UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effects of UATC in addition to a classic moderate-intensity aerobic exercise program on body composition and cardiometabolic risk profile in adults with obesity

Brenda Reynders
Katrien Vilters

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

UHASSELT
KNOWLEDGE IN ACTION

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

2019
2020

UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effects of UATC in addition to a classic moderate-intensity aerobic exercise program on body composition and cardiometabolic risk profile in adults with obesity

Brenda Reynders
Katrien Vilters

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

Acknowledgement

This master's thesis is the pinnacle of our Physiotherapy and Rehabilitation Sciences education. The first part entails a literature study considering information in terms of conducting practical scientific research in the second part of our thesis. Completing this thesis required a lot of work, time and cooperation from various people to whom we would like to express our gratitude. First of all, we would like to thank our promoter, Dr. Kenneth Verboven, for his guidance, feedback and academic support in the realisation of this thesis. Furthermore, we would like to thank the REVAL department of the University of Hasselt, the institute +PresQue (Hasselt) and the clinical laboratory of the Jessa hospital (Hasselt) for the collaboration and the opportunity to conduct this research. Next, special thanks go to the participants for their willingness, motivation and cooperation. Last but not least, we want to thank our fellow students and family for the support and proofreading of our written work.

Akkerstraat 11, 3940 Hechtel (Belgium), June 2020 B.R.

Koningin Astridlaan 44/1, 3500 Hasselt (Belgium), June 2020 K.V.

Research Framework

This master's thesis is situated in the research domain of rehabilitation of internal disorders. The purpose of this research is to investigate the effect of the use of ultrasound-based adipose tissue cavitation (UATC) in addition to a classic aerobic exercise therapy on body composition and cardiometabolic risk profile in adults with obesity.

Previous research shows that fat mass loss plays a major role in augmenting health benefits in adults with obesity (Williamson, Bray, & Ryan, 2015). Hence, further research on non-invasive fat mass reducing interventions remains important. Attention for a new, emerging treatment, namely local UATC, has been increasing over the past years. This technique reduces the overall thickness of the subcutaneous adipose layer by creating small cavities inside the adipocytes' membrane leading to leakage of its content which is then drained by the lymphatic system (Eskici, 2017). This new intervention is currently being used in various beauty institutes, even though only little research on its possible health benefits has been done. To date, its effect on the cardiometabolic risk profile is still unknown.

This duo-thesis is written according to the criteria of a medically oriented scientific peer-reviewed article by two master students physiotherapy and rehabilitation sciences at the University of Hasselt and is supervised by promoter Dr. K. Verboven. Furthermore, a collaboration with the REVAL department of the University of Hasselt, the institute +PresQue and the Jessa Hospital was established.

The students did not contribute to the study design or protocol since the thesis concerned an ongoing research project. Both students assisted promoter Dr. K. Verboven in the recruitment and data acquisition. Data analysis and processing were executed independently by both students under the supervision of Dr. K. Verboven. Academic writing was performed mainly independently by the students. This master's thesis is a product of equal contribution from both students.

References

Eskici, G. (2017). The Effect of Different Methods Used in Regional Slimming and Cellulite Treatment on Regional Weight Loss. *Annals of Medical and Health Sciences Research,* 7(5), 299-304.

Williamson, Donald A., George A. Bray, and Donna H. Ryan. "Is 5% weight loss a satisfactory criterion to define clinically significant weight loss?." *Obesity* 23.12 (2015): 2319. doi: 10.1002/oby.21358

Table of contents

1 Abstract

Background: Ultrasound adipose tissue cavitation (UATC) appears to reduce the overall thickness of the adipose layer. Yet, it is still unknown if UATC could have a significant additional cardiometabolic health benefit considering an exercise-based treatment for individuals with obesity.

Objectives: To investigate the effects of UATC in addition to classic aerobic exercise therapy on body composition and cardiometabolic risk profile in adults with obesity.

Participants: Twenty-six adults with abdominal obesity (age 46 ± 12 years) participated in an aerobic exercise program with either local UATC or sham treatment.

Measurements: Measurements of body composition included body mass index (BMI), waist (WC) and hip circumference (HC), waist-to-hip ratio (WHR), and determinations of android fat mass, whole-body fat mass, and whole-body fat-free mass as assessed by a dual-energy X-ray absorptiometry scan. Parameters of the cardiometabolic risk profile comprise systolic (SBP), diastolic blood pressure (DBP), and a fasting blood sample to determine blood lipid profile, fasting blood glucose (FBG), fasting insulin (FI) and glycated haemoglobin (HbA1c). Secondary outcomes were cardiorespiratory fitness and intervention parameters. Measurements were performed at baseline and after 12 weeks of intervention.

Results: Following the intervention, WC (p_{time} = 0.0478), android fat mass (p_{time} = 0.0430) and whole-body fat mass (p_{time} = 0.0291) decreased significantly in the UATC group, whereas only android fat mass (p_{time} = 0.0343) decreased significantly in the control group. Regarding cardiometabolic risk profile, HbA1c increased significantly (p_{time} = 0.0381) in the control group but not in the UATC group. No significant effects were found for BMI, HC, WHR, whole-body fat-free mass, SBP, DBP, blood lipid profile, FBG and FI after the intervention.

Conclusion: The effect of UATC in addition to classic aerobic exercise therapy concerning body composition and cardiometabolic risk profile in adults with obesity seems limited to significant improvements in body composition only.

Main keywords: obesity, ultrasound, cavitation, exercise, body composition, cardio-metabolic

2 Introduction

The prevalence of obesity has been increasing over the past years, making it a worldwide major health concern (Engin, 2017). Since 1975, the prevalence has nearly tripled (World Health Organization [WHO], 2018). In 2016, about 15% of all women and 11% of all men turned out to be obese (WHO, 2018). If current trends continue, the worldwide prevalence will rise to 20% by 2030 (Kelly, Yang, Chen, Reynolds, & He, 2008).

Most common descriptions of this chronic, multi-component disease are (1) general obesity, based on a body mass index (BMI) of at least 30 kg/m² and (2) abdominal obesity, expressed as waist circumference (WC) of >102 cm for men and >88 cm for women (MacDonald, 2003; Hruby & Hu, 2014). An important correlation was found between a higher BMI or WC and an increased risk of obesity-associated complications and comorbidities, such as hypertension, type 2 diabetes mellitus, dyslipidemia, cardiovascular diseases, certain types of cancers and metabolic syndrome (Jarolimova, Tagoni, & Stern, 2013; Chowdhury, Adnan, & Hassan, 2018). These comorbidities and the higher mortality rate indicate the importance of preventing and treating obesity, with proper education and recommendation of multidisciplinary weight loss programs as key factors (Jarolimova et al., 2013). A combination of physical activity with caloric restriction and behavior management is indicated to manage body weight and prevent weight (re)gain (American College of Sports Medicine [ACSM], 2014). The guidelines of the ACSM (2014), which recommend 150-250 minutes/week of moderate-intensity aerobic exercise for modest weight reduction in overweight and obese adults, are most commonly used and are in line with the recommendations for general health from the WHO (2010) (Cheema et al., 2015; Keating et al., 2017). According to Williamson, Bray and Ryan, (2015), a weight loss of at least 5% is needed to achieve a clinically important difference in metabolic parameters, such as glycemic control, blood pressure and serum lipid levels.

More and more aesthetic interventions are being used to locally reduce body fat, in which liposuction is the standard technique used for this reduction (Coleman, K.M., Coleman, W.P., & Benchetrit, 2009). However, liposuction includes a higher risk for complications such as ectopic fat accumulation and infections (Mohammed, Cohen, Reeds, Young & Klein, 2008; Alam, 2019). Hence, patients now prefer non-invasive methods (Coleman et al., 2009). A new emerging, non-surgical technique is local ultrasound adipose tissue cavitation (UATC), which is applied externally and delivers energy through the skin to the superficial

subcutaneous fat layer (Eldesoky, Abutaleb, & Mousa, 2015). The kinetic and vibrant characteristics of this energy increase tissue temperature and create small, temporary pores in the adipocytes' membrane, without causing tissue damage. This leads to leakage of its content which is then drained by the lymphatic system (Eskici, 2017). Consequently, the overall thickness of the treated adipose layer reduces, but viable adipocytes are preserved which reduces the risk of ectopic fat accumulation (Eldesoky et al., 2015). To date, the effects of UATC on the cardiometabolic risk profile have not been investigated. Hence, it is still unknown if UATC could have a significant additional benefit considering an exercise-based treatment of obesity.

The purpose of this randomized controlled trial is to investigate the effects of UATC in addition to classic aerobic exercise therapy on (1) body composition and (2) cardiometabolic risk profile in adults with obesity. We hypothesize significant improvements in the body composition and cardiometabolic risk profile in both groups, receiving either a UATC or sham treatment in combination with an aerobic exercise program. A greater effect is expected in the cavitation group, indicating an additional benefit of UATC on a classic exercise program in adults with obesity.

3 Method

3.1 Research question

The following research question was formulated: “What are the effects of UATC in addition to a classic moderate-intensity aerobic exercise program on (1) body composition and (2) cardiometabolic risk profile in adults with obesity?”

3.2 Participants

3.2.1 Recruitment

The participants were recruited over 18 months in the central region of Limburg (Belgium) through flyers, distributed by the REVAL department of the University of Hasselt and partner +PresQue.

3.2.2 Selection criteria

Participants were included according to the following criteria: (1) men and women aged 18-65 years, (2) abdominal obesity (WC of >102 cm for men and >88 cm for women) and (3) willing to undergo an interventional treatment. Participants were excluded in presence of following criteria due to an unknown risk for UATC treatment: (1) diabetes or glucose-lowering medication, (2) hypertension (blood pressure > 140/90 mmHg) or anti-hypertensive treatment, (3) cardiovascular or respiratory diseases, (4) venous thrombosis or coagulation diseases, (5) kidney, liver or thyroid diseases, (6) chronic inflammation (e.g. arthritis, dermatitis), (7) malignant diseases, (8) osteoporosis and (9) participants on medication. Due to radiation during the use of the Dual Energy X-ray Absorptiometry (DEXA) scanner, (11) pregnant women were also excluded. Furthermore, participants having (12) a pacemaker or defibrillator, (13) brain or nerve disorders, (14) epilepsy, (15) a copper spiral or (16) a recent (<6 months) bone fracture or metal prosthesis were excluded. Finally, participants who (17) participated in a training program or (18) did not maintain a stable weight in the last six months prior to the intervention were excluded. The presence of these health problems was questioned during an intake meeting using a questionnaire.

3.3 Study design

A double-blind randomized controlled trial was set up to investigate the research question. After careful explanation of the study by the researchers, all participants signed an informed consent form prior to the study and were randomized to either the intervention or the

control group using closed envelopes. The intervention group (UATC group) received local UATC and followed a continuous moderate-intensity aerobic exercise program. The control group received a placebo procedure (sham treatment) and followed the same continuous moderate-intensity exercise program. The use of a sham treatment ensures that the participants were blinded for the UATC intervention. Assessors were blinded to group allocation and all measurements of the participants.

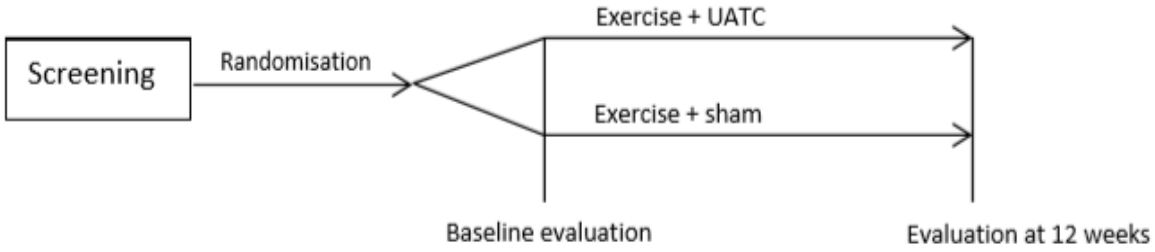


*Figure 1. S*tudy design

3.4 Intervention

The UATC group received UATC in the abdominal region because abdominal obesity has been proven to be more related to metabolic disorders than general obesity (Goktas, Ersoy, Ercan, & Can, 2019). Sessions took place twice a week with at least 48 hours in between. Each session lasted 42 minutes and was administered with ultrasonic energy of 70% of maximum (2 Watt), built up to 100% at the end of the intervention. A vibration frequency of 28-32 Hz was set and administered in cycles of ten seconds followed by a rest period of one second (QB LIPO IIL, QSence, Belgium). In the control group, a sham was applied in which similar procedures were performed but no actual ultrasound treatment was applied. Each day with UATC or sham treatment, participants were asked to drink two liters of water to promote the drainage of the mobilized adipocyte content. All UATC sessions were performed by an experienced and qualified nurse in +Presque in Hasselt, Belgium.

Both UATC and sham sessions were followed by continuous moderate-intensity aerobic exercise training on the same day over a 12-week period. Training sessions consisted of 30 minutes cycling on a stationary bike (Technogym) and 30 minutes of treadmill walking (Technogym). No warming up or cooling down was provided since each 30-minute exercise was continuously performed at the same intensity. Heart rate was monitored during exercise using a Polar Heart Rate monitor to regulate a moderate training intensity of 65% VO_2peak.

All training sessions were individually supervised and performed at the REVAL rehabilitation research center (Hasselt University).

3.5 Procedure

Primary outcome measures were BMI, WC, waist-to-hip ratio (WHR), android fat mass (FM), whole-body FM, whole-body fat-free mass (FFM), systolic (SBP) and diastolic blood pressure (DBP), fasting blood glucose (FBG), fasting insulin (FI), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG) and glycated haemoglobin (HbA1c). Secondary outcome measures were cardiorespiratory fitness and intervention parameters including caloric expenditure (CE) and Borg ratings of perceived exertion (RPE). Measurements of primary outcomes and cardiorespiratory fitness were obtained at baseline and after 12 weeks by the same assessor. Diet and physical activity are the main confounders of this trial. Therefore, participants were asked to maintain their habitual diet and daily physical activity level during the course of the study. The night before each test day, a fasting period (> 10 hours), without limitation of water consumption, was demanded.

3.5.1 Primary parameters

3.5.1.1 Body composition

Body mass index

BMI was calculated based on body weight and height (weight (kg)/ height² (m)). Weight (kg) was measured to the nearest 0.1 kg with a Polar weighing scale. Height (cm) was measured to the nearest 0.5 cm with the participants standing in erect position against a stadiometer. Both measurements were performed barefoot.

Waist and hip circumference

WC was measured horizontal between the inferior border of the ribs and the superior border of the iliac crest and at the end of a normal expiration on bare skin (WHO, 2008). HC was measured horizontal at the widest portion of the buttocks with the participant standing (WHO, 2008). The WHR was calculated by dividing WC by HC.

Results of DEXA scan

Whole-body FM, whole-body FFM and android FM had been determined using a DEXA scan (Hologic Series Delphi-A Fan Beam X-ray Bone Densitometer).

3.5.1.2 Cardiometabolic risk profile

Systolic (SBP) and diastolic blood pressure (DBP)

Following a seven-minute rest period, blood pressure was measured using an automatic blood pressure monitor (Omron). A mean value of three measurements performed at the brachial artery was calculated.

Fasting blood sample

After an overnight fasting period (> 10 hours) a fasting blood sample was taken and sent to a clinical, accredited laboratory (Jessa Hospital, Hasselt) to determine FBG, FI, TC, HDL, LDL, TG (Roche Cobas 8000; Roche Diagnostics International Ltd, Rotkreuz, Switzerland) and HbA1c (Menarini HA-8180 HbA1c autoanalyzer; Menarini Diagnostics, Diegem, Belgium).

3.5.2 Secondary parameters

3.5.2.1 Cardiorespiratory fitness

A cardiopulmonary exercise test (CPET) had been completed on a stationary bike to determine maximal oxygen uptake (VO_2peak) and maximal heart rate (HRmax). The baseline measures were used to determine an individual target heart rate according to the moderate exercise intensity. The testing procedure consisted of cycling on a stationary bike until exhaustion, using an incremental protocol. After a short warming-up, the test was started with a power of 40 Watt (W) and increased with 20 W each minute. Participants had to cycle with a cadence of 70 revolutions per minute. The VO_2 was continuously measured using spirometry (MetaMax). The VO_2peak is defined as the highest observed value and was corrected for whole-body FFM. Heart rate (HR) was continuously monitored using a 12-lead ECG. HRmax is defined as the highest observed value.

The CPET was stopped when following situations occurred: (1) not being able to maintain the cadence, (2) typical chest discomfort, (3) severe arrhythmias, (4) ST-segment depression of >1mm, (5) chest pain suggestive of ischemia, (6) dizziness or (7) faintness.

3.5.2.2 Intervention parameters

Borg ratings of perceived exertion

After completion of each exercise session, RPE was surveyed using a 6 to 20 Borg scale.

Caloric expenditure

The values of the caloric expenditure were displayed on the treadmill and ergometer and added together to obtain the total CE of each session.

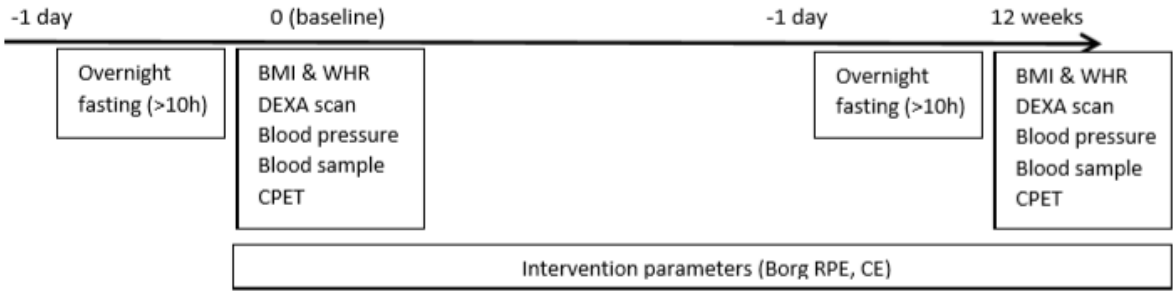


Figure 2. Timeline of measurements

3.6 Data analysis

All statistical analyses were carried out in JMP Pro 14.2, using a significance level of 0.05. The determination of the statistical method is shown in Figure 3.

3.6.1 Baseline

The normality of residuals was tested with the Shapiro-Wilk test while the variance of these residuals was tested using the Brown-Forsythe test. In case both conditions were met, a two-sample t-test was performed to determine between-group differences at baseline since this test uses average values, providing a better representation than the Rank-sum test, which is based on medians. When data were not normally distributed but had equal variances, a Rank-sum test was used, and when data were normally distributed with non-equal variances, Welch's t-test was performed. Data for FI and FBG were based on 17 instead of 22 participants, requiring a Wilcoxon Rank-sum exact test to determine between-group differences for these parameters.

3.6.2 Post-intervention

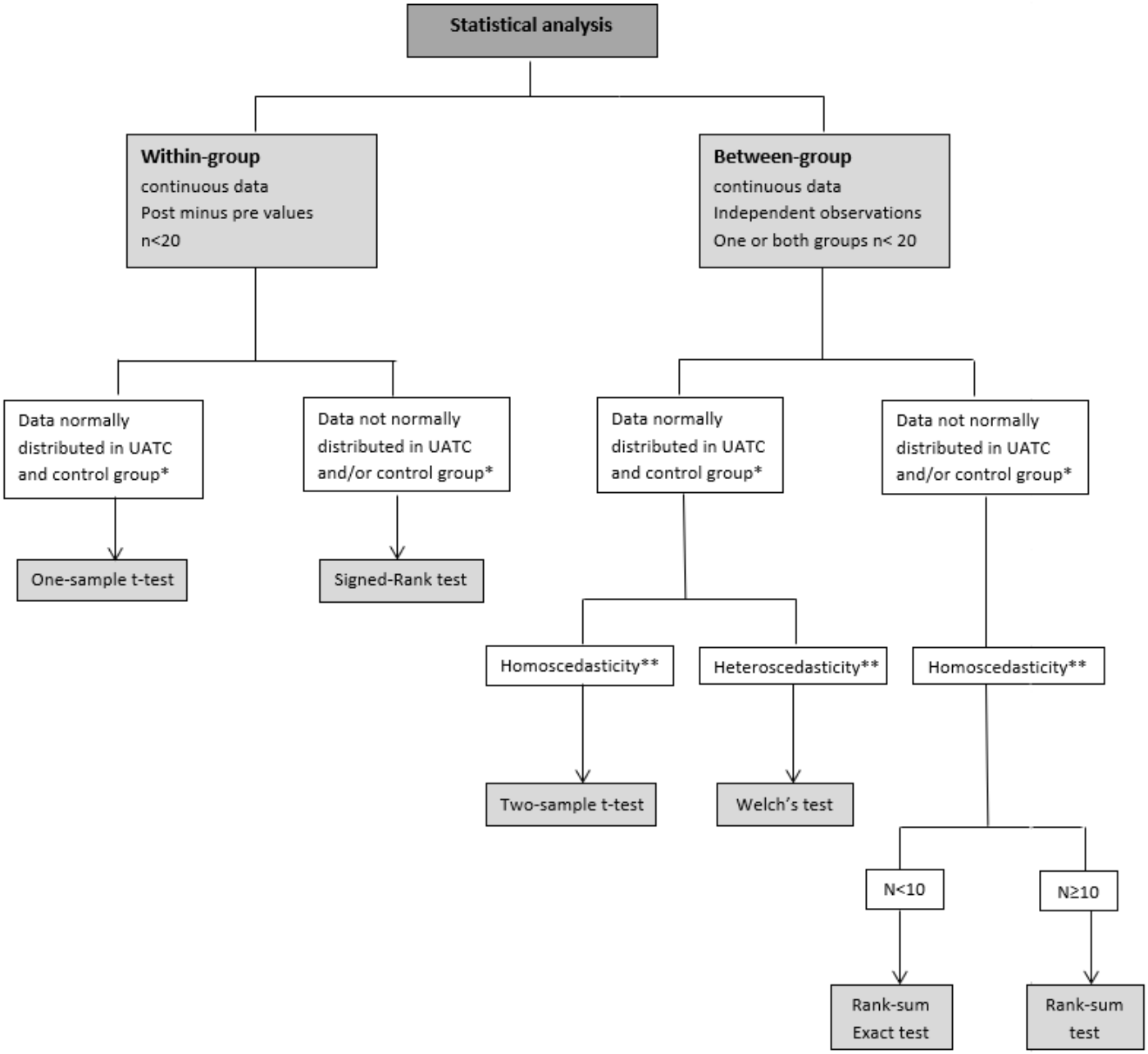
3.6.2.1 Primary parameters and cardiorespiratory fitness

Variance and normality of residuals of the differences between both time points (post minus pre values) were analysed. For parameters of which both conditions were met, only a one-sample t-test was performed since this test uses average values, providing a better representation than the Signed-rank test, which is based on medians. A Signed-rank test was

only used when data were not normally distributed. The statistical method comparing these differences between both groups was similar to that of the baseline.

3.6.2.2 Intervention parameters

To determine whether the intensity of the aerobic exercise therapy was equivalent in both groups, the between-group differences of the intervention parameters were analysed. Based on the variance and normality of the residuals, the most appropriate statistical test was determined by the same method as described for the baseline analysis.



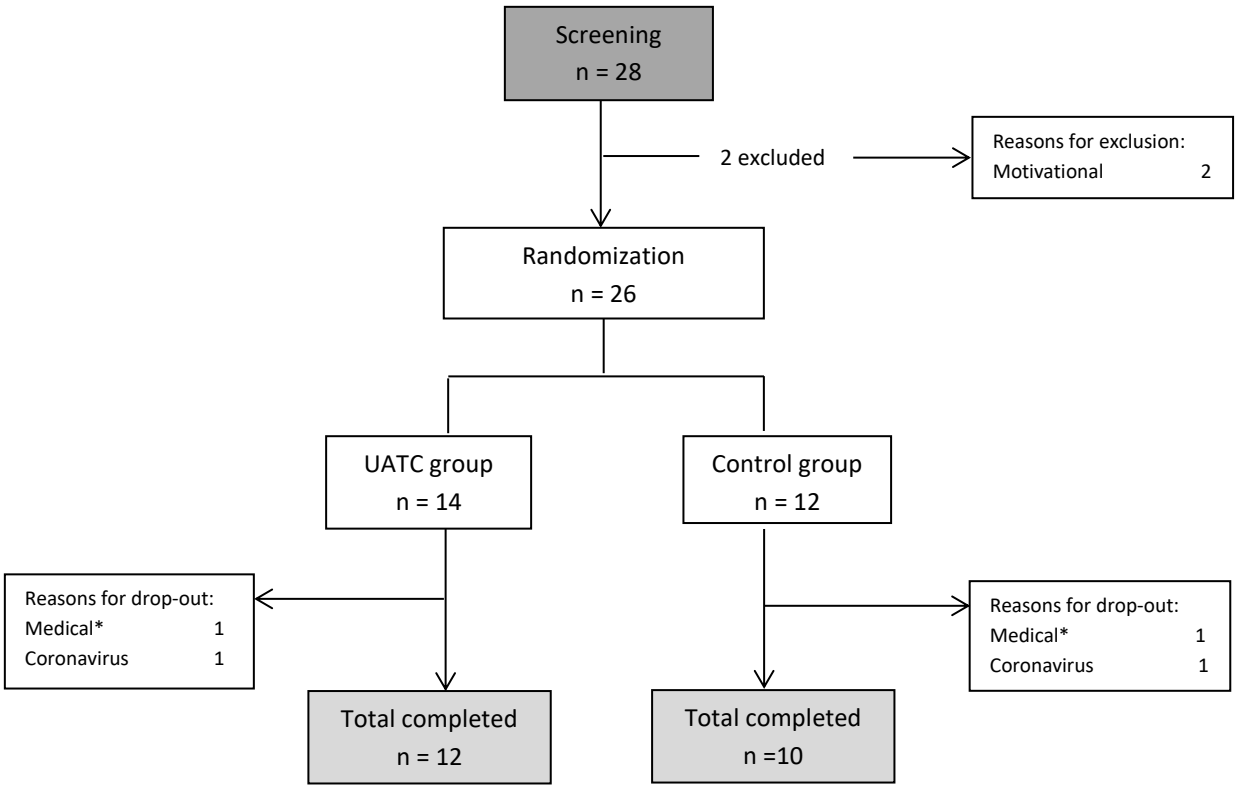
** Based on the Brown-Forsythe test

Figure 3. Flowchart of statistical analysis

4 Results

4.1 Participants

A participant flowchart is displayed in Figure 4. Two drop-outs occurred prior to the intervention due to lack of motivation. Twenty-six participants were randomized to either the UATC or the control group. During the intervention, four more dropouts occurred. Two (1 UATC, 1 control) stopped due to medical reasons not related to the intervention and the other two (1 UATC, 1 control) were unable to complete the intervention due to the circumstances concerning the Coronavirus. Eventually, eight men and 14 women aged 46 ± 12 years with abdominal obesity (WC: 108.05 ± 9.08 cm) completed the intervention. No significant differences in characteristics were observed between both groups at baseline (Table 1).



* not related to the intervention

Figure 4. Flowchart of participants

Table 1
Results - baseline characteristics by group

Characteristic		**UATC** (Mean ± SD)	**Control** (Mean ± SD)	**P1** (P-value) Two-sample t-test	**P2** (P-value) Rank-sum test	**P3** (P-value) Welch's test
Participants		12	10			
Gender	Male	5	3			
	Female	7	7			
Mean age (years)		45 ± 12	47 ± 12	0.7770	/	/
Weight (kg)		92.8 ± 13.6	96.4 ± 13.1	0.5369	/	/
Height (m)		171.5 ± 9.0	171.0 ± 9.5	0.9328	/	/
BMI (kg/m²)		31.6 ± 4.0	32.9 ± 3.6	/	0.3390	/
WC (cm)		107.9 ± 8.7	108.3 ± 10.0	0.9259	/	/
HC (cm)		108.3 ± 7.2	108.1 ± 9.8	/	0.7916	/
WHR		1.0 ± 0.1	1.0 ± 0.1	/	0.3389	/
HRrest (bpm)		60 ± 6	60 ± 7	0.9981	/	/
SBP (mmHg)		127 ± 10	125 ± 16	0.7647	/	/
DBP (mmHg)		80 ± 5	81 ± 19	/	/	0.9474
Android FM (kg)		3.23 ± 0.80	3.40 ± 0.74	0.6220	/	/
Whole-body FM (kg)		33.84 ± 7.98	37.39 ± 7.53	0.2990	/	/
Whole-body FFM (kg)		52.68 ± 9.97	52.33 ± 9.72	0.9361	/	/
HDL (mg/dl)		46.4 ± 10.7	53.2 ± 14.6	/	0.3214	/
LDL (mg/dl)		105.2 ± 31.4	110.6 ± 33.1	0.6973	/	/
TC (mg/dl)		177.0 ± 36.5	185.5 ± 31.1	0.5681	/	/
TG (mg/dl)		125.8 ± 44.4	109.7 ± 29.9	0.3399	/	/
FBG (mg/dl)**		96.4 ± 6.5	98.3 ± 9.5	0.6318	/	/
FI (pmol/l)**		105.5 ± 70.4	84.4 ± 20.9	/	0.8125	/
HbA1c (mmol/mol)		36 ± 3	35 ± 2	/	0.5691	/

UATC: Ultrasound adipose tissue cavitation; BMI: body mass index; WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio; HRrest: resting heartrate; FM: fat mass; FFM: fat-free mass; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglycerides; FBG: fasting blood glucose; FI: fasting insulin; HbA1c: glycated haemoglobin
* Significant < 0.05
**Based on 17 instead of 22 participants: Wilcoxon Exact test

4.2 Effect of UATC on primary outcomes

The results of the primary outcomes are summarized in Table 2.

4.2.1 Body composition

After 12 weeks of aerobic exercise combined with UATC, WC significantly decreased with -1.7 ± 2.7 cm (p = 0.0478), whereas the decrease in the control group did not reach statistical significance (-1.6 ± 2.9 cm; p = 0.1186). Further, there was a significant decrease in android FM (-0.17 ± 0.25 kg; p = 0.0430) and whole-body FM (-1.37 ± 1.89 kg; p = 0.0291) in the UATC group, whereas only a significant decrease in android FM (-0.20 ± 0.25 kg; p = 0.0343) was found in the control group. The results of whole-body FFM show an increase over time in both the UATC and the control group, but did not reach statistical significance (respectively

+0.52 ± 1.01 kg; +0.46 ± 1.39 kg; p = 0.1063; p = 0.3194). There were no significant changes in BMI or WHR for any groups.

4.2.2 Cardiometabolic risk profile

After the combined exercise and sham intervention, a significant increase was found for HbA1c (+2 ± 2 mmol/mol; p = 0.0381), whereas it remained stable in the UATC group (0 ± 3 mmol/mol; p = 0.9191). In addition, a trend towards significance is observed for the decrease in triglycerides (-15.3 ± 28.4 mg/dl; p = 0.0881) in the UATC group. Further, no other effects for cardiometabolic parameters were found.

4.3 Effect of UATC on secondary outcome measures

4.3.1 Cardiorespiratory fitness

Power generation significantly increased in the UATC group compared to baseline (+12 ± 16 W; p = 0.0271), whereas the increase in the control group did not reach statistical significance (+10 ± 29 W; p = 0.2987). There were no significant changes in VO_2peak, HRmax and RER after the intervention. However, a trend towards significance was observed for the decrease in RER in the control group (-0.06 ± 0.09; p = 0.0578) (Table 3).

4.3.2 Intervention parameters

Within both groups, CE initially increased remarkably between timeframes one and two, whereas a negligible difference was observed between timeframes two and three. Additionally, the values of Borg RPE decreased over time with one point in both groups. HR remained quite stable throughout the study course since intensity was adjusted, through speed, inclination or resistance, to reach the set goal HR during exercise. Finally, the adherence was generally excellent with means of 23/24 and 22/24 in the UATC and control group, respectively. No significant between-group differences were found in intervention parameters (Table 4).

Table 2
Results – primary outcomes

Parameter	**Group**	**T1** (Mean ± SD)	**T2** (Mean ± SD)	**T2-T1** (Mean ± SD)	**T2-T1 within-group** (P-value)		**T2-T1 between-group** (P-value)	
					One-sample t-test	Signed-rank test	Two-sample t-test	Rank-sum test
Weight (kg)	UATC	92.8 ± 13.6	92.7 ± 13.1	-0.1 ± 2.0	0.8173	/	0.3301	/
	Control	96.4 ± 13.1	95.4 ± 11.8	-1.0 ± 2.3	0.1839	/		
BMI (kg/m^2)	UATC	31.6 ± 4.0	31.5 ± 3.8	-0.0 ± 0.7	0.8166	/	0.3970	/
	Control	32.9 ± 3.6	32.6 ± 3.6	-0.3 ± 0.7	0.2227	/		
WC (cm)	UATC	107.9 ± 8.7	106.2 ± 8.3	-1.7 ± 2.7	**0.0478** *	/	0.9285	/
	Control	108.3 ± 10.0	106.7 ± 9.9	-1.6 ± 2.9	0.1186	/		
HC (cm)	UATC	108.3 ± 7.2	107.8 ± 7.4	-0.5 ± 4.7	0.7415	/	0.3120	/
	Control	108.1 ± 9.8	109.5 ± 8.7	+1.4 ± 3.5	0.2330	/		
WHR	UATC	1.00 ± 0.05	0.98 ± 0.03	-0.01 ± 0.04	/	0.7334	/	0.0698
	Control	1.00 ± 0.07	0.97 ± 0.04	-0.03 ± 0.04	/	0.0645		
Android FM (kg)	UATC	3.23 ± 0.80	3.07 ± 0.65	-0.17 ± 0.25	**0.0430** *	/	0.7757	/
	Control	3.40 ± 0.74	3.20 ± 0.77	-0.20 ± 0.25	**0.0343** *	/		
Whole-body FM (kg)	UATC	33.84 ± 7.98	32.47 ± 7.30	-1.37 ± 1.89	**0.0291** *	/	0.8923	/
	Control	37.39 ± 7.53	36.14 ± 7.39	-1.25 ± 2.27	0.1166	/		
Whole-body FFM (kg)	UATC	52.68 ± 9.97	53.19 ± 9.80	+0.52 ± 1.01	0.1063	/	0.9200	/
	Control	52.33 ± 9.72	52.80 ± 10.28	+0.46 ± 1.39	0.3194	/		
HRrest (bpm)	UATC	60 ± 6	58 ± 5	-2 ± 6	0.1944	/	0.1207	/
	Control	60 ± 7	61 ± 9	+1 ± 4	0.3729	/		

SBP (mmHg)	UATC	127 ± 10	127 ± 12	0 ± 8	0.8742	/	/	0.9212
	Control	125 ± 16	120 ± 18	-5 ± 18	/	0.9414		
DBP (mmHg)	UATC	80 ± 5	78 ± 5	-2 ± 5	0.1459	/	/	0.4679
	Control	81 ± 19	77 ± 8	-4 ± 16	/	0.7891		
HDL (mg/dl)	UATC	46.4 ± 10.7	47.9 ± 8.6	+1.5 ± 4.6	0.2790	/	0.1790	/
	Control	53.2 ± 14.6	52.3 ± 13.9	-0.9 ± 3.2	0.4036	/		
LDL (mg/dl)	UATC	105.2 ± 31.4	108.8 ± 35.3	+3.7 ± 25.4	0.6263	/	0.4858	/
	Control	110.6 ± 33.1	107.1 ± 42.9	-3.5 ± 21.2	0.6140	/		
TC (mg/dl)	UATC	177.0 ± 36.5	176.7 ± 39.9	-0.3 ± 24.6	0.9634	/	0.5529	/
	Control	185.5 ± 31.1	179.9 ± 35.1	-5.8 ± 15.9	0.2788	/		
TG (mg/dl)	UATC	125.8 ± 44.4	110.5 ± 40.3	-15.3 ± 28.4	0.0881	/	0.1920	/
	Control	109.7 ± 29.9	117.0 ± 43.6	+7.3 ± 49.2	0.6501	/		
FBG (mg/dl)**	UATC	96.4 ± 6.5	98.2 ± 7.7	+1.8 ± 7.2	0.4472	/	0.1961	/
	Control	98.3 ± 9.5	93.1 ± 14.1	-5.1 ± 13.9	0.3665	/		
FI (pmol/l)**	UATC	105.5 ± 70.4	101.7 ± 73.4	-3.8 ± 40.8	0.7748	/	/	0.8451
	Control	84.4 ± 20.9	87.1 ± 46.0	+2.7 ± 38.5	/	0.8125		
HbA1c (mmol/mol)	UATC	36 ± 3	36 ± 3	0 ± 3	0.9191	/	0.1527	/
	Control	35 ± 2	37 ± 3	+2 ± 2	**0.0381** *	/		

T1: timepoint 1 (baseline); T2: timepoint 2 (12 weeks); UATC: ultrasound adipose tissue cavitation; BMI: body mass index; WC: waist circumference; HC: hip circumference; WHR: waist-to-hip ratio; HRrest: resting heartrate; FM: fat mass; FFM: fat-free mass; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; LDL: low-density lipoprotein, TC: total cholesterol; TG: triglycerides; FBG: fasting blood glucose; FI: fasting insulin; HbA1c: glycated haemoglobin

* Significant < 0.05

**Based on 17 instead of 22 participants

Table 3
Results – secondary outcomes: cardiorespiratory fitness

Parameter	**Group**	**T1** (Mean ± SD)	**T2** (Mean ± SD)	**T2-T1** (Mean ± SD)	**T2-T1 within-group** (P-value)		**T2-T1 between-group** (P-value)	
					One-sample t-test	Signed-rank test	Two-sample t-test	Rank-sum test
VO_2peak (l/min)	UATC	2.51 ± 0.62	2.57 ± 0.68	+0.06 ± 0.30	0.4731	/	0.4510	/
	Control	2.33 ± 0.97	2.51 ± 0.84	+0.18 ± 0.41	0.1998	/		
VO_2peak (ml/kgFFM/ min)	UATC	43 ± 15	49 ± 10	+6 ± 19	/	0.4697	/	1.0000
	Control	43 ± 11	47 ± 9	+4 ± 9	0.2374	/		
HRmax (bpm)	UATC	163 ± 16	164 ± 17	+1 ± 10	0.7590	/	0.8131	/
	Control	161 ± 23	164 ± 24	+2 ± 13	0.6240	/		
RER	UATC	1.17 ± 0.09	1.17 ± 0.14	0.00 ± 0.12	0.9274	/	0.1765	/
	Control	1.21 ± 0.09	1.14 ± 0.10	-0.06 ± 0.09	0.0578	/		
Power (W)	UATC	208 ± 37	220 ± 37	+12 ± 16	**0.0271***	/	0.8647	/
	Control	208 ± 55	218 ± 71	+10 ± 29	0.2987	/		

T1: timepoint 1 (baseline); T2: timepoint 2 (12 weeks); UATC: ultrasound adipose tissue cavitation; VO2peak: maximal oxygen uptake; HRmax: maximal heart rate; RER: respiratory exchange ratio

* Significant < 0.05

Table 4
Results – secondary outcomes: intervention parameters

Characteristic	**UATC** (Mean ± SD)	**Control** (Mean ± SD)	**P1** (P-value) Two-sample t-test	**P2** (P-value) Rank-sum test
CE1 (kcal)	354 ± 59	366 ± 77	0.6697	/
CE2 (kcal)	391 ± 67	389 ± 87	/	0.6209
CE3 (kcal)	390 ± 73	386 ± 94	/	0.7169
Borg RPE1	13 ± 1	13 ± 1	0.9208	/
Borg RPE2	13 ± 2	12 ± 1	/	0.3553
Borg RPE3	12 ± 2	12 ± 1	0.9006	/
HR1 walk (bpm)	118 ± 12	123 ± 14	0.3842	/
HR2 walk (bpm)	119 ± 8	126 ± 17	0.2211	/
HR3 walk (bpm)	122 ± 9	125 ± 15	0.6214	/
HR1 cycle (bpm)	122 ± 11	125 ± 11	0.6044	/
HR2 cycle (bpm)	125 ± 8	126 ± 15	0.9508	/
HR3 cycle (bpm)	124 ± 11	123 ± 16	0.7686	/
Goal HR walk (bpm)	137 ± 11	135 ± 15	0.7370	/
Goal HR cycle (bpm)	134 ± 12	133 ± 16	0.8087	/
Adherence	23/24	22/24		

CE: caloric expenditure; HR: heart rate; 1: mean value of sessions 1-8; 2: mean value of sessions 9-16;
3: mean value of sessions 17-24
* Significant < 0.05

5 Discussion

The effect of local UATC on the thickness of the abdominal adipose layer appears to be significant and is thought to positively influence cardiometabolic parameters (Eskici, 2017; Jarolimova et al., 2013). However, the results of the current study reveal only a limited additional effect of UATC on a classic aerobic exercise program. The most important findings of the current study are significant improvements in WC, android FM and whole-body FM considering body composition in the UATC group. Additionally, android FM also improved significantly in the control group. Contrary to our hypothesis, no significant changes for any cardiometabolic parameters, as well as no significant between-group differences were found.

We expected to see more beneficial effects for body composition in both groups, since previous studies have already shown significant improvements in body composition following a 12-week exercise program similar to the one currently implemented (Schjerve et al., 2008; Taghian, Zolfaghari, & Hedayati, 2014). Further, we also expected a greater change in the cardiometabolic risk profile since an indirect influence of improvements in body composition, following aerobic exercise therapy, on cardiometabolic parameters has already been proven (Jarolimova et al., 2013). According to Williamson et al. (2015), a weight loss of at least 5% is required to achieve a clinically important difference in cardiometabolic parameters. Possibly, the duration of the intervention is too short to achieve 5% weight loss and thus a change in cardiometabolic parameters. The current results show no weight loss in any group and only a small decrease in whole-body FM. A possible reason could be the amount of exercise per week in the current intervention, as the ACSM guidelines recommend 150-250 minutes per week of moderate-intensity aerobic exercise for modest weight reduction in overweight and obese adults (Keating et al., 2017). Since participants received two sessions of one hour each week, the total amount of 120 minutes per week may be too low. An additional reason could be the dietary habits of the participants, as the number of expended calories could have been compensated by high-calorie meals. In this regard, the inclusion of a low-calorie diet could have added value to the current results.

Based on the study of Eskici (2017), UATC is stated to be an effective method for body contouring in adults with obesity through the reduction of subcutaneous fat thickness within the treated area, based on a significant reduction in WC. Moreover, the number of UATC

sessions turned out to be a determining factor (Eskici, 2017). Additionally, Akram, Abotaleb, Marry and Abdeen (2019) observed a significant reduction in WC ($p < 0.001$) after receiving two UATC sessions per week for one month. In line with these studies, the current study has found a significant result for WC in the UATC group over time ($p = 0.0478$).

Despite this significant effect on WC, no significant improvement of WHR was found in the current study. Contrary to this result, Maher, Jermeen, Manar and Amira (2019) observed a highly significant improvement of WHR ($p<0.0001$), as well as for BMI ($p<0.0001$) in both the control and UATC group. These contradictory findings to the current study could be explained by differences in the research population and treatment. The research population consisted only of prediabetic women with obesity receiving a combination of a dietary and aerobic exercise intervention for 12 weeks, whether or not in combination with a six-week UATC treatment. This additional dietary intervention, as well as the higher training frequency of three sessions per week, could explain the significant decrease of WHR and BMI in contrast to the current study. Additionally, the low power of the current study, based on a power calculation conducted last year using WC, could also influence the results of the WHR, given the direct link between WC and WHR. Further, Akram et al. (2019) observed a significant reduction ($p<0.001$) of BMI after a one-month treatment consisting of only cavitation. Fonseca et al. (2018), on the other hand, found no significant reduction of BMI nor weight in neither intervention groups ($p = 0.83$ for both). One group received six sessions of UATC once a week whereas the other group received ten sessions twice a week. In the current study, insignificant effects of UATC on BMI and weight were found as well. However, this insignificance could be due to the addition of the exercise program to the UATC treatment, since this has led to an increase in the results of the whole-body FFM in both groups. This increase in muscle mass could have compensated any weight loss caused by a reduction in fat mass.

No research has been published concerning the effect of UATC on outcome measures obtained by the use of a DEXA scan. This might be explained by most research on cavitation focussing on the cosmetic aspect, more specifically body contouring. As this can be easily measured using WC and skinfold measures, an expensive DEXA scan is unnecessary.

To date, only little has been investigated on the influence of UATC on the cardiometabolic risk profile. Eldesoky et al. (2015) and Maher et al. (2019) concluded that no significant

changes had been observed in serum lipid profiles after UATC treatment. These findings are in line with the results of the current study. In addition, Maher et al. (2019) found significant improvements in FBG and HbA1c after the UATC intervention. These results are in contrast with the current study results, which show a significant increase for HbA1c in the control group ($p = 0.0381$) but no changes in the UATC group. This could be explained by the previously stated low power and differences in the intervention and research population. When interpreting the abovementioned study results, the considerable heterogeneity in the parameter settings of the UATC device, as well as combinations of UATC with other interventions, should be considered.

Regarding the limitations of the current study design, one of the most important is the lack of proper monitoring of the main confounders, such as caloric intake and daily physical activity, which can bias the results of the treatment effects. These confounding variables could have been monitored using a food diary and an accelerometer or activity tracker. In addition, no standardized meal was provided in the days prior to testing, which can also influence measures. However, an overnight fasting period was requested prior to testing which reduces the influence of food intake on the blood test results. Furthermore, the determination of the caloric expenditure during the exercise training lacks precision and individualization since it is determined by calculating the sum of the values displayed on the treadmill and ergometer. Therefore, it does not take individual physical characteristics, such as body weight and length, into account. Finally, the moderate training intensity (65% VO_2peak) was determined by setting an individual goal heart rate at baseline, based on CPET results, and monitored during each session using a Polar heart rate monitor. However, the influence of the training effect on the goal heart rate has not been taken into account. A new goal heart rate could have been determined for each participant after a certain time (e.g. every three weeks). Besides, not all participants reached the set goal heart rate during each session, creating uncertainty whether the moderate intensity had always been reached.

The overall risk of biases in the current study is moderate. A selection bias, or more specific a healthy user bias, may be present because the study includes an exercise intervention, which increases the possibility that mainly fitter adults with mild to moderate obesity registered for the study. In addition, the double-blinded study design minimizes the risk of detection

bias. The use of sham and randomisation through closed envelopes minimise the risk of performance bias. Lastly, attrition bias is possible due to the incidence of six drop-outs during the study of which data have been excluded from the statistical analysis. This could have been minimalized using an intention-to-treat analysis. However, all reasons for drop-out are mentioned and are unrelated to the intervention.

Attention should be paid to the low power of the study which increases the risk of type II error. A power calculation, based on the WC parameter, conducted during the drafting of the protocol showed a sample of 94 participants was needed for a power of 80% with significance level 0.05.

Since each session was individually supervised, the adherence of the participants to the intervention is overall high with means of 23/24 and 22/24 in the UATC and control group, respectively. This high adherence reduces the chance of underestimating the treatment effect, resulting in more valid results (Matsui, 2019).

Lastly, based on the mean baseline values of BMI (32.20 ± 3.81), participants are categorized in the first obesity class (BMI 30.0 - 34.9), which influences the external validity. Hence, one should be prudent when extrapolating the findings of this study to adults in more severe categories of obesity.

All participants were informed about the possible complications of UATC prior to the intervention. In case the UATC treatment posed a risk, based on a questionnaire concerning the medical background, possible participants were not admitted to the study. However, previous investigation in obese adults shows that the side-effects of UATC treatment are rather small as they are limited to the following: ecchymoses and significant discomfort (Coleman et al., 2009), transient tenderness, bruising and edema (Saedi & Kaminer, 2013) and numbness (Eldesoky et al., 2015). In the current study, two participants experienced mild discomfort during the UATC treatment due to the ultrasound waves causing an itching feeling. In addition, three participants reported frequent headaches. However, it is uncertain whether these were caused by the UATC intervention since they had experienced frequent complaints of migraines in the past. Besides these cases, no other side-effects were reported during or after the UATC treatment.

The most important advantage of this procedure compared to other fat-reducing treatments is the non-invasive technique. Therefore, periprocedural morbidities, such as infection,

scarring and anaesthesia associated with surgical procedures, are eliminated (Eldesoky et al., 2015). Moreover, UATC turns out to be a cheaper and safer treatment that produces a similar fat mass reduction and improvement of body shape as invasive ultrasound liposuction (Eldesoky et al., 2015).

Further investigation through large-scale RCT's, monitoring all key confounders, is recommended to reinforce these short-term results. However, uniformity in the use of UATC settings must be established through further research about the most effective settings. In addition to the short-term effects of UATC, more research is needed on the preservation of these effects in the long term. Finally, a combination of this UATC treatment with other modalities like exercise and diet can be further investigated to determine the most effective, multidisciplinary approach for the clinical field regarding weight loss in adults with obesity.

6 Conclusion

The effect of UATC in addition to a classic aerobic exercise intervention concerning body composition and cardiometabolic risk profile in adults with obesity seems limited. Body composition improved significantly in the UATC group whereas no significant effects were found for the cardiometabolic risk profile. Future large-scale research considering the long-term effects of UATC in individuals with obesity is warranted.