



저작자표시-비영리-변경금지 2.0 대한민국

이용자는 아래의 조건을 따르는 경우에 한하여 자유롭게

- 이 저작물을 복제, 배포, 전송, 전시, 공연 및 방송할 수 있습니다.

다음과 같은 조건을 따라야 합니다:



저작자표시. 귀하는 원저작자를 표시하여야 합니다.



비영리. 귀하는 이 저작물을 영리 목적으로 이용할 수 없습니다.



변경금지. 귀하는 이 저작물을 개작, 변형 또는 가공할 수 없습니다.

- 귀하는, 이 저작물의 재이용이나 배포의 경우, 이 저작물에 적용된 이용허락조건을 명확하게 나타내어야 합니다.
- 저작권자로부터 별도의 허가를 받으면 이러한 조건들은 적용되지 않습니다.

저작권법에 따른 이용자의 권리는 위의 내용에 의하여 영향을 받지 않습니다.

이것은 [이용허락규약\(Legal Code\)](#)을 이해하기 쉽게 요약한 것입니다.

[Disclaimer](#)

Association between triglyceride glucose index and arterial stiffness in Korean adults

Sang Bae Lee

Department of Medicine
The Graduate School, Yonsei University

Association between triglyceride glucose index and arterial stiffness in Korean adults

Directed by Professor Jong Suk Park

The Master's Thesis
submitted to the Department of Medicine
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

Sang Bae Lee

December 2017

This certifies that the Master's Thesis of
Sang Bae Lee is approved.

Thesis Supervisor : Chul Woo Ahn

Thesis Committee Member#1 : Jong Suk Park

Thesis Committee Member#2 : Byoung Kwon Lee

The Graduate School
Yonsei University

December 2017

ACKNOWLEDGEMENTS

I wish to express my deep sense of gratitude to professor Jong Suk Park for encouraging and inspiring me at all the stages of this work and providing all the necessary help and guiding me to complete this study.

I am also very grateful to professor Chul Woo Ahn and professor Byoung Kwon Lee for their valuable guidance, keen interest and encouragement at various stages of this work.

I'm also appreciate to all of the department of endocrinology in Gangnam Severance Hospital and my family, without whom this thesis would not have been possible at all.

Sang Bae Lee

<TABLE OF CONTENTS>

ABSTRACT	1
I. INTRODUCTION	3
II. MATERIALS AND METHODS	4
1. Study population	
2. Clinical characteristics	
3. Biochemical parameters	
4. Pulse wave velocity	
5. Statistical analysis	
III. RESULTS	8
1. Baseline characteristics	
2. Relationship between baPWV and TyG index quartile	
3. Correlations between baPWV and clinical variables	
4. Regression analysis for high baPWV and TyG index with other variables	
IV. DISCUSSION	18
V. CONCLUSION	22
REFERENCES	23
ABSTRACT(IN KOREAN).....	27

LIST OF FIGURES

Figure 1. Age adjusted value of baPWV for overall population(A), male(B), and female(C).	14
--	----

LIST OF TABLES

Table 1. Clinical characteristics of overall population according to the TyG index	10
Table 2. Clinical characteristics of male population according to the TyG index	11
Table 3. Clinical characteristics of female population according to the TyG index	12
Table 4. Age adjusted value of baPWV for overall, male and female population	13
Table 5. Correlations between baPWV and clinical variables .	16
Table 6. Odds ratios and 95% confidence intervals for high baPWV according to TyG index quartiles.	18

ABSTRACT

Association between triglyceride glucose index and arterial stiffness in Korean adults

Sang Bae Lee

*Department of Medicine
The Graduate School, Yonsei University*

(Directed by Professor Jong Suk Park)

Objective; Insulin resistance is well known risk factor of cardiovascular disease. Recently, triglyceride glucose (TyG) index is considered a simple surrogate marker of insulin resistance. However, few studies have investigated the relationship between TyG index and arterial stiffness, thus we investigated the association between TyG index and arterial stiffness in Korean Adults.

Methods; A total of 4,549 participants underwent arterial plethysmography in health promotion center were enrolled. Anthropometric profiles and multiple cardiovascular risk factors were measured. TyG index was calculates as $\ln[\text{fasting triglycerides}(\text{mg/dl}) \times \text{fasting glucose}(\text{mg/dl}) / 2]$. Automatic plethysmographic instrument was used to measure brachial-ankle pulse wave

velocity(baPWV) as a marker of arterial stiffness.

Results; All subjects were stratified into four groups according to TyG index. There were significant differences in cardiovascular parameters among the groups and the mean value of baPWV was significantly increased with TyG index levels. In the logistic regression analysis after adjustment for multiple risk factors, as compared with the lowest quartile, the odds ratios (95% CI) for the presence of high mean baPWV(defined as >75th percentile) were 1.0, 1.55(1.19-2.01), 1.93(1.47-2.54), 3.19(2.28-4.48) for increasing TyG index level (P<0.05).

Conclusion; There was a significant association between TyG index and mean baPWV as a marker of arterial stiffness. TyG index, a simple measure reflecting insulin resistance, might be useful to the indicator of arterial stiffness. TyG index is even simple to calculate and seems a useful marker of arterial stiffness, and reflect cardiovascular risk.

Key words : triglyceride glucose index, arterial stiffness ,brachial-ankle pulse wave velocity, insulin resistance

Association between triglyceride glucose index and arterial stiffness in
Korean adults

Sang Bae Lee

*Department of Medicine
The Graduate School, Yonsei University*

(Directed by Professor Jong Suk Park)

I. INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of mortality and morbidity worldwide ¹. Brachial-ankle pulse wave velocity (baPWV) is a simple and non-invasive method widely used to assess arterial stiffness, which is strongly associated with cardiovascular diseases, and recent studies have found it to be an independent predictor of not only cardiovascular events, but also cardiovascular mortality ².

Insulin resistance (IR) is one of major risk factor for CVD ³. IR is defined as the inability of insulin to increase cellular glucose uptake and utilization, leading to hyperinsulinemia ⁴. IR and hyperinsulinemia has been associated with hypertension and dyslipidemia, all of which predispose to atherosclerosis and CVD ⁵.

Recently, triglyceride glucose index (TyG index) can be easily calculated with serum triglyceride and fasting plasma glucose level, Some studies have shown

that the TyG index is correlated with IR, as assessed using the hyperinsulinemic euglycemic clamp test and HOMA-IR, and it has been suggested for novel method for measuring IR⁶⁻⁸.

Few studies have examined the relationship between TyG index and CVD, and their results have been inconsistent⁹⁻¹¹. In addition, to date, only three studies have examined the relationship between the TyG index and subclinical atherosclerosis^{9,12,13}. Furthermore, to our knowledge, only one study has examined the relationship between TyG index and arterial stiffness in a small number of women¹⁴.

Therefore, we investigated the relationship between TyG index and arterial stiffness in a large population in Korean adults.

II. MATERIALS AND METHODS

1. Study population

This study population consisted of 5989 Korean subjects who participated in a comprehensive health examination, including cardiac computed tomography, as part of a self referred health checkup program at the Gangnam Severance Hospital Health Promotion Center from January 2008 to February 2015. We excluded subjects who had any malignancy, acute inflammatory disease, or infectious disease or renal disease. We also excluded subjects with a history of

angina, myocardial infarction or cerebrovascular accidents. In addition, subjects whose ankle-brachial index (ABI) was <0.90 were excluded to ensure the accuracy of baPWV measurements. Furthermore, subjects with a history of alcohol consumption in excess of ≥ 20 g/day in women and ≥ 30 g/day in men, were excluded. Subjects who had elevated triglyceride levels (>400 mg/dl) or had taken anti-anginal medication or medications lowering primarily triglycerides (fenofibrate, omega-3) were also excluded. After these exclusions, 4549 subjects were ultimately enrolled in our final analysis. The study protocol was approved by the Institutional Review Board of Yonsei University College of Medicine.

2. Clinical characteristics

Height and weight were measured, and body mass index (BMI) was calculated by dividing the weight (kg) by the square of the height (m^2). Lifestyle, personal medical history of acute and chronic illnesses, and medication history were assessed with a standard questionnaire. Systolic and diastolic blood pressures (SBP, DBP) were measured by an experienced technician by placing the arm at heart level after a five-minute rest period. Diabetes mellitus was defined as fasting plasma glucose ≥ 126 mg/dL or glycated hemoglobin $\geq 6.5\%$ (following American Diabetes Association criteria) or using of hypoglycemic medications. Hypertension was defined as systolic and/or diastolic blood pressures \geq

140/90mmHg or using of anti-hypertensive medications. Current smokers were defined as those who reported having smoked cigarettes regularly over the previous 6 months.

3. Biochemical parameters

Blood samples were taken from all subjects after 8 hours of fasting. Samples were immediately centrifuged, and serum samples were stored at -70°C until analysis. Fasting plasma glucose (FPG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) were determined using enzymatic methods with a Hitachi 7600-120 automated chemistry analyzer (Hitachi, Tokyo, Japan). Low-density lipoprotein cholesterol (LDL-C) was calculated according to the Friedewald formula. TyG index was calculated as $\ln[\text{fasting triglycerides (mg/dl)} \times \text{fasting glucose (mg/dl)} / 2]^6$. Fasting serum insulin was determined by means of chemiluminescence (RIA kit, Daiichi, Japan), and insulin resistance was estimated using the homeostasis model assessment of insulin resistance (HOMA-IR) index calculated from the following formula: $\text{HOMA-IR} = \text{fasting insulin } (\mu\text{U/mL}) \times \text{fasting plasma glucose (mmol/L)} / 22.5$.

4. Pulse wave velocity

Arterial stiffness was measured using an automatic plethysmographic

instrument (VP-1000; Colin, Komaki, Japan) as previously described¹⁵. Electrodes were placed on both wrists, and cuffs were wrapped around both the upper arms and the ankles. After simultaneous measurement of blood pressure and waveforms in all four limbs, the time interval between the brachial and ankle waveforms (ΔT_{ba}) was determined. The distance between the brachium and the ankle ($L_a - L_b$) was estimated automatically according to the subject's height. After these data were collected, baPWV was calculated using the following equation: $baPWV = (L_a - L_b) / \Delta T_{ba}$ (in cm/s). Both baPWV values were measured after allowing the patient to rest in the supine position for at least 5 minutes. We used the mean of the right and left baPWV as a marker of arterial stiffness.

5. Statistical analysis

Continuous variables with normal distributions are expressed as means + SD, whereas continuous variables with skewed distributions are presented as median (interquartile range) and were log transformed for analysis. The intergroup comparisons were performed using ANOVA tests. Chi-square tests were used to compare categorical variables with percentages. Age-adjusted baPWV means and standard errors were calculated using analysis of covariance (ANCOVA) according to TyG quartiles. The relationships between baPWV and various clinical parameters were examined using Pearson's correlation. The odds ratios

(OR) and corresponding 95% confidence intervals (CI) for high PWVs were estimated using a multivariate logistic regression analysis after adjusting for confounding variables across TyG index quartiles. Because an absolute cut-off value of normal baPWV was not available, high baPWV was arbitrarily defined as a value greater than the cut-off level between third and fourth quartiles (>75th percentile), which was 1483.0 cm/s for all subjects, 1495.5 cm/s for men and 1464.0 cm/s for women. Statistical analysis was carried out using SPSS for Windows 23.0 (SPSS Inc., Chicago, IL, USA). P values less than 0.05 were considered statistically significant.

III. RESULTS

1. Baseline characteristics

Table 1 showed the clinical and laboratory characteristics of total study population. The study population was divided into four groups according to TyG index levels. There were significant differences among the groups in terms of many metabolic parameters. SBP, DBP, BMI, FPG, TC, TG, LDL-C, HOMA-IR were gradually increased, and HDL-C was gradually decreased with elevation of TyG index. As TyG index increased, prevalence of Diabetes mellitus(DM) and hypertension, and rate of smoking were increased.

The results of the analysis by dividing total population into male (Table 2) and

female (Table 3) showed similar patterns. There were significant difference in SBP, DBP, BMI, FPG, TC, TG, LDL-C, HOMA-IR, HDL-C, prevalence of DM and hypertension, rate of smoking according to TyG index both in male and female.

Table 1. Clinical characteristics of overall population according to the TyG index

	Q1 (lowest)	Q2	Q3	Q4 (highest)	P value
N	1143	1132	1137	1137	
Age (years)	50.94±9.94	53.63±9.17	53.88±8.93	52.48±8.71	<0.01
Sex (M/F)	403/740	619/513	781/356	930/207	<0.01
SBP (mmHg)	118.85±15.89	123.55±16.67	128.10±16.06	129.45±16.17	<0.01
DBP (mmHg)	73.70±9.93	76.90±10.11	79.99±9.61	81.16±9.89	<0.01
BMI (kg/m ²)	22.17±2.86	23.43±3.08	24.32±2.94	25.38±2.81	<0.01
FPG (mg/dL)	86.49±9.36	93.20±9.88	97.61±12.56	103.42±19.05	<0.01
TC (mg/dL)	184.19±32.90	192.82±33.51	194.78±34.37	202.22±35.02	<0.01
TG (mg/dL)	56 (49-63)	83 (75-91)	114 (103-128)	188(158-232)	<0.01
LDL-C (mg/dL)	110.78±29.59	122.23±30.13	124.05±31.10	123.58±32.17	<0.01
HDL-C (mg/dL)	58.16±13.03	51.77±11.69	47.19±10.53	42.18±8.73	<0.01
TyG index	7.77±0.21	8.25±0.11	8.62±0.11	9.20±0.28	<0.01
HOMA-IR	0.63 (0.43-0.97)	0.94 (0.66-1.36)	1.07 (0.77-1.56)	1.46 (0.95-2.04)	<0.01
Smoking (%)	48 (4.2)	65 (5.7)	97 (8.5)	146 (12.8)	<0.01
Diabetes (%)	2 (0.2)	3 (0.3)	27 (2.4)	94 (8.3)	<0.01
Hypertension (%)	145 (12.7)	214 (18.9)	286 (25.2)	326 (28.7)	<0.01

Data are mean± SD, number (percentage), or median (interquartile range). SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance

Table 2. Clinical characteristics of male population according to the TyG index

	Q1 (lowest)	Q2	Q3	Q4 (highest)	P value
N	684	685	684	685	
Age (years)	53.51±10.58	53.99±8.99	52.57±9.24	51.25±8.03	<0.01
SBP (mmHg)	125.37±15.27	127.31±15.29	128.64±15.05	129.75±15.36	<0.01
DBP (mmHg)	78.34±9.43	80.07±9.36	81.13±9.39	81.85±9.63	<0.01
BMI (kg/m ²)	23.68±2.69	24.49±2.96	25.03±2.63	25.77±2.83	<0.01
FPG (mg/dL)	90.35±10.51	96.25±10.21	99.29±13.52	105.20±19.82	<0.01
TC (mg/dL)	180.78±32.19	187.31±33.00	193.56±33.97	202.22±35.56	<0.01
TG (mg/dL)	64 (55-75)	96 (88-107)	136(120-150)	211 (180-255)	<0.01
LDL-C (mg/dL)	112.97±29.62	121.03±30.36	123.96±31.19	121.87±32.53	<0.01
HDL-C (mg/dL)	51.75±11.47	46.31±9.88	43.76±9.17	41.39±8.57	<0.01
TyG index	7.94±0.23	8.43±0.10	8.79±0.11	9.31±0.25	<0.01
HOMA-IR	0.96±0.69	1.27±0.98	1.44±1.35	1.76±1.14	<0.01
Smoking (%)	48 (7.0)	65 (9.5)	98 (14.3)	146 (21.3)	<0.01
Diabetes (%)	2 (0.3)	3 (0.4)	25 (3.7)	66 (9.6)	<0.01
Hypertension (%)	124 (18.1)	173 (25.3)	176 (25.7)	193 (28.2)	<0.01

Data are mean± SD, number (percentage), or median (interquartile range). SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance

Table 3. Clinical characteristics of female population according to the TyG index

	Q1 (lowest)	Q2	Q3	Q4 (highest)	P value
N	456	454	455	455	
Age (years)	48.38±8.97	51.93±8.97	54.46±8.79	55.66±8.57	<0.01
SBP (mmHg)	114.52±14.87	117.84±16.66	122.26±17.55	128.48±18.94	<0.01
DBP (mmHg)	70.79±9.63	72.91±9.94	74.93±9.97	78.52±10.20	<0.01
BMI (kg/m ²)	21.11±2.52	22.08±2.80	22.61±2.96	23.93±3.15	<0.01
FPG (mg/dL)	83.26±8.69	89.45±8.16	93.10±10.39	99.23±217.54	<0.01
TC (mg/dL)	183.66±30.59	195.93±33.00	202.61±34.52	206.34±34.30	<0.01
TG (mg/dL)	50 (44-55)	69 (63-74)	91 (83-100)	138 (117-174)	<0.01
LDL-C (mg/dL)	106.65±27.22	120.14±30.37	127.24±31.01	127.33±31.95	<0.01
HDL-C (mg/dL)	62.55±12.64	58.57±12.57	54.47±11.30	48.06±10.40	<0.01
TyG index	7.62±0.18	8.02±0.10	8.34±0.10	8.88±0.30	<0.01
HOMA-IR	0.60±0.35	0.93±0.75	1.12±0.94	1.47±0.92	<0.01
Menopause (%)	208 (45.6)	290 (63.9)	319 (70.1)	337 (74.1)	<0.01
Diabetes (%)	0 (0)	0 (0)	3 (0.7)	29 (6.4)	<0.01
Hypertension (%)	21 (4.6)	41 (9.0)	111 (24.4)	132 (29.0)	<0.01

Data are mean±SD, number (percentage), or median (interquartile range). SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance

2. Relationship between baPWV and TyG index quartile

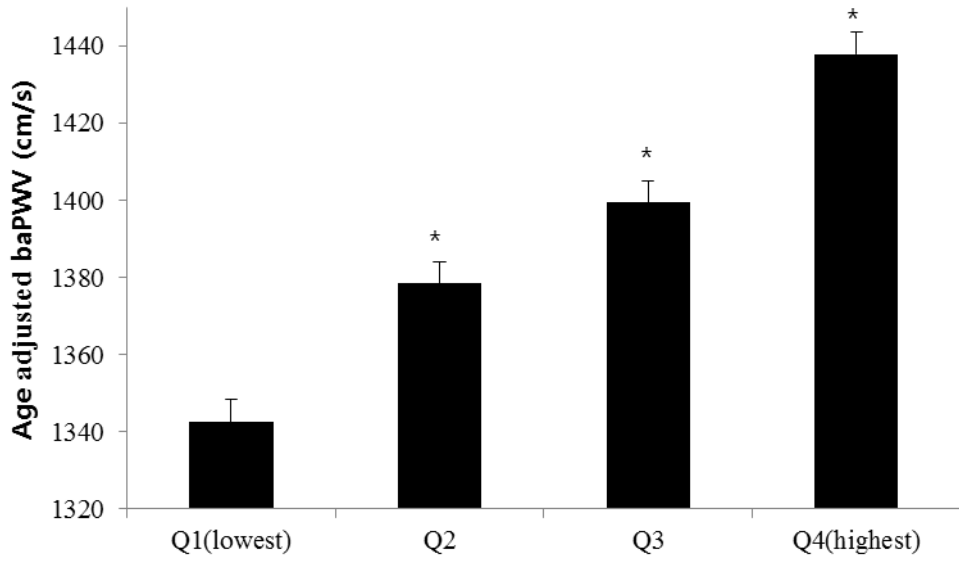
Table 4 and figure 1 to 3 showed the mean value and standard errors of age-adjusted baPWV which were calculated using analysis of covariance (ANCOVA) according to TyG quartiles. Age adjusted baPWV showed gradual increase as increase of TyG index, and showed significant difference between groups of quartiles of TyG index. These results were consistent in total population and also in male and female subgroups. It means that as TyG index increased, value of baPWV also increased regardless of age.

Table 4. Age adjusted value of baPWV for overall, male and female population

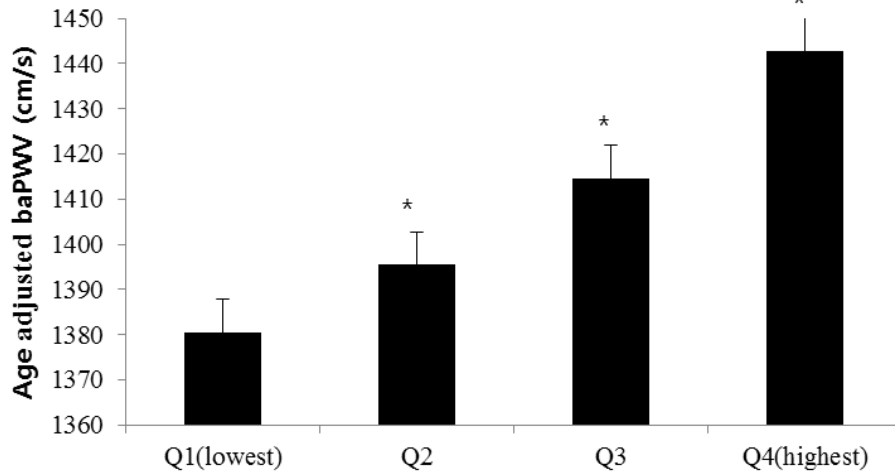
	Q1 (lowest)	Q2	Q3	Q4 (highest)	P value
overall	1342.79±5.71	1378.61±5.73	1399.70±5.72	1437.87±5.71	<0.01
male	1380.50±7.20	1395.46±7.21	1414.58±7.20	1443.22±7.21	<0.01
female	1324.64±9.55	1343.61±9.31	1373.68±9.34	1403.97±9.46	<0.01

Data are mean±SE

A. Overall



B. Male



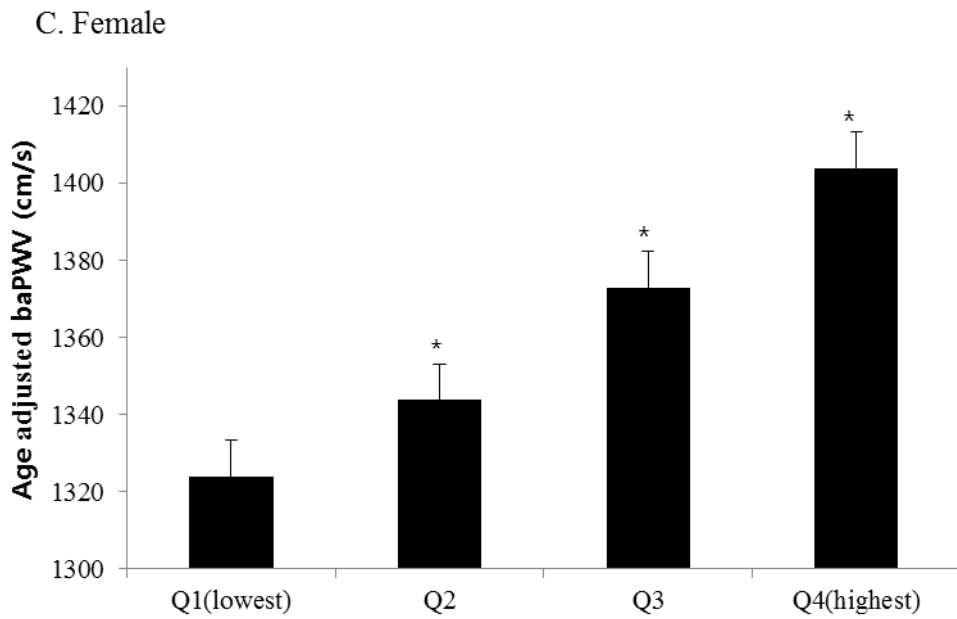


Figure 1. Age adjusted value of baPWV for overall population(A), male(B), and female(C). (* P<0.01 vs Q1)

3. Correlations between baPWV and clinical variables

Correlations between baPWV and clinical variables were examined using Pearson's correlation analysis (Table 5). TG and HOMA-IR were log-transformed because of non-normal distribution. The result showed that baPWV had significant positive correlation with TyG index. SBP, DBP, FPG, log-transformed TG, log-transformed HOMA-IR showed positive correlation with baPWV whereas HDL-C showed negative correlation.

Table 5. Correlations between baPWV and clinical variables

	<i>r</i>	<i>P</i> value
Age	0.525	<0.01
SBP	0.466	<0.01
DBP	0.415	<0.01
BMI	0.082	<0.01
FPG	0.223	<0.01
TC	0.041	<0.01
TG	0.139	<0.01
LDL-C	0.051	<0.01
HDL-C	-0.095	<0.01
TyG index	0.183	<0.01
HOMA-IR	0.240	<0.01

TG and HOMA-IR were log-transformed because of non-normal distribution.

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass

index; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance

4. Regression analysis for high baPWV and TyG index with other variables

Multivariate logistic regression analysis was done to explore further correlation between baPWV and TyG index (Table 6). In this analysis, TyG index was categorized into quartiles and high baPWV was defined as a cut-off value between third and fourth quartiles (>75th percentile).

An unadjusted multivariate logistic regression analysis, compared with first quartile (group Q1, set as reference), TyG index group Q2, Q3, Q4 showed higher OR for presence of high baPWV in total population (Model 1). In univariate analysis adjusted for age, these correlation was significant (Model 2). In multivariate analysis adjusted for age and sex, these correlation was also significant (Model 3). These correlations still remain significant after adjusting for confounding variables, including age, sex, SBP, DBP, BMI, TC, LDL-C, HDL-C, prevalence of DM and hypertension, smoking status in all subjects and menopause in female population. (P for trend <0.01) (Model 4).

Table 6. Odds ratios and 95% confidence intervals for high baPWV according to TyG index quartiles.

	OR (95% CI)				<i>P</i> for trend
	Q1 (lowest)	Q2	Q3	Q4 (highest)	
Unadjusted (Model 1)	1.00	1.73 (1.40-2.13)	2.14 (1.75-2.63)	2.41 (1.97-2.95)	<0.01
Age adjusted (Model 2)	1.00	1.45 (1.15-1.83)	1.87 (1.49-2.36)	2.66 (2.12-3.35)	<0.01
Age,sex adjusted (Model 3)	1.00	1.44 (1.14-1.82)	1.85 (1.47-2.34)	2.62 (2.06-3.32)	<0.01
Multivariable adjusted (Model 4)	1.00	1.55 (1.19-2.01)	1.93 (1.47-2.54)	3.19 (2.28-4.48)	<0.01

Multivariate models were adjusted for age, sex (in overall group), SBP, DBP, BMI, T-C, LDL-C, HDL-C, diabetes, hypertension, and menopause (in women)

IV.DISCUSSION

In this study, we demonstrated that there was a significant association between TyG index and mean baPWV as a marker of arterial stiffness. To our best knowledge, this is the first study that showed relationship between TyG index and arterial stiffness via baPWV in large populations.

According to many previous studies, IR has been recognized as a major risk factor of metabolic diseases including CVD^{3,16,17}. Because of the importance of IR, many methods have been studied and devised for measuring IR. Among these methods, hyperinsulinemic-euglycemic clamp is the gold standard method

for measuring IR¹⁸. However, hyperinsulinemic-euglycemic clamp method is invasive and expensive, so its clinical application is limited due to the ethical and economic reasons. For these reasons, HOMA-IR which is consisted with fasting glucose and insulin is widely used as a marker of IR. Recently, TyG index has been suggested for another surrogate marker of IR in several studies^{6,19,20}. TyG index has high sensitivity and specificity compared with the hyperinsulinemic-euglycemic clamp method⁶. Furthermore, a number of studies have proven that TyG index is more safe, inexpensive, and more accurate than hyperinsulinemic-euglycemic clamp or HOMA-IR method in evaluating of IR⁶⁻⁸. Our result of Pearson's correlation analysis between TyG index and log transformed HOMA IR showed significant correlation($r=0.478$, $P<0.01$, Data not shown). It also supports the fact that TyG index could be a surrogate marker of IR in healthy adults.

In many previous studies, degree of arterial stiffness has been found as an independent risk factor of CVD²¹. BaPWV is simple, safe, validated method to measure arterial stiffness and widely used in clinical settings¹⁵. BaPWV itself also have a strong association with incidence of CVD^{22,23}.

In this study, TyG index showed significant differences according to change in many metabolic parameters. Higher TyG index quartile showed higher SBP, DBP, BMI, FPG, TC, TG, LDL-C, HOMA-IR both in men and women. In many previous studies, these metabolic parameters were proven as risk factors of

CVD and had association with IR^{24,25}. Age, SBP, DBP and proportion of male were increased across quartiles of the TyG index. These result were similar to those of previous study¹⁰. In our study, mean ages decreased as the quartiles of TyG index increased in male, while mean ages increased in female as quartiles of TyG index increased. Younger males who participate in vigorous social activities are generally exposure to more alcohol consumption compared with female. TG levels are increased in females due to the effect of menopause²⁶, so older females showed higher TG than younger females.

We also demonstrated that TyG index showed significant correlation with baPWV. BaPWV is also known to have a close relationship with metabolic parameters such as age, sex, and blood pressure. Tomiyama et al. reported that age and blood pressure variables were potent significant variables for baPWV²⁷. Many studies have shown that IR cause inflammation, changing coagulation status and finally lead to atherosclerosis²⁸⁻³⁰. These change lead to increase of PWV. Our result was consistent with those of other studies. BaPWV showed significant association with age, SBP, DBP, FPG, HOMA-IR and TyG index. This result seems to reflect both physical effect of blood pressure and chemical effect of IR and inflammation in aspect of arterial stiffness. According to our result of Pearson's correlation analysis, log transformed C-reactive protein(CRP) showed significant correlation with TyG index.($r=0.196$, $P<0.01$, Data not shown). That means TyG index could reflect inflammatory status of

vasculature and aortic stiffness. TyG index and baPWV also showed significant association in logistic regression analysis. In logistic regression analysis, a higher quartiles of TyG index showed high ORs for high baPWV for overall study population.

There were few studies that evaluate association between TyG index and CVD, but results showed controversy. Vega et al. reported that TyG index does not predict CVD events¹¹, but according to study from Sanchez-Inigo et al., TyG index showed predictive value for assess development of CVD events¹⁰. In addition, there were only three studies had examined the association between TyG index and subclinical atherosclerosis. Irace et al. reported that TyG index had significant association with carotid artery atherosclerosis which was evaluated by Doppler ultrasonography of carotid artery¹³. Two studies from Lee et al. and Kim et al. showed association between TyG index and coronary artery calcification evaluated by cardiac computed tomography^{9,12}.

Some previous studies reported that HOMA-IR which represents insulin resistance had a relationship with PWV. Nakanishi et al. showed that age-adjusted mean values of baPWV were closely associated with HOMA-IR in Japanese population³¹. Webb et al, also reported that HOMA-IR was the powerful metabolic predictors of arterial stiffness and PWV³². Park et al also demonstrated that HOMA-IR was independently associated with baPWV in normoglycemic, normotensive postmenopausal women³³. Result of this study is

consistent with those previous studies and showed significant association between TyG index which is a surrogate marker of insulin resistance and baPWV in general population.

Our study had some limitations. First, this was a cross-sectional observation study. So we could not explain the causal relationship only by the result of this study. Second, all study population were Korean and enrolled at single institution, so there are some limitations for generalization of this result. Third, proportions of young adult and pre-menopausal women were relatively small, so there is a limitation to applying these result to all ages. Fourth, we could not obtain study population's histories of alcohol consumption and smoking in a quantitative manner. We also could not obtain nutritional data and exercise status of subjects. So we could not adjust these parameters, which can affect blood triglyceride and glucose levels.

V. CONCLUSION

We proved that there was a significant association between TyG index and mean baPWV as a marker of arterial stiffness. TyG index reflecting insulin resistance is a simple to calculate and seems a useful marker of arterial stiffness, and reflect cardiovascular risk.

REFERENCES

1. WHO. Cardiovascular diseases. 2016.
2. Sheng CS, Li Y, Li LH, Huang QF, Zeng WF, Kang YY, et al. Brachial-ankle pulse wave velocity as a predictor of mortality in elderly Chinese. *Hypertension* 2014;64:1124-30.
3. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E, et al. Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus. Prospective studies of Pima Indians. *N Engl J Med* 1993;329:1988-92.
4. Shanik MH, Xu Y, Skrha J, Dankner R, Zick Y, Roth J. Insulin resistance and hyperinsulinemia: is hyperinsulinemia the cart or the horse? *Diabetes Care* 2008;31 Suppl 2:S262-8.
5. Salonen JT, Lakka TA, Lakka HM, Valkonen VP, Everson SA, Kaplan GA. Hyperinsulinemia is associated with the incidence of hypertension and dyslipidemia in middle-aged men. *Diabetes* 1998;47:270-5.
6. Guerrero-Romero F, Simental-Mendia LE, Gonzalez-Ortiz M, Martinez-Abundis E, Ramos-Zavala MG, Hernandez-Gonzalez SO, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *J Clin Endocrinol Metab* 2010;95:3347-51.
7. Vasques AC, Novaes FS, de Oliveira Mda S, Souza JR, Yamana A, Pareja JC, et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. *Diabetes Res Clin Pract* 2011;93:e98-e100.
8. Mohd Nor NS, Lee S, Bacha F, Tfayli H, Arslanian S. Triglyceride glucose index as a surrogate measure of insulin sensitivity in obese adolescents with normoglycemia, prediabetes, and type 2 diabetes mellitus: comparison with the hyperinsulinemic-euglycemic clamp. *Pediatr Diabetes* 2016;17:458-65.
9. Lee EY, Yang HK, Lee J, Kang B, Yang Y, Lee SH, et al. Triglyceride glucose index, a marker of insulin resistance, is associated with coronary artery stenosis in asymptomatic subjects with type 2 diabetes. *Lipids Health Dis* 2016;15:155.
10. Sanchez-Inigo L, Navarro-Gonzalez D, Fernandez-Montero A, Pastrana-Delgado J, Martinez JA. The TyG index may predict the development of cardiovascular events. *Eur J Clin Invest* 2016;46:189-97.
11. Vega GL, Barlow CE, Grundy SM, Leonard D, DeFina LF. Triglyceride-to-high-density-lipoprotein-cholesterol ratio is an index of heart disease mortality and of incidence of type 2 diabetes

- s mellitus in men. *J Investig Med* 2014;62:345-9.
12. Kim MK, Ahn CW, Kang S, Nam JS, Kim KR, Park JS. Relation ship between the triglyceride glucose index and coronary arter y calcification in Korean adults. *Cardiovasc Diabetol* 2017;16:1 08.
 13. Irace C, Carallo C, Scavelli FB, De Franceschi MS, Esposito T, Tripolino C, et al. Markers of insulin resistance and carotid at herosclerosis. A comparison of the homeostasis model assessm ent and triglyceride glucose index. *Int J Clin Pract* 2013;67:66 5-72.
 14. Lambrinouadaki I, Kazani MV, Armeni E, Georgiopoulos G, Tam pakis K, Rizos D, et al. The TyG Index as a Marker of Subclin ical Atherosclerosis and Arterial Stiffness in Lean and Overwei ght Postmenopausal Women. *Heart Lung Circ* 2017; doi:10.101 6/j.hlc.2017.05.142.
 15. Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose K, et al. Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertens Res* 2002;25:359-64.
 16. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted s yndrome responsible for NIDDM, obesity, hypertension, dyslipi demia, and atherosclerotic cardiovascular disease. *Diabetes Car e* 1991;14:173-94.
 17. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Targher G, et al. Prevalence of insulin resistance in metabolic disor ders: the Bruneck Study. *Diabetes* 1998;47:1643-9.
 18. Elahi D. In praise of the hyperglycemic clamp. A method for a ssesment of beta-cell sensitivity and insulin resistance. *Diabe tes Care* 1996;19:278-86.
 19. Du T, Yuan G, Zhang M, Zhou X, Sun X, Yu X. Clinical usefuln ess of lipid ratios, visceral adiposity indicators, and the triglyc erides and glucose index as risk markers of insulin resistance. *Cardiovasc Diabetol* 2014;13:146.
 20. Er LK, Wu S, Chou HH, Hsu LA, Teng MS, Sun YC, et al. Tri glyceride Glucose-Body Mass Index Is a Simple and Clinically Useful Surrogate Marker for Insulin Resistance in Nondiabetic I ndividuals. *PLoS One* 2016;11:e0149731.
 21. Niiranen TJ, Kalesan B, Larson MG, Hamburg NM, Benjamin EJ, Mitchell GF, et al. Aortic-Brachial Arterial Stiffness Gradient and Cardiovascular Risk in the Community: The Framingham H eart Study. *Hypertension* 2017; doi:10.1161/hypertensionaha.11

- 6.08917.
22. Ohkuma T, Ninomiya T, Tomiyama H, Kario K, Hoshide S, Kita Y, et al. Brachial-Ankle Pulse Wave Velocity and the Risk Prediction of Cardiovascular Disease: An Individual Participant Data Meta-Analysis. *Hypertension* 2017;69:1045-52.
 23. Munakata M. Brachial-ankle pulse wave velocity in the measurement of arterial stiffness: recent evidence and clinical applications. *Curr Hypertens Rev* 2014;10:49-57.
 24. Di Angelantonio E, Sarwar N, Perry P, Kaptoge S, Ray KK, Thompson A, et al. Major lipids, apolipoproteins, and risk of vascular disease. *Jama* 2009;302:1993-2000.
 25. Dawber TR, Kannel WB, Lyell LP. An approach to longitudinal studies in a community: the Framingham Study. *Ann N Y Acad Sci* 1963;107:539-56.
 26. van Beek AP, de Ruijter-Heijstek FC, Erkelens DW, de Bruin TW. Menopause is associated with reduced protection from postprandial lipemia. *Arterioscler Thromb Vasc Biol* 1999;19:2737-41.
 27. Tomiyama H, Yamashina A, Arai T, Hirose K, Koji Y, Chikamori T, et al. Influences of age and gender on results of noninvasive brachial-ankle pulse wave velocity measurement--a survey of 12517 subjects. *Atherosclerosis* 2003;166:303-9.
 28. Trovati M, Anfossi G, Cavalot F, Massucco P, Mularoni E, Emanuelli G. Insulin directly reduces platelet sensitivity to aggregating agents. Studies in vitro and in vivo. *Diabetes* 1988;37:780-6.
 29. Kahn AM, Allen JC, Seidel CL, Zhang S. Insulin inhibits migration of vascular smooth muscle cells with inducible nitric oxide synthase. *Hypertension* 2000;35:303-6.
 30. DeFronzo RA. Banting Lecture. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes* 2009;58:773-95.
 31. Nakanishi N, Shiraishi T, Wada M. Brachial-ankle pulse wave velocity and metabolic syndrome in a Japanese population: the Minoh study. *Hypertens Res* 2005;28:125-31.
 32. Webb DR, Khunti K, Silverman R, Gray LJ, Srinivasan B, Lacy PS, et al. Impact of metabolic indices on central artery stiffness: independent association of insulin resistance and glucose with aortic pulse wave velocity. *Diabetologia* 2010;53:1190-8.
 33. Park JS, Nam JS, Cho MH, Yoo JS, Ahn CW, Jee SH, et al. Insulin resistance independently influences arterial stiffness in nor

moglycemic normotensive postmenopausal women. Menopause
2010;17:779-84.

ABSTRACT(IN KOREAN)

논문 제목: 한국 성인에서의 Triglyceride glucose index와
동맥탄성도의 상관관계

<지도교수 박종숙>

연세대학교 대학원 의학과

이 상 배

목적: 인슐린 저항성은 심혈관 질환의 중요한 위험인자로 잘 알려져 있다. 최근 들어 도입된 Triglyceride glucose index (TyG index)는 간단하게 인슐린 저항성을 평가할 수 있는 대체적인 검사 방법으로 알려져 있다. 그러나 TyG index와 동맥탄성도의 연관성을 알아본 연구는 지금까지 많지 않다. 이러한 점에 착안하여 한국 성인에서 TyG index와 동맥탄성도의 상관관계를 연구하였다.

방법: 건강검진 센터를 방문한 4549명의 검사 결과를 이용해 분석하였다. 신체계측 정보 및 심혈관 질환 위험인자로 알려진 다수의 혈액검사 결과를 이용하여 분석하였다. 동맥탄성도를 대변하는 용적맥파기록으로는 상완-발목 맥박파전파속도(brachial-ankle PWV) 값을 사용하여 분석하였다.

결과: 전체 대상자를 TyG index 값에 따라 4개의 그룹으로 나누어 분석한 결과, 각 그룹별로 심혈관 질환의 위험인자가 통계적으로 유의미한 차이를 나타내었다. 또한 TyG index 값이

증가할수록 baPWV 값이 유의미하게 증가하였다. 전체 대상자의 평균 baPWV 값 중 75분위수 값을 기준으로 고 PWV 값을 설정하였을 때, 로지스틱 다중회귀 분석 결과 고 PWV 값이 발생할 상대위험도는 TyG index 값이 가장 낮았던 최소 사분위수 그룹에 비해서 분위수가 올라갈수록 각각 1.0, 1.55(1.19-2.01), 1.93(1.47-2.54), 3.19(2.28-4.48) 으로 증가하는 양상을 보였으며 이는 통계적 유의성을 나타내었다.

결론: TyG index는 동맥탄성도를 반영하는 지표인 평균 baPWV와 밀접한 상관성을 나타내었다. TyG index는 인슐린 저항성을 반영하는 지표로 측정과 계산이 용이하며 동맥탄성도와 심혈관 질환의 위험성을 반영하는 유용한 지표로서의 의미가 있는 것으로 사료된다.

핵심되는 말 : Triglyceride glucose index, 동맥탄성도, 상완-발목 맥박파전파속도, 인슐린저항성