistical analysis are depicted in figure 2. To test for within group comparisons, absolute difference values between two time points were calculated (between baseline and 12 weeks; baseline and 24 weeks; 12 weeks and 24 weeks). In each intervention group separately, normality of these difference values was tested. If the assumption of normal distribution was met, a paired, one-sample t-test was performed. If normal distribution was absent, only the non-parametric Wilcoxon Signed Rank test was performed.
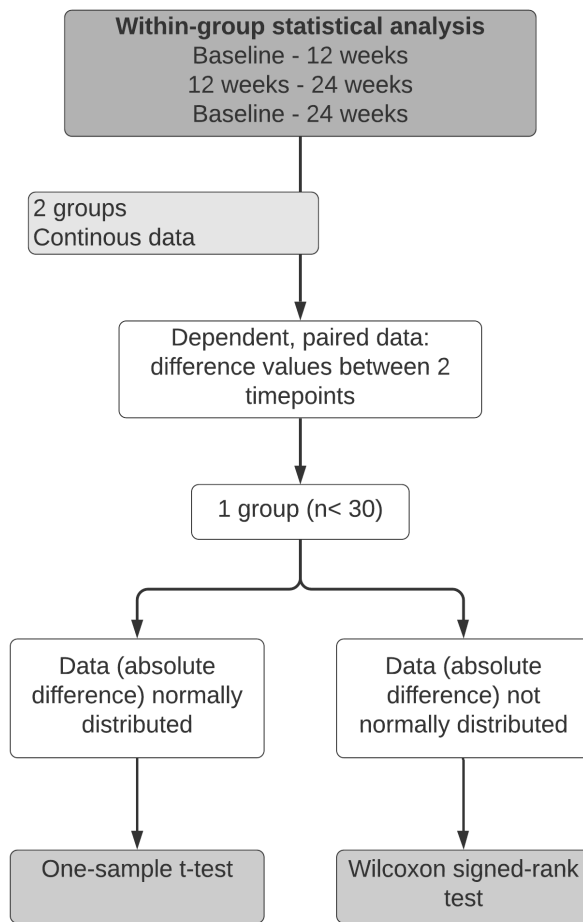
Figure 2. Within-group statistical analysis

3.7.3 Time*group interaction effect

Difference values between two timepoints were used for time*group analysis. Stepwise details are depicted in figure 1. An unpaired, two-sample t-test was performed if normal distribution and homoscedasticity were met in both intervention groups. Only the non-parametric Wilcoxon Rank Sum test (n≥ 10 in both groups) or the Wilcoxon Rank Sum Exact test (n< 10 in one of the groups) was performed if homoscedasticity was met, but normal distribution was absent in of one of two intervention groups.

Statistical significance was set at $p< 0.05$.

All statistical calculations were performed using JMP PRO, version 14.2.0 (SAS Institute Inc., Cary, NC, 1989-2020)

4 Results

4.1 Participants

A flow diagram of the trial is summarized in figure 3. After baseline testing, 27 participants were randomly allocated to one of two intervention groups: MICT (n=12) or HIIT (n=15). After randomization, three participants (n = 1 MICT and n = 2 HIIT) dropped out before starting the program. The reasons were: time constraints, unrelated to the nature of the intervention program, and an orthopedic knee injury. Twenty-four participants initiated the 24-week exercise intervention program. Three participants in the HIIT group dropped out before re-evaluation after 12 weeks of the intervention program and one participant in the MICT group dropped out before re-evaluation after 24 weeks of the program. As a result, 20 patients (10 in HIIT, 10 in MICT) were included in the final analysis.
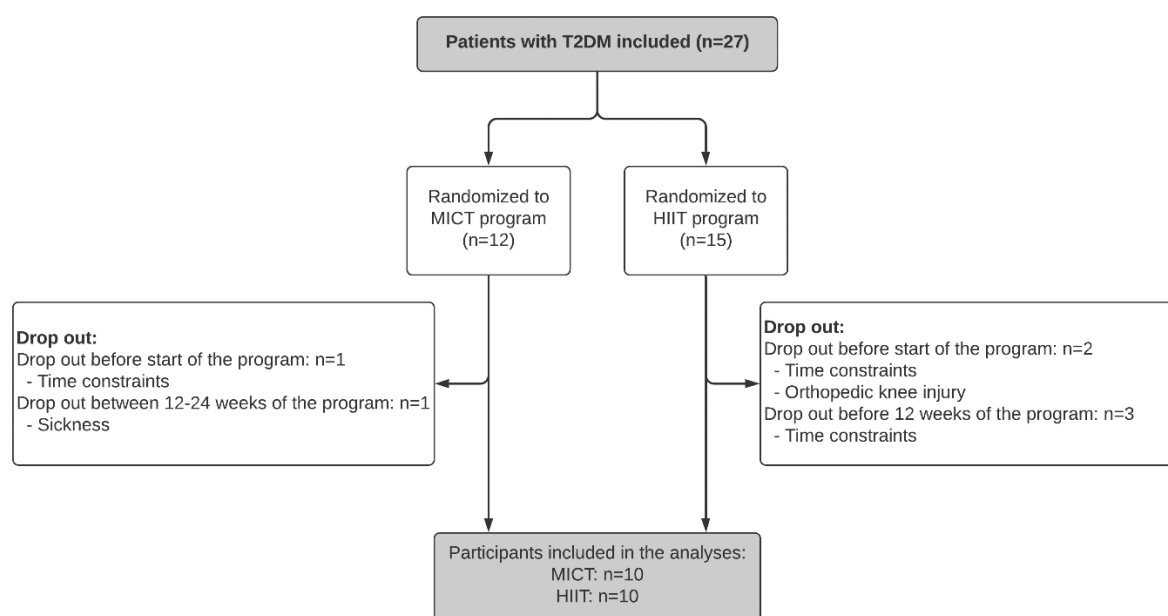
Figure 3. Flow diagram of study participants

Participants included in statistical analyses (n=20, HbA1c 50 ± 8 mmol/mol, BMI 30.0 ± 5.7 kg/m², age 63 ± 10 years) were diagnosed with T2DM. Prior to the intervention, 10 participants structurally engaged in sports or exercise activities every week (playing tennis, hiking, ...), while the other 10 participants did not participate structurally in any physical activity.

Participants' characteristics are summarized in table 4. At baseline, there were no significant differences in primary or secondary outcome measures between groups. All participants included in statistical analysis completed the entire 24 weeks intervention program. On average, 71 ± 3 exercise sessions in the MICT group and 70 ± 5 exercise sessions in the HIIT group of the total 72 exercise sessions were attended by the participants who completed the exercise program, resulting in an overall adherence of 97.9 ± 3.9 % and 96.5 ± 7.3 % in the MICT and HIIT training groups, respectively. Medication usage of the participants is depicted in table 5. The blood-glucose-lowering medication dose did not change during the entire intervention program. Except for one hypoglycemic event in the HIIT group, after which the training session was ended, no adverse events were reported during the exercise program and all participants finished their training sessions successfully. Mean % of missing data was 1.96 %, due to technical errors and absence of participants on testing occasions.

Table 4
Between group differences in baseline participant characteristics

	MICT group	HIIT group	P
N (male/female)	10 (8/2)	10 (10/0)	
Age (years)	64 ± 13	61 ± 5	0.4531
Body weight (kg)	89.1 ± 19.7	96.3 ± 16.6	0.1041
Disease duration (years)	12 ± 9	7 ± 4	
Current smokers (n)	0	0	
Ex smokers (n)	3	5	
Whole body insulin sensitivity and glycemic control			
Fasting glucose (mmol/l)	8.02 ± 2.04	7.29 ± 0.94	0.3137
HbA1c (%)	6.92 ± 0.77	6.60 ± 0.74	0.3571
HbA1c (mmol/mol)	52 ± 9	49 ± 8	0.3927
AUC OGTT (mol/l/min)	1728 ± 372	1609 ± 284	0.3913
Body composition			
BMI (kg/m²)	30.2 ± 6.8	30.0 ± 4.9	0.9137
Subtotal			
Fat mass (kg)	26.43 ± 8.24	26.38 ± 8.00	0.7913
Lean mass + BMC (kg)	55.52 ± 10.21	62.15 ± 8.84	0.1381
Total mass (kg)	81.95 ± 17.09	88.53 ± 15.38	0.1405
% fat mass (%)	31.92 ± 4.63	29.30 ± 5.26	0.2523
Android/gynoid ratio	1.38 ± 0.34	1.49 ± 0.28	0.4109

Data are means ± SD; * $P < 0.05$
MICT, moderate intensity continuous training; HIIT, high intensity interval training; HbA1c, glycated hemoglobin; AUC, area under the curve; OGTT, oral glucose tolerance test; BMI, body mass index; BMC, bone mineral content

Table 5

Medication usage

	MICT group	HIIT group
T2DM related medication (n)		
Metformin	8	7
DPP-4 inhibitor	1	1
Sulfonylurea	2	2
SGLT-2 inhibitor	0	1
DPP-4 inhibitor + metformin	0	1
Repaglinide	0	1
None	1	1
Cardiovascular related medication (n)		
ACE- inhibitor	1	1
ACE- inhibitor + calcium channel blocker	1	0
ACE-inhibitor + thiazide diuretics	0	2
Calcium channel blocker	2	0
Aspirin	2	0
Beta blocker	1	2
Direct oral anticoagulants	1	0
None	6	6
Lipid lowering medication (n)		
Statin	5	3
Fibrate	1	1
Ezetimibe	0	1
None	5	7
Other medication (n)		
Antipsychotics	1	0
Antidepressants	1	0
Proton-pump inhibitor	1	1
Xanthine oxidase inhibitors	0	1
Beta2-andrenergic agonist	0	1
None	8	8

MICT, moderate intensity continuous training; HIIT, high intensity interval training; n, number; T2DM, type 2 diabetes mellitus; DPP-4 inhibitor, dipeptidyl peptidase-4 inhibitor; SGLT-2 inhibitor, sodium-glucose cotransporter 2 inhibitor; ACE- inhibitor, Angiotensin Converting Enzyme inhibitor

4.2 Whole body insulin sensitivity and glycemic control

Outcome measures of whole-body insulin sensitivity and glycemic control were assessed at baseline, after 12 weeks and after 24 weeks of intervention. For outcome measures HbA1c and fasting glucose, all data were obtained. For AUC, there was one missing value at baseline (HIIT n=1) and two missing values after 24 weeks of intervention (HIIT n=1, MICT n=1).

All parameters reflecting whole body insulin sensitivity and glycemic control were comparable at baseline. No significant between-group differences were detected.

Blood HbA1c content decreased from 6.92 ± 0.77 % to 6.49 ± 0.46 % (52 ± 9 mmol/mol to 48 ± 5 mmol/mol) following 12 weeks of exercise training in the MICT group (p<0.05; table 6). At 24 weeks of intervention no significant change (p>0.05; table 6) in blood HbA1c content was measurable in the MICT group (6.60 ± 0.54 %; 48.50 ± 5.84 mmol/mol). In the HIIT group, blood HbA1c content did not change significantly following 12 and 24 weeks of intervention (p>0.05; table 6). No between-group differences were observed at 12 and 24 weeks of intervention (table 7) and no interaction effect (time*group) was observed between exercise intensity and the decrease in blood HbA1c content (% and mmol/mol) (p>0.05; table 8).

In the MICT group, fasting glucose levels decreased from 8.02 ± 2.04 mmol/l to 7.36 ± 1.40 mmol/l following 12 weeks (p<0.05; table 6) and to 7.24 ± 1.55 mmol/l following 24 weeks of intervention (p<0.05; table 6). In the HIIT group, fasting glucose levels did not change following 12 and 24 weeks (p>0.05; table 6). No between-group differences (p>0.05; table 7) and no interaction effect (time*group) was observed between exercise intensity and the decrease in fasting glucose levels (p>0.05; table 8).

AUC OGTT content decreased from 1728 ± 372 mol/min/l to 1519± 323 mol/min/l following 12 weeks (p<0.05; table 6) and to 1461 ± 249 mol/min/l following 24 weeks of intervention in the MICT group. Although the decrease from 12 to 24 weeks of intervention in the MICT group was not significant (p>0,05; table 6), the decrease in the comparison of baseline value with the value after 24 weeks of intervention was significant (p<0,05; table 6). In the HIIT group, AUC OGTT content did not change following 12 weeks of intervention, but decreased from 1609 ± 284 mol/min/l at baseline and from 1510 ± 261 mol/min/l at 12 weeks of intervention to 1385 ± 283 mol/min/l at 24 weeks of the intervention program (both p<0.05; table 6). No between-group differences were observed at 12 or 24 weeks of intervention (p> 0,05; table 7) and no interaction effect (time*group) was observed between exercise intensity and the decrease in AUC OGTT content (p>0.05; table 8).

Table 6

Within group differences in whole body insulin sensitivity and glycemic control

OGTT and venous blood parameters	MICT group (n=10)			P			HIIT group (n=10)			P		
	Baseline	12 w	24 w	Baseline - 12 w	12 w - 24 w	Baseline - 24 w	Baseline	12 w	24 w	Baseline - 12 w	12 w - 24 w	Baseline - 24 w
Fasting glucose (mmol/l)	8.02 ± 2.04	7.36 ± 1.40	7.24 ± 1.55	0.0449*	0.2997	0.0304*	7.29 ± 0.94	7.00 ± 0.74	7.07 ± 0.75	0.1939	0.6350	0.1644
AUC OGTT (mol/min/l)	1728 ± 372	1519 ± 323	1461 ± 249[a]	0.0248*	0.3504[a]	0.0094*[a]	1609 ± 284[a]	1510 ± 261	1385 ± 283[a]	0.1269[a]	0.0279*[a]	0.0059*[a]
HbA1c (%)	6.92 ± 0.77	6.49 ± 0.46	6.60 ± 0.54	0.0131*	0.8370	0.0547	6.60 ± 0.74	6.50 ± 0.72	6.54 ± 0.73	0.2521	0.6936	0.3110
HbA1c (mmol/mol)	52 ± 9	48 ± 5	49 ± 6	0.0196*	0.7900	0.0586	49 ± 8	48 ± 8	48 ± 8	0.2971	0.7125	0.3842

Data are means ± SD; * P < 0.05; [a] n=9

OGTT, oral glucose tolerance test; MICT, moderate intensity continuous training; HIIT, high intensity interval training; AUC, area under the curve; HbA1c, glycated hemoglobin

Table 7

Between group differences in whole body insulin sensitivity and glycemic control

OGTT and venous blood parameters	MICT group (n=10)			HIIT group (n=10)			P		
	Baseline	12 w	24 w	Baseline	12 w	24 w	Baseline	12 w	24 w
Fasting glucose (mmol/l)	8.02 ± 2.04	7.36 ± 1.40	7.24 ± 1.55	7.29 ± 0.94	7.00 ± 0.74	7.07 ± 0.75	0.3137	0.4817	0.7698
AUC OGTT (mol/min/l)	1728 ± 372	1519 ± 323	1461 ± 249[a]	1609 ± 284[a]	1510 ± 261	1385 ± 283[a]	0.4002	0.9466	0.5530
HbA1c (%)	6.92 ± 0.77	6.49 ± 0.46	6.60 ± 0.54	6.60 ± 0.74	6.50 ± 0.72	6.54 ± 0.73	0.3571	0.9707	0.8373
HbA1c (mmol/mol)	52 ± 9	48 ± 5	49 ± 6	49 ± 8	48 ± 8	48 ± 8	0.3927	0.9732	0.8899

Data are means ± SD; * P < 0.05; [a] n=9

OGTT, oral glucose tolerance test; MICT, moderate intensity continuous training; HIIT, high intensity interval training; AUC, area under the curve; HbA1c, glycated hemoglobin

Table 8

*Time * group effect in whole body insulin sensitivity and glycemic control*

Difference in OGTT and venous blood parameters	Baseline - 12 w		P	12 w - 24 w		P	Baseline - 24 w		P
	MICT (n=10)	HIIT (n=10)		MICT (n=10)	HIIT (n=10)		MICT (n=10)	HIIT (n=10)	
Fasting glucose (mmol/l)	-0.66 ± 1.10	-0.28 ± 0.99	0.4290	-0.13 ± 0.74	0.07 ± 0.62	0.5267	-0.79 ± 1.16	-0.21 ± 0.65	0.1896
AUC OGTT (mol/min/l)	-209 ± 292	-98 ± 239[a]	0.3802	-25 ± 187[a]	-126 ± 169[a]	0.2480	-228 ± 233[a]	-224 ± 207[a]	0.9643
HbA1c (%)	-0.43 ± 0.51	-0.10 ± 0.45	0.1490	0.11 ± 0.33	0.04 ± 0.24	0.5983	-0.32 ± 0.57	-0.06 ± 0.37	0.2395
HbA1c (mmol/mol)	-4 ± 6	-1 ± 5	0.1762	1 ± 4	1 ± 3	0.7364	-3 ± 6	-0 ± 4	0.2245

Data are means ± SD; * P < 0.05; [a] n=9

OGTT, oral glucose tolerance test; MICT, moderate intensity continuous training; HIIT, high intensity interval training; AUC, area under the curve; HbA1c, glycated hemoglobin

Mean differences in glucose levels between pre- and post-exercise sessions were similar between groups in phase 2 (w3-6) and phase 3 (w7-12) (p>0.05; table 9). In phase 1 (w1-2) and phase 4 (w13-24), a between-group difference was observed (p<0.05), with an average difference of 66 ± 26 mg/dl in the MICT group and 41 ± 20 mg/dl in the HIIT group in phase 1 and an average difference of 53 ± 21 mg/dl in the MICT group and 25 ± 16 mg/dl in the HIIT group in phase 4 (p<0.05; table 9).

Table 9

Mean Δ glucose per exercise session (mg/dl)

	MICT (n=10)	HIIT (n=10)	P
Phase 1 (w1-2)	66 ± 26	41 ± 20	0.0312*
Phase 2 (w3-6)	51 ± 22	33 ± 19	0.0634
Phase 3 (w7-12)	47 ± 29	33 ± 19	0.2190
Phase 4 (w13-24)	53 ± 21	25 ± 16	0.0033*

Data are means ± SD in mg/dl; * P < 0.05
Δ, difference between pre and post glucose value per session (pre-post); MICT, moderate intensity continous training; HIIT, high intensity interval training

4.3 Body composition

A DEXA scan was obtained at baseline and after 24 weeks of intervention. After 24 weeks, one participant was not re-assessed. Therefore, all outcome measures of body composition had one missing value in the HIIT group, after 24 weeks of intervention. All outcome measures of body composition were comparable between groups at baseline. No significant between-group differences were detected.

Body weight, BMI, and subtotal total mass decreased significantly in the MICT group from 89.1 ± 19.7 kg to 86.8 ± 17.7 kg, from 30.2 ± 6.8 kg/m² to 29.4 ± 6.1 kg/m² and from 81.95 ± 17.09 kg to 80.08 ± 16.80 kg respectively, following 24 weeks of intervention (p<0.05; table 10). No between-group differences were observed in parameters of body weight, BMI and subtotal total mass (p>0.05; table 11). However, there was a significant interaction effect (time*group) for the changes in subtotal total mass after 24 weeks of intervention. Hereby, subtotal total mass decreased to a greater extent in the MICT group (-1.87 ± 1.33 kg) in comparison to HIIT group (+0.41 ± 2.61 kg) after 24 weeks of intervention (p<0.05; table 12).

The application of structured endurance-type exercise training significantly reduced subtotal fat mass in both the MICT (26.43 ± 8.24 kg to 24.38 ± 7.93 kg) and the HIIT (26.38 ± 8.00 kg to 26.16 ± 7.82 kg) intervention groups (p<0.05 in both; table 10). Furthermore, subtotal % fat mass decreased significantly in both the MICT (31.92 ± 4.63 % to 30.15 ± 5.32 %) and HIIT intervention group (29.30 ± 5.26 % to 28.88 ± 5.14 %) following 24 weeks of exercise (p<0.05 in both; table 10). No between-group differences were observed for subtotal fat mass and subtotal % fat mass (p>0.05; table 11). A significant interaction effect (time*group) for the changes in subtotal fat mass after 24 weeks of intervention was measured. Subtotal fat mass decreased to a greater extent in the MICT group than in the HIIT group following the intervention program, -20.50 ± 1.18 kg and -0.84 ± 1.30 kg, respectively (p<0.05; table 12). No within- or between-group differences in values of lean mass + BMC could be seen in the MICT and HIIT groups after 24 weeks of intervention (p>0.05; table 10 and 11).

Mean caloric expenditure per exercise session was similar between intervention groups in phase one (w1-2), two (w3-6) and three (w7-12) (p>0.05; table 13). Only in phase four (w13-24), a between-group difference was observed with an average expenditure of 390 ± 79 kcal in the MICT group and 519 ± 78 kcal in the HIIT group (p<0.05; table 13).

Table 10

Within group differences in body composition

DEXA scan parameters	MICT group (n=10)		P	HIIT group (n=10)		P
	Baseline	24 w	Baseline - 24 w	Baseline	24 w [a]	Baseline-24 w [a]
Body weight (kg)	89.1 ± 19.7	86.8 ± 17.7	0.0029*	96.3 ± 16.6	96.5 ± 17.9	0.4734
BMI (kg/m²)	30.2 ± 6.8	29.4 ± 6.1	0.0097*	29.9 ± 4.9	30.1 ± 5.3	0.4517
Subtotal						
Fat mass (kg)	26.43 ± 8.24	24.38 ± 7.93	0.0002*	26.38 ± 8.00	26.16 ± 7.82	0.0443*
Lean mass + BMC (kg)	55.52 ± 10.21	55.70 ± 10.63	0.2158	62.15 ± 8.84	63.03 ± 10.18	0.0905
Total mass (kg)	81.95 ± 17.09	80.08 ± 16.80	0.0010*	88.53 ± 15.38	89.19 ± 16.54	0.6743
% fat mass (%)	31.92 ± 4.63	30.15 ± 5.32	0.0021*	29.30 ± 5.26	28.88 ± 5.14	0.0273*
Android/gynoid ratio	1.38 ± 0.34	1.37 ± 0.32	0.3721	1.49 ± 0.28	1.47 ± 0.24	0.6488

Data are means ± SD; * P < 0.05; [a] n=9; DEXA, dual-energy X-ray absorptiometry; MICT, moderate intensity continuous training; HIIT, high intensity interval training; BMI, body mass index; BMC, bone mineral content

Table 11

Between group differences in body composition

DEXA scan parameters	MICT group (n=10)		HIIT group (n=10)		P	
	Baseline	24 w	Baseline	24 w [a]	Baseline	24 w [a]
Body weight (kg)	89.1 ± 19.7	86.8 ± 17.7	96.3 ± 16.6	96.5 ± 17.9	0.1041	0.1333
BMI (kg/m²)	30.2 ± 6.8	29.4 ± 6.1	29.9 ± 4.9	30.1 ± 5.3	0.9137	0.7863
Subtotal						
Fat mass (kg)	26.43 ± 8.24	24.38 ± 7.93	26.38 ± 8.00	26.16 ± 7.82	0.7913	0.5490
Lean mass + BMC (kg)	55.52 ± 10.21	55.70 ± 10.63	62.15 ± 8.84	63.03 ± 10.18	0.1381	0.1438
Total mass (kg)	81.95 ± 17.09	80.08 ± 16.80	88.53 ± 15.38	89.19 ± 16.54	0.1405	0.1128
% fat mass (%)	31.92 ± 4.63	30.15 ± 5.32	29.30 ± 5.26	28.88 ± 5.14	0.2523	0.6037
Android/gynoid ratio	1.38 ± 0.34	1.37 ± 0.32	1.49 ± 0.28	1.47 ± 0.24	0.4109	0.4569

Data are means ± SD; * P < 0.05; [a] n=9; DEXA, dual-energy X-ray absorptiometry; MICT, moderate intensity continuous training; HIIT, high intensity interval training; BMI, body mass index; BMC, bone mineral content

Table 12

*Time * group effect in body composition*

Difference in DEXA scan parameters	Baseline - 24 weeks		P
	MICT (n=10)	HIIT (n=9)	
Body weight (kg)	-2.3 ± 2.5	-0.1 ± 2.4	0.1128
BMI (kg/m²)	-0.8 ± 0.8	-0.0 ± 0.8	0.1377
Subtotal			
Fat mass (kg)	-2.05 ± 1.18	-0.84 ± 1.30	0.0236*
Lean mass + BMC (kg)	0.18 ± 1.51	1.25 ± 2.55	0.3562
Total mass (kg)	-1.87 ± 1.33	0.41 ± 2.61	0.0057*
% fat mass (%)	-1.77 ± 1.47	-0.99 ± 1.32	0.2412
Android/gynoid ratio	-0.01 ± 0.10	0.01 ± 0.06	1.0000

Data are means ± SD; * $P < 0.05$

DEXA, dual-energy X-ray absorptiometry; MICT, moderate intensity continuous training; HIIT, high intensity interval training; BMI, body mass index; BMC, bone mineral content

Table 13

Mean caloric expenditure per exercise session

	MICT	HIIT	P
Phase 1 (w1-2)	390 ± 85	401 ± 53	0.7318
Phase 2 (w3-6)	380 ± 79	405 ± 88	0.5051
Phase 3 (w7-12)	381 ± 74	448 ± 94	0.0945
Phase 4 (w13-24)	390 ± 79	519 ± 78	0.0017*

Data are means ± SD; * $P < 0.05$

MICT, moderate intensity continuous training; HIIT, high intensity interval training

5 Discussion

In this study, the clinical benefits of 24 weeks of HIIT versus MICT in patients with T2DM were evaluated. After 24 weeks of intervention, glucose AUC during OGTT and subtotal fat mass (both kg and %) improved in both groups. Only the MICT group demonstrated improvements in fasting glucose, body weight, BMI and subtotal total mass. Additionally, both subtotal fat mass (kg) and subtotal total mass (kg) decreased to a greater extent after MICT. These results show that endurance-type exercise training of two different intensities did not differ in their efficacy to improve whole-body insulin sensitivity and glycemic control in patients with T2DM. Although, subtotal fat mass and subtotal total mass seem to reduce more with moderate intense continuous exercise compared with high intense interval exercise.

5.1 Reflection on results

5.1.1 Outcomes of whole-body insulin sensitivity and glycemic control

As hyperglycemia defines T2DM, the regulation of glycemic control is fundamental in diabetes management. The results in the present study on HbA1c (% and mmol/mol) indicate that 12 weeks of endurance-type exercise significantly lowered HbA1c in the MICT group. Yet, this significant reduction in the MICT group was not longer visible after 24 weeks of intervention. Overall, no significant differences in terms of HbA1c were visible between the intervention groups. These findings are consistent with meta-analyses which could not establish the superiority of HIIT compared to MICT on HbA1c in 120 T2DM patients an average age of 61.7 ± 6 years (De Nardi et al., 2018). Controversially, a more recent meta-analysis by Liu, Zhu, Li, Li, & Xu (2018) comparing HIIT and MICT in nine RCT's with a population of adult T2DM patients, found a 0.37% larger reduction of HbA1c following HIIT compared to MICT which means that HIIT may have additional benefits on the regulation of glycemic control.

Glycemic control is primarily assessed by HbA1c (American Diabetes Association, 2020). HbA1c reflects glycemic control over a period of three months and has also been shown to be an important risk factor for the development of cardiovascular disease in patients with T2DM (Stratton et al., 2000; Woerle et al., 2007). It has been firmly established that regular exercise effectively reduces HbA1c content in T2DM patients (Praet & van Loon, 2009; De Feyter et al.,

2007; Snowling & Hopkins, 2006; Boulé, Haddad, Kenny, Wells, & Sigal, 2001). The overall effect of exercise-induced reductions in HbA1c could be explained by the following mechanisms: (I) although insulin is the chief acute physiologic stimulus of glucose disposal, an insulin-independent stimulus of muscle contractions reduces blood glucose by an increased membrane permeability to glucose and facilitates muscle glucose uptake through activation of intracellular translocation of glucose transporter type 4 (GLUT4) to the muscle cell membrane. Even in an insulin resistant state, exercise enhances the muscle glucose uptake through the insulin-independent pathway (American College of Sports Medicine, 2010) and (II) an exercise-induced improved peripheral insulin sensitivity can explain an improvement in blood glucose concentrations. In the meta-analysis of Jelleyman et al. (2015) peripheral insulin sensitivity of patients with insulin resistance improved more in HIIT compared to MICT. (III) The synergistic effect of insulin and exercise induced muscle contractions triggered by multiple signaling cascades stimulates the redistribution of GLUT4 from the cytoplasmic vesicles through the sarcolemma. This redistribution stimulates the muscular uptake of glucose (Santos, Ribeiro, Gaya, Appell, & Duarte, 2008).

Following Roberts, Little and Thyfault (2013) a theoretical rationale for greater benefits of HIIT for improving HbA1c exists. During HIIT a greater degree of muscle fiber recruitement is required which more rapidly depletes muscle glycogen stores in all muscle fibre types. These combined effects would result in a more robust stimulation of post-exercise muscle glucose uptake and glycogen resynthesis when compared to MICT. The higher degree of muscle fiber recruitement may also lead to metabolic adaptations (increased GLUT4 content and mitochondrial biogenesis) facilitating sustained improvements in metabolic control and insulin sensitivity. Although no rise in overall GLUT4 content was seen after 16 weeks of HIIT in T2DM patients. Yet, higher membrane-bound GLUT4 levels were observed in comparison with energy matched MICT (Karstoft et al., 2014). Paradoxally, Little et al. (2011) reported a significant increase increased total GLUT4 protein content following HIIT in T2DM patients. Further research is needed to determine the mechanisms mediating the improvement in overall glycemic control and HbA1c, following endurance-type exercise interventions of different intensities.

Earlier research already demonstrated that the magnitude of the reduction in HbA1c content following prolonged exercise intervention strongly depends on pre-intervention HbA1c levels (Boulé, et al., 2001). Mean levels of HbA1c in the present study were already below the glycemic target of 7% or 52mmol/mol in both intervention groups before starting the intervention period, which indicates an overall good glycemic control in the included sample of T2DM patients. This could possibly explain why only a significant 0,3% reduction in HbA1c level, from the pre-intervention level of 6.92 ± 0.77 % was observed in the MICT group in the present study without significant between group changes, following 12 weeks of intervention. Nevertheless, these relatively small reductions are of great importance since any reduction in HbA1c is associated with a reduced onset and progression of microvascular and macrovascular complications in T2DM patients (Stratton et al., 2000).

Besides the evaluation of changes in HbA1c, fasting glucose and AUC OGTT were included in outcome measures to have a more comprehensive view on the glycemic control in T2DM patients since HbA1c does not account for glycemic variability in daily life (American Diabetes Association, 2018). No significant interaction effects (time*group) on fasting glucose, a marker reflecting acute glycemic control, was found. However, a significant reduction in the MICT group in fasting glucose was observed following 12 and 24 weeks of intervention, indicating that endogenous glucose production was affected in the group performing MICT. Of other studies assessing fasting glucose in T2DM in interventions comparing different exercise intensities, Mitranun et al. (2014) reported reduced fasting glucose concentrations while others report no change between HIIT and MICT (Terada, Friesen, Chahal, Bell, Mccargar and Boulé, 2013; Karstoft et al., 2014; Maillard et al., 2016). When reductions in fasting glucose are observed, they appear similar in the HIIT and MICT intervention groups (Mitranun et al., 2014). This existing divergence in evidence may be explained by several factors. First, fasting plasma glucose concentration depends entirely on the fasting rate of endogenous glucose production in the liver, and on its insulin sensitivity (Taylor, 2013). Whether exercise training can cause an alteration in endogenous glucose production still remains controversial

(Winnick et al., 2008; Kirwan, Solomon, Wojta, Staten, & Holloszy, 2009). Lastly, the reduction in fasting glucose concentrations following HIIT is smaller when compared with MICT or the application of dietary interventions inducing a very low caloric diet. This suggests a lack of potency for improving hepatic insulin sensitivity with exercise and implies that general body weight loss or a negative energy balance is required to achieve improvements in this short-term marker of glycemic control.

While the AUC OGTT in the MICT group decreased significant after 12 weeks of intervention, a significant decrease AUC OGTT in the HIIT group has only been seen after phase 4 (w 12-24) of the intervention program. Two other RCT's with intervention durations of 11 and 16 weeks, addressing the effect of MICT versus HIIT in T2DM patients, have found no significant reductions in neither of the groups (Karstoft et al., 2014; Winding, Munch, Iepsen, Van Hall, Pedersen, & Mortensen, 2018). Thereby, the longer intervention period of 24 weeks used in the present RCT may provide an explanation for these conflicting results of the exercise-induced improvements in patients with T2DM on AUC OGTT.

Lastly, in other publications comparing MICT with HIIT, the mean duration of the intervention periods is 12 weeks or in publications with a longer intervention period, sessions continued unsupervised until the follow up assessment (Winding et al, 2018; Mitranun et al, 2014). Since significant improvements in fasting glucose, HbA1c and AUC OGTT in the MICT group were only present in the first 12 weeks of intervention, the longer intervention duration of this study did not evoke additional improvements in terms of glycemic control.

5.1.2 Outcomes of body composition

The significant improvements in body composition after both intervention programs are of great interest since most individuals with T2DM included in this study were considered overweight (≥ 25- 29.99 kg/m²) or obese (≥ 30 kg/m²) and relationship between BMI at the time of the T2DM diagnosis and the risk of death has been firmly established (Katzmaryk, Hu, Cefalu, Mire, & Bouchard, 2013; Tobias, Pan, & Hu, 2014). Moreover, at least 10% reduction

in body weight has been associated with a 20% lower incidence risk for the development of cardiovascular diseases (Look AHEAD Research Group, 2016). Additionaly, the significant reduction in subtotal fat mass (kg) in favor of the MICT intervention group is of great importance for the optimization of glucose control since a reduction in fat mass is associated with improved insulin sensitivity (Racette, Evans, Weiss, Hagberg, & Holloszy, 2006).

Other publications comparing MICT and HIIT in T2DM patients have found conflicting evidence. After 12 weeks of intervention, Mitranun et al. (2014) reported reductions in fat mass % and waist to hip ratio in both groups, only in the HIIT group reductions in body mass and BMI were seen. Conversely, other studies have found no additional benefits of HIIT over MICT on body composition (Terada et al., 2013; Cho, Lee, Lee, & Kang, 2011). Terada et al. (2013) concluded that similar results on body composition could be explained by similar energy expenditure in both groups during the training sessions of MICT and HIIT since food intake and physical activity patterns outside the intervention were monitored. Previously, weight loss induced by exercise training is predominantly thought to be caused by the increased energy expenditure during the performed exercise (Slentz, Houmard, & Kraus, 2009). We were not able to underline this statement, since the HIIT group demonstrated a significant higher caloric expenditure per session in comparison to the MICT group during phase 4 (w13-24) of the intervention program. BMI and body weight significantly decreased only in the MICT group following 24 weeks of intervention. However, no between-group effect or interaction effect (time*group) was observed. This higher caloric energy expenditure in the HIIT group in phase 4 can be explained by the design of the exercise program in both intervention groups. The brief high intense bouts in the HIIT group were based on the Wpeak of the CPET while the intensity in the MICT group was depicted by HRmax reached during the CPET.

The results in the present study are in line with those depicted in the meta-analysis of Wewege, Berg, Ward, & Keech (2017) comparing MICT and HIIT for changes in body composition focusing on overweight and obese adults without comorbidities. Their results indicate a modest decrease in body fat mass of 6 % from initial levels after 10 weeks of HIIT and MICT, even in the absence of changes in body weight. These results are of great importance since caloric restriction has been reported as more effective than endurance-type exercise training for weight loss in overweight individuals without T2DM. Yet, exercise is more

effective for decreasing visceral fat stores in this population, even in the absence of weight loss exercise training still induces 6 % drop in visceral fat (Verheggen, Maessen, Green, Hermus, Hopman, & Thijssen, 2016). After 12 weeks of treadmill running a significant decrease (19.5%) in abdominal visceral fat appeared after HIIT in obese women, with no significant decrease after MICT (11.1%) (Zhang, Tong, Qiu, Wang, Nie, & He, 2015). Also, in the T2DM population a greater effect from HIIT over MICT on visceral fat adiposity has been reported in women with T2DM (Maillard et al., 2016). This reduction in visceral fat accumulation is independently associated with improvement in insulin resistance (Fujioka, Matsuzawa, Tokunaga, & Tarui, 1987).

It is plausible that in HIIT and MICT interventions, the different effects on lipid mobilization and oxidation may find a cause in factors related to mitochondrial adaptations in the skeletal muscle (MacInnis, Gibala, 2016). Following other metabolic responses to MICT and HIIT have been depicted: In general, one session of MICT induces a lower rate of energy expenditure but greater proportion of fat as a substrate with a sustained high release and oxidation of free fatty acids (FFA's). In contrast, one session of HITT is associated with high hormonally driven rates of adipose lipolysis but owing to the relatively brevity of the higher intense bout a high rate of FFA oxidation is not necessary. While the higher intense bouts in HIIT are predominantly anaerobic in nature, increased catecholamines (epinephrine and norepinephrine) and growth hormone stimulate lipolysis, while fatty acid oxidation leading to fat loss is not necessarily stimulated (Keating, Johnson, Mielke, & Coombes, 2017). Furthermore, HIIT has demonstrated a significantly greater contribution of carbohydrate at the expense of fat when compared with MICT during an exercise period. Therefore, HIIT does not appear to augment lipolysis or FFA oxidation, but has greater potential for muscle glycogen depletion in comparance to MICT. The benefit on fat reduction in HIIT can be attributed to an elevation in post-exercise metabolic rate and associated fat expenditure because of the greater magnitude and duration of post-exercise oxygen consumption compared to MICT (LaForgia, Withers, & Gore, 2006; Malatesta, Werlen, Bulfaro, Cheneviere, & Borrani, 2009).

The outcomes on body composition could have been masked by compensatory behavioral changes since caloric intake and physical activity outside the intervention programs were not monitored. Hereby, an increase in energy intake could have been caused by different metabolic and behavioural compensatory responses. Expressing the parameters of body composition as a group mean could have caused the concealment of inter-individual variability in these compensatory responses (King, Hopkins, Caudwell, Stubbs, & Blundell, 2008). Furthermore, a decrease in leisure- time physical activity could be present. As King et al. (2007) stated that increased physical demands of a structured exercise intervention may increase physiological and neurobiological fatigue and psychological demands, associated with a proportional increase in recovery time.

5.2   Reflection on drop out and adherence

The present study demonstrated relatively low dropout rates and high adherence. Once participation in the intervention program was started, only four patients (16%) dropped out during the intervention. Three patients discontinued the HIIT intervention program due to time constraints, unrelated to the nature of the intervention program. One patient was not able to continue the MICT intervention program due to sickness. Furthermore, both intervention groups had an overall adherence of 97.9 ± 3.9 % and 96.5 ± 7.3 % in the MICT and HIIT training groups, respectively.

Despite this finding, studies with high adherence are limited since it has been proven difficult to engage sedentary patients with T2DM in more intense exercise intervention programs (Dunstan et al., 2005). As with other research in the field of physical activity in humans, the participants are volunteers who have a possible positive attitude towards exercise and represent a healthier subpopulation of T2DM patients. Thereby, both the low levels of adverse events and high adherence can be attributed to the research process, by screening for exercise contra-indications and study exclusion criteria, and by providing supervision to every exercise session (Wormgoor, Dalleck, Zinn, & Harris, 2017).

5.3 Reflection on limitations

One of the main limitations of the present study is the small number of participants being included (n=20) in the analyses, thereby limiting statistical power. Second, a selection bias is likely present, since patients were physically active, based on their answers on a standardized questionnaire, which impacts on the external validity and generalizability of this study. Third, blinding of patients, assessors and investigators during assessments and training sessions was not possible due to logistic reasons. This could lead to a possible observer bias.

Furthermore, in statistical analyses, significance level was set at $p<0.05$ for every outcome measure in every statistical analysis. Correction for multiple testing was not carried out. This way, controlling the type I error rate was not accomplished.

Another limitation of the present study is the difference in total energy consumption per exercise session per intervention group during phase four (w13-24). Although the intervention protocol was set up to match MICT and HIIT for total energy expenditure, this was not visible in phase four. The MICT group has a significantly lower energy expenditure during a training session in this last phase which makes adequate comparison of the two intervention programs during this phase not possible.

5.4 Reflection on strengths

In contrast to the limitations, this study demonstrated several strengths. First, at baseline, randomisation was successfully executed which made the intervention groups comparable for all outcome measures. Secondly, due to chronotropic incompetence, the inability of the cardiac muscle to contract faster during physical effort, often demonstrated in T2DM patients (Lauer, Okin, Larson, Evans, & Levy, 1996), exercise intensity in the HIIT program was determined based on Wpeak achieved during CPET instead of HRmax achieved during CPET, as in the MICT group. Moreover, all training sessions and investigations went safely. Except for only one hypoglycemic event, after which training session was ended, all patients finished their training sessions.

5.5   Implications for clinical rehabilitation

Both HIIT and MICT lead to modest improvements in glycemic control and body composition after 24 weeks of intervention in this sample of well controlled T2DM patients. When targeting on improving body composition, MICT should be implemented as a treatment strategy since it evokes more beneficial changes in comparison to HIIT. HIIT has the potential to be used as a treatment modality in T2DM patients but strong supporting research is lacking. First, the multitude of different HIIT protocols used in existing research in T2DM needs to be addressed before implementing HIIT in a primary care. A lacking standardised and consistent approach for prescribing HIIT protocols making it difficult to detect dose–response effects when compared with exercise interventions of other intensities. Most clinical HIIT studies have been performed in a laboratory setting in well controlled T2DM patients. The feasibility, acceptability and efficacy of HIIT in a primary care setting requires investigation in studies with larger sample sizes and greater methodological rigor before it can be accepted as an alternative therapy in the heterogenuous T2DM patient population.

6   Conclusion

From the present findings in this RCT, it can be concluded that HIIT is an endurance-type exercise program with at least equivalent benefits compared to MICT on parameters of glycemic control and body composition. However, MICT was able to show significant improvements in glycemic control after 12 weeks, whereas improvements by HIIT were visible after 24 weeks of intervention. Further, larger and more controlled research in a more heterogeneous population of patients with T2DM is warranted to express a recommendation for which type of exercise intensity should be implemented in primary care.

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8 Appendices

Kenneth VERBOVEN

Antw: Discussie MP2

Aan: annelien loverix

Dag Annelien

Hierbij ons gunstig advies om in te dienen in de eerste zittijd.
Je kan de nodige gehandtekende documenten in bijlage terug vinden, inclusief het COVID addendum.

succes met de indiening.

Vriendelijke groet,
Kenneth & Lisa

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Bekijk meer van annelien loverix

PDF	PDF	PDF
COVID-19adden dumM...ien.pdf	Inventarisatiefor mulier...nd.pdf	Inschrijvingsfor mulier...nd.pdf

INVENTARISATIEFORMULIER WETENSCHAPPELIJKE STAGE DEEL 2

DATUM	INHOUD OVERLEG	HANDTEKENINGEN
23/09 12019	algemene inhoud MP2 + bespreken planning	Promotor: *Kenneth Verboven* Copromotor/Begeleider: Student(e): Student(e):
06/04 12020	bespreken methodiscctie	Promotor: *Kenneth Verboven* Copromotor/Begeleider: Student(e): Student(e):
23/04 12020	statistische analyse « uitvoering in JMP	Promotor: *Kenneth Verboven* Copromotor/Begeleider: Student(e): Student(e):
11/05 12020	bespreken discussie, voetgang « verdere verdeling	Promotor: *Kenneth Verboven* Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
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		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):
		Promotor: Copromotor/Begeleider: Student(e): Student(e):

In te vullen door de promotor(en) en eventuele copromotor aan het einde van MP2:

Naam Student(e): *ANNELIEN LOVERIX* .... Datum: 25/05/2020

Titel Masterproef: The effects of high-intensity interval training versus moderate-intensity continuous training on glycemic control and body composition in adult patients with type 2 diabetes mellitus

1) Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:
   - NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
   - 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
   - 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
   - 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering
   - 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering.
   - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	O	O	O	☒	O	O
Methodologische uitwerking	☒	O	O	O	O	O
Data acquisitie	☒	O	O	O	O	O
Data management	O	O	O	O	☒	O
Dataverwerking/Statistiek	O	O	O	O	☒	O
Rapportage	O	O	O	O	O	☒

2) <u>Niet-bindend advies:</u> Student(e) krijgt toelating/~~geen toelating~~ (schrappen wat niet past) om bovenvermelde Wetenschappelijke stage/masterproef deel 2 te verdedigen in bovenvermelde periode. Deze eventuele toelating houdt geen garantie in dat de student geslaagd is voor dit opleidingsonderdeel.

3) Deze wetenschappelijke stage/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) openbaar verdedigd worden.

4) Deze wetenschappelijke stage/masterproef deel 2 mag wel/~~niet~~ (schrappen wat niet past) opgenomen worden in de bibliotheek en docserver van de UHasselt.

Datum en handtekening
Student(e)

25/05/2020

Datum en handtekening
promotor(en)

Kenneth Verboven

25/05/2020

Datum en handtekening
Co-promotor(en)

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Verklaring op Eer

Ondergetekende, student aan de Universiteit Hasselt (UHasselt), faculteit [Revalidatiewetenschappen] aanvaardt de volgende voorwaarden en bepalingen van deze verklaring:

1. Ik ben ingeschreven als student aan de UHasselt in de opleiding [Revalidatiewetenschappen en kinesitherapie], waarbij ik de kans krijg om [in het kader van mijn opleiding] mee te werken aan onderzoek van de faculteit [Revalidatiewetenschappen] aan de UHasselt. Dit onderzoek wordt beleid door [Dr. Kenneth Verboven] en kadert binnen [het opleidingsonderdeel [Wetenschappelijke stage/ masterproef deel 2]]. Ik zal in het kader van dit onderzoek creaties, schetsen, ontwerpen, prototypes en/of onderzoeksresultaten tot stand brengen in het domein van [Cardiorespiratoire en inwendige aandoeningen] (hierna: "De Onderzoeksresultaten").

2. Bij de creatie van De Onderzoeksresultaten doe ik beroep op de achtergrondkennis, vertrouwelijke informatie[1], universitaire middelen en faciliteiten van UHasselt (hierna: de "Expertise").

3. Ik zal de Expertise, met inbegrip van vertrouwelijke informatie, uitsluitend aanwenden voor het uitvoeren van hogergenoemd onderzoek binnen UHasselt. Ik zal hierbij steeds de toepasselijke regelgeving, in het bijzonder de Algemene Verordening Gegevensbescherming (EU 2016-679), in acht nemen.

4. Ik zal de Expertise (i) voor geen enkele andere doelstelling gebruiken, en (ii) niet zonder voorafgaande schriftelijke toestemming van UHasselt op directe of indirecte wijze publiek maken.

5. Aangezien ik in het kader van mijn onderzoek beroep doe op de Expertise van de UHasselt, draag ik hierbij alle bestaande en toekomstige intellectuele eigendomsrechten op De Onderzoeksresultaten over aan de UHasselt. Deze overdracht omvat alle vormen van intellectuele eigendomsrechten, zoals onder meer – zonder daartoe beperkt te zijn – het auteursrecht, octrooirecht, merkenrecht, modelrecht en knowhow. De overdracht geschiedt in de meest volledige omvang, voor de gehele wereld en voor de gehele beschermingsduur van de betrokken rechten.

6. In zoverre De Onderzoeksresultaten auteursrechtelijk beschermd zijn, omvat bovenstaande overdracht onder meer de volgende exploitatiewijzen, en dit steeds voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding:

   - het recht om De Onderzoeksresultaten vast te (laten) leggen door alle technieken en op alle dragers;
   - het recht om De Onderzoeksresultaten geheel of gedeeltelijk te (laten) reproduceren, openbaar te (laten) maken, uit te (laten) geven, te (laten) exploiteren en te (laten) verspreiden in eender welke vorm, in een onbeperkt aantal exemplaren;

---

[1] Vertrouwelijke informatie betekent alle informatie en data door de UHasselt meegedeeld aan de student voor de uitvoering van deze overeenkomst, inclusief alle persoonsgegevens in de zin van de Algemene Verordening Gegevensbescherming (EU 2016/679), met uitzondering van de informatie die (a) reeds algemeen bekend is; (b) reeds in het bezit was van de student voor de mededeling ervan door de UHasselt; (c) de student verkregen heeft van een derde zonder enige geheimhoudingsplicht; (d) de student onafhankelijk heeft ontwikkeld zonder gebruik te maken van de vertrouwelijke informatie van de UHasselt; (e) wettelijk of als gevolg van een rechterlijke beslissing moet worden bekendgemaakt, op voorwaarde dat de student de UHasselt hiervan schriftelijk en zo snel mogelijk op de hoogte brengt.

1

- het recht om De Onderzoeksresultaten te (laten) verspreiden en mee te (laten) delen aan het publiek door alle technieken met inbegrip van de kabel, de satelliet, het internet en alle vormen van computernetwerken;
- het recht De Onderzoeksresultaten geheel of gedeeltelijk te (laten) bewerken of te (laten) vertalen en het (laten) reproduceren van die bewerkingen of vertalingen;
- het recht De Onderzoeksresultaten te (laten) bewerken of (laten) wijzigen, onder meer door het reproduceren van bepaalde elementen door alle technieken en/of door het wijzigen van bepaalde parameters (zoals de kleuren en de afmetingen).

De overdracht van rechten voor deze exploitatiewijzen heeft ook betrekking op toekomstige onderzoeksresultaten tot stand gekomen tijdens het onderzoek aan UHasselt, eveneens voor de hele beschermingsduur, voor de gehele wereld en zonder vergoeding.

Ik behoud daarbij steeds het recht op naamvermelding als (mede)auteur van de betreffende Onderzoeksresultaten.

7. Ik zal alle onderzoeksdata, ideeën en uitvoeringen neerschrijven in een "laboratory notebook" en deze gegevens niet vrijgeven, tenzij met uitdrukkelijke toestemming van mijn UHasseltbegeleider [Dr. Kenneth Verboven].

8. Na de eindevaluatie van mijn onderzoek aan de UHasselt zal ik alle verkregen vertrouwelijke informatie, materialen, en kopieën daarvan, die nog in mijn bezit zouden zijn, aan UHasselt terugbezorgen.

Gelezen voor akkoord en goedgekeurd,

Naam: ANNELIEN LOVERIX

Adres: DRIESSTRAAT 19 , 3971 HEPPEN

Geboortedatum en –plaats : 12/06/1997 LEUVEN

Datum: 24/05/2020

Handtekening:

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AFSPRAKENNOTA

1. Organisatie

Naam	Universiteit Hasselt/transnationale Universiteit Limburg (Hierna: UHasselt/tUL)
Adres	Martelarenlaan 42 3500 Hasselt
Sociale doelstelling	De UHasselt/tUL is een dynamisch kenniscentrum van onderwijs, onderzoek en dienstverlening.
Werking van de organisatie	**Faculteiten** De UHasselt telt <u>zeven faculteiten</u> die het onderwijs en onderzoek aansturen: o faculteit Architectuur en kunst o faculteit Bedrijfseconomische wetenschappen o faculteit Geneeskunde en levenswetenschappen o faculteit Industriële ingenieurswetenschappen o faculteit Rechten o faculteit Wetenschappen o faculteit Revalidatiewetenschappen Elke faculteit stelt per opleiding een <u>onderwijsmanagementteam</u> (OMT) en een <u>examencommissie</u> samen. **Vakgroepen** Binnen de faculteiten opereren diverse <u>vakgroepen</u>. Zij groeperen alle personeelsleden die onderzoek en onderwijs verrichten binnen eenzelfde discipline. Elke vakgroep bestaat vervolgens uit een of meerdere <u>onderzoeksgroepen</u>. Zij staan in voor de organisatie van het gespecialiseerd onderzoek. Deze klassieke boomstructuur van faculteiten, onderzoeksgroepen en vakgroepen wordt doorkruist door de <u>onderzoeksinstituten</u>. De instituten groeperen onderzoekers uit verschillende onderzoeksgroepen die in bepaalde speerpuntdomeinen onderzoek uitvoeren. Daarbij wordt het volledige onderzoekspectrum afgedekt, van fundamenteel over toegepast onderzoek tot concrete valorisatietoepassingen.
Juridisch statuut	Autonome openbare instelling

Verantwoordelijke van de organisatie, die moet verwittigd worden bij ongevallen.

Naam	Kenneth Verboven
Functie	Doctor- Assistent
Tel. - GSM	+32 (0)472 74 36 48

2. De vrijwilliger: student-onderzoeker

Naam	Annelien Loverix
Correspondentieadres	Driesstraat 19, 3971 Heppen (België)
Tel. - GSM	+32 (0)470 52 39 52

3. Verzekeringen

Waarborgen	De burgerlijke aansprakelijkheid van de organisatie.
Maatschappij	Ethias
Polisnummer	45009018

Waarborgen	Lichamelijke schade die geleden is door vrijwilligers bij ongevallen tijdens de uitvoering van het vrijwilligerswerk of op weg naar- en van de activiteiten.
Maatschappij	Ethias
Polisnummer	45055074

4. Vergoedingen

De organisatie betaalt geen vergoeding aan de vrijwilliger.

5. Aansprakelijkheid

De organisatie is burgerrechtelijk aansprakelijk voor de schade die de vrijwilliger aan derden veroorzaakt bij het verrichten van vrijwilligerswerk.

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Ingeval de vrijwilliger bij het verrichten van het vrijwilligerswerk de organisatie of derden schade berokkent, is hij enkel aansprakelijk voor zijn bedrog en zijn zware schuld.
Voor lichte schuld is hij enkel aansprakelijk als die bij hem eerder gewoonlijk dan toevallig voorkomt.

Opgelet: voor het materiaal dat de vrijwilliger zelf meebrengt, is hij/zij zelf verantwoordelijk.

6. Geheimhoudingsplicht – verwerking persoonsgegevens

De vrijwilliger verleent de UHasselt toestemming om de gegevens die in het kader van zijn/haar inschrijving aan UHasselt werden verzameld, ook te gebruiken voor de uitvoering van deze afsprakennota (de evaluatie van de vrijwilliger alsook het aanmaken van een certificaat). UHasselt zal deze informatie vertrouwelijk behandelen en zal deze vertrouwelijkheid ook bewaken na de beëindiging van het statuut student-onderzoeker. De UHasselt neemt hiertoe alle passende maatregelen en waarborgen om de persoonsgegevens van de vrijwilliger conform de Algemene Verordening Gegevensbescherming (EU 2016/679) te verwerken.

De vrijwilliger verbindt zich ertoe om alle gegevens, documenten, kennis en materiaal, zowel schriftelijk als mondeling ontvangen in de hoedanigheid van student-onderzoeker aan de UHasselt als strikt vertrouwelijk te behandelen, ook indien deze niet als strikt vertrouwelijk werd geïdentificeerd. Indien de vertrouwelijke gegevens van de UHasselt ook persoonsgegevens bevatten dient de stagiair hiertoe steeds de Algemene Verordening Gegevensbescherming (EU 2016/679) na te leven en bij elke verwerking het advies van het intern privacycollege van de UHasselt in te winnen. Hij/zij verbindt zich ertoe om in geen geval deze vertrouwelijke informatie mee te delen aan derden of anderszins openbaar te maken, ook niet na de beëindiging van het statuut student-onderzoeker.

7. Concrete afspraken

Functie van de vrijwilliger

De vrijwilliger zal volgende taak vervullen: Data aqcuisitie in het kader van het val wetenschappelijke stage/ masterproef deel 2
Deze taak omvat volgende activiteiten: gegevens verzamelen en bundelen voor de uitwerking van MP2
De vrijwilliger voert zijn taak uit onder verantwoordelijkheid van de faculteit Revalidatiewetenschappen
De vrijwilliger wordt binnen de faculteit begeleid door Kenneth Verboven
Zijn vaste werkplek voor het uitvoeren van de taak is REVAL, gebouw A

De vrijwilliger zal deze taak op volgende tijdstippen uitvoeren: niet bepaald
- op de volgende dag(en):
    - o maandag
    - o dinsdag
    - o woensdag
    - o donderdag
    - o vrijdag
- het engagement wordt aangegaan voor de periode van 16/09/2019 tot 31/12/2019 (deze periode kan maximaal 1 kalenderjaar zijn en moet liggen tussen 1 januari en 31 december).

Begeleiding

De organisatie engageert zich ertoe de vrijwilliger tijdens deze proefperiode degelijk te begeleiden en te ondersteunen en hem/haar van alle informatie te voorzien opdat de activiteit naar best vermogen kan worden uitgevoerd.
De vrijwilliger voert de taken en activiteiten uit volgens de voorschriften vastgelegd door de faculteit. Hij/zij neemt voldoende voorzorgsmaatregelen in acht, en kan voor bijkomende informatie over de uit te voeren activiteit steeds terecht bij volgende contactpersoon:Kenneth Verboven

De vrijwilliger krijgt waar nodig vooraf een vorming. Het volgen van de vorming indien aangeboden door de organisatie, is verplicht voor de vrijwilliger.

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De vrijwilliger heeft kennis genomen van het 'reglement statuut student-onderzoeker' dat als bijlage aan deze afsprakennota wordt toegevoegd en integraal van toepassing is op de vrijwilliger.

Certificaat

Indien de vrijwilliger zijn opdracht succesvol afrondt, ontvangt hij/zij een certificaat van de UHasselt ondertekend door de decaan van de faculteit waaraan de vrijwilliger zijn opdracht voltooide.

8. Einde van het vrijwilligerswerk.

Zowel de organisatie als de vrijwilliger kunnen afzien van een verdere samenwerking. Dat kan gebeuren:
- bij onderlinge overeenstemming;
- op vraag van de vrijwilliger zelf;
- op verzoek van de organisatie.

Indien de samenwerking op initiatief van de vrijwilliger of de organisatie wordt beëindigd, gebeurt dit bij voorkeur minstens 2 weken op voorhand. Bij ernstige tekortkomingen kan de samenwerking, door de organisatie, onmiddellijk worden beëindigd.

Datum: 28/05/2020

Naam en Handtekening decaan

Naam en Handtekening vrijwilliger

_____

_____

Annelien Loverix

Opgemaakt in 2 exemplaren waarvan 1 voor de faculteit en 1 voor de vrijwilliger.

_____

Reglement betreffende het statuut van student-onderzoeker[1]

Artikel 1. Definities

Voor de toepassing van dit reglement wordt verstaan onder:
student-onderzoeker: een regelmatig ingeschreven bachelor- of masterstudent van de UHasselt/tUL die als vrijwilliger wordt ingeschakeld in onderzoeksprojecten. De opdrachten uitgevoerd als student-onderzoeker kunnen op geen enkele wijze deel uitmaken van het studietraject van de student. De opdrachten kunnen geen ECTS-credits opleveren en zij kunnen geen deel uitmaken van een evaluatie van de student in ket kader van een opleidingsonderdeel. De onderzoeksopdrachten kunnen wel in het verlengde liggen van een opleidingsonderdeel, de bachelor- of masterproef.

Artikel 2. Toepassingsgebied

Enkel bachelor- en masterstudenten van de UHasselt/tUL die voor minstens 90 studiepunten credits hebben behaald in een academische bacheloropleiding komen in aanmerking voor het statuut van student-onderzoeker.

Artikel 3. Selectie en administratieve opvolging

§1 De faculteiten staan in voor de selectie van de student-onderzoekers en schrijven hiervoor een transparante selectieprocedure uit die vooraf aan de studenten kenbaar wordt gemaakt.
§2 De administratieve opvolging van de dossiers gebeurt door de faculteiten.

Artikel 4. Preventieve maatregelen en verzekeringen

§1 De faculteiten voorzien waar nodig in de noodzakelijke voorafgaande vorming van student-onderzoekers. De student is verplicht deze vorming te volgen vooraleer hij/zij kan starten als student-onderzoeker.
§2 Er moet voor de betrokken opdrachten een risicopostenanalyse opgemaakt worden door de faculteiten, analoog aan de risicopostenanalyse voor een stagiair van de UHasselt/tUL. De faculteiten zien er op toe dat de nodige veiligheidsmaatregelen getroffen worden voor aanvang van de opdracht.
§3 De student-onderzoekers worden door de UHasselt verzekerd tegen:
🞐 Burgerlijke aansprakelijkheid

🞐 Lichamelijke ongevallen

en dit ongeacht de plaats waar zij hun opdrachten in het kader van het statuut uitoefenen.

Artikel 5. Vergoeding van geleverde prestaties

§1 De student-onderzoeker kan maximaal 40 kalenderdagen, gerekend binnen één kalenderjaar, worden ingeschakeld binnen dit statuut. De dagen waarop de student-onderzoeker een vorming moet volgen, worden niet meegerekend als gepresteerde dagen.

§2 De student-onderzoeker ontvangt geen vrijwilligersvergoeding voor zijn prestaties. De student kan wel een vergoeding krijgen van de faculteit voor bewezen onkosten. De faculteit en de student maken hier aangaande schriftelijke afspraken.

Artikel 6. Dienstverplaatsingen

De student-onderzoeker mag dienstverplaatsingen maken. De faculteit en de student maken schriftelijke afspraken over de al dan niet vergoeding voor dienstverplaatsingen. De student wordt tijdens de dienstverplaatsingen en op weg van en naar de stageplaats uitsluitend verzekerd door de UHasselt voor lichamelijke ongevallen.

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[1] Zoals goedgekeurd door de Raad van Bestuur van de Universiteit Hasselt op 15 juni 2017.

Artikel 7. Afsprakennota

§1 Er wordt een afsprakennota opgesteld die vooraf wordt ondertekend door de decaan en de student-onderzoeker. Hierin worden de taken van de student-onderzoeker alsook de momenten waarop hij/zij de taken moet uitvoeren zo nauwkeurig mogelijk omschreven.
§2 Aan de afsprakennota wordt een kopie van dit reglement toegevoegd als bijlage.

Artikel 8. Certificaat

Na succesvolle beëindiging van de opdracht van de student-onderzoeker, te beoordelen door de decaan, ontvangt hij een certificaat van de studentenadministratie. De faculteit bezorgt de nodige gegevens aan de studentenadministratie. Het certificaat wordt ondertekend door de decaan van de faculteit waaraan de student-onderzoeker zijn opdracht voltooide.

Artikel 9. Geheimhoudingsplicht

De student-onderzoeker verbindt zich ertoe om alle gegevens, documenten, kennis en materiaal, zowel schriftelijk (inbegrepen elektronisch) als mondeling ontvangen in de hoedanigheid van student-onderzoeker aan de UHasselt, als strikt vertrouwelijk te behandelen, ook indien deze niet als strikt vertrouwelijk werd geïdentificeerd. Hij/zij verbindt zich ertoe om in geen geval deze vertrouwelijke informatie mee te delen aan derden of anderszins openbaar te maken, ook niet na de beëindiging van zijn/haar opdracht binnen dit statuut.

Artikel 10. Intellectuele eigendomsrechten

Indien de student-onderzoeker tijdens de uitvoering van zijn/haar opdrachten creaties tot stand brengt die (kunnen) worden beschermd door intellectuele rechten, deelt hij/zij dit onmiddellijk mee aan de faculteit. Deze intellectuele rechten, met uitzondering van auteursrechten, komen steeds toe aan de UHasselt.

Artikel 11. Geschillenregeling

Indien zich een geschil voordoet tussen de faculteit en de student-onderzoeker met betrekking tot de interpretatie van dit reglement of de uitoefening van de taken, dan kan de ombudspersoon van de opleiding waarbinnen de student-onderzoeker zijn taken uitoefent, bemiddelen. Indien noodzakelijk, beslecht de vicerector Onderwijs het geschil.

Artikel 12. Inwerkingtreding

Dit reglement treedt in werking met ingang van het academiejaar 2017-2018.

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COVID-19 Addendum - Masterproef 2

Naam promotor(en) – Verboven Kenneth, PhD

Naam studenten – Annelien Loverix

1)   Duid aan welk type scenario is gekozen voor deze masterproef:

☐ scenario 1: masterproef bestaat uit een meta-analyse - masterproef liep door zoals voorzien
☒ **scenario 2: masterproef bestaat uit een experiment - masterproef liep door zoals voorzien**
☐ scenario 3: masterproef bestaat uit een experiment - maar een deel van de voorziene data is verzameld
  ☐ 3A: er is voldoende data, maar met aangepaste statische procedures verder gewerkt
  ☐ 3B: er is onvoldoende data, dus gewerkt met een descriptieve analyse van de aanwezige data
☐ scenario 4: masterproef bestaat uit een experiment - maar er kon geen data verzameld worden
  ☐ 4A: er is gewerkt met reeds beschikbare data
  ☐ 4B: er is gewerkt met fictieve data

2)   Geef aan in hoeverre de student(e) onderstaande competenties zelfstandig uitvoerde:

- NVT: De student(e) leverde hierin geen bijdrage, aangezien hij/zij in een reeds lopende studie meewerkte.
- 1: De student(e) was niet zelfstandig en sterk afhankelijk van medestudent(e) of promotor en teamleden bij de uitwerking en uitvoering.
- 2: De student(e) had veel hulp en ondersteuning nodig bij de uitwerking en uitvoering.
- 3: De student(e) was redelijk zelfstandig bij de uitwerking en uitvoering

- 4: De student(e) had weinig tot geringe hulp nodig bij de uitwerking en uitvoering. - 5: De student(e) werkte zeer zelfstandig en had slechts zeer sporadisch hulp en bijsturing nodig van de promotor of zijn team bij de uitwerking en uitvoering.

Competenties	NVT	1	2	3	4	5
Opstelling onderzoeksvraag	☐	☐	☐	☒	☐	☐
Methodologische uitwerking	☒	☐	☐	☐	☐	☐
Data acquisitie	☒	☐	☐	☐	☐	☐
Data management	☐	☐	☐	☐	☒	☐
Dataverwerking/Statistiek	☐	☐	☐	☐	☒	☐
Rapportage	☐	☐	☐	☐	☐	☒

Datum

24/05/2020