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碩士學位 請求論文

The association between SIRT1 gene and children obesity:Seoul-Kuro Cohort Study

2013

誠信女子大學校 大學院

食品營養學科

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이 論文을 碩士學位 論文으로 提出함

2012年 11月

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認 准 書

崔 世 琳 의 碩士學位 論文을 認准함.

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Acknowledgement

아무것도 모르는 신입생으로 입학했던 때가 엊그제 같은데 배우고 익히느라 바쁘게 지내다 보니 어느덧 졸업 논문을 완성하게 되었습니다. 힘들고 좌절했던 시간들도 있었지만 잘 이겨낼 수 있도록 도움을 주신 모든 분들께 감사를 드립니다. 대학원 2년 과정동안 많은 가르침을 주시고 조언해주셔서 무사히 논문을 완성하도록 지도해주신 이명숙 교수님께 진심으로 감사드립니다. 더불어 논문이 완성되기까지 조언과 격려를 해주셨던 강대용 교수님과 표영희 교수님께도 진심으로 감사의 말씀을 드립니다. 그리고 학부와 석사과정 동안 많은 가르침을 주신 안홍석 교수님, 한영숙 교수님, 나혜경 교수님, 윤현근 교수님, 이승민 교수님, 고성희 교수님께 깊이 감사드립니다.

2년의 대부분의 시간을 같이 보냈던 실험실 선배, 후배, 박사님들께도 감사의 인사를 드립니다. 석사과정 동안 아무것도 모르는 저에게 많은 것을 가르쳐 주고 힘이 되어준 박미영 박사님, 장유진 박사님, 실험에서부터 논문작성까지 도움을 주신 최정란 박사님, 실험실에서의 롤모델 경민언니, 긍정적인 마인드를 가진 정임언니, 모든 것을 척척 해내는 문지언니, 늘 같이 웃고 울었던 동기 해리, 당차게 일을 해내게 된 소영이, 밝고 씩씩한 민진이, 주현이, 안진표 선생님 모두 감사합니다.

언제나 힘이 되어주고 늘 나의편이 되어주는 정말 고마운 해나언니, 서정이, 예지, 선미언니, 지수, 혜지, 나의 오랜 친구 지은이, 천방지축 진실이, 보아, 아낌없는 격려를 해주었던 강민오빠 모두 감사합니다.

마지막으로 공부를 더 하고 싶다는 제 뜻을 믿고 뒷바라지 해주신 아빠, 엄마 그리고 열심히 응원해준 동생 예림이 사랑하고 정말 감사합니다.

지난 2년 동안 저는 그동안 경험해보지 못했던 많은 일들을 경험했습니다. 그로 인해 많이 성장 할 수 있었고 무엇이든 해낼 수 있다는 자신감을 얻었습니다. 이 경험을 바탕으로 앞으로도 더 큰 사람으로 성장할 수 있도록 노력하겠습니다.

2013년 1월 최세림 올림

Abstract

Sirtuin 1(SIRT1) is a longevity gene that protects cells against oxidative and genotoxic stress. But recent study suggests that SNPs of the SIRT1 gene was associated with body fat, BMI, and visceral obesity. However the association of SIRT1 polymorphism with childhood obesity is not reported.

The purpose of this study is to investigate association of SIRT1(rs7895833) gene and anthropometrics, lipid profile, insulin resistance related profile, and nutrient intake in 3 years of follow-up study(between 2007 and 2010). The original study population consisted of 491(boy: 246, girl: 245) third grade elementary school student and followed up 219(boy: 101, girl: 118) after 3 years. The genotyping was performed using a polymerase chain reaction(PCR) with confronting 2-pair primers(CTPP).

During 3 years, anthropometric parameters were increase but biochemical and nutrient intake were decrease both boy and girl. The distribution of obesity children was increase during 3 years. The 88% of children who had normal BMI of 2007 were also normal in 2010, and the 85% of children who had obesity of 2007 were also obesity in 2010. Also, the children of normal in 2007 were changed obese children in 2010 were 15%.

The frequencies of SIRT1 genotype were GG homozygotes(wild) 57.1%, AA homozygotes(mutant) 4.1%, and GA heterozygotes(hetero) 38.8%. Higher frequency of variant GA+AA in SIRT1 rs7895833 observed significantly in obese girl group than in normal girl group(38.7% vs 64.0%, $P<0.05$). Although energy, protein, fat, and cholesterol intake were decreased in children having GA+AA genotype, the increment of BMI and WC was higher than them with GG. Also, the decrements of TC and LDL in GA+AA were lower than the children having GG. And Obesity children with GG genotype having a negative correlation between mean change of CHO intake and mean change of TG concentration. Also mean change of HOMA-IR was same result with TG.

In conclusion, the SIRT1 polymorphism was found to be associated with obesity. And the children having GG genotype of SIRT1 rs7895833 showed protective effects of TG and HOMA-IR in Korean obesity children during 3 years.

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Ⅰ. Introduction

1. Childhood Obesity

Overweight and obesity in children is epidemic internationally. In the United States, the number of overweight children and adolescents has doubled in the latest two to three decades, and similar doubling rates are being observed worldwide.[1] By 2010, more than 40% of children in the North American and eastern Mediterranean WHO regions, 38% in Europe, 27% in the western Pacific, and 22% in southeast Asia were predicted to be overweight or obese.[2] Developing countries in recent times have also reported an increasing incidence of obesity. In a study from China, Cole et al. have reported a steep rise in body mass index(BMI) in 0-19 year old children from 1986 to 2000 with boys being fatter than girls.[3] South Korea had a relatively low prevalence of overweight and obesity, in part because it was an agricultural society. However, in recent years, rapid economic growth, adoption of fast food, and decreased physical activity have increased overweight and obesity in both children and adults.[4-8] According to the Korean National Health Examination and Nutrition Survey(KNHANES) in 2011, the percentage of Korean children(age 2-18 years)

with obesity is 12.7% among boys. In Korean girls, the prevalence of obesity is 8.6%.[9] The World Health Organization(WHO) defines obesity (in adults: BMI>30kg/m^2)as a disease for which excessive calorie intake, inconjunction with lack of physical exercise, have been identified as major predisposing and aggravating factors.[10, 11] Childhood obesity is associated with an increased risk for other diseases not only during youth but also later in life, including diabetes, arterial hypertension, coronary artery disease, and fatty liver disease.[12]

2. Background of SIRT1

Yeast Sir2(silent information regulator 2) and its mammalian homologue SIRT1 are members of the sirtuin family.[13-15] Sirtuin protein family is a nicotinamide adenine dinucleotide(NAD^+)-dependent histone deacetylase(HDAC) that regulates chromatin silencing.[16-20] In Yeast, there are four sirtuins(NAD^+-dependent histone deacetylases Hst1-Hst4) in addition to Sir2, whereas in mammals 7 homologues of Sir2 termed SIRT1-SIRT7.[21, 22] Sirtuins convert acetylated protein substrates in a reaction that uses NAD^+ into a deacetylated protein, nicotinamide, and the acetyl ester metabolites 2'-O- and 3'-O-acetyl-ADP ribose(AADPR), which are formed by the transfer of the acetyl group to the ADP-ribose portion of NAD^+.[19, 20, 23-26] The 2'-O- and 3'-O-acetyl-ADP riboses are candidate second messengers for putative sirtuin indicated signaling pathways[27, 28], although they have unknown functions in mammalian cells.[28] The deacetylase activity of the sirtuins is controlled by the cellular [NAD+]/[NADH] ratio. NAD+ works as an activator, whereas nicotinamide and reduced nicotinamide adenine dinucleotide(NADH) inhibit their activity.[29-33] Accordingly, sirtuins can act as sensors that detect cellular energy availability. Recent studies suggest

the mammalian SIRT1 in the adequate cellular response to metabolic stess events such as nutrient overload or nutrient deprivation.[34] SIRT1 is the closest human homologue of yeast Sir2 and has been the most studied.[13, 35, 36] Sirt1 has been implicated in the control of lipid and gluose metabolism.[37-39] Sir2(an nicotinamide adenine dinucleotide [11]-dependent histone deacetylase) protein is related to longevity in lower organisms such as yeast, flies, and worms.[24, 40] Sir2 has also been concerned in life-span extension during caloric restriction in these organisms.[30, 41, 42] Mammalian sirtuins have diverse cellular localizations and affect numerous cellular functions.[13] SIRT1, SIRT6 and SIRT7 are classified as the nuclear sirtuins; although SIRT1 is also present in nucleus modulate cytosolic targets. SIRT3, SIRT4 and SIRT5 reside in the mitochondria, whereas SIRT2 is localized predominantly in the cytoplasm. SIRT1, SIRT6 and SIRT3 and SIRT5 are NAD-dependent deacetylases, whereas SIRT4 and SIRT6 are primarily mono-ADP-ribosyl transferases with no deacetylase activity on histone substrates in vivo(Fig 1).[13, 15]Because of their broad distribution in nature it has been proposed that sirtuins play important protective roles that promote the survival of the organism, explaining their conservation throughout evolution[18, 40, 43-45]

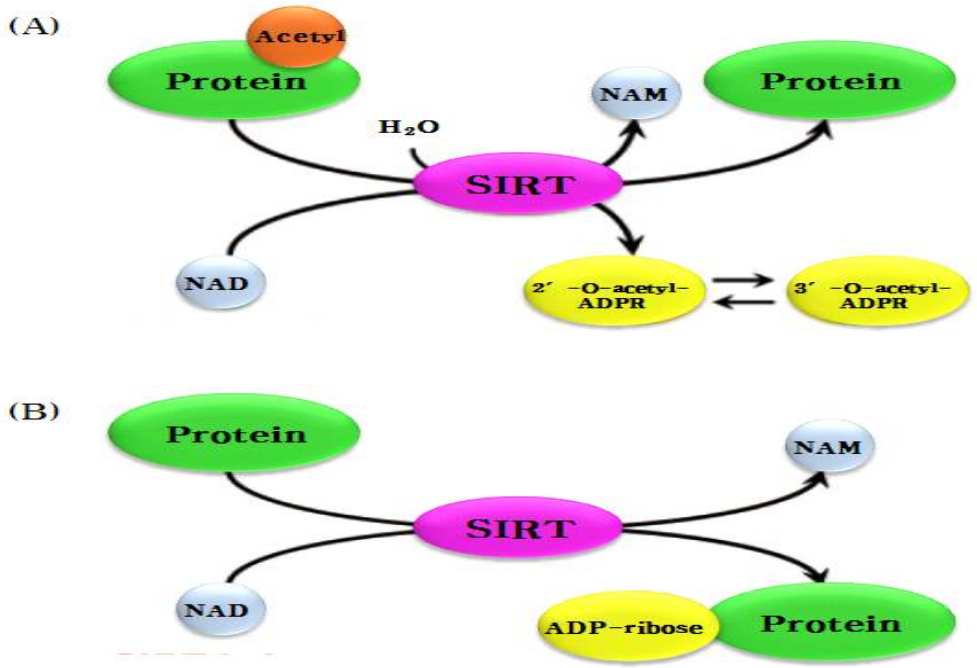


Fig 1. Two Reaction Catalyzed by Sirtuins. (A): Deacetylation (SIRT1-SIRT3, SIRT5). (B): ADP-Ribosylatio(SIRT4, SIRT6). [14]

SIRT1 is an important regulator of chromatin structure and gene expression.[46, 47] SIRT1 has been shown to regulate the expression of adiponectin[48, 49], repress the activity of PPAR-γ, by SIRT1 docking with its negative cofactors NCOR and SMRT at target gene promoters[50, 51], regulate the secretion of insulin[52], lower plasma glucose levels and improve insulin sensitivity[53] and regulate oxygen consumption and mitochondrial capacity[54, 55] and

deacetylates forkhead trancription factor 1(FOXO1) and promotes its activity that may have protective or negative effects on insulin resistance and vascular function.[49, 56-59] All of these metabolic parameters are frequently deregulated in obesity[60]. Interestingly, modest overexpression of SIRT1 also protects mice against high-fat diet induced glucose intolerance and hepatic steatosis.[61] So that SIRT1 may represent a promising future pharmacological target to prevent the metabolic sequela of chronic exposure to a high-fat diet.[62]

(1) The roles of SIRT1 in various tissue

1) Liver effects of SIRT1

The liver is a central metabolic organ that controls key aspects of lipid and glucose metabolism in response to nutritional and hormonal signals.[63] In fed state, insulin stimulates the synthesis of free fatty acids from excess carbohydrates. Fatty acids can then be packaged into lipoprotein particles and transported to adipose tissue for storage as triglycerides.[64] In the fasted conditions, the liver converts lipid and glycogen stores into available energy through the process of fatty acid β-oxidation and

glycogenolysis/gluconeogenesis. Recent reports have shown that SIRT1 is an important regulator of hepatic metabolism.[65] SIRT1 is induced in the fasted liver and interacts and deacetylates PGC1-α to activate gluconeogenic and fatty acid oxidation genes. Perxoisome proliferator-activated receptor-coactivator(PGC1-α) is a transcription coactivator.[66] In the fasted liver, SIRT1 deacetylaetes PGC1-α and activated PGC1-α coactivates FoxO1 and HNF4α on the gluconeogenic genes such as PEPCK and G-6-Pase, increasing transcription of these genes.[67] Concomitant with this effect is a repression of glycolytic genes.[38]

2) Adipose tissue effects of SIRT1

In the adipose tissue, SIRT1 inhibits adipogenesis through increase adiponectin and repression PPARγ. Adipogenesis is the mechanism by wich the preadipocyte differentiates into a mature adipocyte.[60] Several studies have demonstrated that the adipose-derived hormone, adiponectin, is diminished in both obesity and type 2 diabetes and has anti-inflammatory properties.[68] Interestingly, SIRT1 has been demonstrated to be a major regulator of adiponectin transcription in adipocytes[49] as well as adiponectin secretion.[48] Moreover,

SIRT1 protein levels were shown to be significantly lower in epididymal fat tissues from the db/db diabetic mice that have a mutation in the leptin receptor gene and used frequently as a mouse model for type 2 diabetes.[49] Another role of SIRT1 in adipose tissue is repression of PPARγ. SIRT1 induces lipolysis and prevent triglyceride accumulation in white adipocytes is through repression of PPARγ.[69] Early studies established PPARγ as a critical transcription factor capable of promoting the adipogenic program when over expressed in mouse fibroblasts, producing fat cells with similar functions to mature adipocytes.[70] Knockout studies reinforced the importance of PPARγ and linked its involvement with both brown and white fat depots.[71] The mechanism involves SIRT1 binds to PPARγ through transcriptional corepressor NCoR(nuclear receptor corepressor) and SMRT(silencing mediator of retinoid and thyroid hormone receptor), leading to the recruitment of this complex to the PPARγ and aP2(adipose tissue-specific fatty acid binding protein) gene promoters. [69] SIRT1 interferes with PPARγ autoregulatory synthesis, and SIRT1 inhibits PPARγ mediated expression of CEBPα(CCAAT enhancer-binding protein α), CEBPδ(CCAAT enhancer-binding proteinδ) and aP2.[50]

3) Skeletal muscle effects of SIRT1

Skeletal muscle represents a significant percentage of the total body mass, maintain the whole body energy balance and contributes to lipid metabolism by using free fatty acids to generate ATP via β-oxidation in mitochondria.[64, 69] Fasting or exercise when skeletal muscle must switch from using glucose to free fatty acids as its primary fuel to spare glucose for the brain.[72] A central mediator of this switch is PGC-1α. And SIRT1 is regulate PGC-1α. Stimuli that increase ATP consumption, such as exercise, or that decrease ATP production, such as nutrient deprivation, increase the intracellular AMP/ATP ratio and activate AMP-activated protein kinase (AMPK), thereby stimulating fatty acid oxidation and mitochondrial biogenesis.[73] SIRT1 also stimulates AMPK activity by deacetylating LKB1, an upstream activator of AMPK.[74, 75] In turn, AMPK increases NAD^+levels,[76, 77] thereby promoting deacetylation/activation of the SIRT1 targets PGC-1α, FOXO1, and FOXO3a.[76] In this way, SIRT1 and AMPK coordinately regulate the switch to mitochondrial oxidation of fatty acids in response to nutrient limitation.[64]

4) Pancreas effects of SIRT1

Pancreatic β cells constitute very sensitive cellular sensors for systemic glucose levels.[69] SIRT1 modulates insulin secretion in the pancreas and determined a similar mechanism of action.[52, 78] SIRT1 represses UCP2, enhancing ATP production and thereby sensitizing the pancreas to blood glucose.[78]

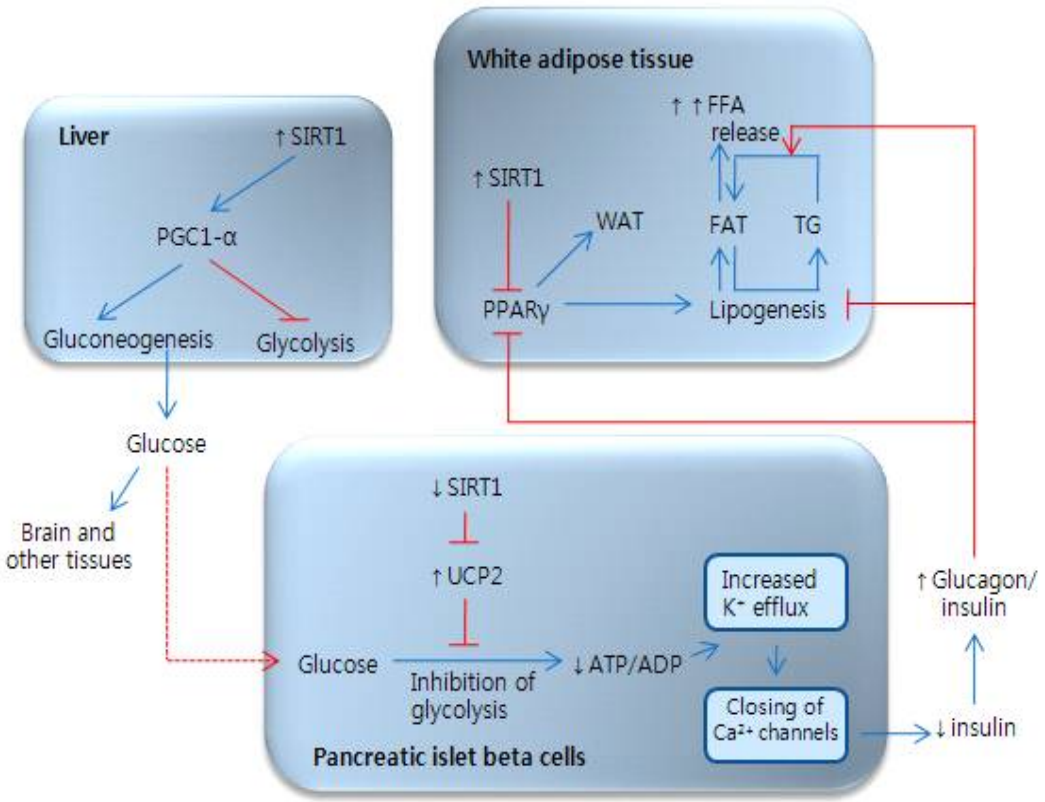


Fig 2. SIRT1 regulation of insulin-signalling pathways in different tissues during fastinf or caloric restriction.[79]

3. Sirt1 polymorphism

The Sirt1 gene is located in chromosome 10q21.3, and the coding region spans 33,715 bp.[80] It encoded in nine exons interrupted by 8 introns.[81] The approximate positions of the single nucleotide polymorphisms(SNPs) are indicated by Figure 3.[82] The rs7895833 in the promoter region.[83] And Figure 3 was DNA sequence of the regions surrounding the polymorphic site of SIRT1 polymorphism.

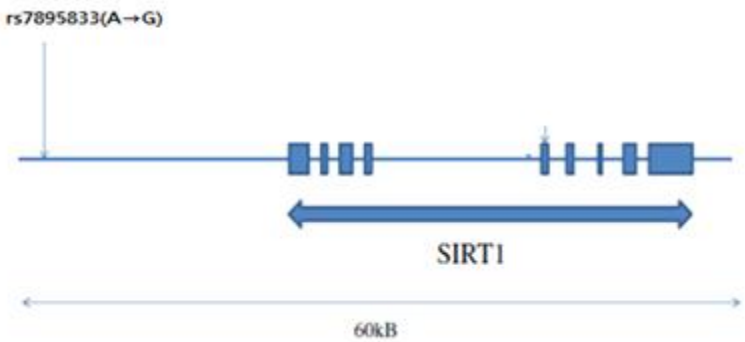


Fig 3. Schematic representation of the SIRT1 gene with the loci of SNPs.[82]

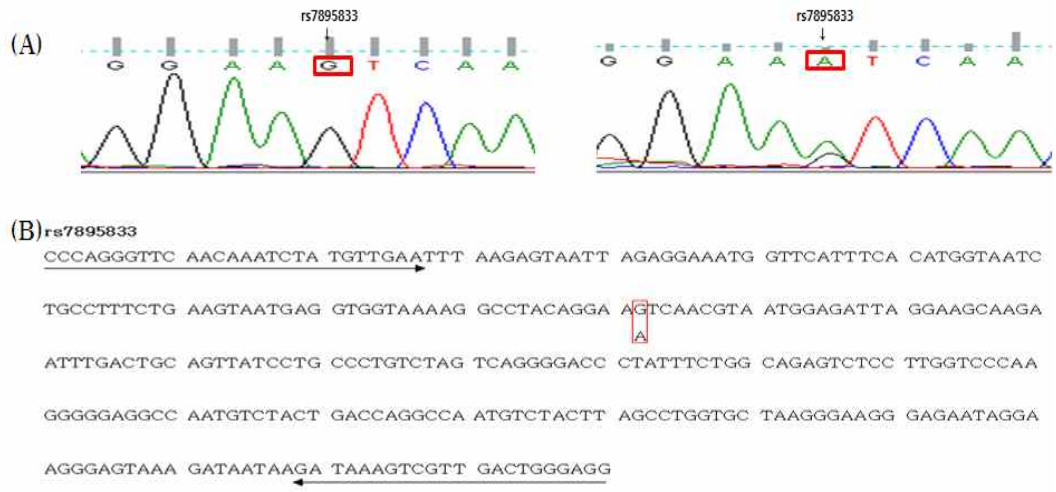


Fig 4. (A): Direct sequencing of the polymerase chain reaction products around the positions of the Sirt1 gene. (B): DNA sequence of the regions surrounding the polymorphic site.

Previous smaller studies, which have examined the relation between variants in SIRT1 and obesity, have led to inconsistent findings.[84] But recent published data suggested that SIRT1 genetic variation is related to obesity and BMI.[84, 85] Case control study of 1,068 obese patients and 313 normal weight control subjects found a SIRT1 single nucleotide polymorphism(SNP) associated with obesity risk.[85] Zillikens e al. reported that the A allele carriers of rs7895833 showed an increase in body mass index.[84] And Lagouge et al. have previously reported an association of SNP rs2273773 in exon 5 of SIRT1 with energy expenditure in

normal weight offspring of probands with type 2 diabetes, and it is plausible that a reduced rate of energy expenditure caused by variants in SIRT1 could predispose an individual to obesity.[86] So the aim of this study is association with Sirt1 gene rs7895833 and rs2273773 in obesity and control.

4. Purpose of the research

In this regard, the purpose of this study is to

a. Examine the SIRT1 genotype in Korean children

b. Investigate the obesity-related anthropometric, biochemical and nutrition variables according to SIRT1 genotype

c. Investigate the mean change of the obesity-related anthropometric, biochemical and nutrition variables according to SIRT1 genotype during 3 years

Ⅱ. Material and method

1. Study subjects and experimental design

This study presents a 3 year follow-up of children in 2007 and 2010. The subjects of this study recruited from eight elementary school in Gurogu, Seoul, Korea. 491 children(3rd grade, 2007) were recruited, of whom 219(6th grade, 2010) completed the study. Baseline data were collected using 3day(2day of weekend and 1day of week) 24-hour diet recall. Subjects enrolled from May 2007 through June 2007 and May 2010 through June 2010. And Figure 5, was the experimental design of this study.

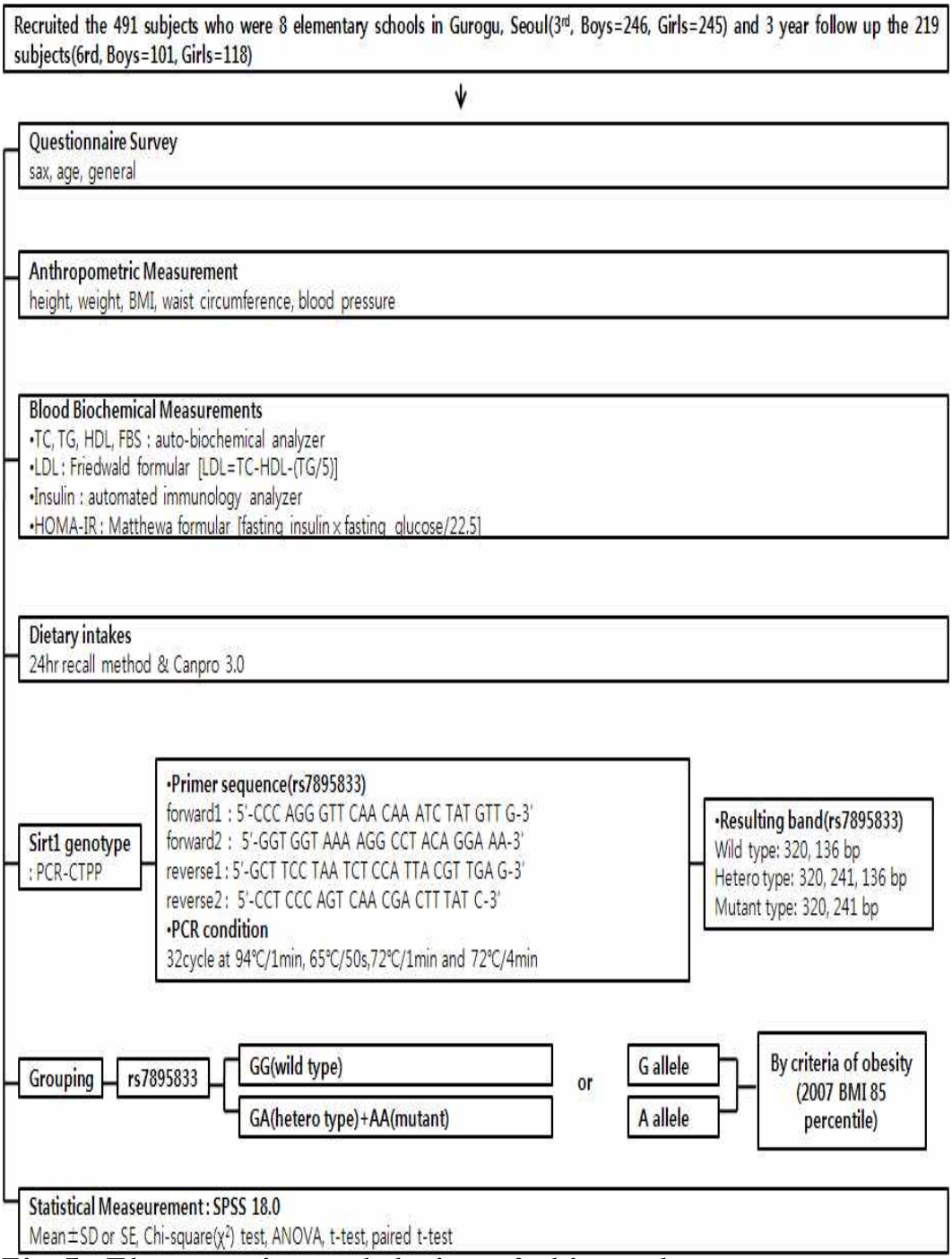


Fig 5. The experimental design of this study

2. Measurement

(1) Anthropometric variables

All measurements were made using standard technicques. The standing height was measured with a standiometer(JENIX) attached to a wall. Weight and height were measured by experienced medical staff. Systolic and diastolic blood pressure was measured after 10-minute rest by using an automatic blood pressure calculator(NISSEI, Japan) in sitting position.

(2) Obesity assessment

Used 『Application of 2007 Korean National Growth Charts』, the subjects were divided according to 2007 Body Mass Index(BMI) 85 percentile.

1) Body Mass Index

BMI was calculated by dividing weight in kilograms by the square of height in meters. Subjects were allocated to two groups according to their calculated BMI percentile values for age and gender, using standard BMI reference data used

『Application of 2007 Korean National Growth Charts』. BMI 85 group 1 were normal(BMI<85th), group 2 were overweight and obesity(BMI≥85).

Body Mass Index=weight(kg)/height(m^2)

(3) Blood biochemistry

Blood samples were collected after 12-hour fasting and were immediately placed on 4℃. For DNA genotyping, whole blood was collected in EDTA-treated tube. For other blood pfofiles, blood samples were collected in SST(serum separator tube) and centrifuged at 3000rpm for 20 min at 4℃. Serum samples were kept frozen at -80℃ until analysis.

1) Lipid profiles

Levels of Total cholesterol(TC), triglyceride(TG), and High density lipoprotein-cholesterol(HDL-c) were measured by using autoanalyzer(Ekachem DTSC module, Johnson & johnson, USA). And Low density lipoprotein-cholesterol(LDL-c) were calculated as described by the Friedewald[87] and Lauer[88] equation.

LDL cholesterol = Total cholesterol - HDL cholesterol - (Triglyceride/5)

2) Insulin resistance related profiles

Levels of fasting glucose were measured by using autoanalyzer(Ekachem DTSC module, Johnson & johnson, USA). Levels of fatsting insulin were measured by ELISA kit and HOMA-IR(homeostasis model assessment of insulin resistance) were calculated as described by Matthewa[89] equation, respectively.

HOMA-IR = [fasting glucose(mmol/l)/22.5×insulin(ul/ml)] [fasting glucose, mmol/l=fasting glucose(mg/ml)×0.0555

3. The genotyping of human Sirt1 gene

(1) Extraction of Genomic DNA from Blood Sample

Genomic DNA was extracted from blood cells using a DNA extraction kit(LaboPass^{TM} Blood MiniKit, Cosmo genetech, korea) as recommended by manufacturer. DNA quantity/quality was evaluated by means of spectrophotometer(Smartspec^{TM} plus, Bio-Rad Laboratories, Richmond, Calif) and gel analysis(2% agarose gel, duchefa biochemie, Haarlem, Netherland), and the genomic DNA was then used for gene amplification by PCR. Extraction DNA was kept frozen at -80℃ until analysis.

(2) SNP validation and genotyping

Two tagging SNPs, rs 7895833 in the SIRT1 gene selected from the public dbSNP(http://www.ncbi.nlm.nih.gov/SNP). Figure 3, show schematic representation of SIRT1 SNPs. The genotyping of rs7895833 in the promoter region was performed using polymerase chain reaction with confronting two-pair primers(CTPP) assay.[90] Table 1 show Confronting pairs of primers(four primers in all) by Yasuhiko Shimoyama et al.[82] The rs7895833 of PCRs were carried out in a total volume of 20㎕, from 100-200ng DNA as template, 10xPCR buffer(20mM Tris-HCL, pH 8.0, 100mM KCl, 0.1mM EDTA, 1mM DTT, 0.5% Tween 20, 0.5% NP-40, 50% Glycerol, 2mM $MgCl_2$), dNTP 2.5mM each, 5 unit Taq DNA polymerase(TaKaRa Bio Inc, Japan) with 5pmol of each primer.

Table 1. PCR primer sequences for genotyping

SNP	Primer	Sequence
rs 7895833	Fowrad1	5'-CCCAGGGTTCAACAAATCTATGTTG-3'
	Foward2	5'-GGTGGTAAAAGGCCTACAGGAAA -3'
	Reverse1	5'-GCTTCCTAATCTCCATTACGTTGAC-3'
	Reverse2	5'-CCTCCCAGTCAACGACTTTATC -3'

1) rs7895833

The PCR cycling profile was as annealing temperature of 94℃ for 1min, 65℃ for 50s, 72℃ for 1min for 32 cycles and final extension at 72℃ for 4 min. The amplification were performed using the PCR machine(iCycleriQ PCR system, BIO-RAD) and the PCR products were analyzed by gel electrophoresis using 2% agarose gel with RedsafeTM Nucleic Acid Staining Solution(iNtRON Biotechnology Inc, Korea) staining. Genotyping was performed as follows: 320, 241 bp for AA genotype; 320,241,136bp for GA genotype; and 320,136bp for GG genotype(Figure 6).

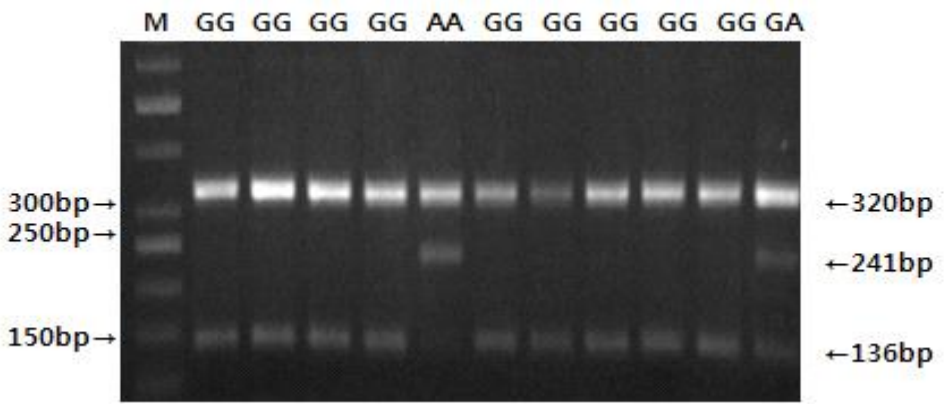


Fig 6. SIRT1 gene polymerase chain reaction (PCR) products. Genontyping of the G/A polymorphism of the SIRT1 gene by PCR-CTPP. Lane M, ladder of molecular size markers.

4. Statistical analysis

Statistical analysis were performed with SPSS 18.0 statistical package(SPSS Inc, Chicago, IL, USA). The results are presented as the means±standard deviations(SD) or number with proportions(%) for categorical variables. Comparison of the mean across the groups was examined using the t-test for normally distributed continuous variables, and with chi-square test for categorical variables. We used paired t test to establish the significance of changes between 2007 and 2010. Logistic regression analysis was used to evaluate the association between gene polymorphism and variation according to the presence of overweight and obesity. And comparisons of the 4 groups were done using one way ANOVA analysis. A p-value less than 0.05 was considered statistically significant.

Ⅲ. Result

1. General characteristics according to gender

(1) General characteristics of the baseline subjects

Table 2 shows the characteristics of anthropometrics in total baseline subjects(n=491). BMI and WC were significantly higher in Boy group after adjusted by energy. OI and DBP were significantly higher in girls group.

Lipid profiles of the groups are summarized in Table 2. According to this results, TC, TG, LDL concentration, and TG/HDL were significantly higher in girl than in boy group. Fasted Insulin and HOMA-IR which were Insulin resistance related profiles were significantly difference according to gender.

Table 2 shows the differentiation of nutrient intake. Compared with girls, boys group had higher intake of nutrient. But protein was no significant difference according to gender after adjustment for energy.

Table 2. General characteristic of baseline subjects

		Total (n=491)	Boys (n=246)	Girls (n=245)	p-value[1)]
Anthropometrics					
Height	cm	133.0±5.6	132.8±0.4	133.1±0.4	NS
Weight	kg	32.6±6.6	32.5±0.1	32.7±0.1	NS
BMI	kg/m^2	18.4±2.9	18.8±0.2	17.9±0.2	0.001
WC	cm	60.8±7.3	61.1±0.2	60.6±0.2	0.042
SBP	mmHg	107.2±13.8	106.6±0.6	107.8±0.6	NS
DBP	mmHg	68.6±10.0	67.8±0.4	69.5±0.4	0.004
Lipid profiles					
TC	mg/dl	169.3±27.2	166.7±1.3	172.1±1.3	0.003
TG	mg/dl	79.2±47.0	69.9±2.1	88.7±2.1	<0.001
HDL	mg/dl	55.2±9.8	56.9±0.4	53.5±0.5	<0.001
LDL	mg/dl	98.3±23.5	95.8±1.1	100.8±1.1	0.001
TG/HDL		1.55±1.2	1.31±0.1	1.80±0.1	<0.001
AST	U/L	26.2±5.4	26.7±0.3	25.6±0.3	0.001
ALT	U/L	24.9±9.2	25.2±0.4	24.5±0.4	NS
Insulin resistance related profiles					
FBS	mg/dl	81.8±15.1	81.1±0.7	82.5±0.7	NS
Insulin	ulU/ml	7.41±5.9	6.70±0.3	8.12±0.3	<0.001
HOMA-IR		1.40±1.4	1.21±0.1	1.59±0.1	<0.001
Nutrient					
Energy	kcal	1672.9±420.7	1755.6±438.5	1589.8±385.4	<0.001
CHO	g	223.1±26.6	233.5±1.1	212.7±1.1	<0.001
Protein	g	72.4±66.4	72.8±3.0	72.0±3.0	NS
Fat	g	57.9±10.2	60.8±0.5	55.1±0.5	<0.001
Cholesterol	mg	322.0±110.0	337.5±107.9	306.5±110.1	<0.001
Na	mg	3555.1±775.1	3659.8±779.5	3449.9±757.9	<0.001
K	mg	2402.0±501.6	2521.4±515.1	2282.2±458.3	<0.001
Na/K		1.5±0.4	1.5±0.3	1.6±0.5	0.004

1) Values are Mean±SE; adjusted by energy NS : No significance, Boy vs Girls
WC: waist circumference, S/(D)BP: systolic/diastolic blood pressure, TC: total cholesterol, TG: triglyceride, HDL: high-density lipoprotein, LDL: low-density lipoprotein, FBS: fasting blood sugar, CHO: carbohydrate

(2) General characteristics of the subjects

The subjects of this study were started 246 boys and 245 girls. But 3-year follow up subjects were 101 boys and 118 girls. The gender ratio of girl had increased. (Figure 7)

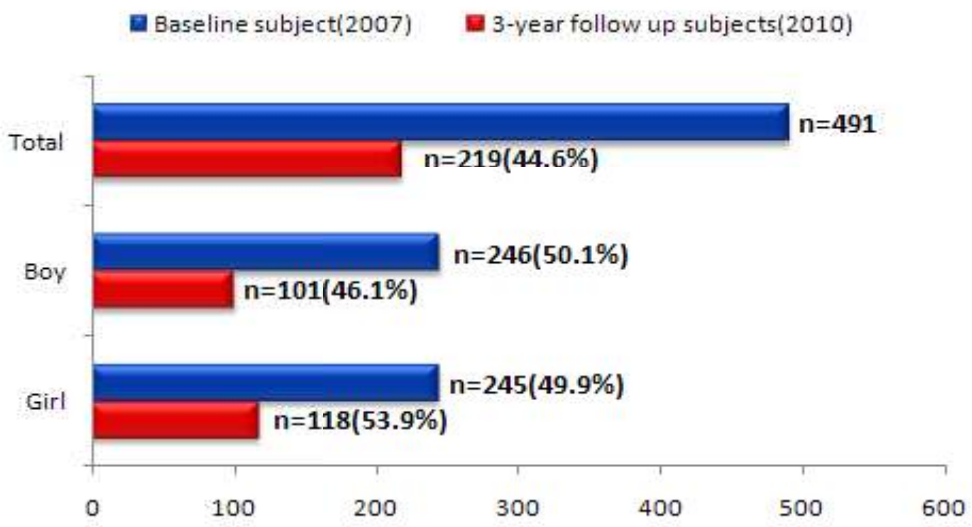


Fig 7. Distribution of the gender in all subjects.

(3) Anthropometric parameters difference between 2007 and 3-years of follow up subjects

Table 3, shows difference of anthropometric parameters between baseline(2007) and 3-years of follow-up(2010) in total subjects. All parameters in 3-years of follow-up total subjects were significantly increased. Total subject's height and weight were 132.6±5.27(cm) and 31.6±6.07(kg) at baseline, 152.0±7.02(cm) and 47.1±8.99(kg) in 3 years of follow up. Both baseline and 3 years of follow-up subject's height and weight were lower when compared to the standard height and weight .

Table 4, shows difference of anthropometric parameters between boy and girl in 3 years of follow up study. At baseline, all parameters no significance between boy and girl. After 3 years, WC of boy was higher than those of girl group and SBP was lower than girl group.

Table 5, shows difference of anthropometric parameters between baseline and 3-years of follow-up(2010) according to gender. For the boys, all parameters were significantly increased after 3 years. For the girls, the result was similar to the total subjects. The mean change of height between boy and girl was higher in girl than boy, in contrast, WC was higher in boy than girl.

Table 3. Difference of anthropometric parameters in 3 years of follow up study

Total		Baseline (n=219)	3 years Follow-up (n=219)	Difference	paired t-test[1)]
<u>Anthropometrics</u>					
Height	cm	132.6±5.2	152.0±7.0	19.4±3.5	<0.001
Weight	kg	31.6±6.1	47.1±9.0	15.5±4.8	<0.001
BMI	kg/m^2	17.9±2.7	20.3±3.2	2.38±1.8	<0.001
WC	cm	59.9±6.5	67.5±8.8	7.65±5.8	<0.001
SBP	mmHg	105.3±13.2	117.2±12.1	11.9±17.0	<0.001
DBP	mmHg	67.2±9.4	73.8±9.0	6.62±12.7	<0.001

1) Values are Mean±SD; NS : No significance, baseline(2007) vs 3 years follow-up(2010)

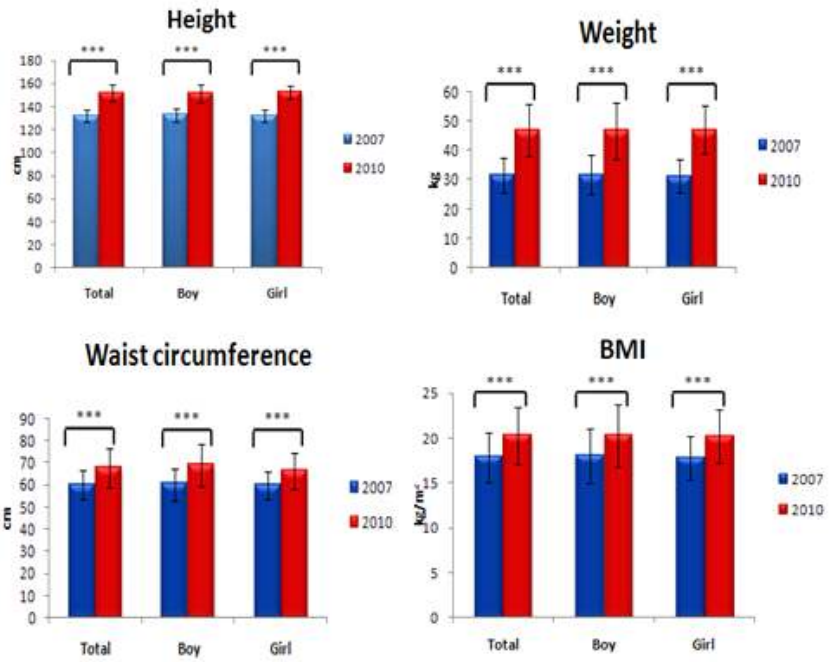


Fig 8. The mean value of height, weight, waist circumference, and BMI

Table 4. Difference of anthropometric parameters between boy and girl in 3 years of follow up study

		Baseline		p-value[1)]	3-years Follow-up		p-value[1)]	p-value[2)]
		Boys (n=101)	Girls (n=118)		Boys (n=101)	Girls (n=118)		
Anthropometrics								
Height	cm	132.7±5.5a	132.5±5.1a	NS	151.4±8.2b	152.5±5.9b	0.046	<0.001
Weight	kg	31.9±6.6a	31.4±5.6a	NS	46.9±9.7b	47.3±8.4b	NS	<0.001
BMI	kg/m^2	18.0±3.0a	17.8±2.4a	NS	20.3±3.5b	20.2±3.0b	NS	<0.001
WC	cm	60.2±7.0a	59.6±6.1a	NS	68.9±9.4c	66.3±8.0b	0.001	<0.001
SBP	mmHg	104.7±13.4a	105.7±12.9a	NS	116.6±12.7b	117.6±11.6b	NS	<0.001
DBP	mmHg	66.3±9.6a	68.0±9.2a	NS	72.2±9.7b	75.2±8.1c	0.001	<0.001

1) mean±SD; adjusted by energy NS : No significance, Boys vs Girls
2) p-value : 4 group(2007 boys vs 2007 girls vs 2010 boys vs 2010 girls)

Table 5. Difference of anthropometric parameters between 2007 and 2010 according to gender

		Boys(n=101)			paired t-test[1)]	Girls(n=118)		
		Baseline	3-year Follow-up	difference		2007	3-years Follow-up	difference
Anthropometrics								
Height	cm	132.7±5.5	151.4±8.2	18.7±4.1	<0.001	132.5±5.1	152.5±5.9	20.0±0.3
Weight	kg	31.9±6.6	46.9±9.7	15.1±5.2	<0.001	31.4±5.6	47.3±8.4	15.9±0.5
BMI	kg/m^2	18.0±3.0	20.3±3.5	2.3±2.0	<0.001	17.8±2.4	20.2±3.0	2.4±0.2
WC	cm	60.2±7.0	68.9±9.4	8.70±5.8	<0.001	59.6±6.1	66.3±8.0	6.7±0.5
SBP	mmHg	104.7±13.4	116.6±12.7	11.9±16.8	<0.001	105.7±12.9	117.6±11.6	12.0±1.6
DBP	mmHg	66.3±9.6	72.2±9.7	5.86±12.6	<0.001	68.0±9.2	75.2±8.1	7.3±1.2

1) mean±SD; NS : No significance, baseline(2007) vs 3 year follow-up(2010)
2) Boys difference vs Girls difference, †<0.05, ††<0.01, †††<0.001

(4) Biochemical parameters difference between 2007 and 3-years of follow up subjects

Table 6, shows difference of biochemical parameters between baseline and 3 years of follow up in total subjects. TG and TG/HDL were increased during 3 years. Other factors were significantly decreased after 3 years.

As shown in Table 7, TC, TG, HDL, LDL, TG/HDL, insulin, and HOMA-IR were significantly different between boy and girl at baseline. HDL was lower in girl than boys and other factors were higher in girl group. However, lipid profiles parameter and insulin resistance parameter were not different between boys and girls. Only AST, ALT, insulin, and HOMA-IR were different between boy and girl. These changes could be related to both age and maturation and likely reflect the influence of sex hormones on serum lipoprotein metabolism.[91]

Table 8, shows difference of biochemical parameters between baseline and 3 years of follow up according to gender. The result of boy and girl was showed same trend with total subject except. Girl lost more TC, LDL, AST, ALT, Insulin, and HOMA-IR during the 3 years than boys.

Table 6. Difference of Lipid profiles and insulin resistance related profiles in 3 years of follow up study

Total		Baseline (n=219)	3-years Follow-up (n=219)	Difference	paired t-test[1)]
Lipid profiles					
TC	mg/dl	169.4±26.3	155.4±25.0	-14.1±19.9	<0.001
TG	mg/dl	79.8±50.9	98.0±44.8	18.2±51.1	<0.001
HDL	mg/dl	55.2±9.9	53.4±11.8	-1.7±7.9	<0.001
LDL	mg/dl	98.3±23.5	82.3±23.6	-16.0±18.9	<0.001
TG/HDL		1.6±1.2	2.1±1.5	0.5±1.4	<0.001
AST	U/L	26.3±5.0	24.3±6.9	-2.0±7.1	<0.001
ALT	U/L	24.9±9.9	17.0±13.4	-7.9±13.2	<0.001
Insulin resistance related profiles					
FBS	mg/dl	80.7±14.1	74.1±6.3	-6.6±14.8	<0.001
Insulin	uIU/ml	7.2±5.2	5.0±4.6	-2.1±6.1	<0.001
HOMA-IR		1.5±1.2	0.9±0.9	-0.6±1.3	<0.001

1) Values are Mean±SD; NS : No significance, baseline(2007) vs 3 year follow-up(2010)

Table 7. Difference of Lipid profiles and insulin resistance related profiles between boy and girl in 3 years of follow up study

		Baseline		p-value[1)]	3-years Follow-up		p-value[1)]	p-value[2)]
		Boys (n=101)	Girls (n=118)		Boys (n=101)	Girls (n=118)		
Lipid profiles								
TC	mg/dl	165.0±29.5b	173.2±22.7c	0.003	154.5±28.2a	156.1±21.9a	NS	<0.001
TG	mg/dl	71.5±44.5a	86.9±54.9b	0.010	93.6±47.7bc	101.7±42.0c	NS	<0.001
HDL	mg/dl	56.5±10.4b	54.0±9.3a	0.006	54.1±12.7a	52.9±11.0a	NS	0.006
LDL	mg/dl	94.2±27.0b	101.8±19.5c	0.001	81.8±27.3a	82.8±19.9a	NS	<0.001
TG/HDL		1.4±1.1a	1.8±1.4b	0.010	2.0±1.5bc	2.1±1.4c	NS	<0.001
AST	U/L	26.6±5.1b	26.1±4.8b	NS	26.5±7.2b	22.5±6.1a	<0.000	<0.001
ALT	U/L	25.1±10.0c	24.7±9.8c	NS	19.2±13.9b	15.2±12.7a	0.004	<0.001
Insulin resistance related profiles								
FBS	mg/dl	79.6±15.2b	81.6±13.1b	NS	74.2±6.1a	74.0±6.5a	NS	<0.001
Insulin	uIU/ml	6.4±3.9b	8.0±6.1c	0.008	4.6±4.8a	5.3±4.5a	0.025	<0.001
HOMA-IR		1.3±0.9b	1.7±1.5c	0.004	0.9±0.9a	10.0±0.8a	0.037	<0.001

1) mean±SD; NS : No significance, Boys vs Girls

2) p-value : 4 group(2007 boys vs 2007 girls vs 2010 boys vs 2010 girls)

Table 8. Difference of Lipid profiles and insulin resistance related profiles between 2007 and 2010 according to gender

		Boys(n=101)			paired t-test[1)]	Girls(n=118)		
		Baseline	3-years Follow-up	difference		Baseline	3-years Follow-up	difference
Lipid profiles								
TC	mg/dl	165.0±29.5	154.5±28.2	-10.5±18.1	<0.001	173.2±22.7	156.1±21.9	-17.1±20.9
TG	mg/dl	71.5±44.5	93.6±47.7	22.0±49.9	<0.001	86.9±54.9	101.7±42.0	14.8±52.0
HDL	mg/dl	56.5±10.4	54.1±12.7	-2.5±8.7	<0.001	54.0±9.3	52.9±11.0	-1.1±7.1
LDL	mg/dl	94.2±27.0	81.8±27.3	-12.4±16.7	<0.001	101.8±19.6	82.8±19.9	-19.0±20.1
TG/HDL		1.4±1.1	2.0±1.5	0.6±1.3	<0.001	1.8±1.4	2.1±1.4	0.4±1.4
AST	U/L	26.6±5.1	26.5±7.2	-0.1±7.7	NS	26.1±4.8	22.5±6.1	-3.6±0.1
ALT	U/L	25.1±10.0	19.2±13.9	-5.9±14.8	<0.001	24.7±9.8	15.2±12.7	-9.5±11.3
Insulin resistance related profiles								
FBS	mg/dl	79.6±15.2	74.2±6.1	-5.5±15.9	<0.001	81.6±13.7	74.0±6.5	-7.6±13.7
Insulin	uIU/ml	6.4±3.9	4.6±4.8	-1.9±4.7	<0.001	8.0±6.1	5.3±4.5	-2.2±7.1
HOMA-IR		1.3±0.9	0.9±0.9	-0.5±1.1	<0.001	1.7±1.5	10.0±0.8	-0.7±1.5

1) mean±SD; NS : No significance, baeline(2007) vs 3 year follow-up(2010)

2) Boys difference vs Girls difference,†<0.05, ††<0.01, †††<0.001

(5) Nutrient and general characteristic and difference between 2007 and 3-years of follow up subjects

2007 and 2010 total subjects nutrient intake is shown in Table 9. Except CHO and Na/K all nutrient decreased during 3 years in total subject. Energy intake and Na/K ratio were not change. When compared with The Korea National Health and Nutrition Examination Survey in 2007, the intake of all nutrients except carbohydrate intake was high. However in 2010, energy, carbohydrate, protein, and fat intake were lower compared to The Korea National Health and Nutrition Examination Survey in 2010.

Table 10, shows difference of nutrient intake between boy and girl in 3 years of follow up study. At baseline, all nutrient intake were higher in boy group than those of girl group. After 3 years, the result was similar to basline but cholesterol was no difference between boy and girl, and Na/K was higher in girl than those of boy group.

Table 11, shows difference of nutrient intake according to gender. CHO intake of boy was decreased but increased in giro group after 3 years.

Table 9. Difference of nutrient intake in 3 years of follow up study

Total		Baseline (n=219)	3-years Follow-up (n=219)	Difference	paired t-test[1)]
Energy	kcal	1667.8±464.7	1618.4±397.9	-49.2±557.6	0.038
CHO	g	230.3±28.2	232.4±26.5	2.0±31.2	NS
Protein	g	69.5±10.9	67.1±17.9	-2.4±19.6	<0.001
Fat	g	58.8±9.5	49.4±9.6	-9.3±12.9	<0.001
Cholesterol	mg	329.7±114.9	300.6±102.0	-29.2±149.4	<0.001
Na	mg	3605.3±741.3	3411.6±768.7	-211.0±861.1	<0.001
K	mg	2406.4±478.1	2231.7±505.3	-179.0±594.7	<0.001
Na/K		1.5±0.3	1.6±0.4	0.0±0.5	NS

1) mean±SD; adjusted by energy, NS : No significance, baseline(2007) vs 3 year follow-up(2010)

Table 10. Difference of nutrient intake between boy and girl in 3 years of follow up study

gender		Baseline		p-value[1)]	3-years Follow-up		p-value[1)]	p-value[2)]
		Boys (n=101)	Girls (n=118)		Boys (n=101)	Girls (n=118)		
Energy	kcal	1762.2±520.6b	1586.3±393.8a	<0.001	1732.3±411.6b	1520.2±358.5a	<0.001	<0.001
CHO	g	248.8±24.1c	214.2±20.9a	<0.001	247.7±24.9c	219.2±19.9b	<0.001	<0.001
Protein	g	73.5±9.8c	66.1±10.7b	<0.001	72.6±22.4c	62.3±10.7a	<0.001	<0.001
Fat	g	61.3±9.6d	56.6±8.8c	<0.001	52.7±10.3b	46.7±8.0a	<0.001	<0.001
Cholesterol	mg	341.8±111.8c	319.2±116.8b	0.041	304.4±106.5ab	297.3±98.0a	NS	<0.001
Na	mg	3731.8±733.8c	3496.3±732.0b	0.001	3564.6±751.4b	3279.5±760.4a	<0.001	<0.001
K	mg	2522.0±477.0d	2306.8±457.1b	<0.001	2425.1±509.5c	2064.6±438.5a	<0.001	<0.001
Na/K		1.5±0.3a	1.5±0.3a	NS	1.5±0.4a	1.6±0.3b	0.004	0.004

1) mean±SE; adjusted by energy, NS : No significance, Boys vs Girls
2) p-value : 4 group(2007 boys vs 2007 girls vs 2010 boys vs 2010 girls)

Table 11. Difference of nutrient intake between 2007 and 2010 according to gender

gender		Boys(n=101)			paired t-test[1)]	Girls(n=118)		
		Baseline	3-years Follow-up	difference		Baseline	3-years Follow-up	difference
Energy	kcal	1762.2±520.6	1732.3±411.6	-23.6±599.6	NS	1586.3±393.8	1520.2±358.5	-71.4±518.7
CHO	g	248.8±24.1	247.7±24.9	-1.2±35.3	<0.001	214.2±20.9	219.2±19.9	4.8±26.8
Protein	g	73.5±9.7	72.6±22.4	-0.8±24.6	NS	66.1±10.7	62.3±10.7	-3.7±13.8
Fat	g	61.3±9.6	52.7±10.3	-8.6±14.3	<0.001	56.6±8.8	46.7±8.0	-9.8±11.5
Cholesterol	mg	341.8±111.8	304.4±106.5	-36.6±159.5	0.007	319.2±116.8	297.3±98.0	-22.8±140.1
Na	mg	3731.8±733.8	3564.6±751.4	-179.2±793.4	0.042	3496.3±732.0	3279.5±760.4	-238.6±916.7
K	mg	2522.0±477.0	2425.1±509.5	-98.3±557.9	NS	2306.8±457.1	2064.6±438.5	-249.1±617.6
Na/K		1.5±0.3	1.5±0.4	0.0±0.5	NS	1.5±0.3	1.6±0.3	0.1±0.4

1) mean±SD; adjusted by energy, NS : No significance, baseline(2007) vs 3 year follow-up(2010)
2) Boys difference vs Girls difference, †<0.05, ††<0.01, †††<0.001

2. General characteristics according to the obesity

(1) Frequencies and distribution of obesity in this study

As indicated in Table 12, the percentage of normal and obesity(overweight+obesity) of boy group were 85.1%, 14.9% in baseline, 79.2%, 20.8% after 3 years of follow-up. In girls, the percentage of normal was 78.8%(2007), 71.2%(2010) and obesity was 21.2%(2007), 28.8%(2010). The percentage of obesity subjects were increased both boys and girls.

Table 12. Distribution of Normal and Obesity subjects in this study

	Total (n=219)		Boy (n=101)		Girl (n=118)	
	2007	2010	2007	2010	2007	2010
Normal	179(81.7%)	164(74.9%)	86(85.1%)	80(79.2%)	93(78.8%)	84(71.2%)
Obesity[1)]	40(18.3%)	55(25.1%)	15(14.9%)	21(20.8%)	25(21.2%)	34(28.8%)
p-value	0.014		0.119		0.056	

1) diveded by BMI 85percentile

The percentage of normal total subjects in 3 years of follow-up who were normal in baseline was 72.1%, normal in baseline and obesity after 3 years was 9.60%, obesity in baseline and normal after 3 years was 2.70% and obesity in baseline and obesity after 3 years was 15.5%(Figure 9).

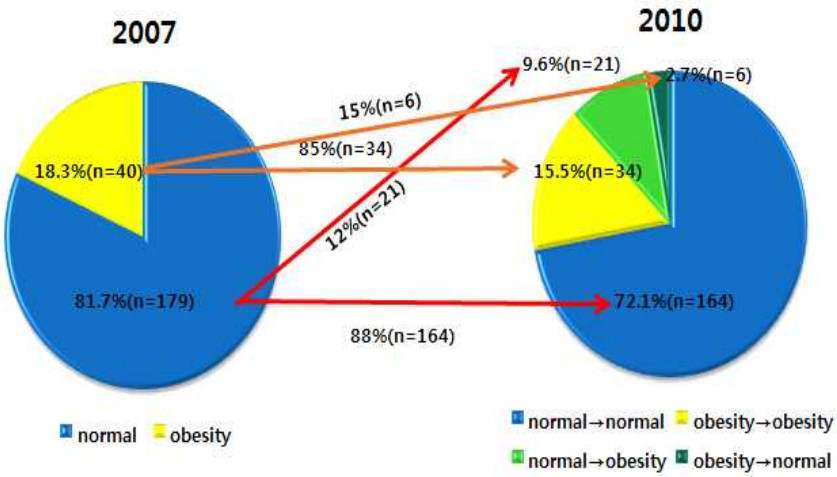


Fig 9. Distribution in the degree of obesity according to BMI 85 percentile.

2) Difference of general characteristic according to obesity

Table 13, shows the characteristics of anthropometric difference between baseline and 3 years of follow-up in total subject, boy, and girl. Mean of all parameters were significantly increased after 3 years both normal and obesity. And increment of obesity girl's WC was more higher than that of normal group.

The characteristics of biochemical profile difference between baseline and 3 years of follow-up in total subject, boy, and girl are shown in Table 14. In normal group, most parameters were decreased but TG and TG/HDL were increased after 3 years. In contrast, mean of TG and TG/HDL had no significantly change in obesity after 3 years. For the subjects who were obesity in boys, the mean change of HDL was higher than normal group. The increment of TG and TG/HDL and decrement of insulin and HOMA-IR in normal group were higher than obesity group in gir subject.

Table 13. Difference of anthropometric parameters between 2007 and 2010 according to obesity

BMI85[1] Total		Normal(n=179)			paired t-test[2]	Obesity(n=40)			paired t-test
		Baseline	3-year Follow-up	difference		Baseline	3-year Follow-up	difference	
Height	cm	132.3±5.2	151.5±7.1	19.3±3.5	<0.001	134.1±5.2	154.1±6.2	20.0±3.4	<0.001
Weight	kg	29.8±4.4	44.8±7.7	15.0±4.9	<0.001	39.6±6.2	57.3±7.0	17.7±3.9	<0.001†† [3]
BMI	kg/m^2	17.0±1.8	19.4±2.6	2.4±1.7	<0.001	21.9±2.4	24.1±2.7	2.2±1.9	<0.001
WC	cm	57.9±4.7	65.3±7.4	7.4±5.7	<0.001	68.8±6.1	77.4±7.6	8.6±6.3	<0.001
SBP	mmHg	103.9±12.3	116.4±12.6	12.5±17.0	<0.001	111.3±15.3	120.3±9.1	9.1±17.0	<0.001
DBP	mmHg	66.0±8.4	73.6±9.4	7.5±12.4	<0.001	72.6±11.5	75.1±6.5	2.6±13.2	NS††
BMI85 Boys		**Normal(n=86)**			**paired t-test**	**Obesity(n=15)**			**paired t-test**
		Baseline	**3-year Follow-up**	**difference**		**Baseline**	**3-year Follow-up**	**difference**	
Height	cm	132.2±5.7	150.9±8.4	18.7±4.1	<0.001	135.3±3.5	154.4±5.7	19.1±4.4	<0.001
Weight	kg	29.9±4.6	44.7±8.3	14.7±5.4	<0.001	42.8±5.6	59.6±7.0	16.8±3.8	<0.001†
BMI	kg/m^2	17.1±1.9	19.5±2.7	2.4±1.9	0.001	23.4±2.7	25.1±3.4	1.7±1.9	<0.001
WC	cm	58.2±4.9	66.9±8.0	8.7±5.7	<0.001	71.7±5.7	80.6±8.6	8.8±6.9	<0.001
SBP	mmHg	102.9±11.8	116.0±13.1	13.1±16.8	<0.001	114.9±17.4	120.2±9.1	5.3±15.9	NS†
DBP	mmHg	65.1±8.3	72.0±10.2	6.8±12.2	<0.001	73.3±12.9	73.7±6.3	0.4±13.7	NS†
BMI85 Girls		**Normal(n=93)**			**paired t-test**	**Obesity(n=25)**			**paired t-test**
		Baseline	**3-year Follow-up**	**difference**		**Baseline**	**3-year Follow-up**	**difference**	
Height	cm	132.3±4.8	152.2±5.6	19.8±2.6	<0.001	133.3±6.0	153.9±6.6	20.6±2.6	<0.001
Weight	kg	29.7±4.2	45.0±7.2	15.3±4.4	<0.001	37.7±5.7	55.8±6.7	18.2±3.9	<0.001†††
BMI	kg/m^2	16.9±1.8	19.4±2.6	2.4±1.5	<0.001	21.1±1.6	23.5±2.0	2.4±1.9	<0.001
WC	cm	57.6±4.5	63.8±6.5	6.3±5.5	<0.001	67.0±5.6	75.5±6.3	8.5±6.0	<0.001†
SBP	mmHg	104.8±12.6	116.8±12.0	12.0±17.2	<0.001	109.1±13.5	120.4±9.3	11.3±17.4	<0.001
DBP	mmHg	66.8±8.4	75.0±0.8	8.2±12.6	0.040	72.2±10.6	76.0±6.6	3.8±12.9	0.040†

1) Divided by BMI85 percentile based on 2007 BMI
2) mean±SD; NS : No significance, baseline(2007) vs 3 year follow-up(2010)
3) Normal difference vs Obesity difference, †<0.05, ††<0.01, †††<0.001

Table 14. Difference of Lipid profiles and insulin resistance related profiles between 2007 and 2010 according to obesity

BMI85[1] Total		Normal(n=179)			paired t-test[2]	Obesity(n=40)		
		Baseline	3-year Follow-up	difference		Baseline	3-year Follow-up	difference
Lipid profiles								
TC	mg/dl	166.7±24.7	153.6±23.9	-13.0±19.4	<0.001	181.8±29.9	163.0±28.3	-18.8±21.4
TG	mg/dl	72.7±40.8	94.7±42.2	22.0±46.5	<0.001	111.5±74.6	112.4±53.1	0.9±65.7
HDL	mg/dl	56.1±9.8	54.5±12.0	-1.63±8.0	<0.001	50.9±8.8	48.8±10.1	-2.1±7.1
LDL	mg/dl	96.0±22.5	80.2±22.6	-15.8±18.1	<0.001	108.6±25.7	91.8±25.5	-16.9±22.3
TG/HDL		1.4±1.0	1.9±1.3	0.5±1.2	<0.001	2.4±2.0	2.6±2.1	0.2±1.8
AST	U/L	26.1±4.5	24.0±5.5	-2.1±5.6	<0.001	27.2±6.6	25.9±11.1	-1.3±11.6
ALT	U/L	23.2±5.6	15.2±8.7	-7.9±9.0	<0.001	32.6±17.9	25.0±24.0	-7.7±24.4
Insulin resistance related profiles								
FBS	mg/dl	80.2±14.3	74.2±6.4	-6.0±15.0	<0.001	82.6±13.5	73.3±5.7	-9.3±13.8
Insulin	ulU/ml	6.5±4.9	4.5±4.2	-1.6±5.7	<0.001	10.7±5.7	7.1±5.8	-4.0±7.6
HOMA-IR		1.3±1.2	0.8±0.8	-0.5±1.3	<0.001	2.2±1.3	1.3±1.1	-1.1±1.5
BMI85 Boys		**Normal(n=86)**			**paired t-test**	**Obesity(n=15)**		
		Baseline	**3-year Follow-up**	**difference**		**Baseline**	**3-year Follow-up**	**difference**
Lipid profiles								
TC	mg/dl	163.1±28.6	153.5±27.2	-9.6±17.2	<0.001	176.0±32.5	160.4±33.1	-15.6±22.4
TG	mg/dl	65.2±30.1	89.3±43.7	24.1±44.3	<0.001	107.4±82.7	117.8±61.3	10.4±74.1
HDL	mg/dl	57.3±10.4	55.4±12.8	-2.0±8.9	0.005	52.0±46.5	46.5±9.3	-5.5±6.4
LDL	mg/dl	92.7±26.6	80.3±26.4	-12.5±14.8	<0.001	102.5±28.1	90.3±30.8	-12.2±25.6
TG/HDL		1.2±0.7	1.8±1.2	0.6±1.1	<0.001	2.3±2.1	2.9±2.6	0.6±2.0
AST	U/L	26.3±4.3	26.0±5.7	-0.3±5.9	NS	28.3±8.2	29.7±12.4	1.5±14.3
ALT	U/L	23.3±3.8	17.2±10.6	-6.1±10.2	<0.001	35.5±21.7	30.5±22.7	-5.0±30.2
Insulin resistance related profiles								
FBS	mg/dl	78.9±16.0	74.0±6.2	-4.9±16.6	<0.001	83.8±8.7	75.1±5.4	-8.7±10.3
Insulin	ulU/ml	5.7±3.6	4.2±4.7	-1.8±4.6	<0.001	9.9±3.7	7.1±4.4	-3.1±5.5
HOMA-IR		1.1±0.8	0.8±0.9	-0.4±1.1	<0.001	2.0±0.8	1.3±0.9	-0.8±1.2

BMI85 Girls		Normal(n=93)			paired t-test	Obesity(n=25)			paired t-test
		Baseline	3-year Follow-up	difference		Baseline	3-year Follow-up	difference	
Lipid profiles									
TC	mg/dl	170.0±19.9	153.8±20.4	-16.2±20.8	<0.001	185.3±28.0	164.6±25.1	-20.7±20.8	<0.001
TG	mg/dl	79.6±47.7	99.7±40.1	20.1±48.5	<0.001	114.0±70.1	109.2±47.9	-4.8±60.2	NS††
HDL	mg/dl	55.0±9.2	53.7±11.1	-1.3±7.1	NS	50.2±8.4	50.1±10.4	-0.1±6.9	NS
LDL	mg/dl	99.0±17.3	80.2±18.5	-18.8±20.2	<0.001	112.3±23.7	92.6±22.1	-19.6±19.8	<0.001
TG/HDL		1.6±1.1	2.0±1.3	0.5±1.4	<0.001	2.5±1.9	2.5±1.7	-0.0±1.7	NS†
AST	U/L	25.9±4.7	22.2±4.7	-3.7±4.8	<0.001	26.6±5.4	23.6±9.6	-3.00±9.5	0.029
ALT	U/L	23.0±6.9	13.4±5.8	-9.6±7.3	<0.001	30.9±15.1	21.6±24.3	-9.3±20.2	0.002
Insulin resistance related profiles									
FBS	mg/dl	81.5±12.4	74.4±6.6	-7.1±13.2	<0.001	81.8±15.7	72.2±5.7	-9.6±15.6	<0.001
Insulin	ulU/ml	7.2±5.7	4.8±3.7	-1.5±6.5	<0.001	11.1±6.7	7.1±6.5	-4.5±8.7	0.001†
HOMA-IR		1.5±1.4	0.9±0.7	-0.6±1.4	<0.001	2.3±1.5	1.3±1.2	-1.3±1.7	<0.001†††

1) Divided by BMI85 percentile based on 2007 BMI
2) mean±SD; NS : No significance, baseline(2007) vs 3 year follow-up(2010)
3) Normal difference vs Obesity difference, †<0.05, ††<0.01, †††<0.001

Table 15. Difference of nutrient intake between 2007 and 2010 according to obesity

BMI85[1] Total		Normal(n=179)			paired t-test[2]	Obesity(n=40)		
		2007	3-year Follow-up	difference		2007	3-year Follow-up	difference
Energy	kcal	1680.6±489.4	1637.8±399.3	-52.8±545.6	NS	1630.9±326.4	1552.4±386.2	-78.4±508.8
CHO	g	231.6±28.3	232.8±26.8	9.4±79.7	0.026	214.1±36.3	223.2±53.3	9.2±67.3
Protein	g	68.9±10.1	67.0±19.2	-2.5±32.7	NS	71.2±23.1	65.0±19.2	-6.3±32.0
Fat	g	58.9±21.7	50.2±16.6	-9.2±26.6	<0.001	57.1±16.4	46.4±14.9	-10.7±18.5
Cholesterol	mg	324.0±139.8	299.5±118.4	-24.5±178.4	0.010	347.8±127.9	307.8±152.8	-40.0±193.8
Na	mg	3634.8±1127.2	3401.8±969.8	-233.0±1313.4	0.001	3480.0±924.1	3431.4±1076.4	-48.6±1337.8
K	mg	2394.9±753.0	2231.1±684.6	-163.8±924.0	0.001	2368.7±660.1	2198.9±630.3	-169.8±947.6
Na_K		1.6±0.3	1.6±0.4	0.0±0.4	NS	1.5±0.4	1.6±0.4	0.1±0.5
BMI85 Boys		**Normal(n=86)**			**paired t-test**	**Obesity(n=15)**		
		2007	**3-year Follow-up**	**difference**		**2007**	**3-year Follow-up**	**difference**
Energy	kcal	1794.9±544.4	1758.6±408.6	-36.3±629.1	NS	1616.7±333.2	1581.3±402.6	-35.4±493.7
CHO	g	236.6±72.1	250.7±57.6	14.1±80.6	0.023	213.8±37.9	232.9±56.2	19.0±71.3
Protein	g	73.8±23.4	73.3±29.1	-0.5±38.4	NS	70.1±16.6	63.9±21.0	-6.2±27.7
Fat	g	63.2±23.2	54.1±18.4	-9.1±29.6	<0.001	54.4±18.1	44.9±14.1	-9.4±17.6
Cholesterol	mg	340.3±155.9	308.2±127.9	-32.1±193.9	0.031	350.0±118.4	288.4±149.3	-61.5±233.9
Na	mg	3760.1±1206.1	3586.8±935.4	-173.3±1291.2	NS	3598.5±934.5	3442.7±724.4	-155.8±1105.2
K	mg	2544.3±836.9	2446.1±681.6	-98.3±947.2	NS	2347.4±692.3	2299.5±794.1	-47.9±1057.8
Na/K		1.5±0.3	1.5±0.4	0.0±0.5	NS	1.6±0.3	1.5±0.4	0.0±0.5
BMI85 Girls		**Normal(n=93)**			**paired t-test**	**Obesity(n=25)**		
		2007	**3-year Follow-up**	**difference**		**2007**	**3-year Follow-up**	**difference**
Energy	kcal	1593.7±443.5	1525.6±363.3	-68.1±562.1	NS	1639.4±325.4	1535.1±379.1	-104.2±520.9
CHO	g	213.9±63.3	219.0±55.1	5.0±78.8	NS	214.2±35.7	217.5±51.2	3.3±64.8
Protein	g	65.1±19.4	60.8±17.1	-4.3±26.2	0.027	71.9±26.4	65.6±18.2	-6.3±34.6
Fat	g	55.9±19.5	46.6±14.0	-9.4±23.4	<0.001	58.8±15.3	47.3±15.4	-11.4±19.1
Cholesterol	mg	308.9±121.5	291.6±108.7	-17.4±163.0	NS	346.5±134.5	319.4±155.1	-27.2±166.5
Na	mg	3519.0±1038.8	3230.8±972.0	-288.2±1334.8	0.004	3408.8±919.9	3424.6±1247.9	15.8±1466.8
K	mg	2256.8±637.8	2032.4±626.4	-224.4±900.2	0.001	2381.5±646.9	2138.5±507.3	-243.0±878.0
Na/K		1.6±0.3	1.6±0.3	0.0±0.4	NS	1.5±0.4	1.6±0.4	0.1±0.5

1) Divided by BMI85 percentile based on 2007 BMI
2) mean±SD; adjusted by energy NS : No significance, baseline(2007) vs 3 year follow-up(2010)
3) Normal difference vs Obesity difference, †<0.05, ††<0.01, †††<0.001

(3) Mean change between boy and girl according to obesity(2007 BMI 85 percentile)

ANOVA measures identified significantly difference in the change of mean height and weight between boys and girls according to obesity. The increment in the height and weight of obesity girl(20.6±2.53, 18.2±3.87) were significantly the greatest among 4 group and mean change of normal boys(18.7±4.09, 14.7±5.38) were the lowest among 4 group. Normal Boy's waist circumference(8.68±5.66) was significantly more raised than normal girl group(6.27±5.45) but same with obesity boy(8.81±6.93) and girl(8.51±5.96). The mean change of DBP was more greater in normal group than obesity and obesity boy subjects observed the lowest increment of DBP mean change. (Fig 10.)

The mean change of TC and LDL was decreased all group. Girls's mean was more decreased than boy's both normal and obesity group. Boy's TG and TG/HDL were more increase than any other group. But no difference between boys and girls in normal group. Mean of HDL was most decrease in obesity boy childeren and decrement of other three group was same. One of insulin resistance related profiles, insulin and HOMA-IR were no difference between boys and girls in normal group. But in obesity group, girl's decrement was

greater than boy's. Mean change of nutrient intake was not statistically significant between 4 group. (Fig 11)

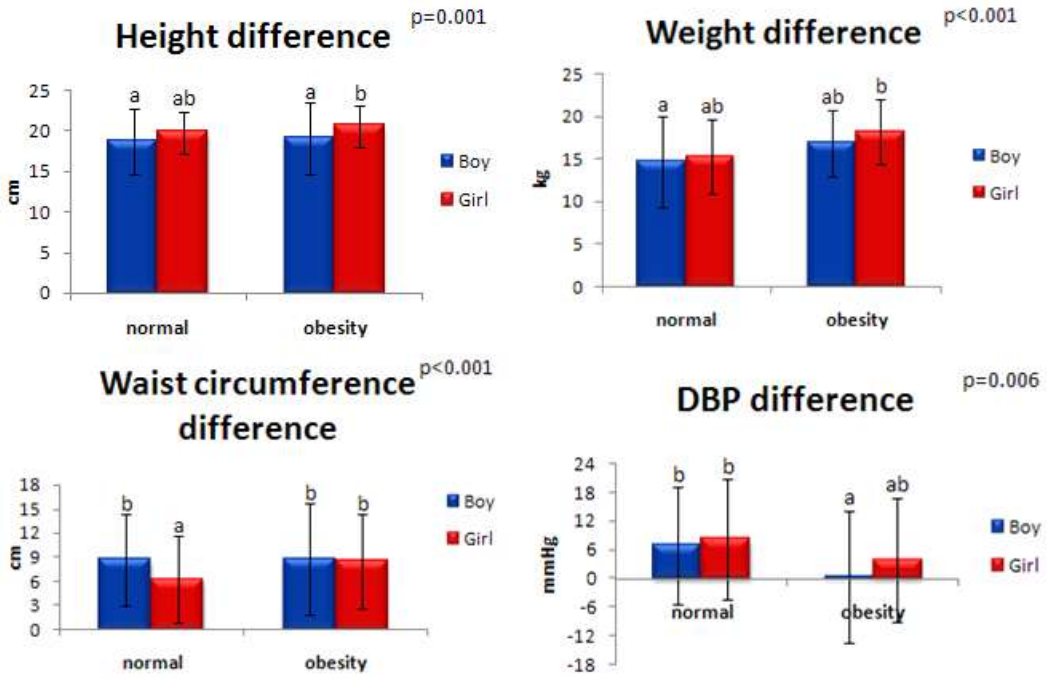


Fig 10. Changes in Height, Weight, WC and DBP between boy and girl according to obesity(2007 BMI 85 percentile)

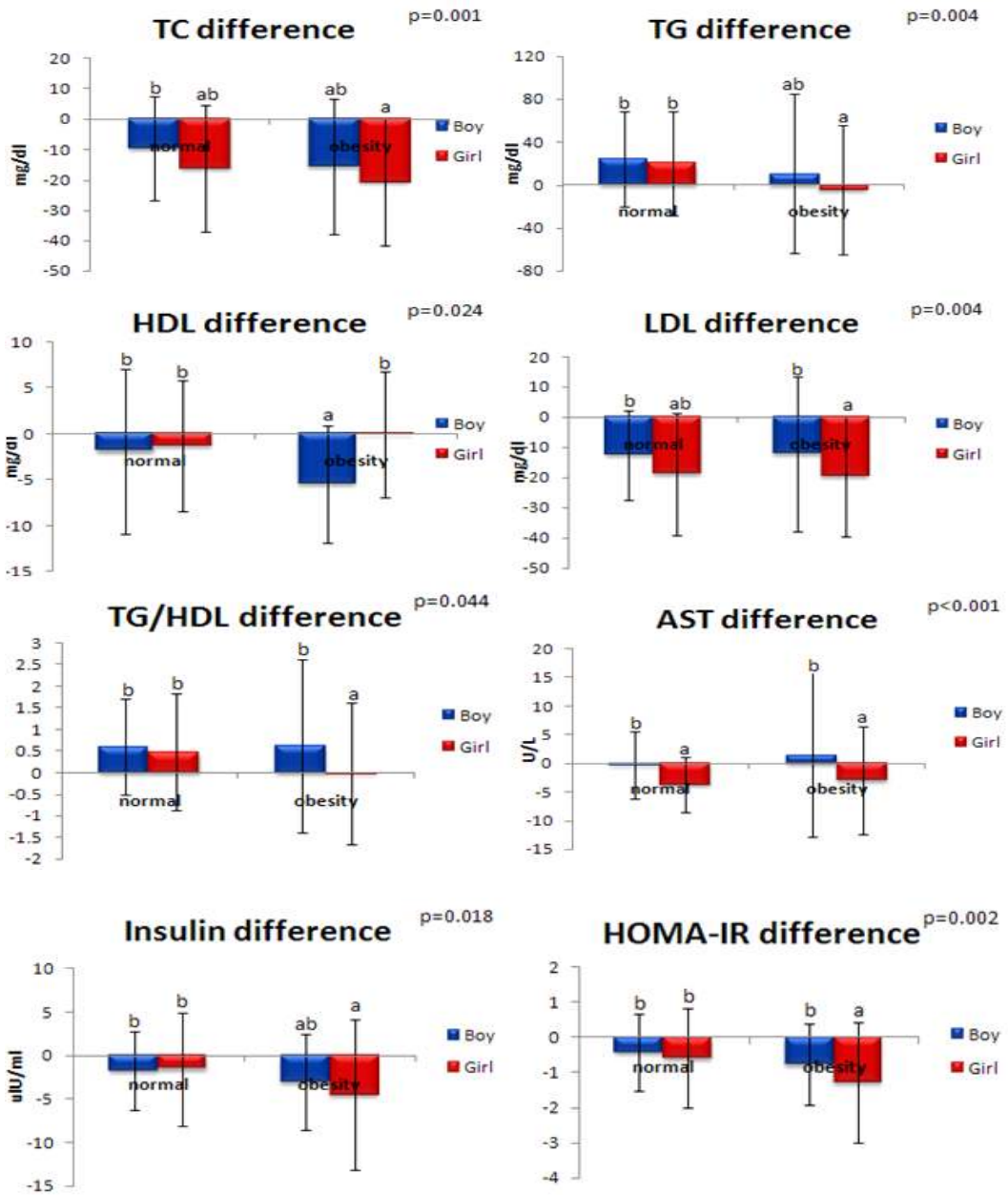


Fig 11. Changes in TC, TG, HDL, LDL, TG/HDL, AST, Insulin and HOMA-IR between boy and girl according to obesity(2007 BMI 85 percentile)

3. SIRT1 rs7895833 polymorphism

(1) SIRT1 rs7895833 polymorphism in total subjects

1) Frequency of SIRT1 rs7895833 polymorphism

The 101 boys subjects and 118 girls subjects were genotyped at SIRT1 rs7895833 polymorphism, and allele frequencies were examined. The genotype frequencies of the SIRT1 rs 7895833 polymorphism in total subjects were 57.1%(n=125) for GG, 38.8%(n=85) for GA, and 4.1%(n=9) for AA genotype. In boys group, 58.4%(n=59) for GG, 39.6%(n=40) for GA, and 2%(n=2) for AA. In girls group, 55.9%(n=66) for GG, 38.1%(n=45) for GA, and 5.9%(n=7) for AA. The allelic frequencies at this polymorphism were 0.765 for G allele and 0.235 for A allele in Total subjects. In boys, allelic frequencies were 0.782 for G allele and 0.218 for A allele. In girls, allelic frequencies were 0.750 for G allele and 0.250 for A allele. (Table 16. and Figure 12.)

Table 16. Frequencies of common allele of the gene locus coading SIRT1 rs7895833 polymorphism according to gender difference of this study

	Total (n=219)	Boys (n=101)	Girls (n=118)
SIRT1 rs7895833 genotype			
GG	125(57.1%)	59(58.4%)	66(55.9%)
GA	85(38.8%)	40(39.6%)	45(38.1%)
AA	9(4.1%)	2(2%)	7(5.9%)
SIRT1 rs7895833 allele			
G allele	0.765	0.782	0.750
A allele	0.235	0.218	0.250

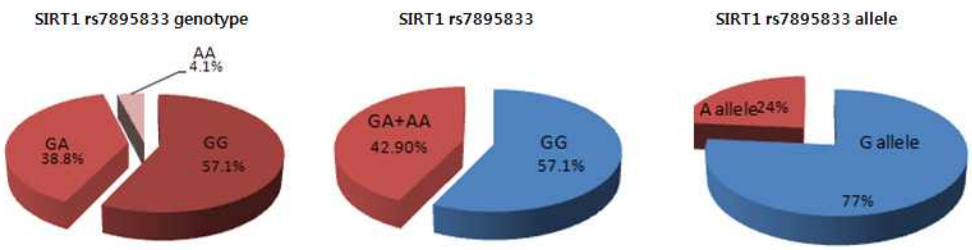


Figure 12. The distribution of SIRT1 rs7895833 polymorphism in this study

SIRT1 rs7895833 genotype frequencies of Japanese and Caucasians are **Table 17.** As Zillikens et al,[84] the "major" alleles for Caucasians are the "minor" alleles for Japanese.[82] And SIRT1 rs7895833 genotype frequencies in this study were the same as Japan. According to the study by Zillikens et al, the A allele frequency of rs7895833 was 0.80 and 0.290 in Japanese study

Table 17. The relative frequencies of common alleles of the gene locus according to SIRT1 rs7895833 of this study comparing the others.

Populations	n	G	A	GG	GA	AA
this study	219	0.765	0.235	125	85	9
Japanese[82]	1274	0.710	0.290	641	528	105
Caucasians (Rotterdam study)[84]	6251	0.200	0.800	2180		3779
Caucasians (ERF study) [84]	2347	0.230	0.770	918		1341

(2) Association between SIRT1 rs7895833 polymorphism and general characteristics in the total subjects

1) Anthropometrics characteristics in the total subjects according to SIRT1 rs7895833 genotype

The result about Anthropometrics characteristics according to SIRT1 rs7895833 genotype showed in Table 18. As indicate in Table 18, the SIRT1 rs7895833 genotype had no significant effect in the anthropometric parameters at baseline, however after 3 years of follow-up, weight, BMI, and WC were higher in GA+AA than those of GG genotype in total subjects. The case of boys, there were no significant effect in all parameters at baseline and after 3 years of follow-up. In contrast, weight, BMI and WC of girl group were significantly higher in GA+AA than those in GG genotype both baseline and 3 years of follow-up.

According to result in Table 19, mean change of BMI and WC of GA+AA in all subjects were significantly higher than those of GG genotype.

Table 18. Difference of anthropometric parameters according to SIRT1 rs7895833 genotype in 3 years of follow up study

Total		Baseline		p-value [1)]	3-years Follow-up		p-value
		GG(n=125)	GA+AA(n=94)		GG(n=125)	GA+AA(n=94)	
Height	cm	132.6±5.2a	132.6±5.4a	NS	152.2±7.0b	151.8±7.1b	NS*** [2)]
Weight	kg	31.5±6.3a	31.8±5.8a	NS	46.3±8.9b	48.2±9.0c	0.035***
BMI	kg/m^2	17.8±2.9a	18.0±2.5a	NS	19.9±3.1b	20.8±3.2c	0.003***
WC	cm	59.6±6.7a	60.2±6.3a	NS	66.3±8.8b	69.1±8.6c	0.001***
SBP	mmHg	106.2±14.0a	103.9±11.9a	NS	117.7±11.8b	116.4±12.4b	NS***
DBP	mmHg	67.8±9.9a	66.5±8.6a	NS	73.8±9.5b	73.9±8.2b	NS***
Boy		**Baseline**		**p-valu**	**3-years Follow-up**		**p-value**
		GG(n=59)	**GA+AA(n=42)**		**GG(n=59)**	**GA+AA(n=42)**	
Height	cm	132.7±5.5a	132.6±5.5a	NS	152.0±8.28b	150.7±7.90b	NS***
Weight	kg	32.4±6.9a	31.0±6.1a	NS	47.1±10.3b	46.6±9.22b	NS***
BMI	kg/m^2	18.3±3.3a	17.6±2.6a	NS	20.3±3.54b	20.4±3.32b	NS***
WC	cm	60.7±7.3a	59.5±6.4a	NS	68.6±9.58b	69.3±9.22b	NS***
SBP	mmHg	105.5±13.3a	103.6±13.7a	NS	117.6±12.1b	115.3±13.3b	NS***
DBP	mmHg	66.7±9.7a	65.8±9.4a	NS	71.8±9.73b	72.8±9.71b	NS***
Girl		**Baseline**		**p-value**	**3-years Follow-up**		**p-value**
		GG(n=66)	**GA+AA(n=52)**		**GG(n=66)**	**GA+AA(n=52)**	
Height	cm	132.5±4.9a	132.6±5.3a	NS	152.5±5.5b	152.7±6.3b	NS***
Weight	kg	30.6±5.5a	32.4±5.6a	0.015	45.6±7.7b	49.4±8.7c	0.001***
BMI	kg/m^2	17.4±2.4a	18.4±2.3b	0.002	19.5±2.7c	21.1±3.1d	<0.001***
WC	cm	58.7±6.0a	60.7±6.1b	0.001	64.3±7.4c	68.9±8.0d	<0.001***
SBP	mmHg	106.9±14.6a	104.3±10.3a	NS	117.8±11.6b	117.3±11.6b	NS***
DBP	mmHg	68.7±10.0a	67.0±8.0a	NS	75.7±9.0b	74.7±6.8b	NS***

1) mean±SD; NS : No significance, GG vs GA+AA

2) p-value: 4group, *<0.05, **<0.01, ***<0.001

Table 19. Difference of anthropometric parameters between 2007 and 2010 according to SIRT1 rs7895833 genotype

Total		GG(n=125)			paired-t-test[1)]	GA+AA(n=94)			paired-t-test
		Baseline	3-years Follow-up	difference		Baseline	3-years Follow-up	difference	
Height	cm	132.6±5.2	152.2±7.0	19.6±3.4	<0.001	132.6±5.4	151.8±7.1	19.2±3.5	<0.001
Weight	kg	31.5±6.3	46.3±8.9	14.8±4.5	<0.001	31.8±5.8	48.2±9.0	16.4±5.1	<0.001††[2)]
BMI	kg/m^2	17.8±2.9	19.9±3.1	2.1±1.6	<0.001	18.0±2.5	20.8±3.2	2.8±1.9	<0.001†††
WC	cm	59.6±6.7	66.3±8.8	6.7±5.4	<0.001	60.2±6.3	69.1±8.6	8.9±6.1	<0.001†††
SBP	mmHg	106.2±14.0	117.7±11.8	11.5±17.4	<0.001	103.9±11.9	116.4±12.4	12.5±16.4	<0.001
DBP	mmHg	67.8±9.9	73.8±9.5	6.0±13.2	<0.001	66.5±8.6	73.9±8.2	7.4±12.0	<0.001
Boy		**GG(n=59)**			**paired-t-test**	**GA+AA(n=42)**			**paired-t-test**
		Baseline	**3-years Follow-up**	**difference**		**Baseline**	**3-years Follow-up**	**difference**	
Height	cm	132.8±5.5	152.0±8.3	19.2±4.3	<0.001	132.6±5.5	150.7±7.9	18.1±3.8	<0.001†
Weight	kg	32.4±6.9	47.1±10.3	14.7±5.2	<0.001	31.0±6.1	46.6±9.2	15.6±5.3	<0.001
BMI	kg/m^2	18.3±3.3	20.3±3.5	1.9±1.8	<0.001	17.6±2.6	20.4±3.3	2.9±2.0	<0.001††
WC	cm	60.7±7.3	68.6±9.6	7.9±5.4	<0.001	59.5±6.4	69.3±9.2	9.8±6.3	<0.001†
SBP	mmHg	105.5±13.3	117.6±12.1	12.1±16.2	<0.001	103.6±13.7	115.3±13.3	11.7±17.8	<0.001
DBP	mmHg	66.7±9.7	71.8±9.7	5.0±12.6	<0.001	65.8±9.4	72.8±9.7	7.0±12.7	<0.001
Girls		**GG(n=65)**			**paired-t-test**	**GA+AA(n=53)**			**paired-t-test**
		Baseline	**3-years Follow-up**	**difference**		**Baseline**	**3-years Follow-up**	**difference**	
Height	cm	132.5±4.9	152.5±5.5	19.9±2.4	<0.001	132.6±5.3	152.7±6.3	20.1±2.9	<0.001
Weight	kg	30.6±5.5	45.6±7.7	15.0±3.8	<0.001	32.4±5.6	49.4±8.7	17.0±4.9	<0.001††
BMI	kg/m^2	17.4±2.4	19.5±2.7	2.2±1.3	<0.001	18.4±2.3	21.1±3.1	2.7±1.8	<0.001†
WC	cm	58.7±6.0	64.3±7.4	5.6±5.3	<0.001	60.7±6.1	68.9±8.0	8.2±5.8	<0.001††
SBP	mmHg	106.9±14.6	117.8±11.6	10.9±18.5	<0.001	104.3±10.3	117.3±11.6	13.1±15.3	<0.001
DBP	mmHg	68.7±10.0	75.7±9.0	6.9±13.6	<0.001	67.0±8.0	74.7±6.8	7.7±11.5	<0.001

1) mean±SD; NS : No significance, baseline(2007) vs 3 year follow-up(2010)
2) GG difference vs GA+AA difference, †<0.05, ††<0.01, †††<0.001

2) Biochemical parameters characteristic in the total subjects according to SIRT1 rs7895833 genotype

Table 20, shows Biochemical parameters characteristic according to rs7895833 genotype in baseline and 3 years of follow-up. All parameters of total subjects were not statistically significant in 2007 but FBS of GG genotype was significantly higher than GA+AA genotype after 3 years. All of insulin resistance related profiles in 3 years of follow-up were higher in GG genotype than GA+AA genotype in boys group. Only FBS and HOMA-IR of girls were significantly higher in GA+AA genotype than GG genotype at baseline but no significance after 3 years.

Table 21, showed the difference of lipid profiles and insulin resistance related profiles according to SIRT1 rs7895833 genotype. Average serum HDL levels of GG in boy subjects decreased during 3 years but decreased in GG with girl group. After adjustment BMI, in girl group, TC and LDL were decreased in GA+AA and TG/HDL was increased in GG(data not shown). The decrement of LDL in total and boy group was higher in GG than GA+AA. In contrast, the decrement of FBS and HOMA-IR in total and girl group were higher in GA+AA than those of GG.

Table 20. Difference of Lipid profiles and insulin resistance related profiles according to SIRT1 rs7895833 genotype in 3 years of follow up study

Total		Baseline		p-value [1)]	3-years Follow-up		p-value
		GG(n=125)	GA+AA(n=94)		GG(n=125)	GA+AA(n=94)	
Lipid profiles							
TC	mg/dl	167.0±28.5b	168.7±23.2b	NS	154.7±26.1a	156.3±23.4a	NS*** [2)]
TG	mg/dl	79.0±47.3a	80.8±55.5a	NS	98.5±49.2b	97.2±38.3b	NS***
HDL	mg/dl	55.2±10.4	55.1±9.1	NS	53.7±12.8	53.1±10.5	NS
LDL	mg/dl	99.0±26.4a	97.4±19.3a	NS	81.3±25.3b	83.7±21.1b	NS***
TG/HDL		1.6±1.3a	1.6±1.3a	NS	2.1±1.7b	2.0±1.2b	NS***
AST	U/L	26.3±5.0b	26.3±4.9b	NS	24.1±6.60a	24.7±7.3a	NS***
ALT	U/L	24.8±9.9c	25.0±9.78c	NS	16.0±11.3a	18.4±15.7b	NS***
Insulin resistance related profiles							
FBS	mg/dl	80.0±13.9b	81.6±14.4b	NS	74.7±6.4a	73.1±6.0a	0.008***
Insulin	uIU/ml	7.1±4.4b	7.4±6.2b	NS	5.3±4.7a	4.7±4.5a	NS***
HOMA-IR		1.4±1.0b	1.5±1.5b	NS	1.0±0.9a	0.9±0.8a	NS***
Boy		**Baseline**		**p-value**	**3-years Follow-up2010**		**p-value**
		GG(n=59)	**GA+AA(n=42)**		**GG(n=59)**	**GA+AA(n=42)**	
Lipid profiles							
TC	mg/dl	165.5±33.5b	164.3±22.8ab	NS	152.9±30.7a	156.8±24.3ab	NS**
TG	mg/dl	70.7±33.3a	72.6±56.9a	NS	92.7±52.4b	94.7±40.3b	NS***
HDL	mg/dl	56.2±11.9	56.9±7.86	NS	54.8±14.6	53.1±9.6	NS
LDL	mg/dl	95.1±32.1b	92.8±17.5b	NS	79.6±30.3a	84.8±22.3a	NS***
TG/HDL		1.4±1.0a	1.3±1.2a	NS	2.0±1.8b	1.9±1.1b	NS***
AST	U/L	26.6±5.2	26.6±5.0	NS	26.4±8.0	26.7±5.9	NS
ALT	U/L	25.3±10.5a	24.8±9.1a	NS	18.5±14.6b	20.1±12.8b	NS***
Insulin resistance related profiles							
FBS	mg/dl	81.2±14.0c	77.4±16.5b	NS	74.9±6.3ab	73.1±5.7a	0.042***
Insulin	uIU/ml	6.7±4.4c	5.9±3.0bc	NS	5.3±5.8b	3.7±2.5a	0.007***
HOMA-IR		1.4±1.0c	1.1±0.6bc	0.038	1.0±1.2b	0.7±0.4a	0.006***
Girl		**Baseline**		**p-value**	**3-years Follow-up2010**		**p-value**
		GG(n=66)	**GA+AA(n=52)**		**GG(n=66)**	**GA+AA(n=52)**	
Lipid profiles							
TC	mg/dl	174.0±22.4b	172.2±23.1b	NS	156.2±21.2a	155.8±22.8a	NS***
TG	mg/dl	86.5±56.0a	86.5±56.0a	NS	103.7±45.8b	99.2±36.7ab	NS*
HDL	mg/dl	54.2±8.8	53.7±9.8	NS	52.8±10.9	53.1±11.2	NS
LDL	mg/dl	102.4±19.4b	101.0±19.9b	NS	82.7±19.8a	82.9±20.2a	NS***
TG/HDL		1.7±1.5a	1.8±1.3a	NS	2.2±1.6b	2.0±1.2ab	NS*
AST	U/L	26.1±4.9b	26.0±4.8b	NS	21.9±4.0a	23.1±7.9a	NS***
ALT	U/L	24.4±9.4c	25.1±10.3c	NS	13.7±6.2a	17.0±17.7b	NS***
Insulin resistance related profiles							
FBS	mg/dl	78.9±13.7b	85.0±11.6c	<0.001	74.6±6.5a	73.1±6.4a	NS***
Insulin	uIU/ml	7.5±4.5b	8.7±7.7b	NS	5.2±3.5a	5.5±5.6a	NS***
HOMA-IR		1.5±1.0b	1.9±1.8c	0.047	1.0±0.7a	1.0±1.0a	NS***

1) mean±SD; NS : No significance, GG vs GA+AA

2) p-value: 4group, *<0.05, **<0.01, ***<0.001

Table 21. Difference of Lipid profiles and insulin resistance related profiles between 2007 and 2010 according to SIRT1 rs7895833 genotype

Total		GG(n=125)			paired-t-test[1)]	GA+AA(n=94)		
		Baseline	3-year Follow-up	difference		Baseline	3-years Follow-up	difference
Lipid profiles								
TC	mg/dl	167.0±28.5	154.7±26.1	-15.3±21.3	<0.001	168.7±23.2	156.3±23.4	-12.4±17.8
TG	mg/dl	79.0±47.3	98.5±49.2	19.5±49.5	<0.001	80.8±55.5	97.2±38.3	16.4±53.3
HDL	mg/dl	55.2±10.4	53.7±12.8	-1.5±7.8	0.003	55.1±9.1	53.1±10.5	-2.1±8.0
LDL	mg/dl	99.0±26.4	81.3±25.3	-17.7±19.9	<0.001	97.4±19.3	83.7±21.1	-13.6±17.2
TG/HDL		1.6±1.3	2.1±1.7	0.5±1.4	<0.001	1.6±1.3	2.0±1.2	0.4±1.3
AST	U/L	26.3±5.0	24.1±6.6	-2.3±7.3	<0.001	26.3±4.9	24.7±7.3	-1.5±6.9
ALT	U/L	24.8±9.9	16.0±11.3	-8.9±13.6	<0.001	25.0±9.8	18.4±15.7	-6.6±12.4
Insulin resistance related profiles								
FBS	mg/dl	80.0±13.9	74.7±6.4	-5.2±14.2	<0.001	81.6±14.4	73.1±6.0	-8.4±15.3
Insulin	uIU/ml	7.1±4.4	5.3±4.7	-1.6±5.3	<0.001	7.4±6.2	4.7±4.5	-2.6±7.0
HOMA-IR		1.4±1.0	10.0±0.9	-0.5±1.2	<0.001	1.5±1.5	0.9±0.8	-0.8±1.5
Boy		GG(n=59)			paired-t-test	GA+AA(n=42)		
		Baseline	3-year Follow-up	difference		Baseline	3-years Follow-up	difference
Lipid profiles								
TC	mg/dl	165.5±33.5	152.9±30.7	-12.6±18.9	<0.001	164.3±22.8	156.8±24.3	-7.5±16.6
TG	mg/dl	70.7±33.3	92.7±52.4	22.1±43.3	<0.001	72.6±56.9	94.7±40.3	22.1±58.2
HDL	mg/dl	56.2±11.9	54.8±14.6	-1.5±8.7	NS	56.9±7.9	53.1±9.6	-3.9±8.6
LDL	mg/dl	95.1±32.1	79.6±30.3	-15.5±15.9	<0.001	92.8±17.5	84.8±22.3	-8.1±16.9
TG/HDL		1.4±1.0	2.0±1.8	0.6±1.2	<0.001	1.3±1.2	1.9±1.1	0.6±1.4
AST	U/L	26.6±5.2	26.4±8.0	-0.2±8.7	NS	26.6±5.0	26.7±5.9	0.1±6.2
ALT	U/L	25.3±10.5	18.5±14.6	-6.8±16.8	<0.001	24.8±9.1	20.1±12.8	-4.8±11.5
Insulin resistance related profiles								
FBS	mg/dl	81.2±14.0	74.9±6.3	-6.3±14.8	<0.001	77.4±16.5	73.1±5.7	-4.2±17.2
Insulin	uIU/ml	6.7±4.4	5.3±5.8	-1.7±5.5	0.001	5.9±3.0	3.7±2.5	-2.3±3.4
HOMA-IR		1.4±1.0	1.0±1.2	-0.5±1.3	<0.001	1.1±0.6	0.7±0.4	-0.5±0.8

Girl		GG(n=66)			paired-t-test	GA+AA(n=52)			paired-t-test
		Baseline	3-year Follow-up	difference		Baseline	3-years Follow-up	difference	
Lipid profiles									
TC	mg/dl	174.0±22.4	156.2±21.2	-17.7±23.0	<0.001	172.2±23.1	155.8±22.8	-16.3±17.8	<0.001
TG	mg/dl	86.5±56.0	103.7±45.8	17.2±54.5	<0.001	86.5±56.0	99.2±36.7	11.8±48.8	0.015
HDL	mg/dl	54.2±8.8	52.8±10.9	-1.5±6.9	0.015	53.7±9.8	53.1±11.2	-0.6±7.3	NS
LDL	mg/dl	102.4±19.4	82.7±19.8	-19.7±22.8	<0.001	101.0±19.9	82.9±20.2	-18.1±16.2	<0.001
TG/HDL		1.7±1.5	2.2±1.6	0.4±1.6	0.002	1.8±1.3	2.0±1.2	0.3±1.2	0.016
AST	U/L	26.1±4.9	21.9±4.0	-4.2±5.0	<0.001	26.0±4.8	23.1±7.9	-2.9±7.2	<0.001
ALT	U/L	24.4±9.4	13.7±6.2	-10.7±9.6	<0.001	25.1±10.3	17.0±17.7	-8.0±13.0	<0.001
Insulin resistance related profiles									
FBS	mg/dl	78.9±13.7	74.6±6.5	-4.3±13.6	0.001	85.0±11.6	73.1±6.4	-11.8±12.7	<0.001††
Insulin	uIU/ml	7.5±4.5	5.2±3.5	-1.6±5.1	<0.001	8.7±7.7	5.5±5.6	-2.9±8.9	0.002
HOMA-IR		1.5±1.0	1.0±0.7	-0.5±1.1	<0.001	1.9±1.8	1.0±1.0	-1.0±1.9	<0.001†

1) mean±SD; NS : No significance, baseline(2007) vs 3 year follow-up(2010)

2) GG difference vs GA+AA difference, †<0.05, ††<0.01, †††<0.001

3) Nutrient characteristic in the total subjects according to SIRT1 rs7895833 genotype

In Table 22, the relationship of SIRT1 rs7895833 with nutrient at baseline and 3 years of follow-up examination. At baseline, In total subjects, all nutrient were no significant difference between GG and GA+AA genotype. However protein, fat and Na/K were higher in GG than GA+AA genotype after 3 years. At baseline of boys group also same with total subjects. But energy, CHO, protein, fat, cholesterol, and Na intake were higher in GG genotype than GA+AA after 3 years. CHO intakes of girls was higher in GA+AA than GG both baseline and after 3 years.

Table 23. shows mean change of nutrient intake between GG and GA+AA genotype. In total subjects, CHO intake of GG was increased but energy and protein intake in children with GA+AA was decreased. Mean change of fat was more decreased in GA+AA than GG. The case of boys, energy, protein, and cholesterol intake were decreased after 3 years in GA+AA but CHO intake of GG was increased. The increment of CHO and protein were highger in children with GG than in children GA+AA. In contrast, the decrement of fat intake was higher in GA+AA than GG. Energy, protein, and cholesterol intake in girl with GG were decreased.

Table 22. Difference of nutrient intake according to SIRT1 rs7895833 genotype in 3 years of follow up study

Total		Baseline		p-value[1)]	3-year Follow-up	
		GG(n=125)	GA+AA(n=94)		GG(n=125)	GA+AA(n=94)
Energy	kcal	1653.6±348.6	1687.2±588.6	NS	1644.9±395.2	1582.9±399.8
CHO	g	217.9±49.6a	229.4±28.8ab	NS	232.6±54.7b	231.7±61.4b
Protein	g	69.5±16.7b	69.8±27.6b	NS	68.7±26.8b	63.5±18.0a
Fat	g	58.3±16.1c	60.0±25.8c	NS	51.4±16.8b	47.0±15.4a
Cholesterol	mg	334.9±125.6b	319.7±152.5b	NS	309.1±127.1ab	290.3±122.3a
Na	mg	3688.3±903.5b	3497.7±1298.8ab	NS	3445.0±967.9a	3357.0±1016.5a
K	mg	2419.6±608.3b	2351.0±878.2ab	NS	2211.3±689.5a	2243.7±655.2a
Na/K		1.6±0.3ab	1.5±0.4a	NS	1.6±0.4b	1.5±0.3a
Boy		**Baseline**		**p-value**	**3-year Follow-up**	
		GG(n=59)	**GA+AA(n=42)**		**GG(n=59)**	**GA+AA(n=42)**
Energy	kcal	1745.5±373.3	1786.3±680.9	NS	1817.3±379.2	1612.8±427.6
CHO	g	230.0±52.5a	237.7±86.3a	NS	257.7±51.2b	234.5±63.5a
Protein	g	73.6±17.7b	72.8±28.0b	NS	77.5±32.1b	64.1±18.9a
Fat	g	61.2±17.4bc	62.8±28.6c	NS	56.4±18.1b	47.6±16.8a
Cholesterol	mg	357.8±113.8b	318.9±105.3b	NS	314.2±116.1b	290.7±90.3a
Na	mg	3760.7±957.5	3701.5±1419.7	NS	3693.2±890.1	3385.8±905.3
K	mg	2532.6±668.3b	2490.5±995.8ab	NS	2475.5±697.4a	2352.4±699.6ab
Na/K		1.5±0.3	1.5±0.4	NS	1.6±0.4	1.5±0.3
Girl		**Baseline**		**p-value**	**3-year Follow-up**	
		GG(n=66)	**GA+AA(n=52)**		**GG(n=66)**	**GA+AA(n=52)**
Energy	kcal	1571.3±303.4	1606.0±489.2	NS	1490.8±343.2	1558.2±375.6
CHO	g	207.2±44.3a	222.6±71.9ab	0.044	210.1±47.8ab	229.4±59.8b
Protein	g	65.8±14.9ab	67.5±27.2ab	NS	60.9±17.5a	62.9±17.3ab
Fat	g	55.7±14.5b	57.7±23.1b	NS	46.9±14.3a	46.6±14.1a
Cholesterol	mg	322.5±121.4	314.8±110.8	NS	296.2±103.3	398.6±91.1
Na	mg	3623.7±850.7b	3333.2±1173.6a	0.035	3223.1±983.8a	3333.8±1101.9a
K	mg	2318.5±531.6b	2238.3±756.7b	NS	1975.2±591.8a	2156.0±606.3b
Na/K		1.6±0.3ab	1.5±0.4a	0.006	1.7±0.3b	1.6±0.3a

1) mean±SD ; NS : No significance, GG vs GA+AA
2) p-value: 4 group , *<0.05, **<0.01, ***<0.001

Table 23. Difference of nutrient intake between 2007 and 2010 according to SIRT1 rs7895833 genotype

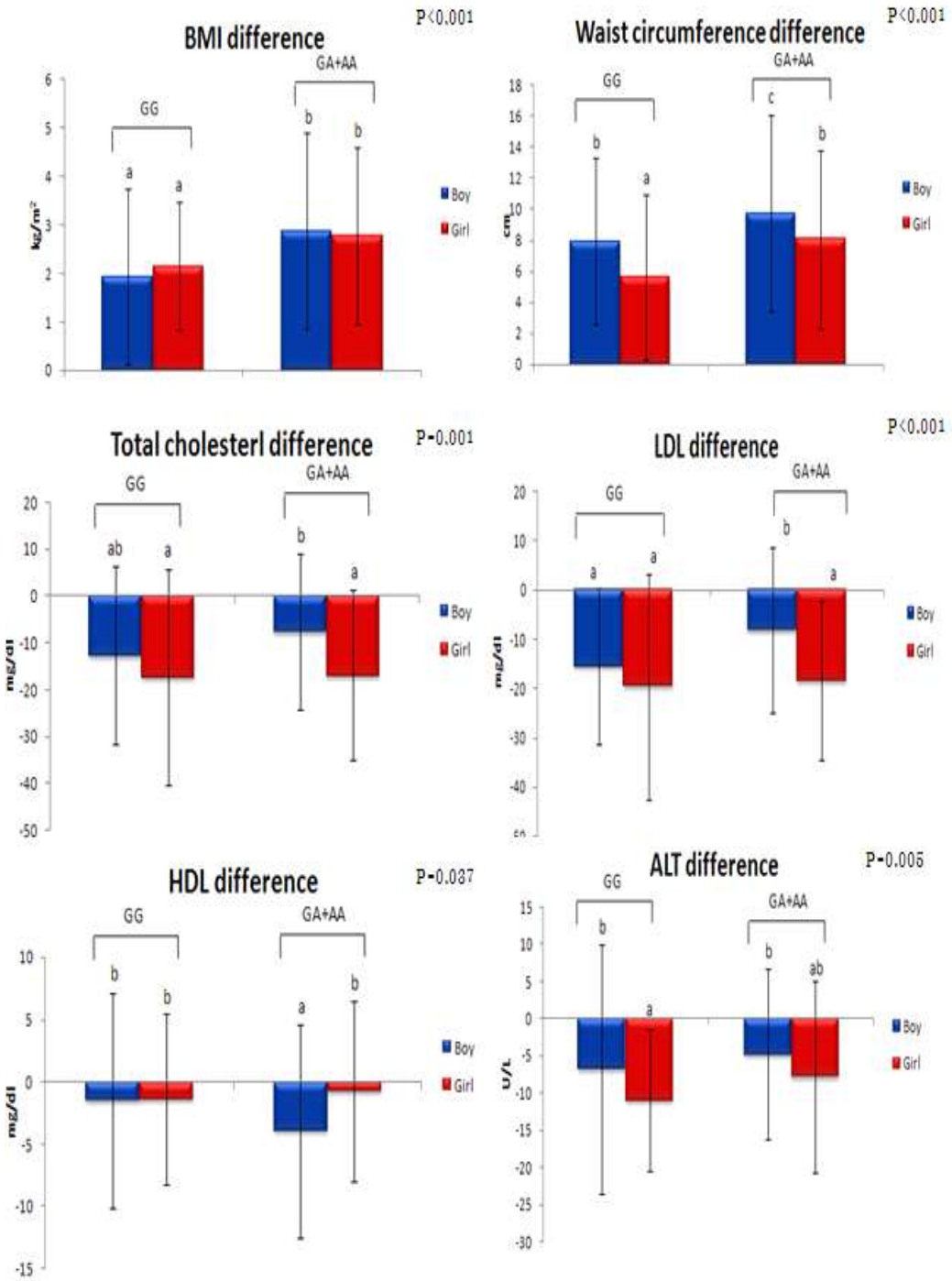
Total		GG(n=125)			paired-t-test[1)]	GA+AA(n=94)			paired-t-test
		Baseline	3-year Follow-up	difference		Baseline	3-year Follow-up	difference	
Energy	kcal	1653.6±348.6	1644.9±395.2	-8.66±489.5	NS	1687.2±588.6	1582.9±399.8	-105.4±637.5	0.028
CHO	g	217.9±49.6	232.6±54.7	14.6±68.3	0.001	229.4±28.8	231.7±61.4	2.3±87.9	NS
Protein	g	69.5±16.7	68.7±26.8	-0.7±32.6	NS	69.8±27.6	63.5±18.0	-6.4±32.3	0.007
Fat	g	58.3±16.1	51.4±16.8	-6.9±21.1	<0.001	60.0±25.8	47.0±15.4	-13.0±29.7	<0.001†[2)]
Cholesterol	mg	334.9±125.6	309.1±127.1	-25.7±175.8	0.021	319.7±152.5	290.3±122.3	-29.4±188.6	0.034
Na	mg	3688.3±903.5	3445.0±967.9	-243.4±1266.1	0.003	3497.7±1298.8	3357.0±1016.5	-140.7±1386.0	NS
K	mg	2419.6±608.3	2211.3±689.5	-208.3±878.8	<0.001	2351.0±878.2	2243.7±655.2	-107.3±987.4	NS
Na/K		1.6±0.3	1.6±0.4	0.1±0.5	NS	1.5±0.4	1.5±0.3	-0.0±0.4	NS
Boy		**GG(n=59)**			**paired-t-test**	**GA+AA(n=42)**			**paired-t-test**
		Baseline	**3-year Follow-up**	**difference**		**Baseline**	**3-year Follow-up**	**difference**	
Energy	kcal	1745.5±373.3	1817.3±379.2	71.8±519.0	NS	1786.3±680.9	1612.8±427.6	-160.9±679.6	0.035
CHO	g	230.0±52.5	257.7±51.2	27.7±72.8	<0.001	237.7±86.3	234.5±63.5	-3.3±84.4	NS††
Protein	g	73.6±17.7	77.5±32.1	3.9±40.0	NS	72.8±28.0	64.1±18.9	-8.7±31.2	0.013†
Fat	g	61.2±17.4	56.4±18.1	-4.75±23.6	0.031	62.8±28.6	47.6±16.8	-15.3±32.7	<0.001 †
Cholesterol	mg	357.8±113.8	314.2±116.1	-22.5±194.6	NS	318.9±105.3	290.7±90.3	-56.2±206.9	0.013
Na	mg	3760.7±957.5	3693.2±890.1	-67.5±1346.5	NS	3701.5±1419.7	3385.8±905.3	-315.7±1126.7	0.012
K	mg	2532.6±668.3	2475.5±697.4	-57.1±942.5	NS	2490.5±995.8	2352.4±699.6	-138.1±992.1	NS††
Na/K		1.5±0.3	1.6±0.4	0.1±0.5	NS	1.5±0.4	1.5±0.3	-0.0±0.4	NS†
Girl		**GG(n=66)**			**paired-t-test**	**GA+AA(n=52)**			**paired-t-test**
		Baseline	**3-year Follow-up**	**difference**		**Baseline**	**3-year Follow-up**	**difference**	
Energy	kcal	1571.3±303.4	1490.8±343.2	-80.6±451.5	0.042	1606.0±489.2	1558.2±375.6	-59.0±599.6	NS
CHO	g	207.2±44.3	210.1±47.8	2.9±62.0	NS	222.6±71.9	229.4±59.8	6.8±90.8	NS
Protein	g	65.8±14.9	60.9±17.5	-4.9±23.5	0.018	67.5±27.2	62.9±17.3	-4.5±33.2	NS
Fat	g	55.7±14.5	46.9±14.3	-8.8±18.4	<0.001	57.7±23.1	46.6±14.1	-11.1±27.0	<0.001
Cholesterol	mg	322.5±121.4	296.2±103.3	-28.7±157.8	0.039	314.8±110.8	398.6±91.1	-7.8±170.3	NS
Na	mg	3623.7±850.7	3223.1±983.8	-400.6±1172.5	<0.001	3333.2±1173.6	3333.8±1101.9	0.6±1555.4	NS†
K	mg	2318.5±531.6	1975.2±591.8	-343.4±797.4	<0.001	2238.3±756.7	2156.0±606.3	-82.3±987.6	NS†
Na/K		1.6±0.3	1.7±0.3	0.1±0.4	NS	1.5±0.4	1.6±0.3	0.0±0.5	NS

1) mean±SD adjusted by energy; NS : No significance, baseline(2007) vs 3 year follow-up(2010)

2) GG difference vs GA+AA difference, †<0.05, ††<0.01, †††<0.001

4) Mean change between boy and girl according to SIRT1 rs7895833 genotype

ANOVA measures identified significantly difference in the change of mean BMI and WC between baseline and follow up according to SIRT1 rs7895833 genotype. The increase in the BMI and WC of GA+AA genotype was significantly greater than that in the GG genotype both girls and boys. Increment of GA+AA genotype in BMI was same with boys(2.87±2.02) and girls(2.74±1.83) but man's WC(9.76±6.32) was significantly more raised than girls(8.15±5.79). The mean change of HDL cholesterol was decreased all genotype both boys and girls. Boy's GA+AA genotype(-3.88±8.55) was more decreased than girl's(-0.71±7.28). And boys's LDL cholesterol(-8.05±16.9) was less decreased than girl's GA+AA genotype(-18.4±16.1). However insulin resistance related profiles were more decreased in girl's GA+AA genotype(FBS:-4.21±17.2,HOMA-IR:-0.46±0.76)than boys(FBS:-11.8±12.6 HOMA-IR:-1.01±1.86).


BMI difference
P<0.001
GA+AA
GG
kg/m²
Boy
Girl
Waist circumference difference
P<0.001
cm
Total cholesterl difference
P=0.001
mg/dl
LDL difference
P<0.001
HDL difference
P=0.037
ALT difference
P=0.005
U/L

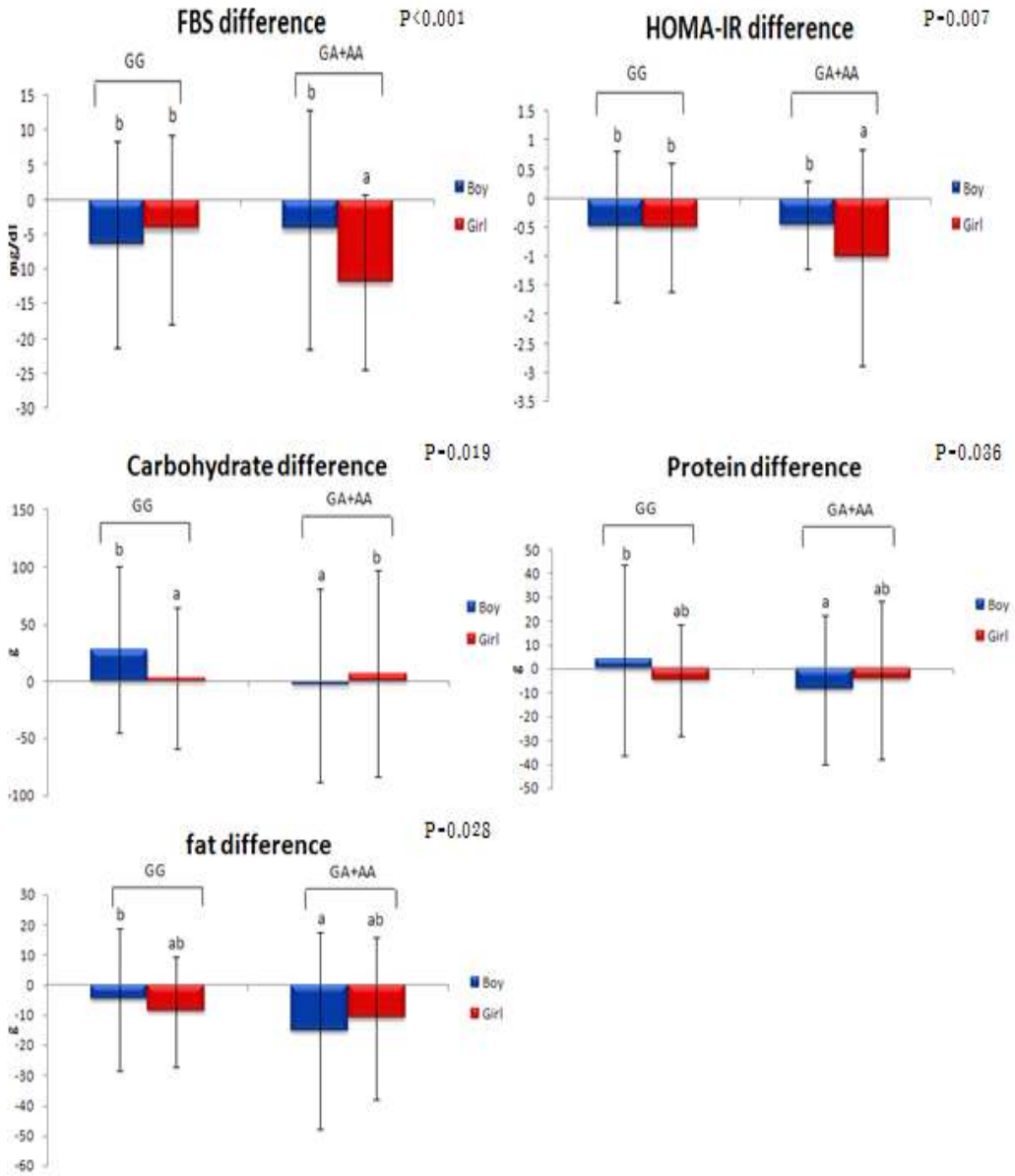


Fig 13. Changes in BMI, WC, TC, HDL, LDL, ALT, FBS, HOMA-IR, CHO, Protein, Fat between boy and girl according to SIRT1 rs7895833 genotype.

(3) SIRT1 rs7895833 polymorphism and the disease difference

1) Frequency of SIRT1 rs7895833 polymorphism according to obesity

The 179 normal subjects and 40 obesity subjects were genotyped at SIRT1 rs7895833 polymorphism, and allele frequencies were examined.

The genotype frequencies of the SIRT1 rs7895833 polymorphism in boy of normal group were 55.8%(n=48) for GG and 44.2%(n=38) for GA+AA genotype. And in girl of normal group, these frequencies were 61.3%(n=57) for GG and 38.7%(n=36) for GA+AA genotype. In case of obesity group, the genotype frequencies of the SIRT1 rs7895833 polymorphism in boy of obesity group were 73.3%(n=11) for GG and 26.7%(n=4) for GA+AA and in girl of obesity group, these frequencies were 36.0%(n=9) for GG and 64.0%(n=16) for GA+AA genotype. The GA+AA genotype and A allele frequencies at this polymorphism significantly higher than in GG genotype and G allele frequencies in female obesity group. The genotype frequency of obesity children who were normal at baseline were higher GA+AA genotype than GG genotype(42.9% vs 57.1%).(Fig 14.)

Table 24. Genotype and allelic frequencies of normal group and obesity group according to SIRT1 rs7895833 polymorphisms

		genotypic frequencies		allelic frequencies	
		GG	GA+AA	G allele	A allele
SIRT1 rs7895833 polymorphism					
Total	normal	105(58.7%)	74(41.3)	0.774	0.226
	obesity	20(50.0%)	20(50.0%)	0.725	0.275
	p-value	0.157		0.353	
Boys	normal	48(55.8%)	38(44.2%)	0.767	0.233
	obesity	11(73.3%)	4(26.7%)	0.867	0.133
	p-value	0.072		0.224	
Girls	normal	57(61.3%)	36(38.7%)	0.780	0.220
	obesity	9(36.0%)	16(64.0%)	0.640	0.360
	p-value	0.001		0.043	

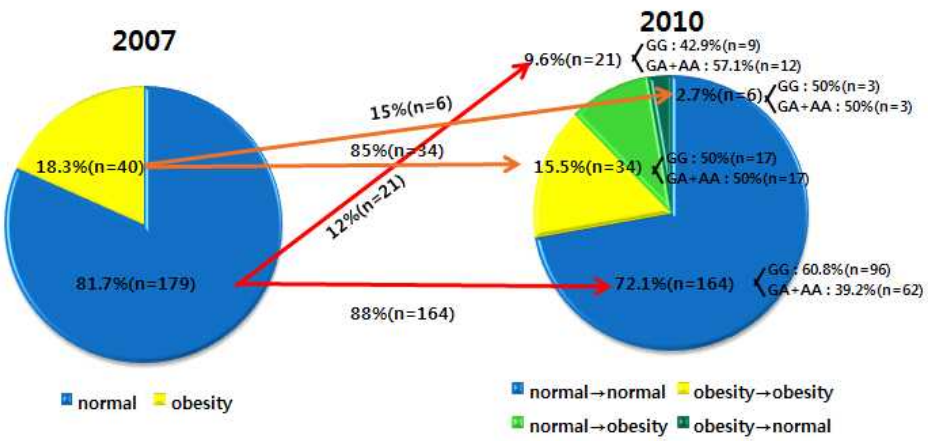


Fig 14. Distribution of genotype in the degree of obesity according to BMI85 percentile

2) General characteristics according to genotype on obesity(2007 BMI 85 percentile)

① Anthropometric characteristics according to SIRT1 rs7895833 genotype

The result about Anthropometric characteristics according to obesity in SIRT1 rs7895833 genotype showed in Table 25. As indicate in Table 25, the SIRT1 rs7895833 genotype had no significantly difference between GG and GA+AA in the anthropometric at baseline total normal group, however after 3 years of follow-up, weight, BMI, and WC were higher in GA+AA than in GG genotype. The case of baseline total obesity group, BMI, WC, SBP, and DBP were higher in GG than GA+AA. But no significantly difference between GG and GA+AA after 3 years in total subjects.

According to result in Table 26, In the case of total subjects, the increment of BMI and WC in normal children with GA+AA were significantly higher than children with GA+AA. And the increment of weight in obesity children with GA+AA showed the same trend with the normal total subjects. Girl's SBP and DBP in obesity were only increased in GA+AA.

Table 25. Difference of anthropometric parameters according to SIRT1 rs7895833 genotype and obesity in 3 years of follow up study

Total		Baseline(n=219)				p-value[1]	p-value[2]	3-years of follow-up(n=219)			
		normal(n=179)		obesity(n=40)				normal(n=179)		obesity(n=40)	
		GG (n=105)	GA+AA (n=74)	GG (n=20)	GA+AA (n=20)			GG (n=105)	GA+AA (n=74)	GG (n=20)	GA+AA (n=20)
Height	cm	132.3±5.3a	132.3±5.1a	134.5±4.3b	133.7±6.1ab	NS	NS*[3]	151.7±7.0a	151.3±7.3a	154.6±6.3b	153.6±6.2ab
Weight	kg	29.7±4.5a	30.0±4.2a	40.8±5.8c	38.4±6.3b	NS	NS***	44.2±7.5a	45.8±8.0a	57.7±7.1b	56.8±7.0b
BMI	kg/m^2	16.9±1.9a	17.1±1.8a	22.5±2.7c	21.4±1.9b	NS	0.027***	19.1±2.4a	19.9±2.9a	24.2±3.1b	24.0±2.3b
WC	cm	57.5±4.6a	58.4±4.8a	70.7±5.0c	66.8±6.5b	NS	0.003***	64.2±7.0a	66.8±7.7b	77.5±8.7c	77.3±6.5c
SBP	mmHg	104.6±12.8a	103.0±11.5a	115.1±16.6b	107.5±12.8a	NS	0.024***	117.1±12.1ab	115.5±13.1a	120.9±9.7b	119.8±8.5ab
DBP	mmHg	66.3±8.3	65.6±8.6	75.7±13.4	69.5±8.2	NS	0.016***	73.5±9.9	73.7±8.7	75.8±6.7	74.5±6.4
Boys		Baseline(n=101)				p-value	p-value	3-years of follow-up(n=101)			
		normal(n=86)		obesity(n=15)				normal(n=86)		obesity(n=15)	
		GG (n=48)	GA+AA (n=38)	GG (n=11)	GA+AA (n=4)			GG (n=48)	GA+AA (n=38)	GG (n=11)	GA+AA (n=4)
Height	cm	132.3±5.9a	132.1±5.4a	134.4±3.3ab	137.7±2.9b	NS	0.019*	151.4±8.6	150.3±8.1	154.6±6.3	154.0±3.9
Weight	kg	30.1±4.7a	29.7±4.6a	42.5±6.2b	43.8±3.6b	NS	NS***	44.3±8.2a	45.2±8.4a	59.2±8.1b	60.7±2.2b
BMI	kg/m^2	17.1±1.9a	17.0±2.0a	23.5±3.1b	23.0±1.2b	NS	NS***	19.2±2.5a	19.9±3.0a	24.9±3.9b	25.6±1.0b
WC	cm	58.2±4.9a	58.3±5.1a	71.7±6.0b	71.8±5.1b	NS	NS***	66.0±7.4a	68.0±8.6a	80.2±9.8b	81.6±4.4b
SBP	mmHg	103.9±11.7a	101.7±11.8a	112.5±17.1b	121.3±17.9c	NS	NS***	117.2±12.5	114.6±13.7	119.4±10.2	122.5±4.6
DBP	mmHg	65.3±7.9a	65.0±8.9a	73.2±13.6b	73.5±11.6b	NS	NS***	71.3±10.2	72.7±10.1	73.6±6.9	73.8±4.4
Girls		Baseline(n=118)				p-value	p-value	3-years of follow-up(n=118)			
		normal(n=93)		obesity(n=25)				normal(n=93)		obesity(n=25)	
		GG (n=57)	GA+AA (n=36)	GG (n=9)	GA+AA (n=16)			GG (n=57)	GA+AA (n=36)	GG (n=9)	GA+AA (n=16)
Height	cm	132.2±4.8	132.5±4.8	134.5±5.3	132.7±6.3	NS	NS	152.1±5.3	152.3±6.1	154.7±6.5	153.5±6.7
Weight	kg	29.3±4.4a	30.3±3.7a	38.8±4.7b	37.1±6.2b	NS	NS***	44.0±6.8a	46.5±7.6a	55.8±5.3b	55.9±7.5b
BMI	kg/m^2	16.7±1.9a	17.2±1.5a	21.3±1.2b	20.9±1.8b	NS	NS***	19.0±2.4a	20.0±2.7a	23.3±1.2b	23.6±2.4b
WC	cm	56.9±4.3a	58.5±4.6a	69.5±3.3b	65.6±6.2c	0.017	0.017***	62.7±6.4a	65.6±6.3a	74.2±5.8b	76.2±6.5b
SBP	mmHg	105.1±13.6a	104.4±11.0a	118.2±16.0b	104.0±8.6a	NS	0.002***	117.0±11.8	116.6±12.4	122.8±9.1	119.1±9.2
DBP	mmHg	67.2±8.5a	66.3±8.3a	78.7±12.9b	68.5±7.0a	NS	0.005***	75.3±9.3	74.7±6.8	78.3±5.4	74.7±6.8

1) mean±SD, NS : No significance, normal GG vs normal GA+AA
2) obesity GG vs obesity GA+AA
3) p-value: 4 group, *<0.05, **<0.01, ***<0.001

Table 26. Difference of anthropometric parameters between 2007 and 2010 according to SIRT1 rs7895833 genotype and obesity

Total		normal(n=179)						paired -t- test[1]	paired -t- test[2]	obesity(n=40)						paired -t- test[1]	paired -t- test[2]
		GG(n=105)			GA+AA(n=74)					GG(n=20)			GA+AA(n=20)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Height	cm	132.3±5.3a	151.7±7.0b	19.5±3.4	132.3±5.1a	151.3±7.3b	19.0±3.6	<0.001***	<0.001	134.5±4.3a	154.6±6.3b	20.2±3.8	133.7±6.1a	153.6±6.2b	19.9±3.0	<0.001***	<0.001
Weight	kg	29.7±4.5a	44.2±7.5b	14.5±4.6	30.0±4.2a	45.8±8.0c	15.8±5.2	<0.0001**	<0.001†[4]	40.8±5.8a	57.7±7.1b	16.9±3.6	38.4±6.3a	56.8±7.0b	18.4±4.1	<0.001***	<0.001††
OI	%	99.7±11.2ab	97.7±12.2a	-2.0±8.3	100.8±10.9ab	102.5±15.4b	1.7±10.5	0.001**	0.003††	130.5±4.4b	121.7±17.3a	-8.8±10.4	126.1±9.4ab	121.8±12.2a	-4.3±11.3	NS***	0.021††
BMI	kg/m2	16.9±1.9a	19.1±2.4b	2.2±1.6	17.1±1.8a	19.9±2.9c	2.8±1.9	<0.001***	<0.001††	22.5±2.7b	24.2±3.1c	1.6±1.7	21.4±1.9a	24.0±2.3c	2.7±2.0	<0.001***	<0.001
WC	cm	57.5±4.6a	64.2±7.0b	6.7±5.2	58.4±4.8a	66.8±7.7c	8.4±6.2	<0.001***	<0.001††	70.7±5.0b	77.5±8.7c	6.8±6.7	66.8±6.5a	77.3±6.5c	10.5±5.3	<0.001***	<0.001
SBP	mmHg	104.6±12.8a	117.1±12.1b	12.5±16.9	103.0±11.5a	115.5±13.1b	12.5±17.0	<0.001***	<0.001	115.1±16.6b	120.9±9.7c	5.8±19.1	107.5±12.8a	119.8±8.5bc	12.3±14.1	<0.001***	<0.001
DBP	mmHg	66.3±8.3a	73.5±9.9b	7.2±12.6	65.6±8.6a	73.7±8.7b	8.0±12.1	<0.001***	<0.001	75.7±13.4b	75.8±6.7b	0.1±14.4	69.5±8.2a	74.5±6.4b	5.00±11.6	<0.001***	<0.001

Boys		normal(n=86)						paired -t- test	paired -t- test	obesity(n=15)						paired -t- test	paired -t- test
		GG(n=48)			GA+AA(n=38)					GG(n=11)			GA+AA(n=4)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Height	cm	132.3±5.9a	151.4±8.6b	19.0±4.2	132.1±5.4a	150.3±8.1b	18.2±3.9	<0.001***	<0.001	134.4±3.3a	154.6±6.3b	20.2±4.7	137.7±2.9a	154.0±3.9b	16.3±1.8	<0.001***	<0.001
Weight	kg	30.1±4.7a	44.3±8.2b	14.2±5.3	29.7±4.6a	45.2±8.4b	15.5±5.5	<0.001***	<0.001	42.5±6.2a	59.2±8.1b	16.8±4.2	43.8±3.6a	60.7±2.2b	17.0±2.7	<0.001***	<0.001
OI	%	99.4±10.9ab	98.4±12.7a	-1.0±9.8	99.0±12.2ab	103.0±16.0b	4.0±11.6	NS**	0.004††	134.6±17.9	124.9±21.5	-9.7±11.7	131.3±10.6	128.9±6.8	-2.4±11.9	0.001	NS
BMI	kg/m^2	17.1±1.9a	19.2±2.5b	2.1±1.8	17.0±2.0a	19.9±3.0b	2.9±2.1	<0.001***	<0.001††	23.5±3.1	24.9±3.9	1.4±2.0	23.0±1.2	25.6±1.0	2.5±1.7	0.003	0.004
WC	cm	58.2±4.8a	66.0±7.4b	7.8±4.9	58.3±5.1a	68.0±8.6c	9.8±6.4	<0.001***	<0.001†	71.7±6.0a	80.2±9.8b	8.4±7.3	71.8±5.1a	81.6±4.4b	9.9±6.1	<0.001***	0.003
SBP	mmHg	103.9±11.7a	117.2±12.5b	13.3±16.2	101.7±11.8a	114.6±13.7b	12.8±17.6	<0.001***	<0.001	112.5±17.1	119.4±10.2	6.8±15.6	121.3±17.9	122.5±4.6	1.3±17.1	NS	NS
DBP	mmHg	65.3±7.9a	71.3±10.2b	6.1±12.0	65.0±8.9a	72.7±10.1b	7.7±12.5	<0.001***	<0.001	73.2±13.6	73.6±6.9	0.5±14.0	73.5±11.6	73.8±4.4	0.3±13.9	NS	NS

Girls		normal(n=93)						paired -t- test	paired -t- test	obesity(n=25)						paired -t- test	paired -t- test
		GG(n=57)			GA+AA(n=36)					GG(n=9)			GA+AA(n=16)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Height	cm	132.2±4.8a	152.1±5.3b	19.9±2.4	132.5±4.8a	152.3±6.1b	19.8±3.0	<0.001***	<0.001	134.5±5.3a	154.7±6.5b	20.2±2.6	132.7±6.3a	153.5±6.7b	20.8±2.6	<0.001***	<0.001
Weight	kg	29.3±4.4a	44.0±6.8b	14.7±3.9	30.3±3.7a	46.5±7.6c	16.2±4.9	<0.001***	<0.001†	38.8±4.7a	55.8±5.3b	17.0±2.6	37.1±6.2a	55.9±7.5b	18.8±4.3	<0.001***	<0.001
OI	%	100.0±11.5ab	97.1±11.9a	-2.9±6.8	105.7±9.1b	102.0±14.8b	-0.7±8.6	<0.001**	NS	125.5±5.8b	117.7±9.3a	-7.8±8.8	124.8±8.8b	120.1±12.6ab	-4.8±11.2	0.002*	0.023
BMI	kg/m^2	16.7±1.9a	19.0±2.4b	2.2±1.3	17.2±1.5a	20.0±2.7c	2.8±1.7	<0.001***	<0.001†	21.3±1.2a	23.3±1.2b	1.9±1.3	20.9±1.8a	23.6±2.4b	2.7±2.1	<0.001***	<0.001
WC	cm	56.9±4.3a	62.7±6.4b	5.8±5.2	58.5±4.6a	65.6±6.3c	7.1±5.7	<0.001***	<0.001	69.5±3.3b	74.2±5.8c	4.7±5.5	65.6±6.2a	76.2±6.5c	10.6±5.2	0.002***	<0.001††
SBP	mmHg	105.1±13.6a	117.0±11.8b	11.9±17.6	104.4±11.0a	116.6±12.4b	12.2±16.6	<0.001***	<0.001	118.2±16.0b	122.8±9.1b	4.6±23.0	104.0±8.6a	119.1±9.2b	15.1±12.1	NS***	<0.001
DBP	mmHg	67.2±8.5a	75.3±9.3b	8.1±13.1	66.3±8.3a	74.7±6.8b	8.3±11.8	<0.001***	<0.001	78.7±12.9b	78.3±5.4b	-0.3±15.3	68.5±7.0a	74.7±6.8b	6.2±10.8	NS***	<0.001

1) mean±SD, NS : No significance, GG 2007 vs GG 3 year follow-up(2010)
2) mean±SD, NS : No significance, GA+AA 2007 vs GA+AA 3 year follow-up(2010)
3) p-value: 4 group, *<0.05, **<0.01, ***<0.001
4) p-value: GG difference vs GA+AA difference, †<0.05, ††<0.01, †††<0.001

② Biochemical parameters characteristics according to SIRT1 rs7895833 genotype

The result about Biochemical parameters characteristics according to obesity in SIRT1 rs7895833 genotype showed in Table 27. As indicate in Table 27, the SIRT1 rs7895833 genotype had no significantly different between GG and GA+AA in all parameters at baseline total normal group, however after 3 years, FBS was higher in GG than in GA+AA genotype. In total obesity group, there were no significant difference between GG and GA+AA all parameters both baseline and 3y follow-up. The case of baseline boy normal group, there were significant effect in HOMA-IR. In boy normal children with GG was higher than GA+AA genotype these parameters. But no significant effect after 3 years. On the contrary normal boy, HDL, insulin and HOMA-IR of obesity boy group were no significance between GG and GA+AA at baseline. But they showed significantly difference after 3 years. FBS of baseline normal girl's result was same with baseline normal boy's HOMA-IR.

According to result in Table 28, In the case of total normal subjects with GA+AA genotype, HDL was only decreased during 3 years. In obesity group with GG genotype, TG was increased and HDL was decreased. But the decrement of TC

and LDL was higher in GG than GA+AA. In contrast, the decrement of insulin and HOMA-IR were higher in GA+AA than in GG.

Table 27. Difference of Lipid profiles and insulin resistance related profiles according to SIRT1 rs7895833 genotype and obesity in 3 years of follow up study

Total		Baseline(n=219)				p-value [1]	p-value [2]	3-years of follow-up(n=219)			
		normal(n=179)		obesity(n=40)				normal(n=179)		obesity(n=40)	
		GG (n=105)	GA+AA (n=74)	GG (n=20)	GA+AA (n=20)			GG (n=105)	GA+AA (n=74)	GG (n=20)	GA+AA (n=20)
Lipid profiles											
TC	mg/dl	167.1±27.0a	166.0±21.0a	185.0±31.4b	178.6±8.4b	NS	NS*** [3]	153.7±26.1a	153.6±20.4a	159.8±25.9ab	166.2±30.4b
TG	mg/dl	73.3±35.4a	71.8±47.5a	109.0±80.4b	114.0±69.4b	NS	NS***	94.8±46.1a	94.6±35.9a	118.1±60.0b	106.7±45.3ab
HDL	mg/dl	56.1±10.4b	56.2±9.1b	50.4±9.5a	51.3±8.1a	NS	NS***	54.9±12.9b	53.9±10.6ab	47.6±10.4a	50.0±9.7ab
LDL	mg/dl	96.4±25.5a	95.4±17.4a	112.8±27.0c	104.5±23.9b	NS	NS***	79.8±25.3a	80.7±18.2ab	88.6±24.0ab	94.9±26.9b
TG/HDL		1.4±0.9a	1.4±1.1a	2.5±0.3b	2.4±1.6b	NS	NS***	1.9±1.5a	1.9±1.0a	2.9±2.4b	2.4±1.6ab
AST	U/L	26.1±4.7	26.1±4.1	27.5±6.2	26.9±7.0	NS	NS	23.6±5.1	24.6±6.1	26.6±11.5	25.2±10.7
ALT	U/L	23.3±6.6a	22.9±4.0a	32.7±8.0b	32.6±17.9b	NS	NS***	14.7±7.7a	16.0±9.9a	22.8±20.9b	27.1±26.8b
Insulin resistance related profiles											
FBS	mg/dl	79.7±14.2	81.0±14.3	81.5±2.1	83.7±14.8	NS	NS	74.9±6.6a	73.2±6.0a	73.8±5.3a	72.8±6.2a
Insulin	uIU/ml	6.6±4.3a	6.3±5.5a	9.8±4.0b	11.6±7.0c	NS	NS***	4.8±4.7a	4.1±3.4a	7.6±4.1b	6.7±7.0b
HOMA-IR		1.3±1.0a	1.3±1.4a	2.0±0.9b	2.4±1.6c	NS	NS***	0.9±0.9ab	0.8±0.6a	1.4±0.8b	1.2±1.3ab
Boy		Baseline(n=101)				p-value	p-value	3-years of follow-up(n=101)			
		normal(n=86)		obesity(n=15)				normal(n=86)		obesity(n=15)	
		GG (n=48)	GA+AA (n=38)	GG (n=11)	GA+AA (n=4)			GG (n=48)	GA+AA (n=38)	GG (n=11)	GA+AA (n=4)
Lipid profiles											
TC	mg/dl	163.8±33.7	162.2±20.5	173.0±32.3	184.3±33.8	NS	NS	152.6±31.3	154.7±21.0	154.3±28.2	177.3±41.6
TG	mg/dl	67.6±29.1a	62.1±31.2a	83.8±46.3a	172.3±123.9b	NS	NS***	85.6±45.9a	94.0±40.7ab	123.7±67.5b	101.5±38.2ab
HDL	mg/dl	57.5±11.9a	57.1±8.0a	50.8±10.2a	55.2±6.7a	NS	NS*	57.0±14.5b	53.3±10.0b	45.0±10.4a	50.8±2.9ab
LDL	mg/dl	92.8±32.2	92.7±17.2	105.4±30.1	94.6±20.9	NS	NS	78.5±30.9a	82.5±19.4a	84.5±27.5a	106.2±35.4b
TG/HDL		1.3±0.7a	1.1±0.6a	1.9±1.7b	3.3±2.7c	NS	NS***	1.7±1.2a	1.9±1.2a	3.3±3.0b	2.0±0.8a
AST	U/L	26.4±4.9	26.2±3.5	27.5±6.3	30.5±12.3	NS	NS	25.6±5.7a	26.5±5.7a	30.1±13.9a	28.8±7.5a
ALT	U/L	23.4±3.9a	23.2±3.7a	33.7±21.5b	40.5±23.0c	NS	NS***	15.8±8.8a	19.0±12.4a	30.7±25.6b	30.0±13.1b
Insulin resistance related profiles											
FBS	mg/dl	80.6±14.9	76.7±17.0	84.0±9.2	83.3±7.8	NS	NS	74.7±6.7	73.2±5.6	76.0±4.6	72.5±6.8
Insulin	uIU/ml	6.2±4.3a	5.2±2.1a	9.2±3.8b	11.8±3.1c	NS	NS***	4.7±5.9a	3.6±2.3a	8.2±4.4b	4.4±3.5a
HOMA-IR		1.2±1.0a	1.0±0.5a	1.9±0.8b	2.4±0.6c	0.028	NS***	0.9±1.2a	0.7±0.4a	1.5±0.9b	0.8±0.6a

Girl		Baseline(n=118)				p-value	p-value	3-years of follow-up(n=118)				p-value	p-value
		normal(n=93)		obesity(n=25)				normal(n=93)		obesity(n=25)			
		GG (n=57)	GA+AA (n=36)	GG (n=9)	GA+AA (n=16)			GG (n=57)	GA+AA (n=36)	GG (n=9)	GA+AA (n=16)		
Lipid profiles													
TC	mg/dl	169.9±19.4a	170.0±20.8a	199.7±23.7b	177.2±27.3a	NS	0.005***	154.6±20.7ab	152.5±19.9a	166.6±21.7b	163.4±27.1ab	NS	NS†
TG	mg/dl	78.1±39.4a	82.0±58.7a	139.8±101.7b	99.4±38.6a	NS	NS***	102.5±45.2	95.3±30.3	111.2±50.3	108.0±47.4	NS	NS
HDL	mg/dl	54.9±8.7b	55.2±10.1b	49.9±8.8a	50.3±8.2a	NS	NS*	53.1±11.1	54.6±11.2	50.7±9.91	49.8±10.8	NS	NS
LDL	mg/dl	99.4±19.5a	98.4±17.2a	121.8±19.9b	107.0±24.3a	NS	0.033***	81.0±19.5a	78.8±16.8a	93.6±18.4b	92.1±24.2b	NS	NS**
TG/HDL		1.5±1.0a	1.6±1.4a	3.1±2.8b	2.1±1.1a	NS	NS***	2.2±1.6	1.84±0.77	2.39±1.45	2.5±1.8	NS	NS
AST	U/L	25.9±4.6	26.0±4.9	27.6±6.3	26.0±4.7	NS	NS	21.9±3.8	22.6±5.8	22.2±5.3	24.3±11.3	NS	NS
ALT	U/L	23.3±8.2a	22.6±4.3a	31.3±13.2b	30.6±16.3b	NS	NS***	13.8±6.5a	12.9±4.6a	13.1±3.6a	26.4±29.4b	NS	0.017***
Insulin resistance related profiles													
FBS	mg/dl	79.0±13.6a	85.5±8.8b	78.3±4.6a	83.8±6.2ab	<0.001	NS**	75.1±6.6b	73.3±6.5ab	71.1±4.8a	72.9±6.2ab	NS	NS*
Insulin	uIU/ml	7.0±4.3a	7.5±7.4a	10.4±4.3b	11.5±7.8b	NS	NS**	4.9±3.4a	4.6±4.2a	6.8±3.6ab	7.3±7.6b	NS	NS*
HOMA-IR		1.4±1.0a	1.6±1.8a	2.0±1.0ab	2.5±1.8b	NS	NS**	0.9±0.7	0.9±0.8	1.2±0.6	1.3±1.4	NS	NS

1) mean±SD, NS : No significance, normal GG vs normal GA+AA
2) obesity GG vs obesity GA+AA
3) p-value: 4 group, *<0.05, **<0.01, ***<0.001

Table 28. Difference of Lipid profiles and insulin resistance related profiles between 2007 and 2010 according to SIRT1 rs7895833 genotype and obesity

Total		normal(n=105)						paired-t-test[1]	paired-t-test[2]	obesity(n=20)					
		GG			GA+AA					GG			GA+AA		
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference
Lipid profiles															
TC	mg/dl	167.1±27.0b	153.7±26.1a	-13.4±20.5	166.0±21.0b	153.6±20.4a	-12.4±17.8	<0.001***	<0.001	185.0±31.4b	159.8±25.9a	-25.2±22.8	178.6±8.4ab	166.2±30.4ab	-12.4±18.1
TG	mg/dl	73.3±35.4a	94.8±46.1b	21.5±43.7	71.8±47.5a	94.6±35.9b	22.8±50.4	<0.001***	<0.001	109.0±80.4	118.1±60.0	9.1±72.6	114.0±69.4	106.7±45.3	-7.3±57.7
HDL	mg/dl	56.1±10.4	54.9±12.9	-1.2±7.8	56.2±9.1	53.9±10.6	-2.2±8.3	NS	0.026	50.4±9.5	47.6±10.4	-2.9±7.4	51.3±8.1	50.0±9.7	-1.4±6.9
LDL	mg/dl	96.4±25.5b	79.8±25.3a	-16.5±19.6	95.4±17.4b	80.7±18.2a	-14.7±15.8	<0.001***	<0.001	112.8±27.0b	88.6±24.0a	-24.2±20.7	104.5±23.9ab	94.9±26.9ab	-9.6±21.7
TG/HDL		1.4±0.9a	1.9±1.5b	0.5±1.3	1.4±1.1a	1.9±1.0b	0.5±1.2	<0.001***	<0.001	2.5±0.3	2.9±2.4	0.4±2.1	2.4±1.6	2.4±1.6	0.0±1.5
AST	U/L	26.1±4.7b	23.6±5.1a	-2.5±5.3	26.1±4.2b	24.6±6.1a	-1.5±6.1	<0.001***	<0.001	27.5±6.2	26.6±11.5	-1.0±13.6	26.9±7.0	25.2±10.7	-1.7±9.3
ALT	U/L	23.3±6.6b	14.7±7.7a	-8.7±8.4	22.9±4.0b	16.0±9.9a	-6.9±9.6	<0.001***	<0.001	32.7±8.0	22.8±20.9	-9.9±28.4	32.6±17.9	27.1±26.8	-5.5±19.6
Insulin resistance related profiles															
FBS	mg/dl	79.7±14.2b	74.9±6.6a	-4.8±14.7	81.0±14.3b	73.2±6.0a	-7.8±15.2	<0.001***	<0.001	81.5±2.1b	73.8±5.3a	-7.7±11.3	83.7±14.8b	72.8±6.2a	-10.9±15.8
Insulin	uIU/ml	6.6±4.3b	4.8±4.7a	-1.6±5.2	6.3±5.5b	4.1±3.4a	-1.7±6.2	<0.001***	<0.001	9.8±4.0ab	7.6±4.1ab	-2.1±5.8	11.6±7.0b	6.7±7.0a	-5.7±8.8
HOMA-IR		1.3±1.0b	0.9±0.9a	-0.5±1.1	1.3±1.4b	0.8±0.6a	-0.6±1.4	<0.001***	<0.001	2.0±0.9b	1.4±0.8a	-0.6±1.1	2.4±1.6b	1.2±1.3a	-1.5±1.8
Boy		normal(n=86)						paired-t-test	paired-t-test	obesity(n=15)					
		GG(n=48)			GA+AA(n=38)					GG(n=11)			GA+AA(n=4)		
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference
Lipid profiles															
TC	mg/dl	163.8±33.7b	152.6±31.3a	-11.2±17.5	162.2±20.5ab	154.7±21.0b	-7.6±16.6	<0.001*	<0.001	173.0±32.3	154.3±28.2	-18.7±23.5	184.3±33.8	177.3±41.6	-7.0±17.3
TG	mg/dl	67.6±29.1a	85.6±45.9b	18.0±43.2	62.1±31.2a	94.0±40.7b	31.9±44.8	<0.001***	<0.001†	83.8±46.3a	123.7±67.5b	39.9±39.6	172.3±123.9b	101.5±38.2a	-70.8±88.1
HDL	mg/dl	57.5±11.9	57.0±14.5	-0.5±8.7	57.1±8.0	53.3±10.0	-3.8±8.9	NS	<0.001†	50.8±10.2ab	45.0±10.4a	-5.8±7.0	55.2±6.7b	50.8±2.9ab	-4.5±4.3
LDL	mg/dl	92.8±32.2b	78.5±30.9a	-14.3±15.5	92.7±17.2b	82.5±19.4a	-10.1±13.6	<0.001***	<0.001	105.4±30.1	84.5±27.5	-20.9±17.1	94.6±20.9	106.2±35.4	11.6±30.6
TG/HDL		1.3±0.7a	1.7±1.2b	0.4±1.0	1.1±0.6a	1.9±1.2b	0.8±1.2	<0.001***	<0.001†	1.9±1.7	3.3±3.0	1.3±1.5	3.3±2.7	2.0±0.8	-1.3±1.9
AST	U/L	26.4±4.9	25.6±5.7	-0.8±5.8	26.2±3.5	26.5±5.7	0.3±6.0	NS	NS	27.5±6.3	30.1±13.9	2.6±16.0	30.5±12.3	28.8±7.5	-1.8±7.3
ALT	U/L	23.4±3.9c	15.8±8.8a	-7.6±9.0	23.2±3.7c	19.0±12.4b	-4.2±11.3	<0.001***	0.002†	33.7±21.5	30.7±25.6	-3.0±34.6	40.5±23.0	30.0±13.1	-10.5±12.1
Insulin resistance related profiles															
FBS	mg/dl	80.6±14.9b	74.7±6.7a	-5.9±15.7	76.7±17.0a	73.2±5.6a	-3.5±17.7	<0.001***	NS	84.0±9.2b	76.0±4.6a	-8.0±10.4	83.3±7.8b	72.5±6.8a	-10.8±10.5
Insulin	uIU/ml	6.2±4.3b	4.7±5.9ab	-1.8±5.6	5.2±2.1ab	3.6±2.3a	-1.7±2.9	0.003**	<0.001	9.2±3.8bc	8.2±4.4b	-1.4±5.2	11.8±3.1c	4.4±3.5a	-7.4±3.9
HOMA-IR		1.2±1.0b	0.9±1.2ab	-0.5±1.3	1.0±0.5ab	0.7±0.4a	-0.3±0.6	0.001***	<0.001	1.9±0.8bc	1.5±0.9b	-0.4±1.1	2.4±0.6c	0.8±0.6a	-1.6±0.9

Girl		normal(n=93)						paired-t-test	paired-t-test	obesity(n=25)						paired-t-test	paired-t-test
		GG(n=57)			GA+AA(n=36)					GG(n=9)			GA+AA(n=16)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Lipid profiles																	
TC	mg/dl	169.9±19.4b	154.6±20.7a	-15.3±22.7	170.0±20.8b	152.5±19.9a	-17.5±17.6	<0.001***	<0.001	199.7±23.7b	166.6±21.7a	-33.1±19.6	177.2±27.3b	163.4±27.1a	-13.8±18.3	<0.001***	<0.001††
TG	mg/dl	78.1±39.4a	102.5±45.2b	24.4±44.1	82.0±58.7a	95.3±30.3b	0.3±1.2	<0.001***	0.042	139.8±101.7	111.2±50.3	-28.6±86.1	99.4±38.6	108.0±47.4	8.6±33.8	NS	NS
HDL	mg/dl	54.9±8.7	53.1±11.1	-1.8±6.9	55.2±10.1	54.6±11.2	-0.6±7.4	0.006	NS	49.9±8.8	50.7±9.9	0.7±6.3	50.3±8.2	49.8±10.8	-0.6±7.3	NS	NS
LDL	mg/dl	99.4±19.5b	81.0±19.5a	-18.4±22.3	98.4±17.2b	78.8±16.8a	-19.6±16.5	<0.001***	<0.001	121.8±19.9c	93.6±18.4a	-28.1±24.2	107.0±24.3b	92.1±24.2a	-14.9±15.3	<0.001***	<0.001†
TG/HDL		1.5±1.0a	2.2±1.6a	0.6±1.4	1.6±1.3b	1.8±0.8ab	0.3±1.2	<0.001**	NS	3.1±2.8	2.4±1.5	-0.7±2.2	2.1±1.1	2.5±1.8	0.4±1.1	NS	NS†
AST	U/L	25.9±4.6b	21.9±3.8a	-4.0±4.3	26.0±4.9b	22.6±5.8a	-3.4±5.6	<0.001***	<0.001	27.6±6.3	22.2±5.3	-5.3±8.5	26.0±4.7	24.3±11.3	-1.7±9.9	0.016	NS
ALT	U/L	23.3±8.2b	13.8±6.5a	-9.5±7.8	22.6±4.3b	12.9±4.6a	-9.7±6.4	<0.001***	<0.001	31.3±13.2b	13.1±3.6a	-18.2±15.6	30.6±16.3b	26.4±29.4b	-4.3±21.0	<0.001*	NS†
Insulin resistance related profiles																	
FBS	mg/dl	79.0±13.6b	75.1±6.6a	-3.8±13.8	85.5±8.8c	73.3±6.5a	-12.2±10.3	0.004***	<0.001††	78.3±4.6ab	71.1±4.8a	-7.2±12.6	83.8±6.2b	72.9±6.2b	-10.9±17.1	0.026**	0.001
Insulin	uIU/ml	7.0±4.3b	4.9±3.4a	-1.3±4.9	7.5±7.4b	4.6±4.2a	-1.8±8.4	0.006***	NS	10.4±4.3ab	6.8±3.6a	-3.1±6.5	11.5±7.8b	7.3±7.6a	-5.3±9.7	NS*	0.006
HOMA-IR		1.4±1.0b	0.9±0.7a	-0.5±1.1	1.6±1.8b	0.9±0.8a	-0.8±1.8	<0.001***	<0.001	2.0±1.0ab	1.2±0.6a	-0.9±1.2	2.5±1.8b	1.3±1.4a	-1.5±1.9	0.009**	<0.001

1) mean±SD, NS : No significance, GG 2007 vs GG 3 year follow-up(2010)
2) mean±SD, NS : No significance, GA+AA 2007 vs GA+AA 3 year follow-up(2010)
3) p-value: 4 group, *<0.05, **<0.01, ***<0.001
4) p-value: GG difference vs GA+AA difference, †<0.05, ††<0.01, †††<0.001

③ Nutrient characteristics according to SIRT1 rs7895833 genotype

The result about Nutrient characteristics according to obesity in SIRT1 rs7895833 genotype showed in Table 29. As indicate in Table 29, the SIRT1 rs7895833 genotype had no significant effect in all parameters at baseline all subjects. After 3 years, protein and fat intake in normal total group were higher in GG than those in GA+AA genotype. In total obesity group, there were no significantly difference all parameters. The case of boy normal group, there were significant effect in CHO, protein, fat and cholesterol. In GG was higher than GA+AA genotype these parameters. But only fat was significant effect in obesity group. On the contrary normal boy, CHO intake of normal girl group was higher in GA+AA than GG after 3 years.

According to result in Table 30, In the case of normal subjects, protein intake was decreased in GA+AA after 3 years. But cholesterol intake was decreased and Na/K is intake was increased in GG during 3 years in normal group.

Table 29. Difference of nutrient intake according to SIRT1 rs7895833 genotype and obesity in 3 years of follow up study

Total		Baseline(n=219)				p-value[1]	p-value[2]	3-years of follow-up(n=219)			
		nomal(n=179)		obesity(n=40)				nomal(n=179)		obesity(n=40)	
		GG (n=105)	GA+AA (n=74)	GG (n=20)	GA+AA (n=20)			GG (n=105)	GA+AA (n=74)	GG (n=20)	GA+AA (n=20)
Energy	kcal	1659.6±360.1	1703.6±633.5	1622.0±282.5	1625.3±372.8	NS	NS	1655.2±400.6	1601.7±397.2	1590.6±365.7	1514.2±406.7
CHO	g	219.1±51.9	232.9±86.3	211.8±34.4	216.3±38.4	NS	NS	233.0±55.4	235.9±62.6	230.5±51.5	216.0±54.7
Protein	g	69.4±16.2	69.0±27.3	69.5±15.6	72.9±28.9	NS	NS	69.5±23.0	63.0±17.5	64.8±18.6	65.1±20.0
Fat	g	58.6±16.2	60.6±27.6	56.6±15.9	57.7±17.1	NS	NS	52.2±17.3b	47.4±15.2ab	47.4±13.7ab	45.5±16.1a
Cholesterol	mg	331.5±123.2	313.3±160.2	352.5±138.0	343.2±118.6	NS	NS	308.1±120.9	287.3±114.1	314.4±157.3	301.2±149.8
Na	mg	3698.5±930.3	3544.5±1356.8	3635.3±755.2	3324.6±1053.6	NS	NS	3420.0±985.5	3376.1±949.8	3576.2±869.5	3286.6±1244.1
K	mg	2460.2±454.5	2302.5±504.4	2293.8±368.7	2443.5±857.4	NS	NS	2196.5±683.7	2280.2±685.2	2288.9±723.1	2108.8±514.9
Na/K		1.6±0.3	1.6±0.4	1.6±0.3	1.4±0.5	NS	NS	1.6±0.4	1.5±0.3	1.6±0.4	1.5±0.3
Boys		Baseline(n=101)				p-value	p-value	3-years of follow-up(n=101)			
		nomal(n=86)		obesity(n=15)				nomal(n=86)		obesity(n=15)	
		GG (n=48)	GA+AA (n=38)	GG (n=11)	GA+AA (n=4)			GG (n=48)	GA+AA (n=38)	GG (n=11)	GA+AA (n=4)
Energy	kcal	1780.6±380.2	1797.4±704.5	1592.4±303.8	1683.5±419.8	NS	NS	1856.8±354.4b	1634.5±439.9ab	1644.9±440.9ab	1406.4±201.6a
CHO	g	234.9±54.6	238.7±89.8	208.5±35.6	228.6±42.6	NS	NS	261.1±48.7b	237.5±65.1ab	242.8±59.5b	205.4±35.7a
Protein	g	74.3±18.8	73.2±28.3	70.5±11.7	69.1±26.9	NS	NS	79.9±33.5b	65.0±19.5ab	67.0±23.4ab	55.6±7.8a
Fat	g	62.8±16.9	63.6±29.5	54.0±18.4	55.3±18.5	NS	NS	58.8±17.9b	48.3±17.3ab	46.3±15.5a	41.1±9.03a
Cholesterol	mg	355.8±129.9	320.7±182.6	342.3±113.7	371.1±136.3	NS	NS	332.8±122.9b	277.1±128.0b	322.3±161.9b	195.4±17.0a
Na	mg	3762.7±1005.0	3756.7±1427.3	3751.7±733.9	3177.1±1313.5	NS	NS	3728.4±909.4	3407.9±943.0	3539.4±801.7	3176.8±368.1
K	mg	2575.8±705.6	2504.7±981.5	2344.1±436.5	2356.4±1189.1	NS	NS	2484.4±652.3	2397.6±718.3	2436.3±884.9	1923.2±206.1
Na/K		1.5±0.3	1.5±0.4	1.6±0.2	1.4±0.3	NS	NS	1.6±0.4	1.5±0.3	1.6±0.5	1.7±0.2
Girls		Baseline(n=118)				p-value	p-value	3-years of follow-up(n=118)			
		nomal(n=93)		obesity(n=25)				nomal(n=93)		obesity(n=25)	
		GG (n=57)	GA+AA (n=36)	GG (n=9)	GA+AA (n=16)			GG (n=57)	GA+AA (n=36)	GG (n=9)	GA+AA (n=16)
Energy	kcal	1557.7±308.8	1604.4±535.9	1658.1±257.9	1609.8±365.5	NS	NS	1485.5±357.2	1566.0±344.5	1524.3±241.1	1541.2±441.8
CHO	g	205.8±45.7	226.8±82.7	215.9±33.4	213.3±37.4	NS	NS	209.3±49.5a	234.2±60.1a	215.3±35.6a	218.7±58.7a
Protein	g	65.4±14.0	64.6±25.7	68.3±19.7	73.9±29.7	NS	NS	60.7±18.5	60.9±14.9	62.2±9.9	67.5±21.4
Fat	g	55.0±14.7	57.4±25.4	59.7±12.1	58.3±17.0	NS	NS	46.6±14.7	46.5±12.6	48.7±11.4	46.6±17.3
Cholesterol	mg	311.1±113.9	305.5±133.4	364.9±165.6	336.2±115.1	NS	NS	287.4±115.7	298.1±97.0	304.7±155.7	327.6±156.7
Na	mg	3644.3±863.2	3320.6±1249.3	3493.0±777.1	3361.5±1000.0	NS	NS	3160.2±975.7	3342.5±962.4	3621.3±967.8	3314.0±1383.0
K	mg	2332.1±2137.4	2137.4±730.5	2232.4±263.2	2465.3±776.7	NS	NS	1954.1±614.1	2156.3±629.8	2108.7±412.1	2155.3±559.4
Na/K		1.6±0.3	1.6±0.3	1.6±0.3	1.4±0.5	NS	NS	1.7±0.3	1.6±0.3	1.7±0.3	1.5±0.3

1) mean±SD; NS : No significance, normal GG vs normal GA+AA
2) obesity GG vs obesity GA+AA
3) p-value: 4 group, *<0.05, **<0.01, ***<0.001

Table 30. Difference of nutrient intake between 2007 and 2010 according to SIRT1 rs7895833 genotype and obesity

Total		normal(n=179)						paired -t- test[1]	paired -t- test[2]	obesity(n=40)						paired -t- test[1]	paired -t- test[2]
		GG(n=105)			GA+AA(n=74)					GG(n=20)			GA+AA(n=20)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Energy	kcal	1659.6±360.1	1655.2±400.6	-4.34±491.9	1703.6±633.5	1601.7±397.2	-99.7±660.6	NS	NS	1622.0±282.5	1590.6±365.7	-31.3±482.4	1625.3±372.8	1514.2±406.7	-126.8±550.1	NS	NS
CHO	g	219.1±51.9	233.0±55.4	13.9±68.7	232.9±86.3	235.9±62.6	3.02±92.9	0.004*[3]	NS	211.8±34.4	230.5±51.5	18.6±66.8	216.3±38.4	216.0±54.7	-0.3±67.3	NS	NS
Protein	g	69.4±16.2	69.5±23.0	0.02±33.7	60.6±27.6	63.0±17.5	-5.98±31.0	NS*	0.020	69.5±15.6	64.8±18.6	-4.71±26.1	72.9±28.9	65.1±20.0	-7.9±37.3	NS	NS
Fat	g	58.6±16.2	52.2±17.3b	-6.44±21.4	60.6±27.6	47.4±15.2ab	-13.2±32.2	<0.001***	<0.001†[4]	56.6±15.9	47.4±13.7ab	-9.2±19.3	57.7±17.1	45.5±16.1a	-12.2±17.7	0.004***	<0.001
Cholesterol	mg	331.5±123.2	308.1±120.9	-23.4±167.1	313.3±160.2	287.3±114.1	-26.0±194.0	0.044*	NS	352.5±138.0	314.4±157.3	-38.1±218.1	343.2±118.6	301.2±149.8	-42.0±168.8	NS	NS
Na	mg	3698.5±930.3	3420.0±985.5	-278.5±1291.1	3544.5±1356.8	3376.1±949.8	-168.5±1346.2	0.002*	NS	3635.3±755.2	3576.2±869.5	-59.1±1122.0	3324.6±1053.6	3286.6±1244.1	-38.1±1538.3	NS*	NS
K	mg	2460.2±454.5	2196.5±683.7	-247.0±888.8	2302.5±504.4	2280.2±685.2	-45.8±962.5	<0.001**	NS†	2293.8±368.7	2288.9±723.1	-4.96±804.8	2443.5±857.4	2108.8±514.9	-334.7±1056.1	NS*	NS
Na/K		1.6±0.3	1.6±0.4	0.1±0.4	1.6±0.4	1.5±0.3	-0.0±0.4	0.048	NS	1.6±0.3	1.6±0.4	0.0±0.5	1.4±0.5	1.5±0.3	0.1±0.5	NS**	NS

Boys		normal(n=86)						paired -t- test	paired -t- test	obesity(n=15)						paired -t- test	paired -t- test
		GG(n=48)			GA+AA(n=38)					GG(n=11)			GA+AA(n=4)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Energy	kcal	1780.6±380.2	1856.8±354.4b	76.2±527.7	1797.4±704.5	1634.5±439.9ab	-148.3±701.5	NS*	NS†	1592.4±303.8	1644.9±440.9ab	52.5±490.9	1683.5±419.8	1406.4±201.6a	-277.1±442.4	NS	NS
CHO	g	234.9±54.6	261.1±48.7b	26.2±73.6	238.7±89.8	237.5±65.1ab	-1.15±86.7	0.001*	NS†	208.5±35.6	242.8±59.5b	34.4±70.6	228.6±42.6	205.4±35.7a	-23.2±57.7	0.033	NS†
Protein	g	74.3±18.8	79.9±33.5b	5.61±42.2	73.2±28.3	65.0±19.5ab	-8.17±31.6	NS**	0.027†	70.5±11.7	67.0±23.4ab	-3.54±27.4	69.1±26.9	55.6±7.79a	-13.5±29.1	NS	NS
Fat	g	62.8±16.9	58.8±17.9b	-4.07±24.6	63.6±29.5	48.3±17.3ab	-15.4±34.1	NS***	<0.001†	54.0±18.4	46.3±15.5a	-7.7±18.7	55.3±18.5	41.1±9.03a	-14.1±13.9	NS	0.024
Cholesterol	mg	355.8±129.9	332.8±122.9b	-23.0±180.5	320.7±182.6	277.1±128.0b	-43.6±210.4	NS**	NS	342.3±113.7	322.3±161.9b	-20.0±252.3	371.1±136.3	195.4±17.0a	-175.7±123.9	NS*	0.005†
Na	mg	3762.7±1005.0	3728.4±909.4	-34.3±1408.3	3736.7±1427.3	3407.9±943.0	-348.9±1110.3	NS	0.008	3751.7±733.9	3539.4±801.7	-212.4±1049.5	3177.1±1313.5	3176.8±368.1	-0.4±1310.7	NS	NS
K	mg	2575.8±705.6	2484.4±652.3	-91.3±944.0	2504.7±981.5	2397.6±718.3	-107.1±957.5	NS	NS	2344.1±436.5	2436.3±884.9	92.2±942.7	2336.4±1189.1	1923.2±206.1	-433.3±1318.3	NS	NS
Na/K		1.5±0.3	1.6±0.4	0.1±0.5	1.5±0.4	1.5±0.3	-0.1±0.4	NS	NS†	1.6±0.2	1.6±0.5	-0.1±0.5	1.4±0.3	1.7±0.2	0.2±0.4	NS	NS

Girls		normal(n=93)						paired -t- test	paired -t- test	obesity(n=25)						paired -t- test	paired -t- test
		GG(n=57)			GA+AA(n=36)					GG(n=9)			GA+AA(n=16)				
		2007	2010	difference	2007	2010	difference			2007	2010	difference	2007	2010	difference		
Energy	kcal	1557.7±308.8	1485.5±357.2	-72.2±450.9	1604.4±535.9	1566.0±344.5	-46.8±613.8	NS	NS	1658.1±257.9	1524.3±241.1	-133.8±464.7	1609.8±365.5	1541.2±441.8	-86.7±575.3	NS	NS
CHO	g	205.8±45.7	209.3±49.5a	3.50±62.8	226.8±82.7	234.2±60.1a	7.43±99.4	NS**	NS	215.9±33.4	215.3±35.6a	-0.6±58.0	213.3±37.4	218.7±58.7a	5.4±69.1	NS	NS
Protein	g	65.4±14.0	60.7±18.5	-4.70±23.4	64.6±25.7	60.9±14.9	-3.67±30.4	0.034	NS	68.3±19.7	62.2±9.9	-6.2±25.1	73.9±29.7	67.5±21.4	-6.5±39.3	NS	NS
Fat	g	55.0±14.7	46.6±14.7	-8.44±18.2	57.4±25.4	46.5±12.6	-10.8±30.0	<0.001***	0.003	59.7±12.1	48.7±11.4	-11.0±20.3	58.3±17.0	46.6±17.3	-11.7±18.7	0.034**	0.001
Cholesterol	mg	311.1±113.9	287.4±115.7	-23.7±155.7	305.5±133.4	298.1±97.0	-7.37±174.5	NS	NS	364.9±165.6	304.7±155.7	-60.1±171.9	336.2±115.1	327.6±156.7	-8.6±163.2	NS	NS
Na	mg	3644.3±863.2	3160.2±975.7	-484.1±1150.0	3320.6±1249.3	3342.5±962.4	22.0±1542.1	<0.001**	NS†	3493.0±777.1	3621.3±967.8	128.3±1208.2	3361.5±1000.0	3314.0±1383.0	-47.5±1608.9	NS	NS
K	mg	2332.1±2137.4	1954.1±614.1	-378.0±820.9	2137.4±730.5	2156.3±629.8	18.9±970.2	<0.001***	NS††	2232.4±263.2	2108.7±412.1	-123.7±600.7	2465.3±776.7	2155.3±559.4	-310.1±1003.9	NS**	NS
Na/K		1.6±0.3	1.7±0.3	0.1±0.4	1.6±0.3	1.6±0.3	0.0±0.5	NS	NS	1.6±0.3	1.7±0.3	0.2±0.5	1.4±0.5	1.5±0.3	0.1±0.5	NS**	NS

1) mean±SD, NS : No significance, GG 2007 vs GG 3 year follow-up(2010)
2) mean±SD, NS : No significance, GA+AA 2007 vs GA+AA 3 year follow-up(2010)
3) p-value: 4 group, †*0.05, **<0.01, ***<0.001
4) p-value: GG difference vs GA+AA difference, †<0.05, ††<0.01, †††<0.001

④ Influence of obesity on the interaction of gene and nutrient

Obesity children with GG genotype having a negative correlation between difference of CHO intake and difference of TG concentration. And difference of HOMA-IR was same result with TG. (Fig 15)

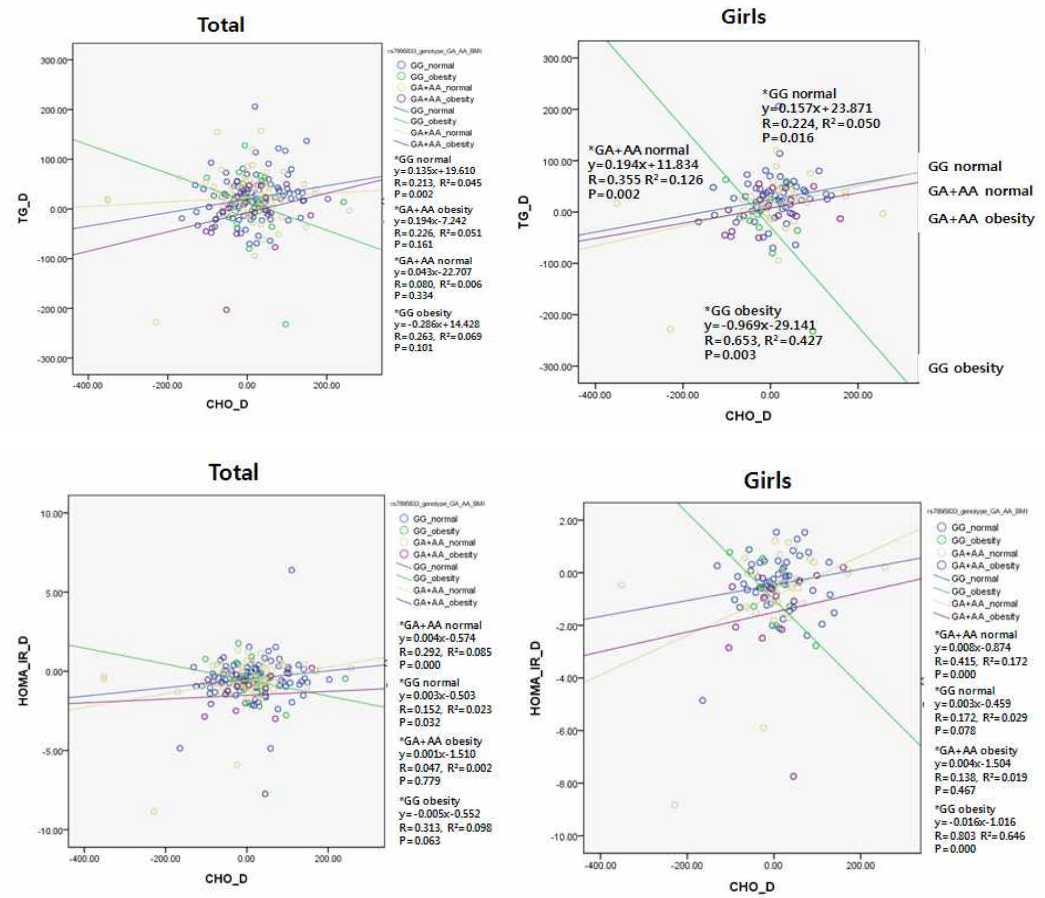


Fig 15. Correlation with difference of Carbohydrate intake and difference of TG and HOMA-IR

Ⅳ. Discussion

In the present study, our study is 3 years of follow up study and the subjects were all Korean boy and girl. At baseline, the number of subject were 491(boy: 246, girl: 245) and 219 subjects(boy: 101, girl: 118) were complete this study. During 3 years, the number of girl were increase but boy were decrease. The mean of lipid profiles were higher in girl than boy at baseline, but there were no significance after 3 years. In contrast, the mean of nutrient intake were higher in boys than those of girl group both 2007 and 2010. During 3 years, anthropometric parameters were increase but lipid, insulin resistance related profiles, and nutrient intake were decrease. Increment of height was higher in girl than boy but increment of WC was higher in boy than girl. The decrement of lipid profiles were higher in girl subjects than those of boy group. Although intake of CHO was decreased during 3 years in boy group, blood TG concentration was increased.

The 88% of children who had normal BMI of 2007 were also normal in 2010, and the 85% of children who had obesity of 2007 were also obesity in 2010. Also, the children of normal in 2007 were changed obese children in 2010 were 15%. The normal and obesity was divided by BMI 85 percentile based on 2007 BMI and observed normal and obesity subjects after 3

years. During 3 years, all anthropometric parameters were increased both normal and obesity. Lipid profiles and insulin resistance related profiles were decreased during 3 years but TG and TG/HDL were increased only normal subjects. This result was because CHO intake was increased in normal group. Although there were no significantly difference in obesity, TG and TG/HDL were higher than normal after 3 years. The decrement of HDL in obesity boy group was greatly higher than normal group. The decrements of insulin and FBS were higher in obesity group than normal group but the mean of insulin and FBS were higher in obesity group. The dietary intake was only significantly decreased in normal group.

we analyzed the association of SIRT1 polymorphism(rs7895833). There's no reference about SIRT1 polymorphism and childhood obesity. So this study is the first study of Korean childhood obesity related SIRT1 polymorphism. In rs7895833 SNP, the frequencies of G/G, G/A, and A/A genotypes was 58.4%, 39.6%, 2.0% for boy subjects and 55.9%, 38.1%, 5.9% for girl subjects. Some studies reported that the frequencies of SIRT1 rs7895833 in different racial population. Major alleles for Caucasians are the minor alleles for Japanese. According to the study by Zillinkens et al, A allele frequency of rs7895833 are 0.80 but 0.290 in Japanese

study[82]. This study subjects showed similar frequencies with previous study of Japanese. Thus, the different allele frequencies of rs7895833 might explain why Korean show less marked obesity compared with Caucasians.

Our result suggest that, although energy, protein, fat, and cholesterol intake were decreased in children having GA+AA genotype, the increment of BMI and WC was higher than them with GG. Also, the decrements of TC and LDL in GA+AA were lower than the children having GG.

We analyzed the differences of various parameter by SIRT1 rs7895833 according to obesity. According to obesity classification, frequency of GA+AA was significantly increased in obesity girl group and the frequency of GA+AA in obesity children in 2010 who were normal in 2007 were higher than GG genotype(42.95 vs 57.1%). Obesity children with GG genotype having a negative correlation between difference of CHO intake and difference of TG concentration. And difference of HOMA-IR was same result with TG.

There were several limitations in this study. First, the number of subjects is small. Also the frequencies of control and obesity is not balance. So this study can not assure the association between SIRT1 polymorphism and obesity. In generally, epigenetic study are needed several thousand subjects and replication study in order to represent the

genetic characteristics of specific population. Second, this study did not prove causality and mechanism. The results of present study were used for only basic data of the association of SIRT1 polymorphism and various biomarkers. Thus, future studies are needed to investigate various cytokine and plasma SIRT1 level and SIRT1 gene expression. And need to investigate long term follow-up.

Ⅴ. Conclusion

In conclusion, the SIRT1 polymorphism was found to be associated with obesity. GG genotype of SIRT1 rs 7895833 in obesity children showed protective effects of plasma TG concentration and HOMA-IR during 3 years. But further large scale studies will be needed to establish the relationship between SIRT1 polymorphisms and obesity risk factor.

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국문 개요

SIRT1 유전자 다형성과 소아비만과의 관련성에 대한 추적연구

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Sirtuin 1(SIRT1)은 노화억제와 관련된 유전자로 알려져 있었으나 최근 연구에서는 SIRT1의 단일염기다형성과 체지방, 체질량지수, 복부비만과의 관련성을 보고하고 있다. SHIMOYAMA 등의 연구에 따르면 SIRT1 rs7895833 SNP의 변이형인 A carrier를 가지면 BMI, 체지방이 증가하고[82], Zillikens 등의 연구에서는 G carrier를 가지면 비만의 위험률이 13-18% 감소하는 것으로 나타났다[84]. 그러나 SIRT1 유전자다형성과 소아비만과의 관련성은 밝혀지지 않았다. 따라서 본 연구는 SIRT1 유전자형과 소아 비만과의 상관성을 조사하기 위해 1차년도(2007) 조사에 참여했던 491명중 2차년도(2010) 조사까지 완료한 44.6%의 소아 219명을 대상으로 진행되었다.

2007년과 비교하여 3년 후에는 신체계측치가 남녀 모두 증가하였고, 혈중 지질농도, 인슐린저항성 관련 인자, 열량영양소 섭취는 모두 감소하였

다. 그러나 중성지방, 중성지방/HDL 콜레스테롤 비는 증가하였다. 성별에 따라 여러 가지 지표들의 변화량을 보았을 때, 허리둘레는 남아에서 많이 증가하였고 혈중지질, 인슐린저항성 관련 지표는 여아가 더 많이 감소하였다. 열량영양소섭취 변화량은 성별에 따른 차이가 없었으나 2007년, 2010년 모두 열량 영양소 섭취량이 남자가 높았다.

2007년과 2010년을 BMI 85percentile을 기준으로 정상과 비만(과체중+비만)으로 나누었을 때 3년 후 비만아가 유의적으로 증가하였으며 2007년에 정상이었던 아동의 88%(n=164)가 2010년에도 정상, 2007년에 비만이었던 아동의 85%(n=34)가 2010년에도 비만이었다. 또한 2007년에 정상이었으나 2010년에는 비만이 된 아동은 12%(n=21)였으며 2007년에는 비만이었으나 3년 후에 정상이 된 아동은 15%(n=6)이었다. 2007년 BMI 85percentile를 기준으로 정상과 비만(과체중+비만)으로 나누었을 때 모든 지표들이 비만아동이 더 높았으며 HDL 콜레스테롤은 비만아동이 더 낮았다. 2007년에 정상이었던 아동과 비만이었던 아동 모두 3년 후 신체계측치가 증가하였고, 혈중 지질, 인슐린 저항성 관련 지표는 감소하였다. 그러나 열량영양소 섭취는 정상아동에서만 변화가 있었고 비만아동에서는 지방섭취만 감소하였다.

SIRT1 rs7895833 유전자다형성에 따른 유전자형 분포는 wild type인 GG 형이 57.1%, mutant type인 AA형이 4.1%, hetero type인 GA형이 38.8%로 나타났다. 비만여부에 따른 SIRT1 유전자형의 분포를 조사하였을 때, 남자는 비만과 무관하지만, 비만 여아에서는 변이형인 A carrier를 가진 GA+AA 유전자형의 빈도가 유의적으로 높게 나타났다. (38.7% vs 64.0%, $p<0.05$). SIRT1 rs7895833의 유전자다형성에 따라 각각 여러 가지 지표들의 차이를 조사하였을 때, GA+AA형을 가질 경

우 GG형을 가진 사람보다 열량영양소 섭취가 감소하였음에도 불구하고 BMI와 허리둘레가 GG형을 가진 사람보다 더 많이 증가하였다 .

1차년 조사인 2007년 대상자들의 BMI를 85percentile을 기준으로 정상과 비만(과체중+비만)군으로 나누어 SIRT1 rs7895833 유전자형에 따라 여러 지표들의 차이를 조사하였을 때, 2007년에 정상이었다가 2010년에 비만이된 아동들의 유전자형 빈도는 GA+AA가 GG 보다 높았다(42.9% vs 57.1%). 또한 2007년에 정상이면서 2010년에도 정상인 아동은 GG형의 빈도가 높았다(60.8% vs 39.2%).

SIRT1 rs7895833과 열량영양소 섭취가 비만에 미치는 영향을 살펴보았을 때 GG형을 가진 비만아동에서 탄수화물 섭취 변화와 중성지방농도 변화가 음의 상관관계를 가졌으며 탄수화물 섭취 변화와 HOMA-IR변화가 음의 상관관계를 가졌다.

위의 연구 결과들을 통해 SIRT1 rs7895833 유전자 다형성과 비만과의 관련성을 확인할 수 있었다. 그러나 본 연구는 대상자의 수가 적어 질병과의 인과관계를 밝히기에는 충분하지 않으며 SIRT1의 유전자다형성과 소아비만과의 관련성을 증명하기 위해서는 앞으로 더 많은 연구가 진행되어야 할 것으로 생각된다.