

## Effects Ala54Thr polymorphism of FABP2 on obesity index and biochemical variable in response to a aerobic exercise training

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### ABSTRACT

The purpose of the current study was to investigate whether or not the FABP2 gene polymorphism modulated obesity indices, hemodynamic factor, blood lipid factor, and insulin resistance markers through 12-week aerobic exercise training in abdominal obesity group of Korean mid-life women. A total of 243 abdominally obese subjects of Korean mid-life women voluntarily participated in aerobic exercise training program for 12 weeks. Polymerase Chain Reaction with Restriction Fragment Length Polymorphism (PCR-RFLP) assay was used to assess the FABP2 genotype of the participants (117 of AA homozygotes, 100 of AT heterozygotes, 26 of TT homozygotes). Prior to the participation of the exercise training program, baseline obesity indices, hemodynamic factor, blood lipid factor, and insulin resistance markers were measured. All the measurements were replicated following the 12-week aerobic exercise training program, and then the following results were found. After 12-week aerobic exercise training program, wild type (Ala54Ala) and mutant type (Ala54Thr+Thr54Thr) significantly decreased weight ( $P > .001$ ), BMI ( $P > .001$ ), %bf ( $P > .001$ ), waist circumference ( $P > .001$ ), WHR ( $P > .001$ ), muscle mass (wild type  $p < .022$ ; mutant type  $P > .001$ ), RHR ( $P > .001$ ), visceral adipose area (wild type  $p < .005$ ; mutant type  $P > .001$ ), subcutaneous area ( $P > .001$ ), insulin (wild type  $p < .005$ ; mutant type  $P > .001$ ) and significantly increased  $VO_2\max$  ( $P > .001$ ). And wild type significantly decreased NEFA ( $P > .05$ ), glucose ( $P > .05$ ), OGTT 120min glucose ( $P > .05$ ) and significantly increased HDLC ( $p > .005$ ). Mutant type significantly decreased SBP ( $P > .001$ ), DBP ( $P > .01$ ), TC ( $P > .01$ ), LPL ( $P > .05$ ), LDL ( $P > .001$ ), HOMA index ( $P > .01$ ). The result of the present study represents that regular aerobic exercise training may beneficially prevent obesity index, blood pressure, blood lipids and insulin resistance markers independent of FABP Ala54Thr wild type and mutant type.

*Keywords:* Fatty acid binding protein 2 gene, aerobic exercise, obesity index, biochemical variable, polymorphism, middle-aged women

### INTRODUCTION

Fatty acid binding protein genes are known to include the 1-kb sequence, upstream of the initiation codon, 3 indel polymorphisms and 4 single nucleotide polymorphisms (SNPs), and there are 9 different types of FABP genes depending on each tissue. Among them, FABP2 genes are 3.4 kb in size and are located in the region of chromosome 4q 28-31, and they consist of 4 exons (700 bp) separated by 3 introns (2,650 bp) [22]. As guanine at codon 54 of FABP2 gene transforms into adenine, the alanine-threonine substitution of amino acid is reported to be associated with insulin resistance [3]. FABP2 is a relatively small protein (15 kDa) which is abundantly distributed in small intestine's epithelial cells, and is known

as one of the genes that participate in the intracellular metabolism and the transport of fatty acids [14]. However, the exact functions of FABP2 have never been revealed clearly. Many studies have mainly focused on the roles of FABP2 as a transcytoplasmic fatty acid carrier and a transmitochondrial fatty acid carrier as well as on its function of relieving intracellular enzymes' hypofunction caused by long chain fatty acids. And it has been reported that FABP2 also serves as a free radical scavenger or removes peroxidized acids from cells [15].

Especially, as the affinity of those FABP2 which contain threonine at Codon 54 of the gene to long chain fatty acids is nearly twice greater than those including alanine [3], it can increase the absorption of fat, and an increased in serum

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free fatty acids (FFA) can cause insulin resistance by accelerating the intracellular oxidization of fat acids. As a matter of a fact, some studies targeting Japanese, Pima Indian and Caucasian people reported that the Ala54Thr polymorphism of FABP2 gene is associated with insulin resistance [23]. Other studies, which used Koreans as their subject groups to assess the correlation between the polymorphs of FABP2 genes and internal energy metabolism, said that in comparison with the control group, the experimental group containing Thr54 allele did not show any significant differences in terms of BMI, blood lipid and blood sugar levels on an empty stomach, but their basal insulin concentration increased and their insulin resistance indicator based on the Homeostatic Model Assessment (HOMA) also went up [1,13]. In addition, although the basal metabolism rate between the polymorphs of the two base sequences showed no significant differences, the fat oxidization rate of the Thr54 allelomorph character was observed to be higher than that of the Ala54 allelomorph character, which indicated that the FABP2 gene polymorphism could cause insulin resistance in Koreans by bringing about a change to fat metabolism [1]. Many previous studies have already found out a possibility of FABP2 as a candidate gene associated with obesity and insulin resistance. It reported that dietary treatments and exercise programs designed to control the FABP2 genes could reduce obesity levels, blood lipid concentrations, blood pressure and insulin resistance by a significant degree, and the variation in control capacity reflected the differences in gene polymorphs [1,2,6].

As diseases with genetic predisposition such as insulin resistance and non insulin-dependent diabetes are increasing at a fast clip at home and abroad due to an increase in obese population, studies have been actively conducted to find out the genetic causes to prevent and cure those diseases and to develop various medical treatments. About 40-70% of obesity and various chronic diseases including all types of Hypokinetic diseases are ascribed to genetic factors [3]. A more systematic experiment verification process needs to be conducted based on scientific logics for studies on the causes of these diseases, prevention by exercise, treatment efficacy, etc. To make this happen, it is the prerequisite to find out those candidate genes associated with obesity and chronic diseases and identify the exercise benefits of these genes. However, those studies which used Korean as a subject group have reported so far that these possible candidate genes had a very limited influence on the exercise benefits. Therefore, this study aims to find out the impact of the Ala54Thr polymorphism of FABP2 on obesity and biochemical indicators through a 12 week-long aerobic exercise training by targeting

**Table 1.** Basic characteristics of study subjects

		mean $\pm$ SD	P
Age (years)	Wild type (N = 117)	45.9 $\pm$ 7.4	.139
	Mutant type (N = 126)	47.3 $\pm$ 7.8	
Waist (cm)	Wild type (N = 117)	90.2 $\pm$ 5.2	.022
	Mutant type (N = 126)	92.0 $\pm$ 6.1	
Height (cm)	Wild type (N = 117)	157.6 $\pm$ 5.2	.448
	Mutant type (N = 126)	156.4 $\pm$ 12.3	
Weight (kg)	Wild type (N = 117)	63.5 $\pm$ 6.8	.224
	Mutant type (N = 126)	64.5 $\pm$ 7.3	
%body fat	Wild type (N = 117)	33.0 $\pm$ 2.8	.216
	Mutant type (N = 126)	33.4 $\pm$ 3.1	
VO <sub>2</sub> max (ml/kg/min)	Wild type (N = 117)	26.7 $\pm$ 4.3	.784
	Mutant type (N = 126)	26.4 $\pm$ 5.6	

Korean middle-aged women with abdominal obesity as its subject group.

## STUDY METHOD

### Study subjects

This study targeted a total of 243 middle-aged women with waist sizes of more than 80cm without obvious medical symptoms (WHO West Pacific Region. The Asia-pacific perspective: refining obesity and its treatment, 2002), and conducted an analysis on the Ala54Thr polymorphism of FABP2. The results showed that 117 women belonged to the wild type (Ala54Ala), while another 126 were categorized as a mutant type. The results of a comparative analysis on basic variables with or without genetic mutation of the study subjects are as shown in [Table 1].

### Exercise programs

To verify the effects on the benefits of the Ala54Thr polymorphism of FABP2 on aerobic exercise training, the study instructed the Korean middle-aged women to walk and do a dance sports for 12 weeks. The study was conducted over a total span of three years, and the number of participants per each session was limited to about 40 people, to whom the one-on-one consulting and program management were provided in order to boost the participation benefits. The walking and dance sports programs consists of the first 2 weeks of introductory phase, another 2 weeks of improvement phase and the remaining 8 weeks of maintenance phase, in order to increase the intensity of exercise on a gradual basis. Each session includes 20 minutes of static and dynamic stretching exercises prior to the main walking or dance sports.

At the maintenance phase, a 60 minute session with the intensity of 50-60% was conducted three times per week. The walking program participants participated in the power walking program which was conducted in the campus of 'S' University under the monitoring of the supervisor, while the dance sports participants performed the basic movements of Cha Cha Cha and Jive in groups of three. During each session of the exercise, participants were required to wear the heart rate monitoring device (POLAR ELECTRO, Finland), and their heart beats were measured after the end of each session to check whether they achieved their exercise intensity goals set prior to the exercise.

### Test methods

#### *Analysis on polymorphism of FABP2 gene*

The analysis on the polymorphism of FABP2 gene was conducted by extracting genomic DNA from blood samples that were collected from veins at empty stomach with a DNA extraction kit and by measuring the restriction enzyme HhaI (New England BioLabs, Beverly, MA, USA) with the extracted genomic DNA as a template based on the Polymerase Chain Reaction with Restriction Fragment Length Polymorphism (PCR-RFLP) method [3].

#### *Analysis on body composition and blood factors*

The height, weight, waist and blood pressure of a test subject were measured by the same person who completed the required training course in accordance with the management guidelines for standardization, while the body composition was calculated by using the X-Scan Body Composition Analyzer (JAWON Medical Co., Seoul, Korea). After the waist and hip circumferences were measured with a tapeline, the waist-hip circumference ratio was calculated by dividing the waist circumference with the hip circumference; the measurements were conducted for more than twice and were averaged for a mean value. The blood pressures were measured two times at an interval of 5 minutes with the FJ-500R (Jawon Medical, S. Korea) and were averaged later. The overall abdominal fat, epidermal subcutaneous fat and intra-abdominal fat were measured at the fourth lumbar vertebra by the abdominal computerized tomography (SCT-7800TE, SHIMADZU, Japan) at the Korea Association of Health Promotion. The analysis of blood lipid, blood sugar level and insulin was conducted by collecting blood samples from participants who were on empty stomach for 10-12 hours and extracting blood serums in a centrifuge at a temperature of 4°C. The Vitros Chemistry DT60 Johnson & Johnson, NY, USA) and a reagent from the same company were used to

analyze the neutral fat, total cholesterol, high-density cholesterol and blood sugar level. The blood insulin concentration was measured with a commercial insulin analysis reagent (Human insulin ELISA-kit, DSL, Texas, USA).

#### *Oral glucose tolerance test*

For the oral glucose tolerance test (OGTT), participants consumed 75 g of glucose. Their blood samples were drawn from the vein before glucose intake and at 30, 60, 90 and 120 min, and were stored in a freezer at a temperature of -80°C until the test began. Glucose tolerance tests were conducted on the collected venous blood samples after analyzing the glucose levels. To measure the glucose response to the OGTT at 120 min, the area under the curve (AUC) was calculated by using the following formula [18], and the homeostasis model assessment index (HOMA<sub>IR</sub>) was assessed based on the following method.

$$AUC = \{(M_2+M_1)/2\} + \{(M_3+M_2)/2\} + \{(M_4+M_3)/2\} + \{(M_2+M_1)/2\}$$

(M<sub>1</sub> = blood glucose in stable condition; M<sub>2</sub> = blood glucose at 30 min; M<sub>3</sub> = blood glucose at 60 min; M<sub>4</sub> = blood glucose at 90 min; M<sub>5</sub> = blood glucose at 120 min)

$$HOMA \text{ index} = [\text{glucose (mM)} \times \text{insulin (uU/ml)}] \div 22.5$$

#### *Cardiorespiratory fitness*

This study measured their cardiorespiratory fitness levels using the Bruce Protocol, a treadmill exercise test that gradually increases in speed and incline until the participant can go no farther, in which a gas analyzer (Treu-one metabolic cart, Parvo-medics, USA) was used to measure the oxygen uptake per minute. This study set up as the cardiorespiratory indicator the oxygen uptake per minute measured at a time when a participant reached 85% of her maximal heart rate in consideration of safety and age of an examinee [13].

#### *Lifestyle survey*

The physical activity of a participant was measured by an accelerometer (LC; Suzuke, Nagoya, Japan) for 24 hours per day except during shower throughout the 12 week exercise program, and the mean of daily recorded data was used for analysis. The dietary intake was measured by using the 24hr recall method. The daily average dietary intake of an individual was measured three times per week (twice during weekdays and once during weekend) for a total of 12 weeks: a participant was required to list all the food, quantity and ingredients that she consumed for breakfast, lunch, dinner, etc. The individual daily average dietary intake was measured by using CAN-Pro 2.0 (Computer Aided Nutritional Analysis

Program) which was developed by the nutrition information center under the Korean Nutrition Society.

#### Data analysis

All data was expressed as the mean and standard variation. The comparison of genetic character differences was conducted by using the Independent T-test, while the comparison of differences in genetic characters before and after test was carried out with the Paired T-test. The Two-way Repeated-Measures ANOVA was used to assess changes in dependent variables among groups to analyze the influence of the Ala54Thr polymorphism of FABP2 on a 12 week long aerobic exercise. All statistic data were calculated by the SPSS-PC (version 18.0-Chicago, IL, USA) and were verified at a significance of  $\alpha = 0.05$ .

## STUDY RESULTS

This study achieved the following results by targeting Korean middle-aged women with abdominal obesity as a

**Table 2.** Comparison of daily total physical activity (step) and energy intake the FABP2 wild and mutant type

		mean $\pm$ SD	P
Total energy intake (Kcal/day)	Wild type (N = 64)	1608 $\pm$ 412	.940
	Mutant type (N = 79)	1603 $\pm$ 366	
PA (steps/day)	Wild type (N = 64)	13983 $\pm$ 3309	.940
	Mutant type (N = 79)	14645 $\pm$ 3396	

**Table 3.** Comparison of responses in body composition to aerobic exercise training across the FABP2 wild and mutant type

			mean $\pm$ SD	P	P-a
Weight (kg)	Wild type (N = 117)	pre	63.5 $\pm$ 6.8	.001	.691
		post	62.0 $\pm$ 6.7		
	Mutant type (N = 126)	pre	64.5 $\pm$ 7.3		
		post	62.9 $\pm$ 6.8		
BMI (kg/m <sup>2</sup> )	Wild type (N = 117)	pre	25.4 $\pm$ 2.4	.001	.528
		post	24.8 $\pm$ 2.4		
	Mutant type (N = 126)	pre	26.0 $\pm$ 2.6		
		post	25.2 $\pm$ 2.4		
%body fat	Wild type (N = 117)	pre	33.0 $\pm$ 2.8	.001	.484
		post	31.9 $\pm$ 3.2		
	Mutant type (N = 126)	pre	33.4 $\pm$ 3.1		
		post	32.5 $\pm$ 3.1		
Muscle (kg)	Wild type (N = 117)	pre	38.8 $\pm$ 3.4	.022	.399
		post	38.5 $\pm$ 3.6		
	Mutant type (N = 126)	pre	39.1 $\pm$ 3.4		
		post	38.7 $\pm$ 3.1		

P: within group effect; P-a: between group effect

subject group and by analyzing the influence of aerobic exercise training on obesity and biochemical indicators due to the Ala54Thr polymorphism of FABP2.

#### Body composition and lifestyle of participants

The results of the study on daily dietary intake and physical activity for 12 weeks of aerobic exercise training are as shown in [Table 2]. The lifestyle survey was carried out on only 143 participants of the second and third year except for those of the first year. The dietary intake and physical activity due to the Ala54Thr polymorphism of FABP2 did not show any significant differences during the exercise training program.

#### Influence of aerobic exercise on body composition and blood pressure due to FABP2 Ala54Thr polymorphism

The results of the analysis on the influence of aerobic exercise training on body composition due to the Ala54Thr polymorphism of FABP2 are as shown in [Table 3]. It was observed that the 12 week-long aerobic exercise training reduced the weight, BMI, body fat and muscles in Korean middle-aged women of a wild type and mutant type of FABP2 Ala54Thr polymorphs, but aerobic exercise participants indicated no significant difference between the wild and

**Table 4.** Comparison of responses in abdominal obesity to aerobic exercise training across the FABP2 wild and mutant type

			mean $\pm$ SD	P	P-a
Waist (cm)	Wild type (N = 117)	pre	90.2 $\pm$ 6.0	.001	.146
		post	86.3 $\pm$ 6.9		
	Mutant type (N = 126)	pre	91.9 $\pm$ 6.1		
		post	87.3 $\pm$ 5.7		
Waist Hip Ratio	Wild type (N = 117)	pre	.93 $\pm$ .04	.001	.225
		post	.91 $\pm$ .06		
	Mutant type (N = 126)	pre	.95 $\pm$ .05		
		post	.93 $\pm$ .05		
Total abdominal area (mm <sup>2</sup> )	Wild type (N = 117)	pre	47367.5 $\pm$ 4210.9	.077	.173
		post	45809.3 $\pm$ 6064.1		
	Mutant type (N = 126)	pre	52389.9 $\pm$ 7100.7		
		post	49134.8 $\pm$ 5562.6		
Visceral area (mm <sup>2</sup> )	Wild type (N = 117)	pre	8751.4 $\pm$ 3411.2	.002	.661
		post	7698.8 $\pm$ 2961.8		
	Mutant type (N = 126)	pre	9616.2 $\pm$ 3213.2		
		post	8721.5 $\pm$ 3275.4		
Subcutaneous area (mm <sup>2</sup> )	Wild type (N = 117)	pre	19589.4 $\pm$ 4397.5	.001	.172
		post	17636.1 $\pm$ 4679.2		
	Mutant type (N = 126)	pre	20093.8 $\pm$ 4875		
		post	18752.1 $\pm$ 5154.7		

P: within group effect; P-a: between group effect

**Table 5.** Comparison of responses in blood pressure, HR, and CRF to aerobic exercise training across the FABP2 wild and mutant type

			mean ± SD	P	P-a
SBP (mmHg)	Wild type (N = 117)	pre	114.0 ± 13.7	.058	.667
		post	112.3 ± 13.5		
	Mutant type (N = 126)	pre	119.5 ± 13.8	.001	
		post	117.6 ± 12.5		
DBP (mmHg)	Wild type (N = 117)	pre	70.1 ± 9.6	.094	.513
		post	68.0 ± 9.5		
	Mutant type (N = 126)	pre	73.2 ± 10.2	.005	
		post	71.8 ± 9.6		
RHR (beats/min)	Wild type (N = 117)	pre	73.4 ± 10.1	.001	.883
		post	72.9 ± 8.9		
	Mutant type (N = 126)	pre	72.9 ± 10.8	.001	
		post	68.6 ± 7.6		
HRmax (beats/min)	Wild type (N = 117)	pre	163.4 ± 12.4	.960	.595
		post	162.5 ± 14.1		
	Mutant type (N = 126)	pre	158.7 ± 14.5	.389	
		post	158.6 ± 13.4		
VO <sub>2</sub> max (ml/kg/min)	Wild type (N = 117)	pre	26.7 ± 4.3	.001	.927
		post	29.0 ± 4.8		
	Mutant type (N = 126)	pre	26.4 ± 5.6	.001	
		post	28.8 ± 5.4		

SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, RHR: Resting heart rate, HRmax: Heart Rate Maximum; P: within group effect; P-a: between group effect

mutant type groups due to the Ala54Thr polymorphism of FABP2. The results of the analysis on the influence of aerobic exercise training on abdominal obesity due to the Ala54Thr polymorphism of FABP are as shown in [Table 4]. It was found that the 12 week-long aerobic exercise training reduced the waist circumference, WHR, visceral fat area and subcutaneous fat area of Korean middle-aged women of a wild type and mutant type of FABP2 Ala54Thr polymorphs, whereas aerobic exercise participants showed no meaningful differences between the wild and mutant type groups due to the Ala54Thr polymorphism of FABP2. The results of the analysis on the influence of aerobic exercise training on blood pressure, heart rate, cardiopulmonary capacity due to the Ala54Thr polymorphism of FABP are as shown in [Table 5]. It was observed that the 12 week-long aerobic exercise training reduced the heart rate but significantly improved the cardiopulmonary capacity of Korean middle-aged women of a wild type and mutant type of FABP2 Ala54Thr polymorphs. The exercise program was found to decrease the blood pressures at both contraction and relation phases in the mutant type group by a meaningful degree, while it reduced those of wild type participants but not to a statistically significant extent. However, there were no profound differences between the wild and mutant type groups of aerobic exercise participants

**Table 6.** Comparison of responses in blood lipids to aerobic exercise training across the FABP2 wild and mutant type

			mean ± SD	P	P-a
TC (mg/dl)	Wild type (N = 117)	pre	203.3 ± 46.0	.190	.312
		post	198.9 ± 41.0		
	Mutant type (N = 126)	pre	208.3 ± 42.8	.003	
		post	199.4 ± 31.6		
TG (mg/dl)	Wild type (N = 117)	pre	112.6 ± 43.8	.214	.732
		post	107.2 ± 41.2		
	Mutant type (N = 126)	pre	121.0 ± 61.1	.568	
		post	118.0 ± 60.2		
HDLC (mg/dl)	Wild type (N = 117)	pre	54.0 ± 19.2	.002	.530
		post	57.3 ± 19.8		
	Mutant type (N = 126)	pre	53.8 ± 18.3	.087	
		post	56.0 ± 20.6		
LPL (mg/dl)	Wild type (N = 117)	pre	156.5 ± 53.9	.066	.517
		post	187.5 ± 53.1		
	Mutant type (N = 126)	pre	164.1 ± 45.2	.045	
		post	213.8 ± 90.9		
NEFA (mg/dl)	Wild type (N = 117)	pre	652.6 ± 250.8	.014	.333
		post	392.6 ± 226.5		
	Mutant type (N = 126)	pre	514.3 ± 228.3	.123	
		post	390.0 ± 184.2		
LDL (mg/dl)	Wild type (N = 117)	pre	128.1 ± 44.9	.065	.261
		post	121.8 ± 43.7		
	Mutant type (N = 126)	pre	130.9 ± 38.0	.001	
		post	119.6 ± 33.9		

TC: Total cholesterol, TG: Triglyceride, HDLC : High density lipoprotein cholesterol, LPL: Lipoprotein Lipase, FFA: Free Fatty Acid, LDL: Low density lipoprotein cholesterol; P: within group effect; P-a: between group effect

due to the Ala54Thr polymorphism of FABP2.

#### *Influence of aerobic exercise on biochemical change due to FABP2 polymorphism*

The results of the analysis on the influence of aerobic exercise training on abdominal obesity indicators due to the Ala54Thr polymorphism of FABP are as shown in [Table 6]. It was found that the 12 week-long aerobic exercise training significantly improved the TC, HDLC, LPL and LDLC in Korean middle-aged women with the mutant type of FABP2, while the wild type showed a meaningful improvement (P) only in the NEFA. However, there were no profound differences between the wild and mutant type groups of aerobic exercise participants due to the Ala54Thr polymorphism of FABP2 (P-a). The results of the analysis on the influence of aerobic exercise training on other abdominal obesity indicators due to the Ala54Thr polymorphism of FABP are as shown in [Table 7]. It was found that the 12

**Table 7.** Comparison of responses in glucose and insulin resistance markers to aerobic exercise training across the FABP2 wild and mutant type

			mean $\pm$ SD	P	P-a
Glucose (mg/dl)	Wild type (N = 117)	Pre	100.1 $\pm$ 11.6	.038	.674
		Post	98.4 $\pm$ 10.1		
	Mutant type (N = 126)	Pre	100.5 $\pm$ 12.9		
		Post	99.3 $\pm$ 11.6		
120min glucose (mg/dl)	Wild type (N = 117)	Pre	141.3 $\pm$ 39.5	.023	.344
		Post	133.6 $\pm$ 36.1		
	Mutant type (N = 126)	Pre	142.1 $\pm$ 39.7		
		Post	138.8 $\pm$ 35.2		
Insulin (mg/dl)	Wild type (N = 117)	Pre	6.3 $\pm$ 3.1	.016	.574
		Post	5.6 $\pm$ 3.0		
	Mutant type (N = 126)	Pre	7.1 $\pm$ 3.7		
		Post	6.2 $\pm$ 3.2		
glucose AUC	Wild type (N = 117)	Pre	573.3 $\pm$ 123.2	.056	.883
		Post	552.0 $\pm$ 116.5		
	Mutant type (N = 126)	Pre	577.9 $\pm$ 114.0		
		Post	554.6 $\pm$ 100.0		
HOMA index	Wild type (N = 117)	Pre	1.5 $\pm$ .8	.141	.597
		post	1.3 $\pm$ .8		
	Mutant type (N = 126)	pre	1.7 $\pm$ .9		
		post	1.5 $\pm$ .8		

Glu : Glucose, T120 : OGTT test 120 min glucose test, AUC : Area under the curve, HOMA index = [glucose (mM)  $\times$  insulin (uU/ml)]  $\div$  22.5; \*the factor of converting [mg/dl] into [mM] = 0.05551; P: within group effect; P-a: between group effect

week-long aerobic exercise training significantly improved the insulin and AUC of Korean middle-aged women of a wild type and mutant type of FABP2 Ala54Thr polymorphs (P), and the wild type showed a profound improvement in blood glucose level and oral glucose tolerance tests, while the mutant type indicated a meaningful improvement in the Homa index. In addition, there were no profound differences between the wild and mutant type groups of aerobic exercise participants due to the Ala54Thr polymorphism of FABP2 (P-a).

## ARGUMENT

The 12 weeks of aerobic exercise training, considering the FABP2 Ala54Thr genetic polymorphism, improved the obesity indices such as weight, %bf, BMI, waist measurement, WHR, visceral fat area (VFA), and subcutaneous fat area, and enhanced the heart rate and cardiorespiratory fitness when resting. It also improved fasting insulin concentration, Oral Glucose Tolerance Test (OGTT) AUC index regardless of the genetic modification of the FABP2 Ala54Thr gene. In a mutant type, which the FABP2 Ala54Thr gene was mutated,

the total area of the abdomen, systolic blood pressure, diastolic blood pressure, total cholesterol, LPL, LDL, and HOMA index were significantly improved and in the wild type, which the gene was not mutated, HDLC, FFA, blood glucose, and the blood glucose level of 120 minutes of OGTT were significantly improved. In other words, the 12 weeks of aerobic exercise training considering the FABP2 Ala54Thr genetic polymorphism, enhanced the obesity indices and biochemical indices of middle-aged Korean women with abdominal obesity in both wild type and mutant type, and the genetic sensitivity toward the enhancement was low.

The currently reported physiological roles of the body of FABP2 are as follows: restraining fatty acid from being combined with cell solute, cell membrane, or various cell components; delivering the fatty acid in cytoplasm to small cell organisms as a fatty acid deliverer. [19]. When the fatty acid does not melt into the aqueous solution, FABP2 minimizes the thermodynamic energy requirements for the fatty acid to melt into the aqueous solution easily, and when the lipid affects the gene expression through peroxisome proliferator-activated receptor (PRAP), FABP2 is able to deliver the regulatory lipid to the cell nucleus [22]. As the results of tracking observation for the study of the FABP2 Ala54Thr gene, obesity, blood lipids, insulin resistance, and the type 2 diabetes, the mutant type of this gene is related to obesity, hyperlipidemia, insulin resistance, and type 2 diabetes depending on age, disease, and lifestyle in specific races such as Pima Indian, Mexican American, Caucasian, Japanese, and Korean. In other words, the FABP2 Ala54Thr gene mutation increases the risk factors related to obesity and insulin resistance when resting, but the improvement effect when participating in an exercise program along with a dietary control such as low-calorie diets, and low fat diets is rather high. However, the researches which have conducted until now to prove the exercise effects according to the gene mutation are insufficient. [1,2,6,7,9,10,11,17,23]. Takakura, who reported the obesity index changes as participating in the FABP2 Ala54Thr intervention program, showed that as the results of participating in 6 months of dietary restriction (1,200kcal/day) and walking 10,000 steps a day, the visceral white adipose tissues reduction was low in the T allelo-morphic character. But this study showed that the abdominal visceral fat and subcutaneous fat were improved as the results of 12 weeks aerobic exercise training regardless of the gene mutation. In this study, only participants lifestyles such the physical activities and dietary intake were investigated, and diet was not controlled, but the results are similar to those of exercising between 3 months and 6 months with dietary control. More interesting results are that this program brought

not only the obesity indices reduction but also the cardiorespiratory fitness increase along with positive symptoms on blood indices. In the Luis study (2006), as the results of aerobic exercise, which took 60 minutes a day and more than 3 times a week along with low calorie diet (1,520 kcal; 52% carbohydrate, 25% fat, 23% protein), FABP2 improved significantly the obesity indices and the cardiorespiratory fitness, and the study also showed that there are differences in obesity indices improvement of the Ala54 allele, and in the systolic blood pressure and the glucose improvement of the Thr54 allele depending on the gene mutation occurrence. Similarly, this study showed the improvement of blood pressure in mutant type. [6-8,10] Furthermore, there was improvement in TC, LPL, LDLC, HOMA index, insulin, OGTT AUC in mutant type, and there was improvement in NEFA, glucose, OGTT 120 minutes glucose in wild type. Like these, the blood lipids and insulin resistance index were improved regardless of the gene mutation.

This study did not monitor the lifestyles of all participants, but at least the participants in this study showed the improvement in obesity indices, blood pressure, blood lipids, and insulin resistance according to the aerobic exercise training regardless of the FABP2 Ala54Thr gene mutation when considering the results presented in <Table 2>, which shows that there is not statistical difference in average intake calories a day and physical activities between FABP2 Ala54Thr polymorphism of 1.43 million people who participated in the program from the 3<sup>rd</sup> round. But the researches, which have been conducted until now, for the FABP2 Ala54Thr gene and lifestyle change, are very limited and the results cannot present a matched genetic effect. Even though this study is not sufficient to prove the genetic effects targeting middle-aged Korean women with abdominal obesity, this study showed low genetic sensitivity of the Ala54Thr mutation of the FABP2 gene compared to other characteristics in the improvement effect as the response to the exercise training stimulation in a large-scale intervention exercise with monitoring of the lifestyles (daily physical activity and dietary intake) of some participants.

The results of studies about relations of FABP2 Ala54Thr gene mutation with obesity, blood lipids, insulin resistance, and the type 2 diabetes, which have been conducted until now, differ depending on the race, and only two studies have been reported in Korea, therefore additional researches may be required. Most of advanced researches in and out of Korea are epidemiological studies, which were conducted once and focus on dependent variable relations in dietary control, complex program with dietary control and exercise. This study can be regarded as meaningful as a research which proves

the genetic sensitivity effect on exercise through the FABP2 Ala54Thr gene through a large-scale aerobic exercise training targeting middle-aged Korean women with abdominal obesity.

## CONCLUSION

As the test results to find if the FABP2 Ala54Thr gene of middle-aged Korean women with abdominal obesity affects the improvement of obesity indices, blood lipids, blood glucose variables, and insulin resistance indices if participating in the 12 weeks of aerobic exercise training, the following conclusion was obtained.

1) The FABP2 genetic polymorphism has a significant effect on the improvement level of obesity indices and cardiorespiratory fitness indicators of middle-aged Korean women with abdominal after they were participating in two weeks of aerobic exercise training. The indices were improved regardless of the gene mutation.

2) The FABP2 genetic polymorphism affects the improvement level on the hemodynamic variable of middle-aged Korean women with abdominal obesity after they were participating in 12 weeks of aerobic exercise, between and within groups. The improvement appears regardless of the gene mutation.

3) The FABP2 genetic polymorphism affects the improvement level on the blood lipids and insulin resistance of middle-aged Korean women with abdominal obesity, after they were participating in 12 weeks of aerobic exercise, between and within groups. The improvement appears regardless of the gene mutation.

As a summary of the conclusions above, the 12 weeks of aerobic exercise targeting middle-aged Korean women with abdominal obesity according to the FABP2 Ala54Thr gene polymorphism, improves obesity indices, cardiorespiratory fitness, blood lipids, and blood glucose and insulin resistance index regardless of the gene mutation.

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