Association of the abdominal adiposity indexes and their interactions with triglyceride-glucose index on hypertension: The Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort

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Dedicated to-

My mother (Ammu)

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GLOSSARY OF TERMS

CMERC:Cardiovascular and Metabolic Diseases Etiology Research Center cohort

QCT: Quantitative Computed Tomography

VFA: Visceral fat area

SFA: Subcutaneous fat area

VSR: Visceral-to-subcutaneous fat ratio

IR: Insulin resistance

TyG index: Triglyceride-glucose index

TG/HDL-C: Triglyceride to high-density lipoprotein cholesterol ratio

HOMA-IR: Homeostasis model measurement of insulin resistance

SD: Standard deviation

SE: Standard error

OR: Odds ratio

CI: Confidence interval

RERI: Relative excess risk of interaction

SNS: Sympathetic nervous system

RAAS: Renin-angiotensin-aldosterone system

ABSTRACT

Association of the abdominal adiposity indexes and their interactions with triglyceride-glucose index on hypertension: The Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort

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Background:

Abdominal obesity is a risk factor for hypertension, but there is scarce evidence on the interaction of abdominal obesity and triglyceride-glucose (TyG) index on hypertension. Therefore, this study aimed to elucidate the association of the

abdominal adiposity indexes and their interactions with triglyceride-glucose index on hypertension in the middle-aged Korean population.

Methods:

This study used the baseline data of the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort. Abdominal computed tomography (CT) scan results were used to quantify three adiposity indexes: visceral fat area (VFA), subcutaneous fat area (SFA), and the visceral-to-subcutaneous fat ratio (VSR). TyG index had calculated using the standard equation $\frac{Ln\,(fasting\ triglyceride)\times(fasting\ glucose)}{2}$. Participants with a mean systolic blood pressure of ≥ 140 mmHg, diastolic blood pressure of ≥ 90 mmHg, or who used antihypertensive drugs had considered hypertensive. To examine the association between adiposity indexes and hypertension, we used multiple logistic regression models. The additive interaction effects were measure by the relative excess risk of interaction (RERI) as well as interactions on a multiplicative scale between each adiposity index and the TyG index.

Results:

Higher VFA, VSR levels had a relatively higher prevalence of hypertension in men and women (p for trend was <0.01). TyG index was positively associated

with hypertension and the presence of a higher TyG index increased the odds ratio (OR) of hypertension in both sexes. There were positive interactions between VFA and TyG index on the multiplicative scale in men (p = 0.030). In addition, the combined measures of the high VFA and TyG index, as well as the high VSR and TyG index showed an additive interaction in men (RERI= 0.56, 95% confidence interval (CI)= 0.44 – 0.68 for VFA), and (RERI= 1.51, 95% CI= 0.60 – 2.44 for VSR), but not in women.

Conclusion:

Increased abdominal adiposity was significantly associated with a higher prevalence of hypertension in the Korean middle-aged population. Furthermore, we observed additive and multiplicative interactions between the TyG index and VFA, and VSR on hypertension prevalence in men, emphasizing the importance of the early prevention of hypertension through lowering the visceral fat, serum triglyceride, and blood glucose level.

Keywords: abdominal adiposity; visceral fat; subcutaneous fat; abdominal adiposity indexes; triglyceride-glucose index; hypertension; additive interaction; multiplicative interaction.

Background:

Hypertension is one of the major contributing factors for cardiovascular disease [1] and is the leading cause of global burden of disease and mortality [2]. The World Health Organization (WHO) reported that nearly 40% of adults had been diagnosed with hypertension worldwide [3]. It is expected that the prevalence of hypertension will increase by 60 percent to 1.56 billion people in 2025 [4]. It has been reported that 9.4 million deaths are attributable to complications from elevated blood pressure per year [5]. This global trend is also apparent in rising mortality and personal costs to treat and control hypertension in the Republic of Korea. The estimated prevalence of hypertension in 2015 was 30.5% in Korean adults aged 30-60 years [6].

Obesity is regarded as one of the world's most significant public health challenges[7]. In the last 20 years, it has become more common throughout the world [8], including in the Republic of Korea. The prevalence of obesity and abdominal obesity was 35.7% and 23.8% in 2018 in Korea, respectively [9]. Prior studies demonstrated that obesity [10-13], especially abdominal obesity, contributes to hypertension significantly [14, 15]. The activation of the sympathetic nervous system (SNS), or the renin-angiotensin-aldosterone system (RAAS), has been considered to be the central mechanism in the pathogenesis of obesity-related hypertension [16-18]. The body mass

index (BMI) is the most conventional metric used for determining the degree of obesity in epidemiological studies. It has been observed that higher BMI has been attributed to elevated blood pressure in several cross-sectional trials [19, 20], and increases in BMI have been linked to the incidence of hypertension in recent prospective cohort studies [21, 22]. However, this index relies on a single measurement that ignores the distribution of truncal adipose tissue and muscle mass, as well as the physiology and pathology of excessive adiposity [23]. Consequently, alternative anthropometric indices have been introduced to assess abdominal adiposity, for example, waist circumference, waist-to-hip ratio, waist-to-height ratio (WHtR), conicity index, and the body adiposity index, and all have shown a strong association with central obesity [24-28]. Nonetheless, it is still difficult to distinguish the visceral and subcutaneous fat by using these indices [29]. Therefore, to resolve the limitations, abdominal adiposity indexes have been developed and a few community-based studies also have explored the discriminatory power of the abdominal adiposity indexes [30-32]. The computed tomography (CT) has been considered the gold standard for measuring whole-body fat mass as well as lean muscle mass and bone mass [33]. The accumulated evidence is suggesting the negative impacts of visceral and subcutaneous fat on the risk of hypertension, metabolic syndrome, and other causes of cardiovascular morbidity and mortality [34-36]. In Caucasian, African American, and Japanese American subjects, some cross-

sectional studies have reported that visceral fat, subcutaneous fat, and hypertension were positively associated, independent of other adipose depots and fasting plasma insulin [37, 38]. A Chinese cross-sectional study examined the association of visceral and total body fat with hypertension and revealed that the higher abdominal obesity or body fat composition, even when BMI was normal, was linked to an increased risk of hypertension [39]. Another meta-analysis involving 309,585 subjects showed that WHtR, which has considered a strong indicator for central obesity, had the strongest association with hypertension risk in both sexes in 19 selected countries [40.] Recently, a Korean research regarding obesity-related hypertension included 16,363 people aged 19 and older who took part in the Korea National Health and Nutrition Examination Survey from 2008 to 2010 (8,184 men and 8,179 women) observed that people with central obesity had a higher risk of prevalent hypertension, which was compatible with previous research [41]. However, instead of using the gold-standard method, all of these studies used waist circumference or other indexes to calculate abdominal obesity. Hitherto, there is a lack of evidence on the association between CT-based abdominal adiposity indexes and the risk of hypertension in the middle-aged Korean population.

Insulin resistance (IR) has been related to hypertension in previous researches [42-44], and it is believed that IR may induce hypertension by compensatory

hyperinsulinemia [45]. In contrast to the homeostasis model, measurement of insulin resistance (HOMA-IR) index, the triglyceride and glucose (TyG) index has emerged as a valid marker for detecting IR among healthy individuals because of easy availability and cost-effectiveness [46, 47]. The TyG index was associated with arterial stiffness, an independent predictor of hypertension, in recent Chinese research, although the HOMA-IR was not [48]. Moreover, some Chinese studies also found the association between increased TyG index and a higher prevalence of both prehypertension and hypertension in adults [49]. Nevertheless, the association between the TyG index and hypertension and its interaction with the abdominal adiposity on hypertension has not been investigated in the Korean population yet. Therefore, our study aimed to elucidate the association between abdominal adiposity indexes and hypertension, and to evaluate the interaction between abdominal adiposity and TyG index on the presence of hypertension in the middle-aged Korean population (Figure- 1).

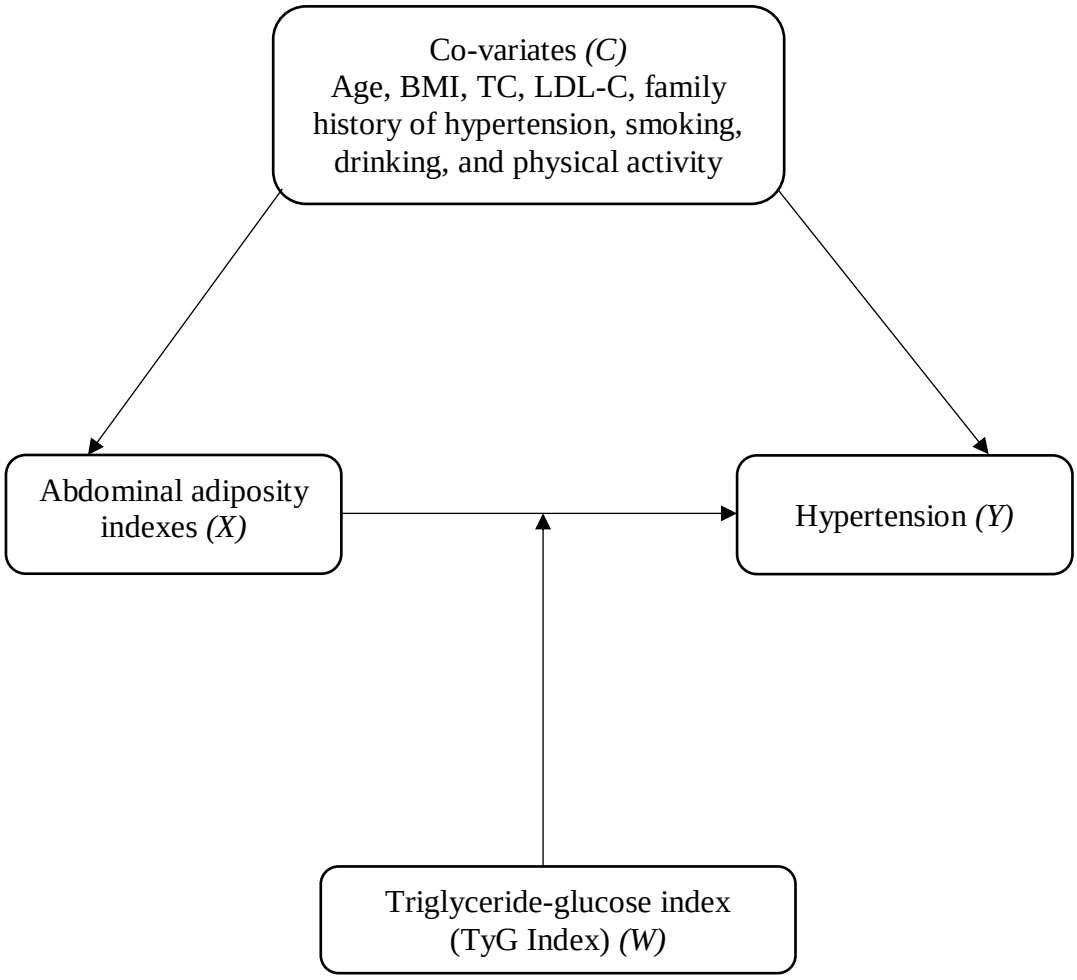

Figure 1. Conceptual framework of the association of abdominal adiposity indexes (exposure; *X*) and triglyceride-glucose index (TyG index) (effect modifier; *W*) with hypertension (outcomes; *Y*) with measured confounders (covariates; *C*).

II. MATERIAL AND METHODS

1. Study population

The study included community dwelling, residents of Seoul city and its western suburbs who had enrolled in the baseline survey (2013-2018) of the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort. The CMERC study was intended to discover novel risk factors and analyze the distribution and consequences of identified cardiac and metabolic disease risk factors, to develop better cardiovascular disease prediction tools for the Korean population. The details of the CMERC study have already been published [50]. Among 4060 participants, people with missing data (n=87) were excluded from the current study, leaving 3,973 participants for the final analysis. The flow diagram of the selection process of the study population has been illustrated in figure 2. The institutional review boards of Severance Hospital, Yonsei University Health System, Seoul, Korea (4–2013-0661) approved this research. Before the baseline survey of the CMERC cohort, all participants signed written informed consent, ensuring that they could withdraw from the study at any time, regardless of the reason.

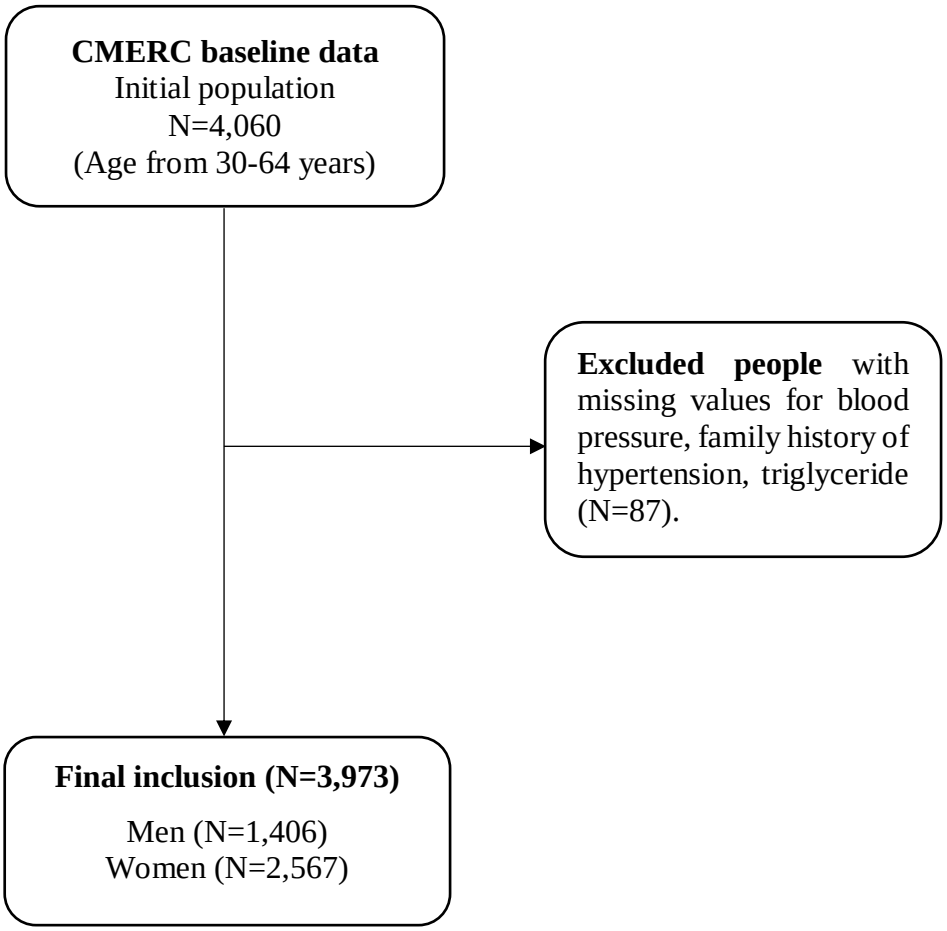

Figure 2. Flow diagram of the selection process of the study population.

2. MEASUREMENT

The well-trained interviewers collected information on socioeconomic status, lifestyle habits, disease history, diet, and psychosocial features using a validated questionnaire. Moreover, anthropometry, blood, and urinal profiles were also tested according to standardized guidelines to identify high-risk persons who would benefit from early intervention.

(1) Abdominal adiposity indexes

Three abdominal adiposity indexes- visceral fat area (VFA), subcutaneous fat area (SFA), and the visceral-to-subcutaneous fat ratio (VSR) were calculated from Quantitative Computed Tomography (QCT) images at the level of the lumber (L4-5) intervertebral space. The participants were in the supine posture for these tests to obtain the best prediction of total body fat volume. A peak kilo voltage of 120 kVp, a current of 150 mA, a pitch of 1.0, and a slice thickness of 3 mm had used in the QCT scan protocol (phantom model 3). The fat area was determined using an Aquarius iNtuition Viewer (version 4.4.12; TeraRecon, Foster City, CA, USA), which was used to set the attenuation values for the region of concern within a range of -190 to 30 Hounsfield units [50]. Then, each index has divided into four groups- quartile 1 to quartile 4. Since there is no standard cut-off value of abdominal

adiposity indexes, the cut-off value of each index has determined by the median value and divided into two groups “low” and “high” for both sexes.

(2) Hypertension

Blood pressure was measured following a standard protocol. After resting for at least 5 minutes and no smoking within 30 minutes prior to the measurement, participants sat in a comfortable position. BP was measured on 3 consecutive occasions each at 2-minutes intervals via the right arm using an automated oscillometric device (HEM-7080; Omron Health, Matsusaka, Japan). The mean of the second and the third measurements was adopted for the data analysis. Participants with mean systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or who used antihypertensive drugs are defined as having hypertension, according to the 2018 Korean Society of Hypertension guidelines for the management of hypertension [51].

(3) Co-variates

Socio-demographic information, medical history, health-related behaviors have been collected by trained interviewers through a systemic face-to-face interview. Age was obtained in years after cross-referencing with government-issued identification. Standing height was measured using a stadiometer (DS-102 Jenix,

Seoul, Korea) to the nearest 0.1cm and weight was measured using a digital scale (DB-150, CAS, Seongnam, Korea) to the nearest 0.1kg. Minimizing the measurement variability, a zero-point adjustment was performed once a week using a standard ruler (170cm) and weights (20, 40, and 60 kg). BMI had calculated as a ratio using the standard equation; weight (kg)/ height squared (m^2).

The history of smoking and alcohol intake was collected through a systemic interview and was categorized into three groups; in the case of smoking, never smokers were defined as those who smoked less than 100 cigarettes in their lifetime. Participants who used to have smoked more than 100 cigarettes but do not smoke in present were classified as the former one, and those who are smoking were classified as current smokers. The same technique was used to calculate the amount of alcohol consumed. Those who answered “no” to the issue of alcohol consumption were classified as non-drinkers, “yes” but not currently drinking were classified as past drinkers, and those who are still drinking alcohol were classified as current drinkers respectively. Physical activity was assessed using the Korean version of the International physical activity questionnaire (IPAQ)- a short form where the last 7 days of activities have been obtained and divided into three groups (low, moderate, high) [52]. Both parental and maternal history of hypertension had considered as family history of hypertension and divided into two groups- “yes” and “no”.

Blood samples were collected in the morning after at least 8 hours of fasting, and bioassays were conducted in a single lab (Seoul Clinical Laboratories R&D Center, Seoul, Korea). Fasting blood glucose, insulin, serum lipid markers, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels were analyzed by ADIVA 1800 Auto Analyzer (Siemens Medical Sol.). Serum insulin concentrations were measured with a radioimmunoassay (SR-300; Stratec, Birkenfeld, Germany).

(4) Triglyceride-glucose index

TyG index was calculated using the equation $\frac{"Ln\,(fasting\ triglyceride)\times(fasting\ glucose)"}{2}$, where both measurements have expressed in mg/dL [47]. TyG index had divided into four groups by the quartiles (Q1, Q2, Q3, and Q4) for each sex. Furthermore, it had divided into “low” and “high” according to the median value for each sex.

HOMA-IR had calculated as follows "$fasting\ plasma\ glucose\ \left(\frac{mg}{dl}\right) \times fasting\ plasma\ insulin(\frac{mIU}{mL})/405$", and further had divided into quartile groups.

TG/HDL-C had calculated from the ratio of TG and HDL-C and had divided in the same way as above.

3. STATISTICAL ANALYSIS

We conducted all analyses separately for men and women considering the substantial sex difference in body composition. The chi-square test for categorical variables and the independent t-test was used to evaluate differences in characteristics between participants with and without hypertension. Data are presented as means with standard deviation or numbers with percentages. To evaluate the independent association between each index of abdominal adiposity and hypertension, we used multiple logistic regression with an adjustment for potential confounders such as age, BMI, serum lipids (TC, TG, HDL-C, and LDL-C), fasting glucose, smoking, drinking, physical activity, family history of hypertension in a single model. VFA, SFA, and VSR were analyzed both as continuous variables and quartile-based categorical variables, and the results were expressed as odds ratios (OR) and 95% confidence intervals (CI). Furthermore, we employed the same statistical procedure to identify the presence of an association between the TyG index and hypertension after adjusting with confounder excluding TG, HDL-C, and fasting glucose level. Further analysis was done to find the association between TG/HDL-C, HOMA-IR, and hypertension, which has provided in Appendix 1.

We examined the multiplicative interaction between each abdominal index and the TyG index as a continuous and categorical variable combining median values by

multiple logistic regression analysis. The presence of additive interactions between each index of abdominal adiposity and the TyG index was measured by the relative excess risk due to interaction (RERI) with the formula, $RERI = OR11 - OR10 - OR01 + 1$, with the corresponding 95% CI using the methods described by Homer and Lemeshow [53]. OR11 indicated the effect of being exposed to two risk factors at the same time, whereas OR10 or OR01 indicated the effect of simply being exposed to one risk factor [54].

Considering age as an important factor for hypertension, we performed a sensitivity analysis to determine the interaction between the TyG index and adiposity indexes on hypertension prevalence stratified by age (age ≤ 45 years and > 45 years) (Appendix 2). Moreover, we repeated the technique on participants over the age of 45, who were divided into sexes (Appendix 3).

The interactions between the TG/HDL-C, HOMA-IR, and adiposity indexes on the prevalence of hypertension were investigated to compare the results of the TyG index, and the findings have presented in Appendix 4 and 5.

All statistical tests were two-sided, with a p-value of 0.05 used to assess statistical significance. SAS version 9.4 was used to do all analyses (SAS Institute Inc., Cary, NC).

III. RESULTS

1. Characteristics of the study population

Table 1 presents the general characteristics of the study participants by sex and the presence of hypertension. A total number of 3,973 adults with an average age of 51.1 ± 9.7 years were enrolled in the present study, including 1,406 men (35.4%) and 2,567 women (64.6%). Men had a higher prevalence of hypertension (26.4%) than women (17.6%) (data not shown).

In comparison to normotensive individuals, hypertensive adults were older, smokers (men only), had higher BMI, fasting plasma glucose, serum lipid levels, SBP, DBP, TyG index, TG/HDL-C, HOMA-IR, and a family history of hypertension. Furthermore, no significant differences were observed in drinking and physical activity between the two groups in both sexes.

Table 1: General characteristics of study participants (n= 3,973) by the presence of hypertension.

Variables	Men (n= 1,406)		P-value [a]	Women (n= 2,567)		P-value [a]
	No (n= 1,035)	Yes (n= 371)		No (n= 2,114)	Yes (n= 453)	
Age, yr	48.5 ± 10.4	54.7 ± 7.6	< 0.001	50.9 ± 9.1	56.8 ± 5.0	< 0.001
BMI, kg/m2	24.6 ± 2.8	25.6 ± 2.9	< 0.001	23.1 ± 2.9	24.8 ± 3.3	< 0.001
SBP, mm Hg	121.6 ± 10.7	134.5 ± 16.2	< 0.001	112.4 ± 12.2	127.4 ± 16.8	< 0.001
DBP, mm Hg	78.5 ± 8.1	86.7 ± 11.9	< 0.001	72.4 ± 8.0	80.1 ± 10.7	< 0.001
Lipid profile						
TC, mg/dL	196.9 ± 34.6	191.2 ± 37.5	0.008	201.6 ± 35.1	193.7 ± 36.1	< 0.001
HDL-C, mg/dL	51.6 ± 12.5	50.5 ± 13.7	0.199	61.9 ± 14.5	56.4 ± 13.4	< 0.001
LDL-C, mg/dL	121.2 ± 31.7	113.1 ± 35.2	< 0.001	119.7 ± 31.6	113.6 ± 32.5	< 0.001
TG, mg/dL	149.4 ± 105.2	174.1 ± 136.2	< 0.001	108.1 ± 59.1	133.7 ± 74.7	< 0.001
FBS, mg/dL	94.1 ± 21.9	101.9 ± 28.3	< 0.001	88.0 ± 13.7	95.1 ± 21.2	< 0.001
TyG Index	4.7 ± 0.3	4.8 ± 0.3	< 0.001	4.5 ± 0.3	4.7 ± 0.3	< 0.001
TG/ HDL-C	3.3 ± 3.1	3.9 ± 4.2	< 0.001	1.9 ± 1.5	2.6 ± 1.9	< 0.001
HOMA-IR	2.15 ± 1.15	2.68 ± 1.51	< 0.001	1.85 ± 0.85	2.42 ± 1.39	< 0.001
Smoking status						
Never smoker	241 (23.3)	77 (20.8)	< 0.001	1964 (92.9)	433 (95.6)	0.107
Former smoker	416 (40.2)	199 (53.6)		82 (3.9)	12 (2.7)	
Current smoker	378 (36.5)	95 (25.6)		68 (3.2)	8 (1.8)	
Alcohol intake						
Non-drinker	92 (8.9)	24 (6.5)	0.253	608 (28.8)	151 (33.3)	0.139
Former drinker	59 (5.7)	26 (7.0)		80 (3.8)	18 (4.0)	
Current drinker	884 (85.4)	321 (86.5)		1426 (67.4)	284 (62.7)	
Physical activity						
Low	313 (30.2)	109 (29.4)	0.645	745 (35.3)	162 (35.8)	0.208
Moderate	337 (32.6)	114 (30.7)		713 (33.7)	135 (29.8)	
High	385 (37.2)	148 (39.9)		656 (31.0)	156 (34.4)	
Family history of hypertension						
No	742 (79.3)	194 (20.7)	< 0.001	1341 (86.4)	211 (13.6)	< 0.001
Yes	293 (62.3)	177 (37.7)		773 (76.2)	242 (23.8)	
Adiposity index						
VFA, cm2	109.3 ± 44.2	140.1 ± 53.8	< 0.001	83.8 ± 36.7	113.9 ± 46.6	< 0.001
SFA, cm2	141.8 ± 57.8	151.2 ± 57.2	< 0.001	167.4 ± 56.5	188.4 ± 64.1	< 0.001
VSR,	0.83 ± 0.33	0.99 ± 0.39	< 0.001	0.52 ± 0.22	0.64 ±0.26	< 0.001

Values are presented as mean ± SD or number (%).
BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TG, triglyceride; FBS, fasting blood sugar; TyG index, triglyceride-glucose index; TG/ HDL-C, triglyceride to high-density cholesterol ratio; HOMA-IR, homeostasis model assessment of insulin resistance, VSA, visceral fat area; SFA, subcutaneous fat area; VSR, Visceral to subcutaneous fat ratio.
[a] P value are calculated by independent t-tests & chi-square tests.

2. Association of abdominal adiposity indexes with the presence of hypertension

The OR of hypertension was increased in higher VFA and VSR quartiles compared with the lowest quartile (p for trend < 0.001) in both sexes after adjusting for age, BMI, blood lipid parameters (TC, TG, HDL-C, and LDL-C), fasting glucose, family history of hypertension, smoking, drinking, and physical activity (Table 2). Participants in the highest VFA quartile had a higher prevalence of hypertension (OR: 3.69, 95% CI: 2.17– 6.28) for men and (OR: 1.83, 95% CI: 1.13–2.97) for women than the first VFA quartile. The multivariable-adjusted OR was 1.11 (95% CI: 1.06 – 1.15) per 10 cm^2 higher VFA in men and was 1.05 (95% CI: 1.01 – 1.09) per 10 cm^2 higher VFA in women when the VFA was used as a continuous variable in this model. Similarly, the presence of hypertension was significantly increased with higher VSRs (OR for Q4: 1.94, 95% CI: 1.26 – 3.01 in men and OR for Q4: 1.75, 95% CI: 1.18 – 2.59). However, we did not observe a significant association between SFA (either as categorical or continuous) and the higher prevalence of hypertension, regardless of sex.

Table 2: Association between computed tomography-based abdominal adiposity indexes and the presence of hypertension.

Abdominal adiposity index	Men (n= 1,406)				Women (n= 2,567)			
	Range	No. of participants	No. of cases (%)	OR (95% CI) [a]	Range	No. of participants	No. of cases (%)	OR (95% CI) [a]
VFA								
Q1	≤ 82.1	352	43 (11.6)	1.00 (Ref)	≤ 59.3	641	40 (8.8)	1.00 (Ref)
Q2	82.2 - 111.7	351	74 (19.9)	1.61 (1.02 - 2.55)	59.4 - 83.0	643	80 (17.7)	1.27 (0.83 - 1.95)
Q3	111.8 - 146.5	352	98 (26.4)	2.09 (1.29 - 3.39)	83.1 - 109.7	642	115 (25.4)	1.33 (0.86 - 2.06)
Q4	≥ 146.6	351	156 (42.1)	3.69 (2.17 - 6.28)	≥ 109.8	641	218 (48.1)	1.83 (1.13 - 2.97)
p for trend				<.0001				0.013
Continuous (per 10 cm2)				1.11 (1.06 - 1.15)				1.05 (1.01 - 1.09)
SFA								
Q1	≤ 105.2	352	74 (19.9)	1.00 (Ref)	≤ 131.5	641	75 (16.6)	1.00 (Ref)
Q2	105.3 - 136.1	351	89 (23.9)	1.04 (0.70 - 1.56)	131.6 - 164.6	643	103 (22.7)	1.01 (0.70 - 1.43)
Q3	136.2 - 174.7	352	103 (27.8)	1.17 (0.76 - 1.82)	164.7 - 204.5	643	113 (24.9)	0.81 (0.55 - 1.18)
Q4	≥ 174.8	351	105 (28.3)	1.21 (0.71 - 2.09)	≥ 204.6	640	162 (35.8)	0.89 (0.58 - 1.39)
p for trend				0.439				0.364
Continuous (per 10 cm2)				1.01 (0.97 - 1.05)				0.98 (0.95 - 1.01)
VSR								
Q1	≤ 0.61	351	53 (14.3)	1.00 (Ref)	≤ 0.38	610	49 (10.8)	1.00 (Ref)
Q2	0.62 - 0.79	352	89 (23.9)	1.32 (0.86 - 2.02)	0.39 - 0.49	646	102 (22.5)	1.43 (0.96 - 2.13)
Q3	0.80 - 1.04	351	96 (25.9)	1.42 (0.92 - 2.19)	0.50 - 0.64	665	125 (27.6)	1.49 (1.01 - 2.20)
Q4	≥ 1.05	352	133 (35.9)	1.94 (1.26 - 3.01)	≥ 0.65	646	177 (39.1)	1.75 (1.18 - 2.59)
p for trend				0.003				0.009
Continuous (per 0.1 SD)				1.08 (1.04 - 1.13)				1.06 (1.01 - 1.11)

VSA, visceral fat area; SFA, subcutaneous fat area; VSR, visceral to subcutaneous fat ratio.
[a] Results were derived from multiple logistic regression models after adjusted for age, body mass index (BMI), total cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride, family history of hypertension, smoking, drinking, and physical activity.

3. Association of triglyceride-glucose index with the presence of hypertension

A significant association was observed between the TyG index and hypertension in both men and women (Table 3). After adjustment for potential confounders, hypertension prevalence in the fourth TyG index quartile group had shown to be higher than the reference group (OR: 2.82 95% CI: 1.71 – 4.65), and p for trend was <0.0001 in men. Following the same pattern, the fourth TyG index quartile for women had an increased odds ratio (OR: 2.54 95% CI: 1.63 – 3.97), with a p for trend of <0.0001.

Additionally, we performed the same analysis for the association of TG/HDL-C and HOMA-IR with the presence of hypertension and observed significant results in both sexes (Appendix 1). However, compared to the other two indices, the TyG index had a stronger association with hypertension in men and women.

Table 3: Association between triglyceride-glucose index and the presence of hypertension.

Variable	Men (n= 1,406)				Women (n= 2,567)			
	Range	No. of participants	No. of cases (%)	OR (95% CI) [a]	Range	No. of participants	No. of cases (%)	OR (95% CI) [a]
TyG index								
Q1	≤ 4.52	368	64 (17.4)	1.00 (Ref)	≤ 4.36	642	58 (9.0)	1.00 (Ref)
Q2	4.53 - 4.70	354	90 (25.4)	1.66 (1.11 - 2.50)	4.37 - 4.53	670	89 (13.3)	1.11 (0.76 - 1.63)
Q3	4.71 - 4.90	334	101 (30.2)	2.13 (1.38 - 3.26)	4.54 - 4.71	649	120 (18.5)	1.41 (0.95 - 2.06)
Q4	≥ 4.91	350	116 (33.1)	2.82 (1.71 - 4.65)	≥ 4.72	606	186 (30.7)	2.54 (1.63 - 3.97)
p for trend				<.0001				<.0001

TyG index, triglyceride-glucose index.
[a] Results were derived from multiple logistic regression models after adjusted for age, body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

4. Interaction between abdominal adiposity indexes and triglyceride-glucose index on hypertension

Compared with the lower VFA and TyG index, the OR in the higher VFA and TyG index subgroup was relatively increased (OR: 3.35, 95% CI: 2.39 – 4.17). Moreover, significant additive interactions between VFA and TyG index were observed. The result of RERI was 0.56 (95% CI: 0.44 – 0.68), p= <0.001, suggesting that there would be 0.56 relative excess risk due to the interaction (Table 4).

Furthermore, men who had concurrent higher VSR and the TyG index had a higher prevalence of hypertension compared to other groups (OR: 3.60, 95% CI: 1.04 – 5.54). The additive interaction of VSR and the TyG index was observed by significant RERI= 1.51 (95% CI 0.60 – 2.44), p= <0.001. However, the significant additive interaction of SFA and the TyG index had not found in men. In the multiplicative model, the interaction between adiposity indexes and the TyG index as categorical and continuous variables on hypertension was examined; however, no significant interaction was found, except for VFA when considered as a continuous variable (p for interaction = 0.030).

Conversely, any significant additive interaction was not found between each index of abdominal adiposity and TyG index on hypertension in women. Moreover, no

significant multiplicative interaction was observed between adiposity indexes and the TyG index either as continuous variables or categorical variables on hypertension prevalence, with the exception of VSR as a continuous (p for interaction = 0.035).

Subsequently, we performed a sensitivity analysis to find the interaction between abdominal adiposity indexes and the TyG index divided into two age groups (Appendix 2). In individuals over 45 years old, the OR for the presence of hypertension was greater in those with high VFA and the TyG index than in the reference group (OR: 4.21, 95% CI: 3.46 – 5.12). We also observed significant additive interaction between these two factors as RERI=0.94 (95% CI 0.34 – 1.57), p= 0.038. However, we did not find significant interactions between SFA, VSR, and TyG index on hypertension. In addition, no significant interaction was observed between adiposity indexes and TyG index on hypertension prevalence in the participants aged ≤ 45 years. A further analysis was conducted for adults over the age of 45 stratified by sex, to validate the age effect on the significant interaction between adiposity indexes and TyG index and no significant interaction was observed in both sexes (Appendix 3). As shown in Appendix 4 and 5, there was no interaction between the TG/HDL-C, HOMA-IR, and adiposity indexes in either men or women in multivariate-adjusted models.

Table 4: Interaction between abdominal adiposity indexes and TyG index on the presence of hypertension

Combined variables	Men (n= 1,406)				Women (n= 2,567)			
	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]	No of participant	No of cases (%)	OR (95% CI) [a]	*P* [b]
VFA and TyG index								
Low VFA and low TyG	473	74 (15.6)	1.00 (Ref)	0.415	917	62 (6.8)	1.00 (Ref)	0.229
High VFA and low TyG	249	80 (32.1)	2.56 (1.82 – 3.59)		395	85 (21.5)	1.56 (1.04 - 2.32)	
Low VFA and high TyG	230	43 (18.7)	1.23 (0.83 - 1.83)		367	58 (15.8)	1.89 (1.28 - 2.81)	
High VFA and high TyG	454	174 (38.3)	3.35 (2.39 – 4.71)		888	248 (27.9)	2.18 (1.55 - 3.06)	
Continuous	1406	371 (26.4)		0.030	2567	453 (17.6)		0.228
SFA and TyG index								
Low SFA and low TyG	420	77 (18.3)	1.00 (Ref)	0.371	778	62 (8.0)	1.00 (Ref)	0.127
High SFA and low TyG	302	77 (25.5)	1.24 (0.80 - 1.91)		534	85 (15.9)	1.95 (1.35 - 2.82)	
Low SFA and high TyG	283	86 (30.4)	1.90 (1.22 - 2.94)		506	116 (22.9)	2.61 (1.85 - 3.66)	
High SFA and high TyG	401	131 (32.7)	1.84 (1.14 - 2.97)		749	190 (25.4)	3.13 (2.22 - 4.39)	
Continuous	1406	371 (26.4)		0.717	2567	453 (17.6)		0.335
VSR and TyG index								
Low VSR and low TyG	405	72 (17.8)	1.00 (Ref)	0.250	801	59 (7.4)	1.00 (Ref)	0.126
High VSR and low TyG	317	82 (25.9)	1.97 (1.28 - 3.05)		511	88 (17.2)	2.61 (1.81 - 3.77)	
Low VSR and high TyG	298	70 (23.5)	1.11 (0.59 - 2.07)		455	92 (20.2)	4.76 (3.39 - 6.68)	
High VSR and high TyG	386	147 (38.1)	3.60 (1.04 - 5.54)		800	214 (26.8)	4.57 (3.37 - 6.19)	
Continuous	1406	371 (26.4)		0.687	2567	453 (17.6)		0.035

VSA, visceral fat area; SFA, subcutaneous fat area; VSR, visceral to subcutaneous fat ratio; TyG index, triglyceride-glucose index.

[a] Results were derived from multiple logistic regression models after adjusted for age, body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

[b] P-value is for multiplicative interaction.

[c] Additive interaction in men: relative excess risk due to interaction, RERI= 0.56 (95% CI: 0.44 – 0.68), p= < 0.001; In women, RERI= - 0.26 (95% CI: - 1.06 – 0.52), p= 0.576.

[d] Additive interaction in men: RERI= - 0.29 (95% CI: - 1.22 – 0.64), p= 0.610; In women, RERI= - 0.44 (95% CI: - 1.45 – 0.57), p= 0.470.

[e] Additive interaction in men, RERI= 1.51 (95% CI: 0.60 – 2.44), p= <0.001; In women, RERI= - 1.80 (95% CI: - 3.27 – -0.32), p= 0.576.

IV. DISCUSSION

1. Summary of findings

The present study was conducted with the cross-sectional data from the CMERC cohort to investigate the association of abdominal obesity with hypertension and the interaction with the TyG index on this association. The results revealed a positive association of VFA and VSR with the prevalence of hypertension independent of other risk factors, whereas SFA did not exert any significant association in both sexes. We also found a stronger association between the TyG index and the increased prevalence of hypertension than TG/HDL-C and HOMA-IR. Furthermore, men with higher levels of concurrent VFA and the TyG index, VSA and the TyG index had more prevalence of hypertension than those with a high level of the individual index of abdominal obesity. The additive and multiplicative interaction effect of the TyG index, VFA, and VSR on hypertension prevalence is concerning for early hypertension prevention, especially in Korean men. In addition, the additive interaction between VFA and the TyG index had observed on hypertension adults over age 45 years old.

2. Discussion of study results

BMI cannot differentiate between adipose tissue and lean mass due to its single body composition estimate [23]. Despite the fact that QCT measurement is the gold standard procedure for measuring visceral and subcutaneous fat, it is not preferred for an epidemiological study due to its expense [33]. We used data from an abdominal CT scan, which revealed a strong positive association of VFA and VSR, on hypertension prevalence. Our study pinpointed that excess body fat deposited viscerally rather than elsewhere in the body might increase the prevalence of hypertension. For instance, per 10 cm^2 increase of visceral fat area would lead to a 1.11 fold increase in the prevalence of hypertension in men and 1.05 fold in women. Moreover, we illustrated the sex difference between adiposity indexes and hypertension. Men consistently had a higher hypertension prevalence for both measures of VFA and VSR than women. Our finding can be supported by other studies, where a strong correlation for visceral adiposity with hypertension was seen in men. A cross-sectional study involving 687 Japanese men demonstrated that greater visceral adiposity defined using abdominal CT was associated with increased odds of the prevalence of hypertension [36]. Another cross-sectional research conducted in the United States with White and African-American participants (n= 2,969) showed that visceral fat was the most important factor in

associated hypertension, particularly in white men, and that could be especially important for thinner people with a lot of visceral fat [38]. Furthermore, a previous Korean study reported the associations between the prevalence of hypertension and VSR in both sexes, which is consistent with our results [32]. We did not observe that the increased SFA was associated with a higher risk of hypertension in Korean adults, which is supported by the previous studies [36, 37].

The TyG index is considered a surrogate marker of insulin resistance, also found to be linked to hypertension and CVD risk factors. An elevated TyG index was significantly associated with the presence of hypertension in an earlier study conducted with 3,589 children aged 6-9 years and adolescents aged 10-15 years [55]. Several cross-sectional and cohort studies from China have shown that the TyG index can predict the incidence of hypertension among the Chinese population [56-58]. This study also revealed that the prevalence of hypertension is associated with increasing the TyG index quartiles in both men and women, which coincides with prior studies.

Further analysis was done in the present study to examine the possible multiplicative and additive interaction between adiposity indexes and the TyG index on hypertension. A Chinese study stated that the TyG index has a significant association with hypertension and additive interactions with WHtR and percent body fat on this association [49]. Nevertheless, researchers did not show the results

by age or gender stratification, which has been shown in our study. Our study found that the multiplicative interaction of VFA and TyG index and additive interactions of VFA, VSR, and the TyG index on hypertension in Korean men, whereas women did not exhibit significant interactions. These results suggest that lowering visceral fat, serum triglyceride, and blood glucose level could lead to a greater proportional reduction in hypertension prevalence in men. The implication for health policy lies in that within a given limited cost, hypertension prevention would be more effective if it focuses on the people with higher visceral fat.

The precise factors that underpin visceral fat excessive impact on hypertension are unknown. However, it can be explained by several plausible mechanisms. First, the adipose tissue is believed to play a key role in the development of both hypertension and other problems associated with IR. According to a cohort report, men with IR had a two-fold elevated risk of hypertension relative to average people [59]. Hyperinsulinemia is thought to activate both the RAAS and SNS, resulting in vascular smooth cell and endothelial cell hypertrophy, which contributes to increased peripheral vascular resistance and hypertension [43, 44, 60]. Another hypothesis is that visceral fat increases blood pressure by direct activation of the SNS, improving RAAS, and possibly inducing physical repression of the kidneys [61]. Moreover, both TG and glucose have been considered important risk factors for hypertension [62-64]. Therefore, it can be hypothesized that the positive interaction

between visceral fat and the TyG index was found in this study due to visceral fat compensating for hyperinsulinemia, which might induce hypertension.

VSR represents an individual's relative fat distribution which might varies by gender. Since estrogen encourages the accumulation of peripheral fat while androgen encourages the accumulation of visceral fat [65]. To get a higher level of VSR, the visceral fat area has to be greater compare to the subcutaneous fat area. That might be a possible explanation that in this study VSR had found to be substantially correlated with hypertension and showed an additive interaction with the TyG index only in men [67]. However, it is still worthwhile to investigate further the exact mechanism of interaction between visceral fat and the TyG index on hypertension.

3. Strength and Limitations

To the best of our knowledge, this study is the first in the Korean population that carried out interaction analyses to examine the potential multiplicative and additive interaction between abdominal adiposity and TyG index concerning hypertension. Second, prior studies have used conventional anthropometric measurements, while the current study used abdominal CT scan data to quantify visceral fat, subcutaneous fat, and their ratio, potentially increasing the precision of the results.

However, there are limitations to be considered. First, since it is a cross-sectional analysis, causality inference on adiposity and hypertension is limited. Second, although analysis with adjustment for potential confounders has been performed, we did not take into account the impact of dietary intake, especially sodium intake, on hypertension, which is a major risk factor for the prevalence of hypertension. Lastly, the participants were all middle-aged adults living in the capital region, therefore, these observations might not be extended to the entire adult Korean community.

V. CONCLUSION

Abdominal obesity, especially visceral fat was associated strongly with hypertension in both sexes. Furthermore, our research provides novel information, since multiplicative and additive interactions were observed with concurrent visceral fat and TyG index, suggesting a higher prevalence of hypertension in men. Hence, considering the public health burden of both obesity and hypertension in the Korean middle-aged population, the current study result can be used as important content for the early prevention of hypertension. Further study needs to investigate the underlying mechanisms involved.

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Appendix 1: Association between triglyceride to HDL-cholesterol ratio, HOMA-IR and the presence of hypertension.

Variables	Men (n= 1,406)				Women (n= 2,567)			
	Range	No. of participants	No. of cases (%)	OR (95% CI) [a]	Range	No. of participants	No. of cases (%)	OR (95% CI) [a]
TG/HDL-C								
Q1	≤ 1.65	352	64 (18.2)	1.00 (Ref)	≤ 1.10	643	58 (9.0)	1.00 (Ref)
Q2	1.66 - 2.61	349	97 (27.8)	1.56 (1.05 - 2.32)	1.11 - 1.62	644	90 (14.0)	1.14 (0.78 - 1.67)
Q3	2.62 - 4.22	353	104 (29.5)	1.63 (1.09 - 2.44)	1.63 - 2.50	637	128 (20.1)	1.39 (0.96 - 2.01)
Q4	≥ 4.23	352	106 (30.1)	1.68 (1.11 - 2.57)	≥ 2.51	643	177 (27.5)	1.81 (1.26 - 2.59)
p for trend				0.022				<.0003
HOMA-IR								
Q1	≤ 1.49	353	66 (18.7)	1.00 (Ref)	≤ 1.34	638	62 (9.7)	1.00 (Ref)
Q2	1.50 - 1.99	348	76 (21.8)	1.20 (0.80 - 1.80)	1.34 - 1.70	646	92 (14.2)	1.26 (0.87 - 1.81)
Q3	2.00 - 2.74	354	95 (26.8)	1.36 (0.91 - 2.04)	1.70 - 2.28	642	113 (17.6)	1.24 (0.86 - 1.78)
Q4	≥ 2.75	351	134 (38.2)	2.20 (1.42 - 3.40)	≥ 2.29	641	186 (29.0)	1.59 (1.09 - 2.31)
p for trend				<.0004				0.020

Results were derived from multiple logistic regression models.
TG/HDL-C, triglyceride to high-density lipoprotein cholesterol ratio; HOMA-IR, homeostasis model assessment of insulin resistance.
[a] adjusted for age, body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

Appendix 2: Interaction between abdominal adiposity indexes and TyG index on the presence of hypertension by age.

Combined variables	≤ 45 years (n= 965)				> 45 years (n= 3,008)			
	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]
VFA and TyG index								
Low VFA and low TyG	372	3 (0.8)	1.00 (Ref)	0.529	609	66 (10.8)	1.00 (Ref)	0.342
High VFA and low TyG	112	3 (0.3)	3.94 (2.80 – 5.53)		906	215 (23.7)	1.56 (1.04 - 2.32)	
Low VFA and high TyG	111	2 (0.2)	2.27 (1.53 – 3.36)		143	30 (21.0)	1.89 (1.28 - 2.81)	
High VFA and high TyG	370	44 (11.9)	5.99 (4.54 – 7.90)		1350	461 (34.2)	2.18 (1.55 - 3.06)	
Continuous	965	52 (5.4)		0.604	3008	772 (25.7)		0.297
SFA and TyG index								
Low SFA and low TyG	296	2 (0.7)	1.00 (Ref)	0.876	817	132 (16.2)	1.00 (Ref)	0.690
High SFA and low TyG	188	4 (2.1)	1.67 (1.26 - 2.19)		698	149 (21.4)	1.95 (1.35 - 2.82)	
Low SFA and high TyG	187	16 (8.6)	3.19 (2.41 - 4.21)		687	227 (33.0)	2.61 (1.85 - 3.66)	
High SFA and high TyG	294	30 (10.2)	3.01 (2.28 - 3.96)		806	264 (32.8)	3.13 (2.22 - 4.39)	
Continuous	965	52 (5.4)		0.726	3008	772 (25.7)		0.802
VSR and TyG index								
Low VSR and low TyG	327	5 (1.5)	1.00 (Ref)	0.743	963	144 (15.0)	1.00 (Ref)	0.961
High VSR and low TyG	157	1 (0.6)	1.49 (1.13 - 1.97)		552	137 (24.8)	2.61 (1.81 - 3.77)	
Low VSR and high TyG	156	7 (4.5)	2.20 (1.67 - 2.91)		535	144 (26.9)	4.76 (3.39 - 6.68)	
High VSR and high TyG	325	39 (12.0)	3.13 (2.36 - 4.13)		958	347 (36.2)	4.57 (3.37 - 6.19)	
Continuous	965	52 (5.4)		0.491	3008	772 (25.7)		0.728

VSA, visceral fat area; SFA, subcutaneous fat area; VSR, visceral to subcutaneous fat ratio; TyG index, triglyceride-glucose index.

[a] Results were derived from multiple logistic regression models after adjusted for gender, body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

[b] P-value is for multiplicative interaction.

[c] Additive interaction in ≤ 45 years: relative excess risk due to interaction, RERI= 0.78 (95% CI: -0.21 – 1.78), p= 0.456 ; In > 45 years, RERI= 0.94 (95% CI: 0.34 – 1.57), p= 0.038.

[d] Additive interaction in ≤ 45 years: RERI= - 0.85 (95% CI: -1.84 – 0.13), p= 0.793 ; In > 45 years, RERI= - 0.01 (95% CI: - 0.91 – 0.70), p= 0.540.

[e] Additive interaction in ≤ 45 years: RERI= 0.43 (95% CI: - 0.38 – 1.24), p= 0.627 ; In > 45 years, RERI= 0.40 (95% CI: - 0.27 – 1.06), p= 0.831.

Appendix 3: Interaction between abdominal adiposity indexes and TyG (> age 45 years) on the presence of hypertension.

Combined variables	Men (n= 956)				Women (n= 2,052)			
	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]
VFA and TyG index								
Low VFA and low TyG	322	75 (23.3)	1.00 (Ref)	0.413	697	84 (12.1)	1.00 (Ref)	0.396
High VFA and low TyG	173	65 (37.6)	1.68 (1.09 - 2.61)		344	84 (24.4)	1.56 (1.04 - 2.32)	
Low VFA and high TyG	156	43 (27.6)	1.21 (0.75 - 1.95)		329	60 (18.2)	1.89 (1.28 - 2.81)	
High VFA and high TyG	305	144 (47.2)	2.61 (1.71 - 3.99)		682	217 (31.8)	2.18 (1.55 - 3.06)	
Continuous	956	327 (34.2)		0.489	2052	445 (23.9)		0.523
SFA and TyG index								
Low SFA and low TyG	290	65 (22.4)	1.00 (Ref)	0.726	603	78 (13.0)	1.00 (Ref)	0.298
High SFA and low TyG	205	75 (36.6)	1.03 (0.63 - 1.66)		438	90 (20.6)	1.95 (1.35 - 2.82)	
Low SFA and high TyG	188	70 (37.2)	1.99 (1.29 - 3.09)		424	107 (25.2)	2.61 (1.85 - 3.66)	
High SFA and high TyG	273	117 (42.9)	1.62 (0.99 - 2.62)		587	170 (29.0)	3.13 (2.22 - 4.39)	
Continuous	956	327 (34.2)		0.698	2052	445 (23.9)		0.478
VSR and TyG index								
Low VSR and low TyG	287	78 (27.2)	1.00 (Ref)	0.457	607	76 (12.5)	1.00 (Ref)	0.349
High VSR and low TyG	208	62 (29.8)	1.20 (0.78 - 1.81)		434	92 (21.2)	2.61 (1.81 - 3.77)	
Low VSR and high TyG	204	73 (35.8)	1.34 (0.86 - 2.07)		395	101 (25.6)	4.76 (3.39 - 6.68)	
High VSR and high TyG	257	114 (44.4)	1.95 (1.32 - 2.89)		616	176 (28.6)	4.57 (3.37 - 6.19)	
Continuous	956	327 (34.2)		0.379	2052	445 (23.9)		0.214

VSA, visceral fat area; SFA, subcutaneous fat area; VSR, visceral to subcutaneous fat ratio; TyG index, triglyceride-glucose index.

[a] Results were derived from multiple logistic regression models after adjusted for body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

[b] P-value is for multiplicative interaction.

[c] Additive interaction in men: relative excess risk due to interaction, RERI= 0.72 (95% CI: - 0.24 – 1.68), p= 0.926 ; In women, RERI= 0.42 (95% CI: - 0.29 – 1.12), p= 0.829.

[d] Additive interaction in men: RERI= - 0.40 (95% CI: - 1.22 – 0.41), p= 0.660 ; In women, RERI= - 0.58 (95% CI: - 1.32 – 0.15), p= 0.403.

[e] Additive interaction in men: RERI= - 0.42 (95% CI: - 0.39 – 1.23), p= 0.219 ; In women, RERI= - 0.33 (95% CI: - 1.14 – 0.49), p= 0.315.

Appendix 4: Interaction between abdominal adiposity indexes and TG/HDL-C on the presence of hypertension.

Combined variables	Men (n= 1,406)				Women (n= 2,567)			
	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]
VFA and TG/HDL-C								
Low VFA and low TG/HDL-C	458	73 (15.9)	1.00 (Ref)	0.541	909	71 (7.8)	1.00 (Ref)	0.276
High VFA and low TG/HDL-C	243	88 (36.2)	1.80 (1.18 - 2.75)		378	77 (20.4)	1.35 (0.91 - 2.00)	
Low VFA and high TG/HDL-C	245	44 (18.0)	1.16 (0.74 - 1.81)		375	49 (13.1)	1.38 (0.92 - 2.09)	
High VFA and high TG/HDL-C	460	166 (36.1)	2.16 (1.45 - 3.22)		905	256 (28.3)	1.86 (1.32 - 2.62)	
Continuous	1406	371 (26.4)		0.319	2567	453 (17.6)		0.308
SFA and TG/HDL-C								
Low SFA and low TG/HDL-C	418	80 (19.1)	1.00 (Ref)	0.457	774	73 (9.4)	1.00 (Ref)	0.520
High SFA and low TG/HDL-C	283	81 (28.6)	1.30 (0.83 - 2.02)		513	75 (14.6)	0.84 (0.56 - 1.25)	
Low SFA and high TG/HDL-C	285	83 (29.1)	1.53 (1.03 - 2.26)		510	105 (20.6)	1.55 (1.09 - 2.20)	
High SFA and high TG/HDL-C	420	127 (30.2)	1.42 (0.91 - 2.21)		770	200 (26.0)	1.18 (0.81 - 1.72)	
Continuous	1406	371 (26.4)		0.624	2567	453 (17.6)		0.425
VSR and TG/HDL-C								
Low VSR and low TG/HDL-C	392	75 (19.1)	1.00 (Ref)	0.430	782	61 (1.8)	1.00 (Ref)	0.335
High VSR and low TG/HDL-C	223	86 (27.8)	1.12 (0.75 - 1.66)		505	87 (17.2)	1.66 (1.14 - 2.42)	
Low VSR and high TG/HDL-C	311	67 (21.5)	0.92 (0.60 - 1.41)		474	90 (18.9)	1.66 (1.13 - 2.44)	
High VSR and high TG/HDL-C	394	143 (36.3)	1.68 (1.15 - 2.44)		806	215 (26.7)	2.06 (1.47 - 2.89)	
Continuous	1406	371 (26.4)		0.364	2567	453 (17.6)		0.417

VSA, visceral fat area; SFA, subcutaneous fat area; VSR, visceral to subcutaneous fat ratio; TG-HDL-C, triglyceride to high-density lipoprotein cholesterol ratio.

[a] Results were derived from multiple logistic regression models after adjusting for age, body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

[b] P-value is for multiplicative interaction.

[c] Additive interaction in men: relative excess risk due to interaction, RERI= 0.70 (95% CI: 0.14 – 1.42), p= 0.251 ; In women, RERI= 0.14 (95% CI: - 0.08 – 0.36), p= 0.532.

[d] Additive interaction in men: RERI= 0.51 (95% CI: - 0.12 – 1.15), p= 0.987 ; In women, RERI= - 0.02 (95% CI: - 0.72 – 0.32), p= 0.158.

[e] Additive interaction in men: RERI= 0.64 (95% CI: 0.05 – 0.73), p= 0.296 ; In women, RERI= 0.25 (95% CI: - 0.45 – 0.95), p= 0.276.

Appendix 5: Interaction between abdominal adiposity indexes and HOMA-IR on the presence of hypertension.

Combined variables	Men (n= 1,406)				Women (n= 2,567)			
	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]	No of participants	No of cases (%)	OR (95% CI) [a]	*P* [b]
VFA and HOMA-IR								
Low VFA and low HOMA-IR	466	72 (15.5)	1.00 (Ref)	0.325	870	76 (8.7)	1.00 (Ref)	0.453
High VFA and low HOMA-IR	235	70 (29.8)	2.01 (0.70 - 1.69)		411	78 (19.0)	1.67 (1.15 - 2.41)	
Low VFA and high HOMA-IR	237	45 (19.0)	1.09 (1.30 - 3.12)		413	44 (10.7)	1.52 (1.03 - 2.25)	
High VFA and high HOMA-IR	468	184 (39.3)	2.45 (1.46 - 4.12)		873	255 (29.2)	1.91 (1.36 - 2.68)	
Continuous	1406	371 (26.4)		0.891	2567	453 (17.6)		0.398
SFA and HOMA-IR								
Low SFA and low HOMA-IR	464	92 (19.8)	1.00 (Ref)	0.645	789	85 (10.8)	1.00 (Ref)	0.719
High SFA and low HOMA-IR	237	50 (21.1)	0.84 (0.54 - 1.29)		492	69 (14.0)	0.76 (0.51 - 1.12)	
Low SFA and high HOMA-IR	239	71 (29.7)	1.22 (0.82 - 1.82)		495	93 (18.8)	1.32 (0.93 - 1.85)	
High SFA and high HOMA-IR	466	158 (33.9)	1.57 (1.02 - 2.41)		791	206 (26.0)	1.06 (0.73 - 1.54)	
Continuous	1406	371 (26.4)		0.462	2567	453 (17.6)		0.582
VSR and HOMA-IR								
Low VSR and low HOMA-IR	367	60 (16.4)	1.00 (Ref)	0.834	739	62 (8.4)	1.00 (Ref)	0.332
High VSR and low HOMA-IR	334	82 (24.6)	1.32 (0.90 - 1.96)		542	92 (17.0)	1.23 (0.84 - 1.80)	
Low VSR and high HOMA-IR	336	82 (24.4)	1.30 (0.87 - 2.05)		517	89 (17.2)	1.09 (0.72 - 1.66)	
High VSR and high HOMA-IR	369	147 (39.4)	1.55 (1.38 - 3.00)		769	210 (27.3)	1.73 (1.22 - 2.45)	
Continuous	1406	371 (26.4)		0.090	2567	453 (17.6)		0.408

VSA, visceral fat area; SFA, subcutaneous fat area; VSR, visceral to subcutaneous fat ratio; HOMA-IR, homeostasis model assessment of insulin resistance.

[a] Results were derived from multiple logistic regression models after adjusting for age, body mass index (BMI), total cholesterol, LDL-cholesterol, family history of hypertension, smoking, drinking, and physical activity.

[b] P-value is for multiplicative interaction.

[c] Additive interaction in men: relative excess risk due to interaction, RERI= 0.35 (95% CI: - 0.88 – 1.59), p= 0.265 ; In women, RERI= - 0.28 (95% CI: - 1.06 – 0.49), p= 0.954.

[d] Additive interaction in men: RERI= 0.51 (95% CI: - 0.12 – 1.15), p= 0.987 ; In women, RERI= - 0.02 (95% CI: - 0.53 – 0.49), p= 0.135.

[e] Additive interaction in men: RERI= 0.36 (95% CI: - 0.33 – 1.07), p= 0.192 ; In women, RERI= 0.40 (95% CI: - 0.24 – 1.05), p= 0.729.

ABSTRACT (KOREAN)

고혈압에 대한 복부 지방 혈증 지수와 중성지방-포도당 지수의 상호 작용

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배경 및 목적:

비만은 고혈압의 대표적인 위험요인이다. 선행 연구에 따르면, 중성지방-포도당(Triglyceride-glucose, TyG) 지수는 인슐린 저항성을 평가하는 지표임에도 불구하고 고혈압과 긍정적인 연관성을 보였다. 현재 고혈압과 비만의 연관성은 활발하게 연구 되고 있지만, 고혈압에 대한 복부 지방과 중성지방-포도당 지수의 연관성에 대해서는 거의 연구되지 않고 있다. 따라서 본 연구는 한국 중년 인구의 고혈압에 대한 복부 지방 지수와 중성 지방-포도당 지수의 연관성과 상호 작용 효과를 알아보고자 한다.

연구방법:

본 연구는 심혈관 및 대사질환 원인연구센터(CMERC) 코호트의 기반 조사 데이터를 활용한 단면 연구이다. 복부 지방 지수는 정량적골염량측정법(Quantitative Computed Tomography, QCT)을 통하여 측정되었으며, 내장지방면적(Visceral Fat Area, VFA), 피하지방면적(Subcutaneous Fat Area, SFA), 내장지방면적 대 피하지방면적 비율(Visceral-to-Subcutaneous fat Ratio, VSR)의 세 가지 지표로 구분하였다. 고혈압은 수축기혈압 ≥ 140mmHg 및 / 또는 이완기혈압 ≥ 90mmHg, 고혈압 진단력, 또는 고혈압 약물 복용력으로 정의하였다. 중성지방-포도당 (Triglyceride-glucose, TyG) 지수는 방정식 (공복 중성지방(fasting triglycdride(mg/dl))×공복 포도당(fasting glucose(mg/dl)))/2 으로

정의하였다. 복부 지방 지수와 고혈압 사이의 연관성은 다중 로지스틱 회귀 모델을 사용하여 분석하였다. 가법 상호작용(additive interaction) 효과는 상호작용의 상대 초과 위험(RERI) 및 각 복부 지방 지수와 중성 지방-포도당 지수 사이의 승법 상호작용을 통해 측정되었다.

연구결과 :

내장지방면적이 높을수록 내장지방면적 대 피하지방면적 비율 수치는 남성 및 여성에서 상대적으로 고혈압 유병률이 더 높았다 (p for trend <0.01). 중성지방-포도당 지수는 고혈압과 긍정적인 연관성이 있으며, 중성지방-포도당 지수가 높아질수록 남녀 모두에서 고혈압의 높은 승산비(OR)를 보였다. 남성의 승법 척도에서 내장지방면적과 중성지방-포도당 지수 사이에는 긍정적인 상호작용을 보였다. 높은 내장지방면적 및 중성지방-포도당 지수의 결합 된 측정 값과 높은 내장지방면적 대 피하지방면적 비율 및 중성지방-포도당은 남성에서 가법 상호 작용을 보였으나 (내장지방면적, RERI = 0.56, 95 % 신뢰구간 [0.44 – 0.68]), p= <0.001; (내장지방면적 대 피하지방면적 비율, RERI= 1.51, 95% 신뢰구간 [0.60 – 2.44]), p= <0.001), 여성에서는 통계적으로 유의하지 않았다.

결론 및 고찰:

복부 지방의 증가는 한국 중년 인구의 고혈압 유병률과 유의한 관련성이 있었다. 또한 남성의 고혈압 유병률에 대한 중성지방-포도당 지수와 내장지방면적 및 내장지방면적 대 피하지방면적 비율 간의 가법적, 승법적 상호작용을 관찰한 결과는 생활습관 개선을 통한 고혈압의 조기 예방의 중요성을 강조한다.

핵심어: 복부비만; 내장지방; 피하지방; 중성지방-포도당 지수; 고혈압; 상호 작용배경 및 목적: