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A Study on the Relationship between Carotid Artery Intima–Media Thickness and Clinical Chemistry Tests

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경동맥 초음파 결과와 임상화학 검사의 상관성 연구

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Carotid Intima–Media Thickness (CIMT) testing is a test that precisely assesses cerebrovascular and coronary heart diseases. According to many previous studies, CIMT predicts atherosclerosis and is highly correlated to cardiovascular disease risk factors. It has also been reported that CIMT is an independent predictor of risk factors for myocardial infarction and stroke. Therefore, the purpose of this study is to investigate CIMT and other independent factors through a correlation study with the clinical laboratory test results of a blood test. As a result, this study could not prove the correlation between CIMT and risk factors of cardiovascular disease (TC, TG, LDL cholesterol, and HDL cholesterol) due to an insufficient number of subjects. Nevertheless, a positive correlation was demonstrated between CIMT and ALT ($p < 0.05$), GGT ($p < 0.05$), Uric acid ($p < 0.05$), and CEA ($p < 0.05$) at a statistically significant level, suggesting a continuation of the study.

Keywords: Carotid artery intima–media thickness (CIMT), Clinical chemistry

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Introduction

Carotid Artery Ultrasonography is a test that accurately assesses cerebrovascular and coronary heart diseases through measuring the Carotid Intima-Media Thickness (CIMT) and is a simpler, faster, and safer test compared to Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) (Salonen *et al.*, 1990). The carotid is composed of intima, media, and adventitia, and generally the thickness of the intima and media in the inner side of the adventitia with higher brightness are measured. CIMT of a normal person is different by race, gender, and age. According to a prospective domestic study in 2004 that investigated 470 subjects, the average CIMT of a healthy adult was 0.63 ± 0.11 mm on the right and 0.64 ± 0.11 mm on the left, and the average CIMT of an adult with hypertriglyceridemia and hypertension was 0.70 ± 0.13 mm on the right and 0.71 ± 0.14 mm on the left (Bae *et al.*, 2005). In general, standard CIMT of a normal person is set as less than 0.7 mm in clinical setting, and it was reported that a 0.1 mm increase of CIMT follows with $10 \sim 5\%$ increase of myocardial infarction, and $13 \sim 18\%$ increase of stroke (Freedman *et al.*, 2004). CIMT is used as an indicator for early prediction of cardiovascular diseases, as it has an interrelationship with cardiovascular risk factors such as age,

male, obesity, hypertension, hyperlipidemia, diabetes, and smoking (Burke *et al.*, 1995). Among the individual risk factors of cardiovascular diseases, total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglyceride are blood test categories that are commonly used to evaluate hyperlipidemia (Chambless *et al.*, 1997). In modern days, many people take advantage of health check-ups for early detection and treatment of diseases. Moreover, South Korea has been providing free health check-ups, including general health check-up, cancer screening, and health check-up for infants based on the Framework Act on Health Examination that was established on March 21st, 2008, to the public after establishing the National Health Insurance Law on December 31st, 1997 (Sung, 2014). Based on this setting, this study aimed to investigate the relationship between the various blood test items that are generally included in the national health check-up category and CIMT by ultrasonography, which is not included in the basic health check-up category.

Materials and Methods

1. Subjects

A total of 47 healthy adults in the age of 30~55 were investigated through carotid ultrasonography and clinical laboratory blood test at a large comprehensive health examination center located in the southern part of Gyeonggi-do in 2014. Subjects were grouped into the category of 30's for age 30~40, 40's for 41~50, and 50's for 51~55.

2. Anthropometric data and blood test

An automatic anthropometric instrument that measures the height and weight at the same time was used. Body Mass Index (BMI) was calculated using the SPSS statistical package by dividing weight by height squared and was treated as a variable. Blood test was performed by collecting venous blood samples after fasting for more than 8 hours, and Aspartate aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline phosphatase (ALP), Gamma(γ)-glutamyl transpeptidase (GGT), Total bilirubin (T-Bil), Uric acid, Total Cholesterol (TC), High density lipoprotein cholesterol (HDL), Low density lipoprotein cholesterol (LDL), Triglyceride (TG),

Lactate dehydrogenase (LDH), Creatine Phosphokinase (CPK), and carcinoembryonic antigen (CEA) were tested. Blood test were measured using Hitachi 7180 (Hitachi, Japan).

3. Carotid ultrasonography test

CIMT was measured using Accuvix V20 (Medison, South Korea) on 3 parts: the common carotid, the carotid bulb (Bulb), and the area in between the two. Study subjects were facing the left side and laid down comfortably to set the probe around the central part of the sternocleidomastoid, which is below the thyroid cartilage. The probe was manipulated vertically to show the cross section of the vein (internal jugular) and artery (common carotid) on the screen of Accuvix V20 and horizontally for the longitudinal side of the vein and artery. The angle of the probe was slightly inclined towards the back of the neck to check the absence of the vein and presence of the common carotid artery and the oral region on the screen. A dot was marked on the starting point of the dark area of the intima-media and end point of the bright area and CIMT was measured in mm.

4. Statistical analysis

Statistical analysis was performed using the SPSS, PC, Version 21.0 (SPSS Inc., Chicago, IL, USA) program. A frequency analysis and mean (M) and standard deviation (SD) were calculated for the physical features, blood test results, and CIMT of the subjects. An independent t-test was performed for homogeneity test, and ANOVA test for the difference, Post-test was used for Dunnett 3 ways and a correlation analysis was performed for relational analysis. All statistical significance level was set as $p < 0.05$.

Results

1. General characteristics of subjects

The total number of subjects who participated in this study is 67 with 35 males and 32 females. The average age of the subjects was 45.64 ± 5.05, showing a difference ($p < 0.01$) between 47.00 ± 4.70 for male and 44.16 ± 5.98 for female. There was a difference ($p < 0.01$) in weight with 73.72 ± 8.55 kg for males and 56.38 ± 8.19 kg for females. The average BMI

for males was 24.97±2.30 and 24.17±12.05 for females, showing no significant difference between the male and female group. The average systolic blood pressure was 120.34±13.96 mmHg in males and 108.47±12.51 mmHg in females, showing a statistically significant difference ($p<0.01$) between the groups. The average diastolic blood was 81.43±9.61 mmHg in males and 70.97±10.31 mmHg in females, displaying a significant difference ($p<0.01$). The general characteristics of the subjects are described on Table 1.

2. Clinical laboratory test results by gender

Clinical laboratory test result by gender showed a significant difference ($p<0.01$) between 31.57±14.18 IU in the male group and 19.72±5.68 IU in the female group, with the male group displaying a higher average value. The average ALT was higher in the male group, showing a significant difference ($p<0.01$) between 32.89±18.00 IU in males and 15.34±7.23 in females. The average GGT was higher in the male group, showing a significant difference ($p<0.01$) between 74.89±62.05 IU in males and 17.16±10.74 IU in females. ALP was higher in the male group, showing a significant difference ($p<0.01$) between 59.63±17.94 IU in males and 49.56±10.38 IU in females. Total bilirubin was higher in the male group, showing a significant difference ($p<0.01$) between 1.48±1.17 mg/dL in males and 0.87±0.27 mg/dL in females. Uric acid was higher in the male group ($p<0.01$) with 6.23±1.22 mg/dL in males and 4.06±0.95 mg/dL in females. Total cholesterol was higher in the male group,

Table 1. General characteristics of subjects

Character	Total N=67	Male N=35	Female N=32	F/t
	M±SD			
Age	45.64±5.50	47.00±4.70	44.16±5.98	1.08/2.17*
Height (cm)	165.86±8.66	172.09±5.81	159.03±5.52	1.74/.19[†]
Weight (kg)	65.44±12.05	73.72±8.55	56.38±8.19	.76/8.45[†]
BMI (kg/m^2)	24.59±8.43	24.97±2.30	24.17±12.05	2.79/.38
SBP (mmHg)	114.67±14.48	120.34±13.96	108.47±12.51	.11/3.65[†]
DBP (mmHg)	76.43±11.19	81.43±9.61	70.97±10.31	.57/4.29[†]

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.
*$p<0.05$, [†]$p<0.01$.

Table 2. Results of blood test by gender

Variable	Total N=67	Male N=35	Female N=32	F/t
	M±SD			
AST (IU/L)	25.91±12.42	31.57±14.18	19.72±5.68	18.66/4.41[†]
ALT (IU/L)	24.51±16.41	32.89±18.00	15.34±7.23	11.94/5.14[†]
ALP (U/L)	54.82±15.55	59.63±17.94	49.56±10.38	4.74/2.78[†]
GGT (U/L)	47.31±53.68	74.89±62.05	17.16±10.74	31.21/5.18[†]
T.Bil (mg/dL)	1.19±0.91	1.48±1.17	0.87±0.27	5.79/2.83[†]
Uric acid (mg/dL)	5.19±1.54	6.23±1.22	4.06±0.95	1.77/8.15[†]
T.Cho (mg/dL)	196.07±31.26	203.46±31.91	188.00±28.89	0.28/2.07*
HDL-Cho (mg/dL)	51.16±11.83	46.66±12.11	56.09±9.43	3.68/-3.53[†]
LDL-Cho (mg/dL)	122.49±34.54	126.66±41.28	117.94±25.10	10.59/1.03
TG (mg/dL)	153.64±136.62	212.83±165.08	88.91±39.64	25.81/4.14[†]
LDH (IU/L)	383.57±78.71	415.77±90.35	348.34±42.26	12.98/3.85[†]
CPK (IU/L)	200.97±570.21	327.12±784.70	70.88±34.99	8.38/1.85
CEA (ng/mL)	1.18±0.41	1.30±0.53	1.04±0.13	40.35/2.77[†]

Abbreviation: AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma(γ)-glutamyl transpeptidase; T-Bil, total bilirubin; T.Cho, total cholesterol; HDL-Cho, high density lipoprotein cholesterol; LDL-Cho, low density lipoprotein cholesterol; TG, triglyceride; LDH, lactate dehydrogenase; CPK, creatine phosphokinase; CEA, carcinoembryonic antigen.
*$p<0.05$, [†]$p<0.01$.

showing a significant difference ($p<0.05$) between 203.46± 31.91 mg/dL in males and 188.00±28.89 mg/dL in females. On the contrary, males and females showed a statistically significant difference ($p<0.01$) in HDL cholesterol where females showed higher level of HDL cholesterol with an average of 56.09±9.43 mg/dL than males with an average of 46.66±12.11 mg/dL . The male and female group showed a statistically significant difference ($p<0.01$) in triglyceride level, with an average of 212.83±165.08 mg/dL in males and 88.91±39.64 mg/dL in females. Males and females showed a statistically significant difference ($p<0.01$) in LDH where males showed higher level of LDH with an average of 415.77±90.35 mg/dL than females with an average of 348.34± 42.26 mg/dL. CEA was higher in males with an average CEA of 1.30±0.53 ng/dL in males and 1.04±0.13 ng/dL in females, showing a statistically significant difference between males and females ($p<0.01$). On the other hand, there was a statistically significant difference in TSH level ($p<0.01$) and CA19-9 ($p<0.05$), where females showed higher level of TSH with an average of 2.75±1.35 than males with an average of 1.92±1.04, and higher level of CA19-9 with an average of 7.38±4.81 than males with an average of 4.86±3.47. There was no statistically significant difference in LDL cholesterol and CPK. The clinical laboratory results of the subjects are displayed in Table 2.

Table 3. Results of CIMT by gender

Variable	Total N=67	Male N=35	Female N=32	F/t
	M±SD			
CIMT (mm)	0.51±0.06	0.53±0.54	0.47±0.65	0.73/4.07[†]

Abbreviation: CIMT, carotid intima media thickness.
*$p<0.05$, [†]$p<0.01$.

3. CIMT test results by gender

The average total CIMT was 0.51±0.06 mm, and males and females showed a statistically significant difference ($p<0.01$), where males showed an average of 0.06 mm thicker CIMT than females with an average of 0.53±0.54 mm in males and 0.47±0.65 mm in females. The CIMT test results by the gender of the subjects are displayed in Table 3.

4. CIMT test results by age

According to the CIMT test results by age, the 30's group showed an average of 0.47±0.05 mm, 40's an average of 0.50± 0.06 mm, and 50's an average of 0.54±0.06 mm. The analysis of variance *F-value* appeared as 3.86, showing difference in variation. The 40's group showed a tendency of higher CIMT test result than the 30's group, but there was no significant difference between the groups. The 50's group showed a tendency of higher CIMT test result than the 40's group, but there was also no significant difference between the groups. The 50's showed an average of 0.07 mm higher value than that of 30's group, and displayed a statistically significant difference ($p<0.05$) in CIMT test results between the groups. The CIMT test results by the age of the subjects are displayed in Table 4.

5. Correlation between carotid artery ultrasonography, clinical laboratory test results, and general characteristics

According to an analysis of the correlation between the results from the carotid artery ultrasonography, each variable of the general characteristics of the subjects, and results from the blood test, the results of carotid artery ultrasonography and CIMT showed a positive correlation with general charac-teristics, where age group showed a positive relationship (*p*

Table 4. Results of Carotid Artery Ultrasonography by age

Variable	30s group[a] N=8	40s group[b] N=42	50s group[c] N=17	F/p	Dunnett T3
	M±SD				
CIMT (mm)	0.47±0.05	0.50±0.06	0.54±0.06	3.86/0.02	a<c*

Abbreviations are the same as those in Table 3.
*$p<0.05$.

Table 5. Correlation of carotid artery ultrasonography, blood test and general characteristics

	CIMT	Age	Height	Weight	SBP	ALT	GGT	Uric acid	CEA
CIMT (mm)	1	.400†	.456†	.400†	.270*	.259*	.278*	.285*	.286*
Age		1	−.022	.098	.217	.251*	.296*	.282*	−.067
Height (cm)			1	.799†	.322†	.247†	.361†	.513†	.398
Weight (kg)				1	.348†	.397†	.409†	.601†	.240
SBP (mmHg)					1	.323†	.455†	.316†	.344†
ALT (IU)						1	.518†	.517†	.155
GGT (IU)							1	.252*	.283*
Uric acid (mg/dL)								1	.289*
CEA (mg/dL)									1

Abbreviations are the same as those in Table 1, 2, 3.
*$p<0.05$, †$p<0.01$.

<0.01). For physical characteristics, height and weight both showed a positive relationship ($p<0.01$), and systolic blood pressure also displayed a positive relationship ($p<0.05$). ALT, GGT, Uric acid, and CEA all showed a positive correlation ($p<0.05$) with the clinical laboratory blood test. The correlation between results of the carotid artery ultrasonography and each variable is displayed in Table 5.

Discussion

The purpose of this study was to investigate the correlation between CIMT by the carotid artery ultrasonography and clinical laboratory test, which is part of the blood test item in a physical examination category that is generally being conducted. The clinical laboratory blood test and CIMT test results analyzed in this study was conducted at a large comprehensive health examination center located in Gyeonggi-do. The subjects of this study were 67 healthy adults in the age of 30~55, with 35 males and 32 females. The age distribution of the subjects was 8 in the 30's group, 42 in the 40's group, and 17 in the 50's group, with the 40's group displaying the highest distribution. Average BMI of the subjects was 24.97± 2.30 in males and 24.17±12.05 in females, showing no difference between the male and female group. There was a statistically significant difference ($p<0.01$) in systolic blood pressure with an average of 120.34±13.96 mmHg in males and 108.47±12.51 mmHg in females. The average diastolic blood pressure in males was 81.43±9.61 mmHg and 70.97±10.31 mmHg in females, showing a significant difference ($p<0.01$) in diastolic blood pressure level. Hyper-

tension is a risk factor of cardiovascular disease (O Donnell CJ et al., 1997) and blood pressure is associated with CIMT (Pall et al., 2003). In this study, systolic blood pressure showed a positive relationship with CIMT ($p<0.01$), as well as with age ($p<0.01$). These results are shown in the results that the thickness of the carotid artery increases with age is increased CIMT (Veller et al., 1993). These results correlate with results from previous studies that reported an association of age and systolic pressure with CIMT (Urbina et al., 2002). This may be due to the small number of subjects investigated in this study (Park et al., 2005). However, different from the results of previous studies that reported CIMT measured by a carotid artery ultrasonography as an independent indicator for predicting risk factors of atherosclerosis, cardiovascular disease, and myocardial infarction, there was no significant correlation between CIMT and risk factors for cardiovascular disease, such as total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride level (Pearson, 2002). This may be due to the small number of subjects investigated in this study (Bae et al., 2005).

In conclusion, this study investigated the correlation between CIMT and clinical laboratory test results, in addition to the relationship between CIMT and blood pressure and cardiovascular risk factors that was previously studies. Results of this study showed that CIMT has a positive correlation with ALT ($p<0.05$), GGT ($p<0.05$), Uric acid ($p<0.05$), and CEA ($p<0.05$), and therefore further studies should be considered for continuous investigation.

요 약

경동맥 내중막 두께는 뇌혈관질환과 관상동맥질환을 정밀하게 측정하는 검사이다. 많은 선행논문에 따르면 경동맥 내중막 두께는 죽상동맥경화를 예측하고 심혈관질환의 위험인자와 연관성이 높으며, 심근경색이나 뇌졸중 발생 위험을 예측할 수 있는 독립인자로 연구되었다. 따라서 본 연구는 혈액검사 중 임상화학적 검사결과와의 상관관계 연구를 통해 경동맥 내중막 두께와 다른 독립인자를 확보하는 것이 목적이었다. 연구결과 피험자의 부족으로 인해 심혈관계관련 임상화학적 요인과는 상관관계를 입증하지 못했으나, 경동맥 내중막 두께와 ALT ($p<0.05$), GGT ($p<0.05$), Uric acid ($p<0.05$), CEA ($p<0.05$)와 양의 상관관계를 통계적인 유의수준으로 입증하여 지속적인 연구의 문제를 제기하였다.

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