THE IMPACT OF UCP-2 Ala55Val GENE POLYMORPHISM ON WAIST CIRCUMFERENCE AND WAIST-HIP RATIO (WHR) CHANGE POST CONTINUOUS TRAINING INTERVENTION IN OBESE WOMEN

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ABSTRACT

Introduction: Obesity is characterized by waist circumference of more than 90cm for men and 80cm for women. The waist-hip ratio (WHR) is a method to measure the accumulation of abdominal fat. One factor that influences obesity is genetic factors, including uncoupling protein (UCP)-2 Ala55Val gene polymorphism. Continuous training (CT) exercise can increase change in waist circumference and WHR in obese individuals. Still, the impact of the UCP-2 Ala55Val gene polymorphism on waist circumference and WHR change after CT intervention is unclear. **Objective:** To determine the impact of UCP-2 Ala55Val genetic variation on waist circumference and WHR change post continuous training intervention in obese women. **Methods:** This study used a Quasi-Experimental Pre and Post Design Without Control Group design. Subjects were 14 people chosen based on purposive sampling. Waist circumference and WHR were examined before and after ten-week intervention, while UCP-2 Ala55Val gene polymorphism was examined before intervention. Gene examination used Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR–RFLP) method. Univariate and bivariate tests analyzed data. Bivariate analysis was using dependent t-test and independent t-test. **Results:** The results indicate that waist circumference before intervention is 86,82±9,14cm, and after the intervention is 82,64±7,73cm, which is significant using dependent t-test (p=0,000). WHR pre-intervention was 0,79 ± 0,06 and post-intervention was 0,78 ± 0,06. CT can reduce WHR 0,1 which was significant using dependent t-Test (p=0,048). Waist circumference change post-intervention in CC genotype is 3,59±3,08 cm, and TT genotype is 6,33±4,16 cm, which is not significant using independent t-test (p=0,224). There was no significant difference in WHR between CC and TT genotypes (p = 0,119) using the independent t-test. **Conclusion:** There is an effect of continuous training (CT) on waist circumference and WHR. There is no significant difference in waist circumference and WHR changes in the UCP-2 Ala55Val gene polymorphism genotypes.

Keywords: Continuous Training, Obesity, UCP-2 Ala55Val, Waist Circumference, Waist to Hip Ratio

INTRODUCTION

The imbalance of energy in and out can lead to fat accumulation in the body, which, if left unchecked, can lead to obesity (Sherwood, 2017). Obesity is a complex, multifactorial, and largely preventable disease (Hruby, 2016). Obesity is defined as the accumulation of excess fat in the body that interferes with health, characterized by a Body Mass Index (BMI) of 25 kg/m2 (WHO, 2000). In conducting obesity screening, the method used is anthropometric measurements such as BMI measurements (WHO, 2008). However, waist circumference and WHR are superior to BMI for measuring abdominal fat accumulation, which can be used to predict cardiovascular disease risk (Tchernof & Després, 2013). Obesity is characterized by a waist circumference of more than 90 cm for men and 80 cm for women (Kemenkes RI, 2018). The WHR will interpret the type of obesity as central or peripheral. The limit value for central obesity for men is 0.90 and for women 0.80 if less than this value is categorized as peripheral obesity (WHO, 2008). Obesity is a risk factor for chronic diseases such as diabetes, dyslipidemia, cardiovascular disease, cancer, and others (WHO, 2020). Obesity requires a comprehensive approach to achieve successful management (Kahan, 2016).

Physical activity is one way to prevent obesity (Kahan, 2016). The World Health Organization (WHO)(2020) recommends adults do at least 150 minutes of moderate-intensity physical activity a week. One of the physical activities that can be done is continuous training. Continuous training is physical activity with moderate intensity and is carried out continuously to achieve aerobic metabolism, which allows burning more fat than anaerobic metabolism (McArdle et al., 2010). Wewege et al. (2017) wrote that continuous training had been shown to increase changes in waist circumference and body fat percentage in obese patients.

Other factors, namely genetic factors, also influence obesity. Recent studies have examined the gene uncoupling protein (UCP)-2 as a candidate for a new gene associated with obesity. The UCP-2 gene has been widely studied because it is present in many body tissues (Brondani et al., 2014). The UCP gene is one of the genes that influence obesity because it is related to the regulation of energy expenditure. The UCP gene increases the efficiency of the oxidative phosphorylation pathway by transferring protons from the intermembrane space to the mitochondrial matrix for further use in the process of thermogenesis (Busiello et al., 2015). The meta-analysis of Brondani et al. (2014) concluded that the UCP-2-866G/A polymorphism was associated with protection against obesity in European races while the UCP-2 Ala55Val polymorphism was associated with obesity susceptibility in Asian races.

Previous studies have studied the effect of physical exercise on obesity and the effect of genetics on obesity. However, to the best of our knowledge, no one has assessed the effect of gene polymorphism on changes in waist circumference and WHR after the intervention. Therefore, researchers are interested in examining the effect of UCP-2 Ala55Val gene polymorphism on changes in waist circumference and WHR after the continuous training intervention.

METHODS

This study was a Quasi-Experimental Pre and Post Design Without Control Group. The subjects were given Continuous Training (CT) as an intervention by comparing the data before and after the intervention. The intervention was conducted for ten weeks. A purposive sampling method was used to collect this study population. The sample size required 14 obese women (BMI≥25 kg/m2). The inclusion criteria for study subjects were 18–34 years old, had a history of inactive lifestyle for the last six months, were declared healthy and fit for physical exercise, and were willing to be the subjects. Subjects taking weight-loss drugs/supplements were excluded. The dropout criteria were that they could not finish the intervention according to the predetermined program.

Measurement of Research Variables

Waist circumference and WHR measurements were performed before and after the intervention. Meanwhile, an examination of genetic variation of UCP2-Ala55Val was carried out before the intervention was carried out. Waist circumference was measured using a tape measure at the midpoint between the edge of the lowest rib and the curved end of the pelvic bone. WHR measurement is done by dividing waist circumference by hip circumference. The examination of the genetic variation of UCP2-Ala55Val used the Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) method.

Training Intervention

Training interventions were conducted for ten weeks, with a frequency of 3 times per week and based on the COVID-19 prevention health protocol. The type of training is cycling. Training begins with a 10-minute warm-up at 50% maximum Heart Rate, and continues with core training for 30 minutes at 60%-85% maximum HR, then ends with a 5-minute cooldown at 50% maximum HR.

Data analysis

The body weight, BMI, waist circumference, and WHR before – after the intervention were analyzed using the Dependent T-Test. Independent T-Test used to determine the effect of the UCP2 Ala55Val gene on changes in waist circumference and WHR. The test results were considered significantly different if $p<0.05$.

Research Ethics

The study has received an Ethics Committee Approval from the Medical and Health Research Ethics Committee (MHREC) Faculty of Medicine, Public Health and Nursing Universitas Gadjah Mada-DR. Sardjito General Hospital (Ref. No: KE / FK / 0258 / EC / 2020).

RESULTS

Univariate analysis was carried out to determine the characteristics of the research subjects with the results as shown in table 1.

Table 1. Distribution of Age, BMI, Weight, Waist Circumference and WHR

Variable (n=14)	Mean±SD	Median	Minimum - Maximum
Age	21,85±2,90	22,00	18,0 - 28,0
BMI			
Pre-Intervention	30,18±4,40	29,70	25,2 - 41,8
Post-Intervention	28,86±3,84	28,45	24,2 - 38,7
BW			
Pre-Intervention	74,32±11,46	72,15	55,7 - 92,8
Post-Intervention	71,05±10,11	69,25	55,9 - 86,6

Waist circumference			
Pre-Intervention	86,82±9,14	85,5	72,5 - 104,0
Post-Intervention	82,64±7,73	82,0	70 – 97
Waist to Hip Ratio			
Pre-Intervention	0,79 ±0,06	0,80	0,64 – 0,87
Post-Intervention	0,78 ±0,06	0,78	0,66 – 0,91

Description: n: number of samples; SD: standard deviation

All subjects had two genotypes of the UCP-2 Ala55Val gene, namely homozygous Ala55 (CC) and homozygous Val55 (TT). The CC genotype group amounted to 11 people (78.57%), and the TT group amounted to 3 people (21.43%). There was no CT genotype in this subject.

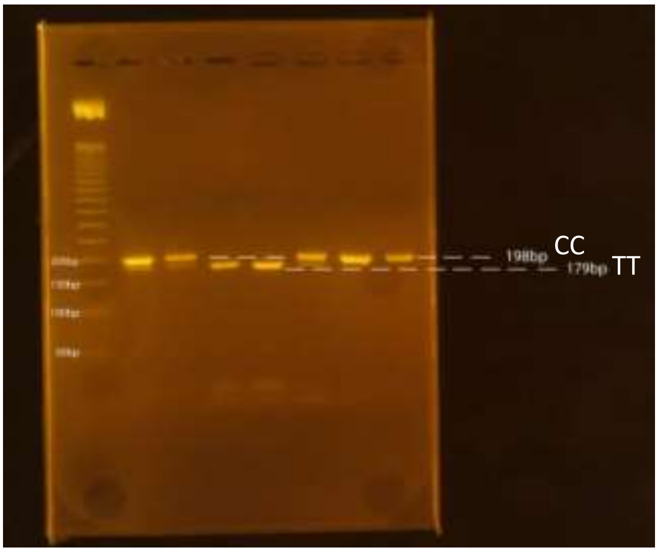

Figure 1. UCP-2 Ala55Val Gene Electrophoresis

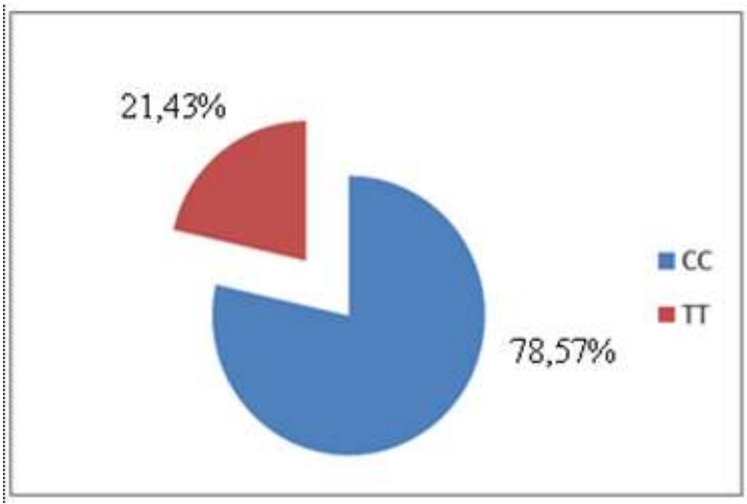

Figure 2. The number of subjects per genotype of the UCP-2 Ala55Val gene

Table 2. The effect of the intervention on waist circumference and WHR

Variable	n	Mean±SD	p-*value*	Description
Waist circumference (cm)				
Pre-Intervention	14	86,82±9,14	0,000	There is a significant difference
Post-Intervention	14	82,64±7,73		
Waist to Hip Ratio (WHR)				
Pre-Intervention	14	0,79 ± 0,06	0,048	There is a significant difference
Post-Intervention	14	0,78 ±0,06		

Description :
n : number of samples; SD : standard deviation; p-value significant p<0.05; p-value is not significant p>0.05

The results of the paired t-test analysis (table 2) showed that there was a significant difference between the mean waist circumference (p=0.000) and WHR (p=0.048) before and after the intervention in obese women.

Table 3. The waist circumference and WHR changes between genotypes

Genotypes	n	Mean±SD	p-*value*	Description
Waist Circumference (cm)				
CC	11	3,59±3,08	0,224	There is no a significant difference
TT	3	6,33±4,16		
Waist to Hip Ratio (WHR)				
CC	11	0,01 ± 0,02	0,119	There is no a significant difference
TT	3	0,02 ± 0,04		

Description :
n : number of samples; SD : standard deviation; CI 95% : Confidence Interval 95%; p value significant p<0.05; p value is not significant p>0.05

Unpaired t-test was used to determine the effect of UCP-2 Ala55Val genetic on waist circumference and WHR changes as training response (table 3). Table 3 shows no significant relationship between the two groups of UCP-2 Ala55Val genotype on changes in waist circumference (p=0.224) and WHR (p=0.119) after CT intervention in obese women.

DISCUSSION

This study shows a significant difference between the mean waist circumference and WHR before and after the intervention. This is in accordance with Wewege et al. (2017) research that continuous training for ten weeks has been shown to reduce waist circumference and WHR. Keating et al. (2014) stated that CT with cycling mode, which was carried out with a frequency of 3 times per week for 12 weeks, could reduce the mean waist circumference before the intervention from 90.8 ± 2.1 cm to 87.2 ± 1.7 cm after the intervention. Martins (2016) conducted a similar study to determine the effect of HIIT and MICT physical exercise on body composition in obese women, showing a change in waist circumference of 2.6 cm after 12 weeks of intervention. Another study conducted by Lemes

(2018) showed a decrease in waist circumference of 2.18 cm after doing regular aerobic exercise for six weeks.

Continuous Training is a form of aerobic exercise. Continuous Training can reduce adipose cell size and fat body mass, both visceral fat and subcutaneous fat. This is due to repeated activation of the lipolysis pathway during exercise to produce ATP (Rodrigues, 2020). The decrease in fat mass in the body causes changes in body anthropometry, such as waist circumference and WHR (Airin, 2014). Therefore, in this study, there was a change in waist circumference and WHR before and after CT intervention.

Bivariate analysis of unpaired t-test was used to determine whether there were differences in changes in waist circumference and WHR in the genetic variation group UCP-2 Ala55Val. The genotypes found in this study were CC with base length at 198bp as many as 11 subjects and TT genotype with base length at 179bp and 17bp as many as 3 subjects. This study showed no significant difference between changes in waist circumference and WHR of subjects between CC genotypes and TT genotypes in obese women. The results of this study are different from the results of previous studies. Brondani (2014) conducted a meta-analysis study, concluding that the UCP-2 Ala55Val polymorphism is associated with susceptibility to obesity in Asian races. Research conducted by Qin (2013) also obtained similar results. Research conducted by Matinez-Hervas (2012) stated that the Ala55Val polymorphism TT genotype had a significant relationship with higher waist circumference compared to other genotypes. Gamboa (2018) obtained results from his research that the TT genotype has a high abdominal visceral fat level compared to other genotypes. High levels of visceral fat allow an increase in the size of a person's waist circumference.

The UCP-2 gene is associated with energy expenditure with Ala55Val as a form of polymorphism (Brondani, 2014). Ala55Val mutations affect a decrease in resting energy expenditure 24 hours (REE-24h) and a decrease in the rate of fat oxidation which is often associated with the risk of obesity (Surniyantoro, 2016), which is greater than other individuals (Mexitalia, 2013; Nicoletti, 2016; Zhang, 2014). However, the results of this study showed that there was no significant difference between genotypes in changes in waist circumference and WHR after Continuous Training intervention.

The limitation of this study was that it was unable to obtain a complete genetic variation of UCP2. From 14 research participants, only two genotype alleles were obtained, which are CC and TT. This study did not find genotype CT as UCP2 Ala55Val variation gene, so it is difficult to conclude the effect of UCP2 gene variation on improving waist circumference and WHR on Continuous Training interventions. The small number of participants may decrease the power to detect differences between the genotype groups. Based on the study's limitations, it can be suggested to take more participants and meet the availability of three types of genotypes in the UCP2 Ala55Val genetic variation.

CONCLUSION

The research concludes that the 10-week Continuous Training interventions improved waist circumference and WHR in obese women. Continuous Training can be used as a therapy for obese patients, mainly to improve the body compositions such as waist circumference and WHR. There was no effect of the UCP2 Ala55Val genetic variation on the response to training intervention.

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