Association Study of Health-Related Physical Fitness, Metabolic Syndrome, Biomarkers, and Lifestyle Factors

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A Master's Thesis
Submitted to the Department of Medicine
and the Graduate School of Yonsei University
in partial fulfillment of the
requirements for the degree of
Master of Science in Medicine

Ji Yeong Choi

December 2021

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The Graduate School
Yonsei University
December 2021

ACKNOWLEDGEMENTS

From the moment I started my studies at Yonsei University Wonju College of Medicine, many people around me have helped me and encouraged me immensely.

I would like to express my gratitude to Professor In Deok Kong, who supervised me throughout my master's degree course. His words are still in my mind. Being a member of the exercise medicine lab has been a valuable experience, leading me to be a great researcher and therapist.

I am also grateful to Professor Dae Ryong Kang and Seung-Kuy Cha, who have provided me with sincere academic advice about statistics and physiology, which has considerably helped improve the quality of my thesis.

I sincerely thank Professor Seong-Woo Jeong and Kyu-Sang Park for their warm encouragement during my degree course. I am also grateful to Professor Byung-Il Yeh, a designer of a happy life, for his warm attention to me.

Special thanks go to my seniors, especially Jae Seung Chang, Ji-Hee Kim and Ji Hee Min. They guided me with the experimental techniques and everything related to the research that I undertook for the first time. I am also grateful to all my colleagues in the Department of Physiology, Center for Exercise Medicine and National Fitness Award Center. Their warm encouragement has helped me at every step of my degree completion. I would also like to thank my friend and senior, Joon Young Chang, who led me to a new academic world.

I would like to mention my precious friend Kyeong-A Choi, who always understood my situation and cheered me during challenging times. Hui Young Kim, an old friend of mine, was always on my side and gave me comfort. Thanks to my precious friends who know me better than me, due to whom I was able to complete my degree happily.

Lastly, I would like to thank my dear family, father Kyung Heum Choi, mother Mi Jung Kim, older sister Mun Yeong Choi and younger brother Seung Bin Choi, always on my side with infinite love. They have always supported my thoughts and choices. With my family's trust in me, I can dream of a future that I have always hoped to experience.

I sincerely express my appreciation once again to everyone who helped me and stayed by my side throughout my master's degree course.

Every moment in Wonju would remain in my heart and I will never forget those memories. This valuable master's degree course definitely leads to my future happiness. Thank you all again.

December 2021

Ji Yeong Choi

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ABBREVIATIONS

Abbreviation	Full name
ALT	Alanine transferase
ANCOVA	Analysis of covariance
AST	Aspartate aminotransferase
BDI	Beck's Depression Inventory
BMI	Body mass index
CRF	Cardiorespiratory fitness
DBP	Diastolic blood pressure
ELISA	Enzyme linked immune sorbent assay
FGF21	Fibroblast growth factor
FLI	Fatty liver index
GDF15	Growth differentiation factor 15
GLU	Fasting glucose
HbA1c	Glycated hemoglobin
HDL-C	High-density lipoprotein cholesterol
HGS	Handgrip strength
HOMA-IR	Homeostatic model assessment for insulin resistance
hs-CRP	High sensitive C-reactive protein

IPAQ	International Physical Activity Questionnaire
LDL-C	Low density lipoprotein cholesterol
MetS	Metabolic syndrome
mtDNA-CN	Mitochondrial DNA copy number
NCDs	Non-communicable diseases
NCEP-ATPIII	National Cholesterol Education Program Adult Treatment Panel
PBMCs	Peripheral blood mononuclear cells
PSQI	Pittsburgh Sleep Quality Index
PSS	Perceived Stress Scale
r-GTP	Gamma glutamyl transpeptidase
SBP	Systolic blood pressure
STAI	State-Trait Anxiety Inventory
TC	Total cholesterol
TG	Triglyceride
TL	Telomere length
VO2max	Maximal oxygen uptake
WHOQOL-BREF	World Health Organization Quality of Life
2MWT	2-minute walk test

ABSTRACT

Association Study of Health-Related Physical Fitness, Metabolic Syndrome, Biomarkers, and Lifestyle Factors

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The aim of this study was to explore the relationship between health-related physical fitness, metabolic syndrome, biomarkers and lifestyle factors using a cross-sectional study design. A total of 98 subjects (19 men and 79 women) participated in this study.

Physical fitness, metabolic syndrome risk factors, and aging biomarkers including telomere length, mitochondrial DNA copy number, and serum soluble α-Klotho level, in addition to mitochondrial stress biomarkers including FGF21 and GDF15 were measured for all the participants. Lifestyle factors such as stress, anxiety, depression, quality of life, physical activity, and sleep were surveyed using validated questionnaires.

In a group analysis of YMCA step test, WC, heart rate, BMI, body fat percentage, HOMA-IR, insulin, anxiety, and depression were significantly different between two groups. In a group analysis according to HGS, WC, heart rate, weight, BMI, body fat percentage, mtDNA-CN, FGF21, HOMA-IR, HDL-C, r-GTP, TG, insulin, and quality of life were significantly different between two groups.

According to the result of logistic regression analyses, VO_{2max} and relative handgrip strength are negatively associated with MetS independently and after adjustment for age, sex, education, and house income. Our results suggest that a VO_{2max} and relative handgrip strength could predict metabolic syndrome. Additionally, various health outcomes, associated with VO_{2max} and relative handgrip strength, could be the therapeutic target to metabolic syndrome.

Keywords: Physical fitness, Metabolic syndrome, Biomarker, Lifestyle

I. INTRODUCTION

1.1 Background

The increase in the prevalence of non-communicable diseases (NCDs), also known as chronic diseases, in recent decades has been a major challenge in the world (1, 2). A number of NCDs have various risk factors that are modifiable to some degree (3, 4). Thus, preventing NCDs through lifestyle interventions and controlling modifiable risk factors is essential (5).

Metabolic syndrome and physical fitness

Metabolic syndrome (MetS) is a clustering of specific risk factors, including insulin resistance, high glucose obesity, high blood triglycerides, low levels of high-density lipoprotein cholesterol (HDL-C) and high blood pressure (6). Studies have reported that MetS is related to type 2 diabetes, cardiovascular disease, chronic kidney disease and all-cause mortality (6-9). Therefore, the sustained management of metabolic syndrome and its independent components can prevent metabolic and cardiovascular diseases (7, 10). A growing number of studies have shown that physical fitness, especially for health-related physical fitness such as cardiorespiratory fitness (CRF) and handgrip strength (HGS) are strongly linked to MetS (11, 12). Collectively, managing metabolic syndrome risk factors and increasing physical fitness levels are necessary to improve health outcomes.

Aging biomarker

Telomere length (TL) is considered a biomarker for biological aging, and also related to cardiovascular disease, diabetes and cancer (13, 14). However, the association between metabolic syndrome and that of its individual components with TL remains controversial (14).

Another hallmark of aging is the mitochondrial DNA copy number (mtDNA-CN) which reflects mitochondrial dysfunction (15, 16). Mitochondrial dysfunction is strongly associated with pathological conditions including cardiovascular diseases (15, 16).

Klotho is an anti-aging protein that plays an important role in aging and age-related diseases in humans (17). Several previous studies support that Klotho functions as a human aging-suppression molecule (17) and that the serum level of Klotho decreases with age in humans (17, 18).

Mitochondrial stress biomarker

Mitochondria are crucial for cellular energy metabolism and cellular stress mediation (19). Fibroblast growth factor (FGF21) and growth differentiation factor 15 (GDF15) are involved in energy metabolism (20, 21). They are primarily produced by the liver and regulate glucose and lipid metabolism (22-24). Serum FGF21 levels are significantly associated with obesity and type 2 diabetes (24, 25) and are suggested to be myokines induced by exercise (21, 26). Our study explored the relationship between FGF21, metabolic syndrome and physical fitness.

1.2 Purposes

Several studies have explored the relationship between physical fitness, body composition and metabolic syndrome risk factors. However, comprehensive research on the association between various biomarkers and lifestyle factors is still poorly investigated.

The aim of this study was to explore the relationship between health-related physical fitness, metabolic syndrome, biomarkers and lifestyle factors using a cross-sectional study design. Through this valuable information, future directions will be suggested to confirm the causal effect of the findings in this current study.

1.3 Hypothesis

The hypothesis of this study include

1.3.1 Physical fitness is related to metabolic syndrome risk factors, aging and mitochondrial biomarkers, and lifestyle factors.

1.3.2 Higher levels of health-related physical fitness are related to better health outcomes.

II. MATERIALS AND METHODS

2.1 Study design and ethics approval

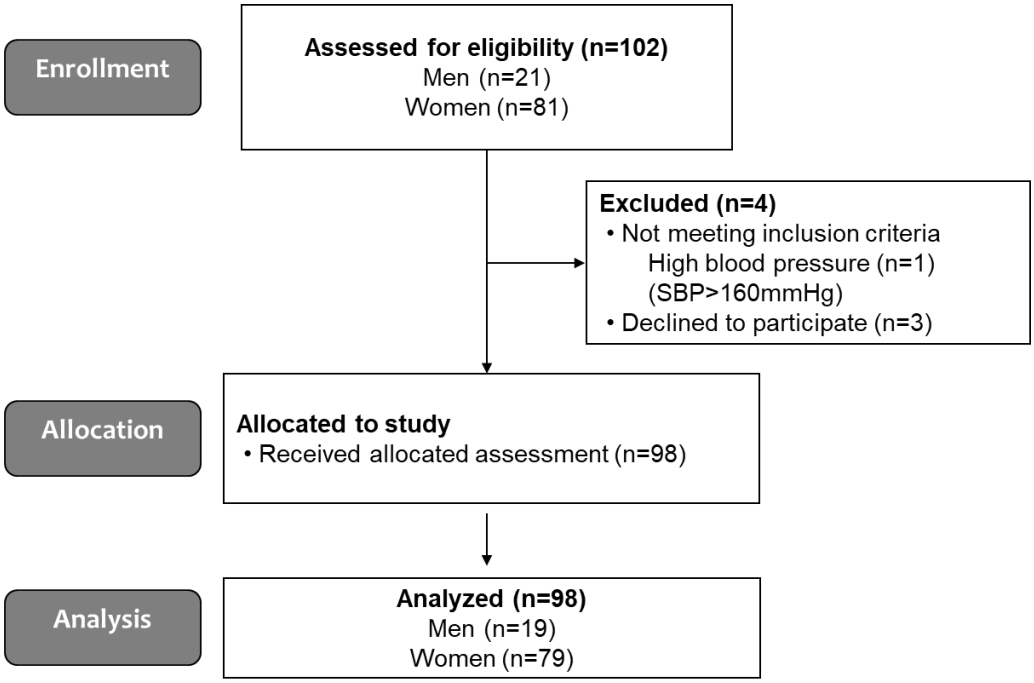
This study is a single-center, descriptive cross-sectional design. We measured physical fitness levels and metabolic syndrome risk factors to determine whether these factors are associated with aging and mitochondrial biomarkers such as telomere length, mitochondrial DNA copy number, serum soluble α-Klotho level, serum FGF21 level and serum GDF15 level.

The Institutional Review Board of Wonju Severance Christian Hospital approved this study (IRB No. CR320130). Written informed consent was obtained from all the participants in this study.

2.2 Study participants and procedures

A total of 98 healthy individuals aged 40 years and above were recruited from April to June 2021 at the Center for Exercise Medicine (Yonsei University Wonju College of Medicine, Gangwon-do, Korea). A flowchart of the study is shown in **Figure 1.**

Figure 1. Flow chart of the study



2.3 Definition of metabolic syndrome

According to the criteria of the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATPIII) (27-29), metabolic syndrome is defined based on the presence of at least three of the following risk factors: 1) central obesity (waist circumference ≥ 90cm for men or ≥ 85cm for women) defined by the Korean Society of Obesity (30); 2) serum triglycerides ≥ 150 mg/dL or specific treatment for hyperglyceridemia; 3) serum HDL-C < 40 mg/dL for men or < 50 mg/dL for women, or specific treatment for low HDL-C level; 4) systolic blood pressure (SBP) ≥ 130 mmHg or diastolic blood pressure (DBP) ≥ 85 mmHg, or treatment with antihypertensive agents; 5) fasting serum glucose level ≥ 100 mg/dL or the current use of antidiabetic medication. **(Table 1)**

Table 1. C**riteria of metabolic syndrome in the study**

Component	Cutoff value
Central obesity	≥ 90cm for men ≥ 85cm for women
Triglycerides	≥ 150 mg/dL
HDL Cholesterol	<40 mg/dL for men <50 mg/dL for women
Blood pressure	SBP ≥ 130 mmHg DBP ≥ 85 mmHg
Fasting glucose	≥ 100 mg/dL

2.4 Measurements

The primary outcomes were aging biomarkers including telomere length from peripheral blood mononuclear cells, mitochondrial DNA copy number and serum soluble α-Klotho level, in addition to mitochondrial stress biomarkers including FGF21 and GDF15. Physical fitness, various health outcomes, and primary outcomes were measured for all the participants. The detailed methods of each measurement were as follows:

2.4.1 Anthropometry and body composition

Body weight and height were measured for all participants. Body mass index (BMI, kg/m^2) was calculated as body weight divided by height in meters squared. Waist circumference, a metabolic syndrome risk factor, was measured at the midpoint between the lower rib cage and the iliac crest in a standing position. Blood pressure, was measured in the sitting position using an automated blood pressure monitoring device. Multi frequency bioelectrical impedance analysis (Inbody 720, Biospace, Centennial, CO, Korea) was used to study body composition including skeletal muscle mass and body fat percentage.

2.4.2 Physical fitness

We measured handgrip strength, sit and reach, and implemented a 2-minute walking test (2MWT) for all participants. For younger participants aged over 40 and under 65 years, we conducted the YMCA step test, sit up, reaction time test, and standing-board jump. For older participants aged 65 years and over, we measured 30 second chair stand test, timed up and go and figure-of-8 walk around test **(Table 2).** Handgrip strength, sit and reach, 2MWT, YMCA step test, sit up and 30 second chair stand test, and health-related physical fitness tests were also conducted. Handgrip strength test evaluates muscular strength and the sit-and-reach test evaluates flexibility. The YMCA step test and 2MWT represent CRF for younger and older participants respectively. However, the 2MWT was additionally performed for the younger participants to confirm CRF in all participants. Sit up represents muscular endurance in the younger participants and 30 second chair test represents muscle function in the older participants. Skill-related physical fitness was also assessed. The reaction time and standing-board jump, which represent power and agility, respectively, were measured in the younger participants. The timed up and go test and figure-of-8 walk around test, which represent balance and coordination, respectively, were measured in the older participants.

Table 2. Physical fitness measurements

Measurement	Physical fitness
<65 years	
Health-related physical fitness	
Handgrip strength (kg)	Muscular strength
Sit and reach (cm)	Flexibility
2-minute walking test	Cardiorespiratory fitness
YMCA step test (ml/kg/min)	Cardiorespiratory fitness
Sit up (n)	Muscular endurance
Skill-related physical fitness	
Reaction time (sec)	Agility
Standing-board jump (cm)	Power
≥65 years	
Health-related physical fitness	
Handgrip strength (kg)	Muscular strength
Sit and reach (cm)	Flexibility
2-minute walking test (n)	Cardiopulmonary fitness
30 second chair stand test (n)	Muscular function
Skill-related physical fitness	
Timed up and go (sec)	Balance
Figure-of-8 walk around (sec)	Coordination

2.4.3 Blood collection

Nurses at the exercise medicine center collected whole blood from the antecubital vein. Blood was collected in the morning after overnight fasting for more than 8 h. Serum separating tubes (BD Vacutainer® SST blood collection tube, 367988) were used to separate the serum. The tubes were centrifuged at 3,000 rpm for 15 min. Separated serum was immediately stored at -80℃. Stored serum was used for biochemical analysis and enzyme-linked immunosorbent assay (ELISA). Peripheral blood mononuclear cells (PBMCs) were collected in different tubes (BD Vacutainer® CPT tube with polymer gel and sodium citrate for mononuclear cell preparation, 365761). Blood separation was performed within 2 h after whole blood collection. Genomic DNA was extracted using an extraction kit (QIAGEN DNeasy Blood & Tissue Kit, 69504) from the PBMCs for telomere length analysis.

2.4.4 Biochemical analysis

The metabolic syndrome risk factors including HDL-C, fasting glucose (GLU), and triglyceride (TG) levels; and insulin, high sensitive C-reactive protein (hs-CRP), gamma glutamyl transpeptidase (r-GTP) were measured by company (SCL, Seoul Clinical Laboratories, Korea). Other biomarkers including creatinine, alanine transferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and glycated hemoglobin (HbA1c) were measured using an automatic chemical blood analyzer (Samsung® IVD-A10A, Korea). Homeostatic model assessment for insulin resistance (HOMA-IR) and fatty liver index (FLI) were calculated using the following formulae (31, 32):

$$\text{HOMA-IR} = (\text{fasting glucose} \times \text{fasting insulin}) / 405$$

$$\text{FLI} = (e^{0.953\times\log_e(\text{triglycerides}) + 0.139\times\text{BMI} + 0.718\times\log_e(\text{r-GTP}) + 0.053\times\text{waist circumference} - 15.745}) / (1 + e^{0.953\times\log_e(\text{triglycerides}) + 0.139\times\text{BMI} + 0.718\times\log_e(\text{r-GTP}) + 0.053\times\text{waist circumference} - 15.745}) \times 100$$

2.4.5 Measures of telomere length and mtDNA copy number

Real-time PCR was used to measure telomere length and mtDNA copy number (33). Genomic DNA was extracted from PBMCs using the QIAGEN DNeasy kit, according to the manufacturer's protocol. DNA was eluted in 200μl AE buffer and stored in a -80°C deep freezer immediately after DNA extraction.

Absolute Human Telomere Length and Mitochondrial DNA Copy Number Dual Quantification qPCR Assay Kit (AHDQ) (#8958, Sciencell) was used, and the experiment was performed according to the commercial guidelines. We used the Applied Biosystems 7900HT Fast Real-Time PCR System (Applied Biosystems).

2.4.6 Enzyme-linked immunosorbent assay

Serum levels of GDF15, FGF21 and soluble α-Klotho were measured by ELISA using a commercial kit. Serum was used for the assay. An R&D Systems (DGD150) ELISA kit was used to analyze serum GDF15 levels. Serum was diluted 4-fold. The R&D Systems (DF2100) ELISA kit was used to analyze serum FGF21 levels without dilution. Soluble α-Klotho was analyzed with 3-fold diluted serum using a Human soluble α-Klotho Assay Kit (#27998, IBL, Japan).

2.4.7 Lifestyle questionnaires

We adopted six lifestyle-related or psychological status questionnaires. We used the International Physical Activity Questionnaire (IPAQ) Short Form to monitor physical activity status. We used the Beck Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI) for depression and anxiety respectively. Perceived Stress Scale (PSS), World Health Organization Quality of Life (WHOQOL-BREF), and Pittsburgh Sleep Quality Index (PSQI) were used to measure stress, quality of life, and sleep, respectively **(Table 3)**. The questionnaires used in this study are shown in **Appendix 1**.

Table 3. Lifestyle questionnaires

	Questionnaires	Questions (N)
Stress	Perceived Stress Scale (PSS)	10
Anxiety	State-Trait Anxiety Inventory (STAI)	20
Depression	Beck's Depression Inventory (BDI)	21
Quality of Life	World Health Organization Quality of Life (WHOQOL-BREF)	26
Physical activity	Modified International Physical Activity Questionnaire (IPAQ) - Short Form	10
Sleep	Pittsburg Sleep Quality Index (PSQI)	11

2.4.8 Statistical analysis

All data were analyzed using SPSS software (version 25.0; SPSS, Inc., Chicago, IL, USA). Pearson's correlation tests were conducted to determine the association between the variables. We used an independent t-test or analysis of covariance (ANCOVA) to analyze the two groups. Logistic regression analysis was used to confirm the effects of health-related physical fitness on metabolic syndrome. Statistical significance was set at $P < 0.05$.

III. RESULTS

3.1 Characteristics of the participants

The descriptive demographic and anthropometric data of all participants are shown in **Table 4**. A total of 98 subjects (19 men and 79 women) participated in this study. Categorical variables are shown as numbers with percentages, while continuous variables are shown as mean with standard deviations. The average age of all participants was 59.71, (ranging between 40 to 85 years).

Table 4. Characteristics of participants

	Total (n=98)
Demographic	
Age (years)	59.71±9.34
<65 years (n, %)	76 (77.6)
≥65 years (n, %)	22 (22.4)
Gender (n, %)	
Male	19 (19.4)
Female	79 (80.6)
Education (n, %)	
middle school or less	18 (18.3)
High school	26 (26.5)
Bachelor's degree or higher	46 (47.0)
No response	8 (8.2)
House income (n, %)	
High	5 (5.1)
Medium	75 (76.5)
Low	10 (10.2)
No response	8 (8.2)
Marital status (n, %)	
Unmarried	3 (3)
Married	75 (76.5)
Divorced	9 (9.2)
Widowed	4 (4.1)
No response	7 (7.1)
Anthropometric	
Height (cm)	158.09±7.23
Weight (kg)	59.42±10.23
BMI (kg/m^2)	23.70±3.28
Skeletal muscle mass (kg)	25.26±30.24
Body fat percentage (%)	23.09±9.23
Waist circumference (cm)	80.45±9.19

Data presented as mean±SD or number (%).

3.2 Physical fitness variables

Table 5 shows the number of participants and the mean with the standard deviation of each physical fitness test. Maximal oxygen uptake (VO_2max, mL/kg/min) was predicted using the YMCA step test (34). The equation validated by the Korean Institute of Sport Science for predicting VO_2max is as follows:

For women:

VO_2max (mL/kg/min) = 54.337 – 0.185 × (age) + 0.097 × (height) – 0.246 × (weight) – 0.122 × (1 minute recovery heart rate)

For men:

VO_2max (mL/kg/min) = 70.597 – 0.246 × (age) + 0.077 × (height) – 0.222 × (weight) – 0.147 × (1 minute recovery heart rate)

We used relative handgrip strength divided by body weight (relative handgrip strength = handgrip strength [kg] / body weight [kg]) to normalize the confounding effects of body size (7, 35). The data on handgrip strength were analyzed by relative handgrip strength.

Table 5. Physical fitness variables

	N	Mean±SD
Total		
Handgrip strength (kg)	97	0.48±0.10
Sit and reach (cm)	96	12.92±8.09
2-minute walking test (n)	97	121.05±20.02
<65 years		
Handgrip strength (kg)	75	0.48±0.10
Sit and reach (cm)	74	13.29±8.49
2-minute walking test (n)	75	122.71±20.19
YMCA step test (ml/kg/min)	71	33.23±4.08
Sit up (n)	74	16.96±10.99
Reaction time (sec)	74	1.37±3.73
Standing-board jump (cm)	72	140.46±31.07
≥65 years		
Handgrip strength (kg)	22	0.45±0.09
Sit and reach (cm)	22	11.63±6.50
2-minute walking test (n)	22	115.14±18.70
30 second chair stand test (n)	22	16.67±4.34
Timed up and go (sec)	22	6.28±0.99
Figure-of-8 walk around (sec)	22	24.74±7.14

Data presented as mean±SD

3.3 Correlations

Correlations between physical fitness and other health outcomes are presented in three Tables **(Table 6–8).** r = Pearson correlation coefficient. The additional correlation results are presented in **Appendix 2**.

3.3.1 Correlations between physical fitness and metabolic syndrome risk factors

The correlations between all physical fitness variables and metabolic risk factors are presented in **Table 6.**

3.3.2 Correlations between physical fitness and biomarkers

The correlations between all physical fitness variables and the main biomarkers are presented in **Table 7**.

3.3.3 Correlations between physical fitness and lifestyle questionnaires

The correlations between all physical fitness variables and lifestyle-related or psychological questionnaires are shown in **Table 8**.

Table 6. Correlations between physical fitness level and metabolic syndrome risk factors

	Physical fitness variables									
	VO_2max	2MWT	HGS	Sit and reach	Sit up	Reaction time	Standing -board jump	30 sec chair stand test	Timed up and go	Figure-of-8 walk around
Metabolic syndrome risk factors										
WC	-0.160	**-.241***	**-.296****	-0.180	0.003	-0.186	0.048	-0.270	0.425	0.222
GLU	0.154	-0.044	-0.014	**-.203***	0.391	-0.031	-0.027	-0.137	0.321	0.153
HDL-C	-0.091	0.083	0.066	**.291****	-0.107	0.125	-0.058	0.305	-0.403	-0.346
TG	-0.008	-0.115	-0.096	-0.133	0.064	-0.123	-0.015	-0.238	**.439***	0.288
SBP	-0.068	0.008	-0.022	0.173	-0.150	**-.282***	-0.013	0.084	-0.391	-0.377
DBP	-0.042	0.174	0.185	0.100	0.018	**-.297***	0.191	0.232	-0.425	-0.407

Data presents as r. r = Pearson correlation co-efficient. *p<0.05, **p<0.01.

Table 7. Correlations between physical fitness level and biomarkers

	Physical fitness variables									
	VO_2max	2MWT	HGS	Sit and reach	Sit up	Reaction time	Standing-board jump	30 sec chair stand test	Timed up and go	Figure-of-8 walk around
Biomarkers										
TL	-0.178	-0.198	-.257*	-0.073	-0.064	**.233***	-0.226	-0.072	0.061	0.203
mtDNA-CN	0.105	-0.119	-0.110	-0.028	0.029	0.144	-0.123	0.132	-0.019	0.222
α-Klotho	-0.146	0.028	0.090	-0.008	0.173	-0.066	0.132	0.149	0.140	-0.020
FGF21	-0.024	-0.143	**-.221***	-0.132	-0.201	-0.058	-0.146	-0.095	**.446***	0.214
GDF15	0.016	-0.127	-0.094	-0.153	-0.159	0.035	-0.080	-0.140	0.349	-0.029

Data presents as r. r = Pearson correlation co-efficient. *p<0.05, **p<0.01.

Table 8. Correlations between physical fitness level and lifestyle questionnaire scores

	Physical fitness variables									
	VO_2max	2MWT	HGS	Sit and reach	Sit up	Reaction time	Standing-board jump	30 sec chair stand test	Timed up and go	Figure-of-8 walk around
Lifestyle questionnaires										
Stress	-0.134	-0.110	-0.037	-0.005	-0.057	0.005	-0.182	-0.318	0.378	0.289
Anxiety	-0.163	-0.150	-0.039	0.022	-0.116	-0.008	-0.137	-0.192	0.070	-0.022
Depression	-0.225	-0.139	**-.211***	0.150	-0.217	**.244***	-0.220	-0.388	0.365	**.514***
Quality of Life	0.171	0.194	0.205	-0.027	0.226	-0.114	**.308***	0.190	-0.200	-0.204
Physical activity	0.137	0.137	0.196	-0.017	**.248***	0.015	0.191	**.492***	**-.462***	-0.091
Sleep	-0.155	0.036	-0.138	0.083	-0.062	0.063	-0.153	-0.165	-0.018	0.208

Data presents as r. r = Pearson correlation co-efficient. *p<0.05, **p<0.01

3.4 Metabolic syndrome and health outcomes

Among the 98 participants, 22 had MetS. **Table 9** describes the differences between the two groups with or without MetS. There were significant differences in the metabolic syndrome risk factors and related biomarkers, including WC, DBP, HDL-C, GLU, TG, HOMA-IR, and insulin which were expected. Body composition outcomes were significantly different in terms of weight, BMI, and body fat percentage. The FLI was also significantly different between the two groups. FGF21 levels were significantly different, whereas levels of GDF15 and aging markers were not.

Table 9. Health outcomes by metabolic syndrome

	Normal (n= 76)	MetS (n= 22)	P
Anthropometric			
WC (cm)	77.47±7.11	90.72±8.15	**<0.001**
SBP (mmHg)	126.36±16.34	132.50±14.53	0.115
DBP (mmHg)	71.97±11.09	77.91±9.50	**0.025**
Heart Rate (bpm)	74.34±11.10	71.32±6.61	0.117
Height (cm)	157.71±6.51	159.40±9.38	0.436
Weight (kg)	56.49±8.13	69.52±10.48	**<0.001**
Skeletal muscle mass (kg)	25.34±34.26	24.98±5.68	0.962
BMI (kg/m^2)	22.64±2.35	27.36±3.46	**<0.001**
Body fat percentage (%)	21.48±8.63	28.67±9.26	**0.001**
Aging biomarker			
Soluble a-Klotho (pg/mL)	1013.24±300.13	1199.67±734.49	0.257
Telomere length (kb)	2.39±0.82	2.32±0.90	0.730
mtDNA-CN	272.71±111.49	302.57±159.27	0.324
Mitochondrial stress biomarker			
FGF21 (pg/mL)	157.25±87.88	256.34±146.50	**0.006**
GDF15 (pg/mL)	709.70±358.30	770.47±415.17	0.501

Data presented as mean±SD.

Table 9. Cont'd

	Normal (n= 76)	MetS (n= 22)	P
Blood profile			
Creatinine (mg/dL)	0.90±0.18	0.95±0.25	0.308
ALT (U/L)	33.45±13.77	39.45±16.77	0.090
AST (U/L)	28.91±7.83	36.23±21.57	0.132
TC (mg/dL)	188.80±38.31	179.41±34.62	0.304
LDL-C (mg/dL)	98.78±35.61	92.30±31.59	0.461
HOMA-IR	1.54±0.88	2.95±1.49	**<0.001**
HDL-C (mg/dL)	58.96±13.44	42.27±7.09	**<0.001**
r-GTP (IU/L)	18.59±15.41	26.59±22.42	0.058
Fasting glucose (mg/dL)	95.24±9.88	106.32±17.35	**<0.001**
Triglyceride (mg/dL)	110.05±50.20	210.95±143.06	**<0.001**
Insulin (μU/mL)	6.45±3.36	11.26±5.62	**<0.001**
hs-CRP (mg/L)	0.92±0.97	1.17±0.95	0.299
HbA1c (%)	5.47±0.70	5.82±0.81	0.068
FLI	15.15±13.69	48.96±21.51	**<0.001**
Lifestyle-related Questionnaires			
Stress	14.18±4.19	15.45±4.25	0.215
Anxiety	32.96±8.54	35.68±9.43	0.205
Depression	6.44±5.42	6.77±4.45	0.792
Quality of Life	97.01±15.00	92.76±11.35	0.234
Physical activity	1927.16±2083.56	2839.41±3319.87	0.124
Sleep	1.72±1.20	2.14±1.25	0.164

Data presented as mean±SD.

3.5 Physical fitness and health outcomes

3.5.1 Health outcomes by VO_2max in middle-aged adult

VO_2max was calculated by the YMCA 3-minute step test in 71 young adults aged 40–64 years (13 men, 58 women). Men and women were divided into two groups (VO_2max Low and VO_2max High) according to their VO_2max values. The high VO_2max group included seven men (VO_2max ≥ 38.48) and 29 women (VO_2max ≥ 31.90). The low VO_2max group included six men (VO_2max < 38.48) and 29 women (VO_2max < 31.90).

Group analysis was performed using ANCOVA as the age of the two groups was significantly different, leading to the number of participants getting diminished because of missing data. The result of ANCOVA adjusted by age is presented in **Table 10**.

There were significant differences in WC, HOMA-IR and insulin levels, which are metabolic syndrome risk factors. Regarding psychological outcomes, depression (p=0.033) and anxiety (p=0.015) levels were significantly higher in the low CRF group compared with those of the high CRF group.

Table 10. Health outcomes by VO_2max in middle-aged adult aged 40~64 years

	VO_2max Low (n= 26)	VO_2max High (n= 24)	P
Anthropometric			
WC (cm)	83.30±7.70	76.50±8.05	**0.004**
SBP (mmHg)	125.42±14.72	123.17±13.57	0.864
DBP (mmHg)	73.77±10.33	72.58±11.21	0.714
Heart Rate (bpm)	77.85±8.71	71.46±9.06	**0.015**
Height (cm)	158.76±7.38	160.31±7.60	0.895
Weight (kg)	62.63±9.33	58.24±11.35	0.093
Skeletal muscle mass (kg)	22.77±4.30	35.26±60.48	0.242
BMI (kg/m^2)	24.84±3.20	22.47±2.62	**0.011**
Body fat percentage (%)	27.71±9.50	19.40±8.36	**0.003**
Aging biomarker			
Soluble a-Klotho (pg/mL)	1013.96±302.00	985.33±320.69	0.782
Telomere length (kb)	2.14±0.77	2.14±0.67	0.970
mtDNA-CN	248.84±106.29	265.18±99.09	0.958
Mitochondrial stress biomarker			
FGF21 (pg/mL)	185.43±122.39	163.91±112.92	0.608
GDF15 (pg/mL)	606.85±209.71	652.51±347.58	0.132

Data presented as mean±SD.

Table 10. Cont'd

	VO_2max Low (n= 26)	VO_2max High (n= 24)	*P*
Blood profile			
Creatinine (mg/dL)	0.87±0.14	0.89±0.22	0.762
ALT (U/L)	36.23±14.43	33.25±14.44	0.669
AST (U/L)	31.35±14.76	28.29±8.53	0.691
TC (mg/dL)	186.50±33.3	185.04±33.35	0.814
LDL-C (mg/dL)	100.19±32.04	93.96±30.40	0.460
HOMA-IR	2.21±1.17	1.35±0.84	**0.013**
HDL-C (mg/dL)	52.35±11.45	57.67±14.45	0.135
r-GTP (IU/L)	19.81±12.5	19.50±11.08	0.804
Fasting glucose (mg/dL)	97.19±9.63	94.50±8.07	0.544
Triglyceride (mg/dL)	120.00±46.87	109.38±57.60	0.564
Insulin (μU/mL)	9.03±4.09	5.66±3.21	**0.006**
hs-CRP (mg/L)	1.18±0.96	0.82±0.66	0.240
HbA1c (%)	5.62±0.79	5.50±0.51	0.647
FLI	26.43±21.52	16.55±14.73	0.098
Lifestyle-related Questionnaires			
Stress	14.58±3.49	13.38±3.79	0.214
Anxiety	36.42±9.49	30.08±7.76	**0.033**
Depression	7.27±4.90	3.83±2.97	**0.015**
Quality of Life	94.73±14.48	99.17±13.31	0.436
Physical activity	2055.88±2039.19	2497.96±2688.71	0.389
Sleep	2.08±1.06	1.58±1.10	0.121

Data presented as mean±SD.

3.5.2 Health outcome by relative hand grip strength

Relative handgrip strength (HGS) was measured in 95 participants (18 men, 77 women). Men and women were divided into two groups (HGS Low and HGS High) according to their HGS values. The high HGS group included nine men (HGS ≥ 0.59) and 37 women (HGS ≥ 0.46). The low HGS group included nine men (HGS < 0.59) and 40 women (HGS < 0.46). Group analysis was performed by using an independent t-test analysis. (**Table 11)** There were significant differences in the metabolic syndrome risk factors including WC ($p < 0.001$), HOMA-IR ($p = 0.009$), HDL-C ($p = 0.038$), TG ($p = 0.012$) insulin ($p = 0.011$) and r-GTP ($p = 0.041$). Heart rate ($p = 0.031$), body weight ($p = 0.006$), BMI ($p < 0.001$) and body fat percentage ($p = 0.002$) were also significantly different between the two groups. One of the aging markers, mtDNA-CN ($p = 0.044$) was significantly lower in the high HGS group. FGF21 levels ($p = 0.014$) were significantly lower in the high HGS group. Among the lifestyle-related questionnaires, quality of life ($p = 0.046$) was the only variable that showed significance.

Table 11. Health outcomes by handgrip strength

	HGS Low (n= 49)	HGS High (n= 46)	P
Anthropometric			
WC (cm)	84.06±9.34	76.74±7.59	**<0.001**
SBP (mmHg)	127.47±16.33	128.09±15.95	0.853
DBP (mmHg)	72.02±9.11	74.78±12.91	0.234
Heart Rate (bpm)	71.61±8.85	76.15±11.30	**0.031**
Height (cm)	157.48±7.63	158.49±6.51	0.491
Weight (kg)	62.29±10.73	56.60±8.80	**0.006**
Skeletal muscle mass (kg)	22.27±4.80	28.62±43.84	0.316
BMI (kg/m^2)	25.04±3.46	22.45±2.48	**<0.001**
Body fat percentage (%)	26.08±9.56	20.19±7.86	**0.002**
Aging biomarker			
Soluble a-Klotho (pg/mL)	658.95±427.32	799.25±823.03	0.312
Telomere length (kb)	2.48±0.86	2.27±0.82	0.227
mtDNA-CN	300.27±129.14	249.56±106.77	**0.044**
Mitochondrial stress biomarker			
FGF21 (pg/mL)	273.23±175.53	199.96±98.97	**0.014**
GDF15 (pg/mL)	784.10±487.15	693.22±375.88	0.310

Data presented as mean±SD.

Table 11. Cont'd

	HGS Low (n= 49)	HGS High (n= 46)	*P*
Blood profile			
Creatinine (mg/dL)	0.91±0.21	0.92±0.19	0.733
ALT (U/L)	37.90±17.03	32.24±11.01	0.056
AST (U/L)	32.88±16.13	28.61±6.83	0.094
TC (mg/dL)	187.08±42.36	186.96±32.50	0.987
LDL-C (mg/dL)	97.36±39.27	96.98±30.17	0.958
HOMA-IR	2.19±1.43	1.55±0.81	**0.009**
HDL-C (mg/dL)	52.80±15.40	58.76±11.95	**0.038**
r-GTP (IU/L)	24.22±22.61	16.87±8.68	**0.041**
Fasting glucose (mg/dL)	99.33±14.38	96.07±10.82	0.217
Triglyceride (mg/dL)	156.29±113.86	109.41±50.46	**0.012**
Insulin (μU/mL)	8.71±5.38	6.41±2.86	**0.011**
hs-CRP (mg/L)	1.11±1.12	0.84±0.79	0.182
HbA1c (%)	5.62±0.74	5.48±0.74	0.363
FLI	31.82±24.05	14.06±12.74	<0.001
Lifestyle-related Questionnaires			
Stress	14.46±4.02	14.37±4.50	0.922
Anxiety	33.50±8.76	34.07±9.07	0.763
Depression	6.89±5.17	6.27±5.34	0.576
Quality of Life	92.51±13.34	98.58±14.74	**0.046**
Physical activity	2125.20±2735.02	2225.37±2196.65	0.847
Sleep	1.91±1.33	1.74±1.14	0.509

Data presented as mean±SD.

3.6 Effect of health-related physical fitness on metabolic syndrome

Logistic regression analysis was performed to confirm the effects of health-related physical fitness on metabolic syndrome. Among the health-related physical fitness tests, the YMCA step test, 2MWT and handgrip strength were included in the analysis. The YMCA step test was analyzed in younger adults, while 2MWT and HGS were analyzed in all participants.

The YMCA step test and HGS have the power to predict both crude and adjusted analyses. The 2MWT including all participants did not have the power to predict the risk of metabolic syndrome.

Table 12. Effects of health-related physical fitness on metabolic syndrome (Logistic regression)

Variables	Crude Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
YMCA step test (n=71)		
Low	**10.05 (2.06-48.89)**	**12.56 (1.57-100.63)**
High	**1.00 (Ref)**	**1.00 (Ref)**
2MWT (n=97)		
Low	1.70 (0.65-4.46)	1.30 (0.42-3.98)
High	**1.00 (Ref)**	**1.00 (Ref)**
HGS (n=97)		
Low	**4.36 (1.45-13.08)**	**3.64 (1.09-12.17)**
High	**1.00 (Ref)**	**1.00 (Ref)**

Data are represented OR (95% CI). **BOLD=** Significantly different from the High physical fitness group (p<0.05). Adjusted for age, sex, education, and house income

IV. DISCUSSION

In this cross-sectional study, we evaluated the relationships among physical fitness, metabolic syndrome risk factors, aging and mitochondrial biomarkers, and lifestyle factors.

We explored the correlations between all physical fitness variables and health outcomes. According to the result of correlations, we conducted group analysis in health-related physical fitness variables including YMCA step test and HGS.

In a group analysis of YMCA step test, WC, heart rate, BMI, body fat percentage, HOMA-IR, insulin were significantly different between two groups. Additionally, lifestyle-related questionnaires including anxiety and depression were significantly high in the low VO_2max group. In a group analysis according to HGS, WC, heart rate, weight, BMI, body fat percentage, mtDNA-CN, FGF21, HOMA-IR, HDL-C, r-GTP, TG, and insulin were significantly different between two groups. Also, high HGS group shows better quality of life according to questionnaire scores.

In a group analysis of HGS, serum FGF21 levels were significantly lower in the high HGS group. Also, FGF21 levels were significantly low in participants without metabolic syndrome. High serum FGF21 levels were positively linked to metabolic diseases such as diabetes, obesity, mitochondrial diseases, and aging (36). The correlations between serum FGF21 levels and health outcomes are shown as scatter plot in **Appendix 2-2**. Elevated serum FGF21 level could be a compensatory mechanism to control insulin level. FGF21 could be the therapeutic target to metabolic disorders.

The prevalence of metabolic syndrome differed according to health-related physical fitness level. The prevalence of metabolic syndrome was significantly higher in the group with low cardiorespiratory fitness according to the VO_2max level predicted by the YMCA step test. The low HGS group also have higher risk of metabolic syndrome than high HGS group. This result suggests that VO_2max and relative handgrip strength are strong predictors of metabolic syndrome. On the other hand, 2MWT did not have the power to predict the risk of metabolic syndrome.

V. CONCLUSION

In conclusion, health-related physical fitness are associated with various health outcomes. VO_{2max} and relative handgrip strength are negatively associated with MetS independently and after adjustment for age, sex, education, and house income.

There were some limitations in this study. The proportion of male was small and the distribution of participants in the age group was different. Also, this cross-sectional study could not ensure a causal effect among the variables. Therefore, future studies including randomized controlled trials are needed to confirm our findings. Also, we discussed the results of all the participants. Subgroup analyses according to age and sex were necessary. In spite of some limitations, comprehensive data collected from cell to clinical practice is a strong value of this study.

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VII. APPENDIX

Appendix 1-1. International Physical Activity Questionnaire (IPAQ) Short Form

ID:_____

작성일: _____년 _____월 _____일

설 문 지

안녕하십니까?
이 설문조사는 연구에 필요한 내용을 조사하기 위함입니다. 귀하께서 응답하신 내용은 연구에 귀중한 자료가 될 것입니다. 정성껏 모든 항목에 답변해 주시기를 부탁드립니다. 설문 시간은 약 30분 정도 소요될 것입니다. 본 설문 결과는 비밀이 철저히 보장되며 연구 이외의 목적으로 사용되지 않습니다.

1. 주관적 신체활동량

이 설문은 **지난 7일간** 귀하가 신체활동에 소모한 시간에 대해 물을 것입니다. 귀하 스스로 활동적이지 않다고 생각되시더라도 각 질문에 응답해 주시기 바랍니다. 직장에서 집에서 하는 활동, 교통수단을 이용할 때 하는 활동, 여가 시간에 시행하는 활동, 운동 또는 스포츠 모두를 포함하여 생각해 주시기 바랍니다.
귀하가 **지난 7일간** 하신 모든 격렬한 활동을 생각해 보십시오. **격렬한 신체활동** 이란 힘들게 움직이는 활동으로서 평소보다 숨이 훨씬 더 차게 만드는 활동입니다. 한번에 적어도 10분 이상 지속한 활동만을 생각하여 응답해주시기 바랍니다.

1. 지난 7일간 무거운 물건 나르기, 달리기, 에어로빅, 빠른속도로 자전거 타기 등과 같은 격렬한 신체활동을 며칠간 하였습니까?

일주일에_____일

☐ 격렬한 신체활동 없었음 → *3번으로 가세요*

2. 그런 날 중 하루에 격렬한 신체활동을 하면서 보낸 시간이 보통 얼마나 됩니까?

하루에_____시간_____분

☐ 모르겠다/확실하지 않다

귀하가 **지난 7일간** 하신 모든 중간정도 신체활동을 생각해 보십시오. **중간정도 신체활동**이란 중간정도 힘들게 움직이는 활동으로서 평소보다 숨이 훨씬 더 차게 만드는 활동입니다. 한번에 적어도 10분 이상 지속한 활동만을 생각하여 응답해주시기 바랍니다.

3. **지난 7일간**, 가벼운 물건나르기, 보통속도로 자전거타기, 복식 테니스 등과 같은 **중간정도** 신체활동을 며칠간 하였습니까? 걷기는 포함시키지 마십시오.

일주일에_____일

☐ 중간정도 신체활동 없었음 → *5번으로 가세요*

ID:_____

4. 그런 날 중 하루에 **중간정도**의 신체활동을 하면서 보낸 시간이 보통 얼마나 됩니까?

하루에_____**시간**_____**분**

☐ 모르겠다/확실하지 않다

지난 7일간 걸은 시간을 생각해보십시오. 직장이나 집에서, 교통수단을 이용할 때 걸은 것 뿐만아니라 오락활동, 스포츠, 운동, 여가 시간에 걸은 것도 포함됩니다.

5. **지난 7일간** 한번에 적어도 10분 이상 **걸은 날**이 며칠입니까?

일주일에_____**일**

☐ 걷지 않았음 → 7번으로 가세요

6. 그런 날 중 하루에 **걸으면서** 보낸 시간이 보통 얼마나 됩니까?

하루에_____**시간**_____**분**

☐ 모르겠다/확실하지 않다

지난 7일간 주중에 앉아서 보낸 시간에 관한 것입니다. 여기에는 직장과 집에서 학업이나 여가시간에 앉아서 보낸 시간이 포함됩니다. 또한 책상에 앉아 있거나, 친구를 만나거나, 독서할 때 앉거나, 텔레비전을 앉아서 또는 누워서 시청한 시간이 포함됩니다.

7. 지난 7일간, 주중에 앉아서 보낸 시간이 보통 얼마나 됩니까?

하루에_____**시간**_____**분**

☐ 모르겠다/확실하지 않다

마지막 질문은 **지난 7일간** 근력운동을 하신 시간을 생각해 보십시오. 근력운동이란 특정부위 (배, 팔, 다리, 등, 엉덩이)의 근육을 단련하기 위해 물건이나 기구를 이용하거나 또는 물건이나 기구의 도움 없이도 근육의 반복적인 수축과 이완을 일으키는 운동입니다.

8. 지난 7일간, 한번이상 근력운동을 며칠간 하였습니까? **일주일에**_____**일**

9. 지난 7일간, 근력운동을 하셨다면 얼마정도 하셨습니까? **하루에**_____**시간** _____**분**

10. 근력운동에 참가해 온 기간은 얼마나 되십니까? _____**년**_____**개월**

Appendix 1-2. Beck's Depression Inventory (BDI)

ID:_____

2. 우울

문항	V	내 용
1	0	나는 슬프지 않다.
	1	나는 슬프다.
	2	나는 언제나 슬픔에 젖어 헤어날 수가 없다.
	3	나는 너무나 슬프고 불행해서 도저히 견딜 수 없다.
2	0	나는 앞날에 대해 별로 비관적이지 않다.
	1	나는 앞날에 대해서 비관적이다.
	2	나는 앞날에 대한 기대가 아무것도 없다.
	3	나의 앞날은 아주 절망적이고 나아질 가망도 없다.
3	0	나는 실패자라고 생각하지 않는다.
	1	나는 다른 사람들보다 더 많이 실패한 것 같다.
	2	내가 살아온 과거를 돌이켜 보면 생각나는 것은 실패 뿐이다.
	3	나는 인간으로서 완전한 실패자인 것 같다.
4	0	나는 전과 같이 일상생활에서 만족하고 있다.
	1	나는 일상생활은 전처럼 즐겁지가 않다.
	2	나는 더 이상 어떤 것에도 참된 만족을 느끼지 못한다.
	3	나는 모든 것이 다 불만스럽고 지겹다.
5	0	나는 별로 죄책감을 느끼지 않는다.
	1	나는 죄책감을 느낄 때가 많다.
	2	나는 거의 언제나 죄책감을 느낀다.
	3	나는 항상 죄책감을 느낀다.
6	0	나는 벌을 받고 있다고 생각하지 않는다.
	1	나는 벌을 받을지도 모르겠다.
	2	나는 벌을 받아야 한다고 생각한다.
	3	나는 지금 벌을 받고 있다고 생각한다.
7	0	나는 나 자신에게 실망하지 않는다.
	1	나는 나 자신에게 실망하고 있다.
	2	나는 나 자신에게 화가 난다.
	3	나는 나 자신을 증오한다.
8	0	나는 내가 다른 사람보다 못한 것 같지는 않다.
	1	나는 나의 약점이나 실수에 대해서 내 자신을 책망한다.
	2	내가 한일이 잘못되어 있을 때 언제나 나를 탓한다.
	3	나는 주위에서 일어나는 모든 안 좋은 일을 내 탓으로 돌린다.
9	0	나는 자살 같은 것은 생각지 않는다.
	1	나는 자살할 생각은 하고 있으나, 실제로 하지는 않을 것이다.
	2	나는 자살하고 싶다.
	3	나는 기회만 있으면 자살하겠다.
10	0	나는 평소보다 더 울지는 않는다.
	1	나는 평소보다 더 많이 운다.
	2	나는 요즈음 항상 운다.
	3	나는 전에는 울고 싶을 때 울 수 있었지만, 요즈음은 울래야 울 수도 없다.
11	0	나는 요즈음 평소보다 더 화를 내는 편은 아니다.
	1	나는 평소보다 더 쉽게 화가 나고 짜증이 난다.
	2	나는 요즈음 항상 화가 난다.
	3	전에는 화나던 일에 요즈음은 전혀 화조차 나지 않는다.

ID:_____

문항	V	내 용
12	0	나는 다른 사람들에게 여전히 관심을 가지고 있다.
	1	나는 평소보다 다른 사람들에게 관심이 줄었다.
	2	나는 다른 사람들에게 거의 관심이 없어졌다.
	3	나는 다른 사람들에게 관심이 완전히 없어졌다.
13	0	나는 평소처럼 결정을 잘 내린다.
	1	나는 평소보다 결정을 미루는 때가 많다.
	2	나는 결정 내리는 것이 전보다 더 힘들다.
	3	나는 이제 아무 결정도 내릴 수가 없다.
14	0	나는 평소보다 내 모습이 더 나빠졌다고 생각하지 않는다.
	1	나는 나이 들어 보이거나 호감을 못 줄 것 같아 걱정이다.
	2	나는 내 모습이 아주 볼품이 없어져 버린 것 같다.
	3	나는 내가 추하게 보인다고 생각한다.
15	0	나는 평소처럼 일을 할 수 있다.
	1	어떤 일을 하려면 평소보다 더 힘이 든다.
	2	무슨 일이든 하려면 무척 힘이 든다.
	3	나는 전혀 아무 일도 할 수가 없다.
16	0	나는 평소처럼 잠을 잘 수 있다.
	1	나는 평소보다 새벽에 일찍 깨고 다시 잠들기가 어렵다.
	2	나는 평소보다 몇 시간이나 일찍 깨고 다시 잠들 수가 없다.
	3	나는 너무나 피곤해서 아무 일도 할 수가 없다.
17	0	나는 평소보다 더 피곤하지는 않다.
	1	나는 평소보다 더 쉽게 피곤해진다.
	2	나는 무엇을 해도 언제나 피곤해진다.
	3	나는 너무나 피곤해서 아무 일도 할 수가 없다.
18	0	내 식욕은 평소와 다름 없다.
	1	나는 요즈음 평소보다 식욕이 없다.
	2	나는 요즈음 식욕이 많이 떨어졌다.
	3	요즈음에는 전혀 식욕이 없다.
19	0	요즈음 체중이 별로 줄지 않았다.
	1	전보다 몸무게가 2킬로그램 가량 줄었다.
	2	전보다 몸무게가 5킬로그램 가량 줄었다.
	3	전보다 몸무게가 7킬로그램 가량 줄었다.
20	0	나는 건강에 대해 전보다 더 염려하고 있지는 않다.
	1	나는 여러 가지 통증, 소화불량 또는 변비 등으로 염려된다.
	2	나는 건강이 매우 염려되어서 다른 일을 거의 생각할 수가 없다.
	3	나는 건강이 너무 염려되어서 다른 일은 아무 것도 생각할 수가 없다.
21	0	나는 요즈음 성(性)에 대한 관심이 별다른 변화가 있는 것 같지는 않다.
	1	나는 평소보다 성에 대한 관심이 줄었다.
	2	나는 요즈음 성에 대한 관심이 상당히 줄었다.
	3	나는 성에 대한 관심을 완전히 잃었다.

Appendix 1-3. State-Trait Anxiety Inventory (STAI)

ID:_____

3. 불안

다음 문장은 귀하가 이 순간에 느끼고 있는 상태에 대한 내용들입니다.
각 문장을 잘 읽으시고 오른편 네 개의 항목 중에서 당신이 일상생활에서 일반적으로 느낄 수 있는 바를 가장 잘 나타내주는 문항 하나를 골라 V표 하십시오.

문항	지금 이순간에 나는	전혀 없음	조금	보통	매우
1	평안하다.	1	2	3	4
2	안정된 느낌이다.	1	2	3	4
3	긴장감을 느낀다.	1	2	3	4
4	심하게 긴장된다.	1	2	3	4
5	마음이 평안하다.	1	2	3	4
6	속상하다.	1	2	3	4
7	불행이 닥쳐올까봐 지금 걱정이다.	1	2	3	4
8	흡족하다.	1	2	3	4
9	두렵다.	1	2	3	4
10	편안하다.	1	2	3	4
11	자신감을 느낀다.	1	2	3	4
12	안절부절 못한다.	1	2	3	4
13	초조하다.	1	2	3	4
14	무엇을 어찌해야 좋을지 모르겠다.	1	2	3	4
15	느긋한 기분이다.	1	2	3	4
16	만족감을 느낀다.	1	2	3	4
17	불안하다.	1	2	3	4
18	혼란스럽다.	1	2	3	4
19	마음이 동요되지 않고 안정되어 있다.	1	2	3	4
20	기분이 좋다.	1	2	3	4

Appendix 1-4. Perceived Stress Scale (PSS)

ID:_____

4. 스트레스

다음의 문항들은 최근 1개월 동안 당신이 느끼고 생각한 것에 대한 것입니다.
각 문항에 해당하는 내용을 얼마나 자주 느꼈는지 표기해 주십시오.

문항	최근 1개월 동안	전혀 없었다	거의 없었다	때때로 있었다	자주 있었다	매우 자주 있었다
1	최근 1개월 동안, 예상치 못했던 일 때문에 당황했던 적이 얼마나 있었습니까?	0	1	2	3	4
2	최근 1개월 동안, 인생에서 중요한 일들을 조절할 수 없다는 느낌을 얼마나 경험하였습니까?	0	1	2	3	4
3	최근 1개월 동안, 신경이 예민해지고 스트레스를 받고 있다는 느낌을 얼마나 경험하였습니까?	0	1	2	3	4
4	최근 1개월 동안, 당신의 개인적 문제들을 다루는 데 있어서 얼마나 자주 자신감을 느꼈습니까?	0	1	2	3	4
5	최근 1개월 동안, 일상의 일들이 당신의 생각대로 진행되고 있다는 느낌을 얼마나 경험하였습니까?	0	1	2	3	4
6	최근 1개월 동안, 당신이 꼭 해야 하는 일을 처리할 수 없다고 생각한 적이 얼마나 있었습니까?	0	1	2	3	4
7	최근 1개월 동안, 일상생활의 짜증을 얼마나 자주 잘 다스릴 수 있었습니까?	0	1	2	3	4
8	최근 1개월 동안, 최상의 컨디션이라고 얼마나 자주 느끼셨습니까?	0	1	2	3	4
9	최근 1개월 동안, 당신이 통제할 수 없는 일 때문에 화가 난 경험이 얼마나 있었습니까?	0	1	2	3	4
10	최근 1개월 동안, 어려운 일들이 너무 많이 쌓여서 극복하지 못할 것 같은 느낌을 얼마나 자주 경험하셨습니까?	0	1	2	3	4

Appendix 1-5. World Health Organization Quality of Life (WHOQOL-BREF)

ID:_____

5. 삶의 질

문 항		전혀 그렇지 않다	그렇지 않다	보통이다	그렇다	매우 그렇다
1	나의 삶의 질은 좋다.					
2	나는 나의 건강상태에 대해 만족하고 있다.					
3	신체적 통증으로 인해 내가 해야 할 일들을 방해받고 있다.					
4	일상생활을 잘 하기 위해 치료가 필요하다.					
5	나는 인생을 즐긴다.					
6	나의 삶은 매우 의미가 있다.					
7	나는 정신을 잘 집중할 수 있다.					
8	나는 일상생활에서 안전하다고 느낀다.					
9	나는 건강에 좋은 주거환경에 살고 있다.					
10	일상생활을 위한 에너지를 충분히 가지고 있다.					
11	나는 나의 신체적 외모에 만족한다.					
12	나는 나의 필요를 만족시킬 수 있는 충분한 돈을 가지고 있다.					
13	나는 매일의 삶에서 내가 필요로 하는 정보를 쉽게 구할 수 있다.					
14	나는 레저(여가) 활동을 위한 기회를 충분히 가지고 있다.					
15	나는 잘 돌아다닐 수 있다.					
16	나는 수면(잘 자는 것)에 충분히 만족한다.					
17	나는 일상생활을 수행하는 나의 능력에 대해 만족하고 있다.					
18	나는 내가 일할 수 있는 능력에 대해 만족하고 있다.					
19	나는 나 스스로에 대해 만족하고 있다.					
20	나는 나의 개인적 대인관계에 대해 만족하고 있다.					
21	나는 나의 성생활에 대해 만족하고 있다.					
22	나는 나의 친구들로부터 받고 있는 도움에 대해 만족하고 있다.					
23	나는 내가 살고 있는 장소에 대해 만족하고 있다.					
24	나는 의료서비스를 쉽게 받을 수 있다는 점에 만족하고 있다.					
25	나는 내가 사용하는 교통수단에 대해 만족하고 있다.					
26	나는 침울한 기분, 절망, 불안, 우울감과 같은 부정적인 감정을 자주 느낀다.					

Appendix 1-6. Pittsburg Sleep Quality Index (PSQI)

ID:_____

6. 수면의 질

다음은 지난 1달(4주) 동안 당신의 일상적인 수면습관에 관한 질문들입니다.

지난 1달 동안 대부분의 일상에서 가장 적절한 답변에 빠짐없이 V표시 혹은 기록을 해주시기 바랍니다.

1. 지난 한 달 동안, 당신은 평소에 몇 시에 잠자리에 들었습니까?	보통 오전 ( ) | 오후 ( ) _____시 _____분에 잠자리에 든다.
1. 지난 한 달 동안, 당신은 밤에 잠자리에 들어서 잠이 들기까지 보통 얼마나 오래 걸렸습니까?	_____시간 _____분이 걸린다.
1. 지난 한 달 동안, 당신은 평소 몇 시에 일어났습니까?	보통 오전 ( ) | 오후 ( ) _____시 _____분에 일어난다.
1. 지난 한 달 동안, 당신이 실제로 잠잔 시간은 얼마나 됩니까? (이것은 잠자리에서 보낸 시간과 다를 수 있습니다)	하루 밤에 _____시간 _____분

다음 각 문항에서 가장 적절한 응답을 하나만 고르십시오.

모든 질문에 응답해주시기 바랍니다.

1. 최근 한 달 동안 당신은 아래의 이유로 잠자는 데 얼마나 자주 문제가 있었습니까? (우측 칸에 □에 표시하세요)	지난 한 달 동안 없었다 (없다)	한 주에 한 번보다 적게 (주1회 미만)	한 주에 1~2번 정도 (주1~2회)	한 주에 3번 이상 (주3회 이상)
a. 취침 후 30분 이내로 잠들 수 없었다.	□	□	□	□
b. 한밤중이나 새벽에 깼다.	□	□	□	□
c. 화장실에 가려고 일어나야 했다.	□	□	□	□
d. 편안하게 숨을 쉴 수가 없었다.	□	□	□	□
e. 기침을 하거나 시끄럽게 코를 골았다.	□	□	□	□
f. 너무 춥다고 느꼈다.	□	□	□	□
g. 너무 덥다고 느꼈다.	□	□	□	□
h. 나쁜 꿈을 꾸었다.	□	□	□	□
i. 통증이 있었다.	□	□	□	□
j. 그 외에 다른 이유가 있었다면 기입해 주세요.(이유:) 지난 한 달 동안, 당신은 위에 기입한 이유들 때문에 잠자는 데 얼마나 자주 어려움이 있었습니까?	□	□	□	□

ID:_____

6. 지난 한 달 동안, 당신은 전반적으로 수면의 질이 어느 정도라고 스스로 평가하십니까?

☐ 매우 좋음 ☐ 좋음 ☐ 나쁨 ☐ 매우 나쁨

7. 지난 한 달 동안, 당신은 잠이 들기 위해 얼마나 자주 약을 먹었습니까?
(처방약 또는 약국에서 구입한 약)

☐ 지난 한 달 동안 없었다. ☐ 한 주에 1번보다 적게

☐ 한 주에 1~2회 정도 ☐ 한 주에 3회 이상

8. 지난 한 달 동안, 운전하거나 식사 때 또는 사회생활을 하는 동안 얼마나 자주 졸음을 느꼈습니까?

☐ 지난 한 달 동안 없었다. ☐ 한 주에 1번보다 적게

☐ 한 주에 1~2회 정도 ☐ 한 주에 3회 이상

9. 지난 한 달 동안, 당신은 일에 열중하는 데 얼마나 많은 문제가 있었습니까?

☐ 전혀 없었다. ☐ 매우 조금 있었다. ☐ 다소 있었다. ☐ 매우 많이 있었다.

10. 당신은 다른 사람과 같은 잠자리에 들거나 집을 같이 쓰는 사람이 있습니까?

☐ 같은 잠자리에 들거나 집을 같이 쓰는 사람이 없다.

☐ 집에 다른 방을 쓰는 사람이 있다.

☐ 방을 같이 쓰지만 같은 잠자리에 들지 않는다.

☐ 같은 잠자리에 드는 사람이 있다.

11. 만일 같은 방을 쓰거나 같은 잠자리에 드는 사람이 있다면, 그 사람에게 지난 한 달간, 당신이 다음과 같은 행동을 얼마나 자주 했는지 물어보십시오. (우측 칸에 ☐에 표시하세요)	지난 한 달 동안 없었다 (없다)	한 주에 한 번보다 적게 (주1회 미만)	한 주에 1~2번 정도 (주1~2회)	한 주에 3번 이상 (주3회 이상)
a. 심하게 코골기	☐	☐	☐	☐
b. 잠잘 때 숨을 한동안 멈추고 다시 숨쉬기	☐	☐	☐	☐
c. 잠잘 때 다리를 갑자기 떨거나 흔들기	☐	☐	☐	☐
d. 잠자다가 잠시 시간, 장소, 상황을 인식하지 못하거나 혼란스러워함	☐	☐	☐	☐
e. 잠자는 동안 다른 뒤척거리는 행동들이 있었으면 직접 기입해 주십시오.				

Appendix 1-7. Demographic questionnaire

ID:_____

7. 일반 설문

1. 귀하의 학력은 무엇입니까? ① 무학 ② 초졸 ③ 중졸 ④ 고졸 ⑤ 대졸 ⑥ 대학원 이상

2. 귀하의 결혼상태는 무엇입니까? ① 미혼 ② 기혼 ③ 이혼 ④ 사별 ⑤ 기타 ( )

3. 귀하의 종교는 무엇입니까? ① 기독교 ② 천주교 ③ 불교 ④ 무교 ⑤ 기타 ( )

4. 귀하의 직업은 어떻게 되십니까? ① 무직 ② 사무직 ③ 기술직 ④ 전문직 ⑤ 자영업
⑥ 기타 ( )

5. 귀하의 경제 상태는 어느 정도입니까? ① 상 ② 중 ③ 하

6. 귀하의 동거인은 누구입니까? ① 혼자 ② 배우자 ③ 자녀 ④ 배우자와 자녀
⑤ 친척 ⑥ 친구 ⑦ 기타 ( )

7. 현 직장에서의 근무 형태를 표시해주시기 바랍니다.
① 주간 8시간 ② 2교대 ③ 3교대 ④ 격일제(24시간) ⑤ 고정 야간근무 ⑥ 해당 없음

8. 지금까지 야간작업을 포함한 교대 근무에 종사한 기간은 몇 년입니까?
① 5년 미만 ② 5~9년 ③ 10~14년 ④ 15~19년 ⑤ 20년 이상 ⑥해당 없음

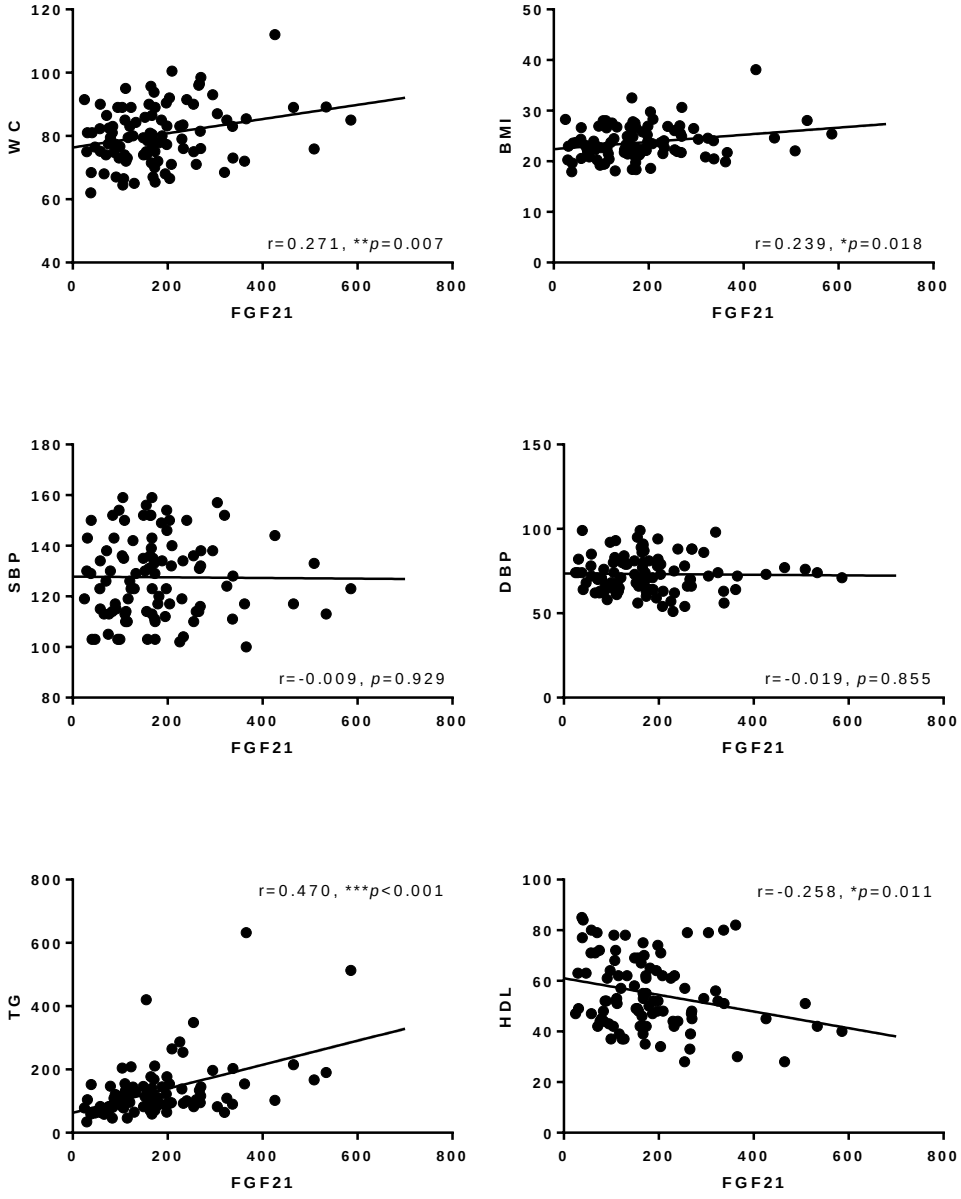
9. 귀하는 평소에 스트레스를 많이 받는 편이라고 생각하십니까? ① 예 ② 아니오

10. 스트레스를 받은 기간은 얼마 정도입니까? ( )년 ( )개월

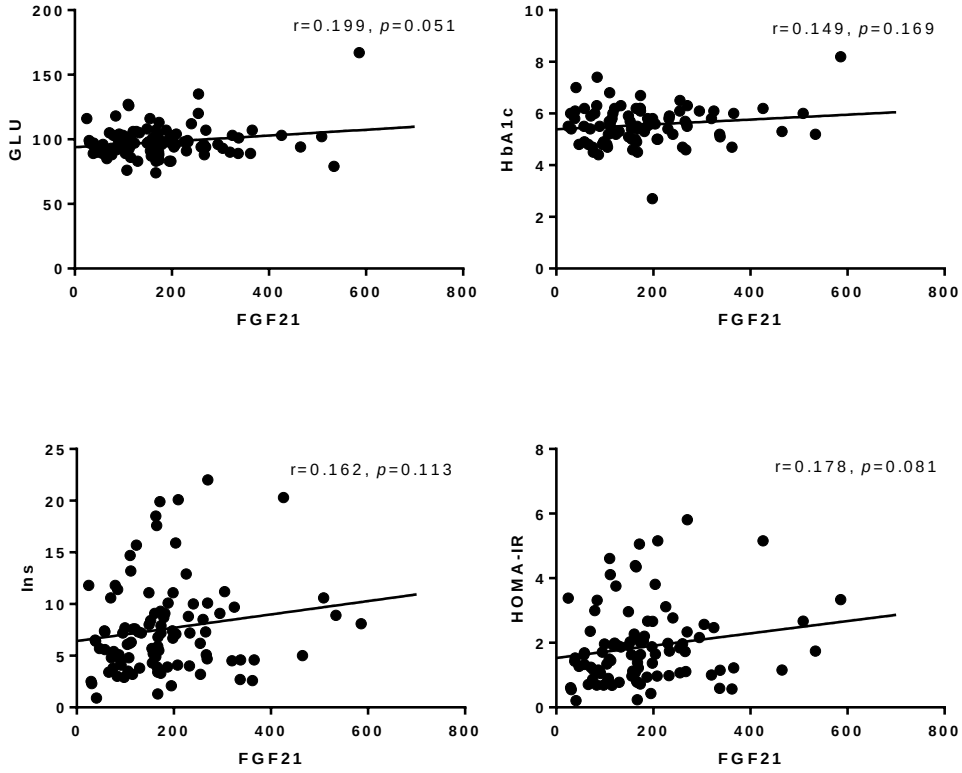
Appendix 2-1. Correlations among physical fitness variables.

variables	1	2	3	4	5	6	7	8	9	10
1. VO_2max	1									
2. 2MWT	0.128	1								
3. HGS	**.474****	0.067	1							
4. Sit and reach	**-.445****	0.060	**-.320****	1						
5. Sit up	**.452****	0.197	**.541****	-0.157	1					
6. Reaction time	0.035	-0.074	-0.083	-0.003	0.015	1				
7. Standing-board jump	**.518****	0.189	**.728****	-0.231	**.639****	0.015	1			
8. 30 second chair stand test		**.550***	0.203	0.316				1		
9. Timed up and go		**-.755****	-0.171	-0.236				**-.766****	1	
10. Figure-of-8 walk around		-0.175	-0.131	-0.055				-0.269	**.433***	1

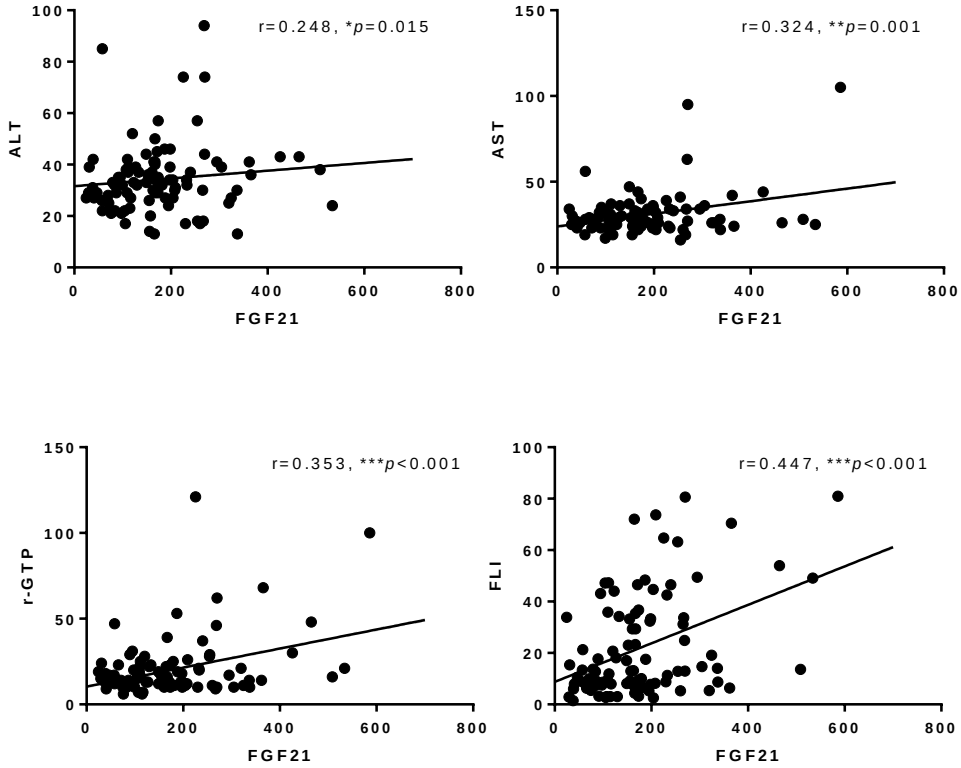
Appendix 2-2-1. Correlations between FGF21 and health outcomes.



Appendix 2-2-2. Correlations between FGF21 and health outcomes.



Appendix 2-2-3. Correlations between FGF21 and health outcomes.



VIII. CURRICULUM VITAE

Education and Training

2020.3-2021.12	Master's degree course Department of Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea
2017.3-2017.12	Language training program Shandong Institute of Business and Technology, Yantai, China
2016.9-2016.12	Exchange student program Saint Mary's University, Halifax, Nova Scotia, Canada
2014.3-2020.2	Bachelor's degree course Department of Physical Therapy, College of Health Science, Yonsei University, Wonju, Korea

Awards

2021.11	Best Poster Award 2021 Fall Congress of Korean Society Lifestyle Medicine Title: High Cardiorespiratory Fitness is Linked to Low Metabolic Risk Factors, Anxiety and Depression in the Middle-Aged Women.

Publications

Chang JY, You SJH, Grant ME, Lee JH, Kim TG, Kim KS, Chang JS, Choi JY, Lee YH, Kong ID. Review of physiotherapy service for athletes of 2018 Olympic Winter games: Consideration of preparation for two polyclinics. Phys Ther Sport. 2021 May;49:106-111.

Min J, Chang JS, Choi JY, Kong ID. Association Between Skeletal Muscle Mass, Physical Activity, and Metabolic Syndrome: the Korean National Health and Nutrition Examination Survey 2008-2011. Metab Syndr Relat Disord. 2021 Dec 23.

IX. ABSTRACT IN KOREAN

건강체력 수준에 따른 대사증후군, 생체지표, 생활습관 간의 연관성 연구

연세대학교 대학원

의학과 최지영

본 연구의 목적은 단면 연구를 통해 건강체력, 대사증후군, 생체지표 및 생활습관 간의 연관성을 알아보는데 있다. 성인 98명 (남성 19명, 여성 79명)이 연구에 참가하였다.

건강체력, 대사증후군 위험 인자, 노화관련 생체지표인 텔로미어 길이와 미토콘드리아 DNA 복제수, 그리고 미토콘드리아 스트레스 생체지표인 FGF21 및 GDF15을 모든 대상자에게서 측정하였다. 생활습관 관련 설문을 통해 스트레스, 불안, 우울, 삶의 질, 신체활동 및 수면에 대해 조사하였다.

건강체력 수준에 따라 두 그룹으로 나누어 분석한 결과, 심폐체력이 높은 그룹과 낮은 그룹 사이에서 허리둘레, 심박수, 체질량지수, 체지방률, HOMA-IR, 인슐린, 불안 및 우울에서 그룹 간 차이를 보였다. 상대악력이 높은 그룹과 낮은 그룹에서는 허리둘레, 심박수, 체중, 체질량지수, 체지방률, 미토콘드리아 DNA 복제수, FGF21, HOMA-IR, 고밀도 콜레스테롤, r-GTP, 중성지방 그리고 삶의 질에서 그룹 간 차이를 보였다.

심폐체력과 상대악력이 대사증후군에 미치는 영향을 알아보기 위해 로지스틱 회귀분석을 수행하였다. 심폐체력이 낮은 그룹은 높은 그룹에 비해 대사증후군이 생길 위험이 10.05배 높았으며, 나이, 성별, 학력, 경제수준을 보정했을 때에는 12.56배 높았다. 상대악력이 낮은 그룹은 높은 그룹에 비해 대사증후군이 생길 위험이 4.36배 높았으며, 나이, 성별, 학력, 경제수준을 보정했을 때에는 3.64배 높았다. 결과적으로, 심폐체력과 상대악력은 대사증후군의 예측 인자로 제시될 수 있으며, 관련된 생체지표는 치료적 타겟으로 간주될 수 있다. 본 연구는 건강 체력, 대사증후군, 다양한 건강 결과 간의 연관성을 보여주었고, 앞으로 대사증후군의 예방과 치료에 대한 연구에 중요한 기초 자료를 제공할 것이라 생각된다.

핵심 되는 말: 건강체력, 대사증후군, 생체지표, 생활습관