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Dietary flavan-3-ols intake and metabolic syndrome risk in Korean adults

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Abstract

Flavan-3-ols are a subclass of flavonoids found in a variety of foods including teas. The effects of flavan-3-ols on the risk of metabolic syndrome (MetS) have been investigated, generally focusing on tea catechins or individual flavan-3-ol rich foods, but there is little information on dietary flavan-3-ols intake and risk of MetS in population-based studies. In this cross-sectional study, we examined the association between dietary flavan-3-ols intake and the risk of MetS in Korean adults. Subjects comprised 1,827 men and 2,918 women aged 20-69 years whose data was included in the 2008 Korean National Health and Nutrition Examination Survey. This survey was conducted between January 2008 and December 2008. Total flavan-3-ols intakes were calculated from 24-hour dietary recalls using a flavonoids database. Thirty percent of the male subjects and 24% of the female subjects were reported as having MetS. In the female subjects, flavan3-ols intake was inversely associated with the risk of MetS after adjusting for potential confounders (5th vs. 1st quintile, OR = 0.64, 95% CI = 0.45-0.91, P for trend = 0.384). The main food source of flavan-3-ols was green tea followed by apples and grapes. Among MetS components, flavan3-ols intake was inversely associated with the risk of high blood pressure after adjusting for potential confounders (5th vs. 1st quintile, OR = 0.64, 95% CI = 0.45-0.90, P for trend = 0.005). No significant association between flavan-3-ols intake and risk of MetS was found in the male subjects. After stratified analysis by obesity (BMI $\geq$ 25 or BMI < 25), however, flavan3-ols intake was inversely related to the risk of hypertension in non-obese men. These results suggest that dietary flavan-3-ols intake may have beneficial effects on MetS risk by reducing the risk of hypertension. The effects of flavan-3-ols intake dependent on obesity need further investigation.

Key Words: Flavan-3-ols, metabolic syndrome, flavonoids, hypertension, hyperglycaemia

Introduction

Flavonoids are a class of plant secondary metabolites and are the most common group of polyphenolics in the human diet. According to their chemical structure, flavonoids are classified into several groups including flavonols, flavones, flavan-3-ols, flavanones, anthocyanidins, and isoflavonoids. Differences in the chemical structures of flavonoid subclasses alter their biological efficacy and bioavailability [1,2]. Flavan-3-ols are the collective term for the catechin group of compounds that have a 2-phenyl-3,4-dihydro-2H-chromen-3-ol skeleton. Catechin, epigallocatechin, epicatechin, epicatechin 3-gallate, epigallocatechin 3-gallate (EGCG), theaflavin, thearubigins, theaflavin-3,3-digallate, theaflavin-3-gallate, theaflavin-3'-gallate, gallocatechin, and catechin 3-gallate are included in flavan-3-ols. Food sources of flavan-3-ols include apples, hops, tea, beer, wine, fruit juice, and black tea [3].

Metabolic syndrome (MetS) is characterized by a clustering of metabolic abnormalities including abdominal obesity, hyperglycemia, hypertension, and dyslipidemia [4]. MetS is associated with developing type 2 diabetes, cardiovascular disease, and all-cause mortality [5,6]. Based on the 2005 Korean National Health and Nutrition Examination Survey (KNHANES), the prevalence of MetS in men and women was 32.9% and 31.8%, respectively. MetS is a complicated interaction between genetic, metabolic, and environmental factors, in which diet is a potent modifiable environmental factor. A number of foods, nutrients, and dietary patterns have been reported to be associated with MetS [7-9].

In recent years the effects of flavan-3-ols on the risk of MetS have been investigated. Green tea is rich in polyphenols, about 70% of which are catechins. Tea catechins have shown a relation with reduced serum cholesterol, serum triacylglycerol, and visceral fat area in animal studies [10-12]. Several epidemiological studies also have reported the beneficial effects of green tea consumption against cardiovascular disease risk [13-15]. Flavan-3-ols rich foods such as fruits, red wine, cocoa, and black tea also have been shown to reduce the risk of MetS or its components in human studies [16-19]. However, to our knowledge, no study has investigated the association of total flavan-3-ols intake from various kinds of flavan-3-ols [catechin, epigallocatechin, epicatechin, epicatechin 3-gallate, epigallocatechin 3-gallate (EGCG), theaflavin, thearubigins, theaflavin-3,3-digallate, theaflavin-3-gallate, theaflavin-3'-gallate, gallocatechin, and catechin 3-gallate] and the risk of

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MetS. Therefore, we examined the association between total flavan-3-ols intake and risk of MetS and its components (high blood pressure, hyperglycaemia, abdominal obesity, low HDL cholesterol, and hypertriglyceridaemia) in Korean adults.

Subjects and Methods

Study population

The Korean National Health and Nutrition Examination Survey (KNHANES) is a series of surveys designed to assess the health and nutritional status of the Korean population. The KNHANES began in 1998 and was conducted in 1998, 2001, and 2005. Since 2007, the KNHANES has been conducted annually. The KNHANES consists of a health interview, health examination (physical examination, clinical measurements, and tests), and a dietary interview. The subjects of the KNHANES were aged ≥ 1 year and were from stratified multistage samples of the South Korean population from multiple geographic areas, ages, and of both genders.

A total of 8,631 people participated in the 2008 KNHANES. We excluded subjects aged < 20 years or > 69 years (n = 3339), those who did not take the health examination (n = 310), those who reported implausible dietary intakes (< 500 kcal/d or > 4500 kcal) (n = 79), and those who did not have data on waist circumference, blood pressure, blood glucose, triglycerides, or high density lipoprotein (HDL)-cholesterol (n = 158). Finally, 4,745 subjects aged 20-69 years were included in the analysis. This study was approved by the Institutional Review Board (IRB) of Ewha Womans University. Written informed consent was obtained from all subjects.

General characteristics, anthropometrics, and biochemical variables

A structured questionnaire including information on demographics, education, smoking, alcohol intake, exercise, medical history, and female reproductive history was administered by trained interviewers. Height was measured within 0.1 cm and weight was measured with a metric weight scale to the nearest 0.01 kg in light clothing without shoes. Body mass index (BMI) was calculated as weight (kg)/ height (m^2). Waist circumference (WC) was measured according to the WHO guideline at the end of a normal expiration. Blood pressure measurements were taken three times, and the average of the second and third measurements for systolic blood pressure and diastolic blood pressure were used (Baumanometer, New York, USA). Blood samples were collected in the morning after at least ten hours of fasting and all biochemical markers were analyzed on the same day. Plasma total cholesterol, triglycerides, glucose, and high density lipoprotein (HDL) cholesterol were measured by an ADVIA1650 Automatic Analyzer (Siemens, New York, USA).

Diagnosis of metabolic syndrome

Metabolic syndrome was diagnosed if the subjects had three or more risk determinants according to the modified National Cholesterol Education Program Adult Treatment Panel III guidelines [20] using the standard waist circumference for Koreans [21]. The determinants were as follows: 1) a waist circumference ≥ 90 cm for men and ≥ 85 cm for women; 2) a plasma TG concentration of 150 mg/dL; 3) a plasma concentration of HDL-C < 40 mg/dL for men and < 50 mg/dL for women; 4) a systolic BP ≥ 130 mmHg and diastolic BP ≥ 85 mmHg; and 5) a fasting plasma glucose concentration ≥ 100 mg/dL.

Dietary assessment and flavonoid database

Trained dietitians interviewed each subject to collect dietary data through 24 hr dietary recalls. The daily flavan-3-ols intake from foods was estimated using a flavonoid database. Since a national nutrient database for flavonoids is not available in Korea, we constructed the flavonoid database for plant foods consumed by 8,631 subjects in the 2008 KNHANES from January 2008 to December 2008 using the United States Department of Agriculture (USDA) Flavonoid Content of Food Database [22], the Japan Functional Food Factor Database [23], and the Rural Development Administration Food Functional Composition Table [24]. For Korean foods with flavonoid analytic data, only data satisfied with a certain quality by the USDA nutrient data evaluation system were added to the database. Flavonoid contents for combination foods were calculated using standard recipes. If we could not find the same plant in other countries' database, we used data of a similar plant, based on species, genus, nutrients, shape, and color. The subjects of the 2008 KNHANES consumed 1,549 plant foods based on 24hr dietary recall data. The flavonoid database with 1,317 food items covered 85% of the plants foods consumed by the subjects of the 2008 KNHANES. When 1,549 foods were sorted by intake amounts from high to low, we defined the foods ranked ≤ the 95th percentile as 'commonly consumed food'. A total of 922 plant foods were classified into the commonly consumed food group, of which the flavonoids database covered 96%. Flavan-3-ols intake was the sum of catechin, epigallocatechin, epicatechin, epicatechin 3-gallate, epigallocatechin 3-gallate (EGCG), theaflavin, thearubigins, theaflavin-3,3-digallate, theaflavin-3-gallate, theaflavin-3'-gallate, gallocatechin, and catechin 3-gallate intakes.

Statistical analysis

Nutrient intakes were adjusted for total energy intake by the residual method. The subjects were categorized into quintiles by dietary flavan-3-ols intake. The Student's *t*-test and the Chi-square test were applied to determine differences in means and the distribution between the MetS group and control group. The

general linear model (GLM) and Cochran Mantel Haenzel analysis were used to determine the linear trends across the flavan-3-ols intake groups. Non-conditional logistic regression analysis was applied to obtain the odds ratios (ORs) and corresponding 95% confidence intervals for MetS. Potential confounders were identified by examining the differences in means and distributions between the MetS group and control group. The variables that showed significantly different means or distributions between the MetS group and control group or showed significant linear trends across quintiles of flavan3-ols were considered as potential confounders and adjusted in the analyses. Three different models were applied to examine the associations of flavan-3-ols intake and MetS. Age and BMI were adjusted as confounders in the first model, and potential confounders except dietary factors were further adjusted in the second model. The final model additionally adjusted for dietary factors such as intakes of total energy, fat, fiber, and carbohydrate. All statistical analyses were performed using the SAS software (version 9.1 SAS Institute Inc., Cary, NC, USA), and P values < 0.05 were considered significant.

Results

The numbers of subjects for 20-29, 30-39, 40-49, 50-59, 60-69 years were 606, 1144, 1094, 966, and 935, respectively. Men made up 39% of the total subjects, and 30% of the male subjects and 24% of the female subjects were diagnosed as having MetS. Estimated means of daily total flavan3-ols intake for the men and women were 30.0 mg/d and 22.5 mg/d, respectively. The general characteristics of subjects are shown in Table 1. The means for age and BMI in the MetS group were higher than those in the control group for both male and female subjects. Education levels were higher in the control group than the MetS group for both the male and female subjects. In the male subjects, the mean intakes of energy, carbohydrate, fat, protein, and vegetables were higher in the control group than in the MetS group. There were no significant differences in flavan3-ols intake. In the female subjects, the proportions of current drinkers (defined as drinking alcohol more than once a month), and vitamin/mineral supplement use were higher in the control group than in the MetS group. In addition, mean intakes of energy, fat, protein, fruits, and flavan3-ols were higher in the control group than in the MetS group. The mean intakes of epigallocatechin, epicatechin, epicatechin 3-gallate, and EGCG were higher in the control group than in the MetS group.

To determine potential confounding factors, the distributions of selected characteristics were examined across quintiles of flavan-3-ol intake as shown in Table 2. In the male subjects, functional food use (%) and intakes of carbohydrate, fiber, and fruits increased across the quintiles of flavan3-ol intake. Conversely, regular exercisers (%) and intakes of energy and vegetables decreased across the quintiles of flavan3-ols intake. In the female subjects, height, current drinkers (%), multivitamin users (%) and intakes of carbohydrate, fiber, and fruits increased across the quintiles of flavan3-ol intake, but current smokers (%) and intakes of energy and vegetables decreased across the quintiles of flavan3-ols intake.

The top ten foods contributing flavan-3-ols in the diets of the male and female subjects are shown in Table 3. The main food source of flavan-3-ols was green tea followed by grapes, apples, and beer in the male subjects. In the females, green tea was the main food source of flavan-3-ols followed by apples, grapes, and pears.

The relationships between flavan-3-ols intake and the risk of MetS and MetS components are given in Table 4. No significant association between flavan-3-ols intake and the risk of MetS was found in male subjects. In the female subjects, flavan3-ols intake was inversely associated with the risk of MetS after adjusting for potential confounders (5th *vs.* 1st quintile, OR = 0.64, 95% CI = 0.45-0.91, P for trend = 0.384). When associations between flavan3-ols and each MetS component were determined, flavan3-ols intake was inversely associated with the risk of high blood pressure in female subjects after adjusting for potential confounders (5th *vs.* 1st quintile, OR = 0.64, 95% CI = 0.45-0.90, P for trend = 0.005).

To evaluate if the relationship between flavan3-ols intake and MetS risk was different according to the presence of obesity, a stratified analysis was applied based on BMI ≥ 25 or BMI < 25, as shown in Fig. 1 and 2. The proportions of obese subjects with BMI ≥ 25 were 37% and 28% of the male and female subjects, respectively. In the male subjects, flavan3-ols intake was inversely related to the risk of hypertension only in non-obese men. Among the female subjects, flavan3-ols intake was inversely associated with MetS risk after adjusting for potential confounders only in obese women. Among the components of MetS, flavan3-ols were inversely related to risks of hypertension and hyperglycaemia only in obese women. However, no significant relationships were found in non-obese women.

Discussion

In the present cross-sectional study, the relationship between flavan-3-ols intake and risk of MetS was investigated in male and female adult populations. Flavan-3-ols intake was not found to be related to the risk of MetS among the male subjects. Among the female subjects, flavan-3-ols intake was inversely associated with the risk of MetS. In particular, among the MetS components, flavan3-ols intake was inversely related to the risk of hypertension among the female subjects. After stratified analysis by obesity, flavan3-ols intake was inversely related to the risk of hypertension only in non-obese men. Among the female subjects, flavan3-ols intake was also inversely associated with risks of MetS, hypertension, and hyperglycaemia after adjusting for

Table 1. Characteristics of subjects with and without metabolic syndrome (MetS)

Variables[1)]	Males		*P*-value	Females		*P*-value
	Control	MetS		Control	MetS	
N	1286	541		2230	688	
Age (yr)	44.5 ± 13.6[2)]	50.5 ± 11.4	< 0.0001	42.2 ± 12.4	55.0 ± 11.1	< 0.0001
Height (cm)	169.8 ± 6.6	168.7 ± 6.3	0.001	157.8 ± 6	155.4 ± 5.7	< 0.0001
Weight (kg)	67.3 ± 9.9	74.1 ± 10.1	< 0.0001	56.0 ± 7.7	63.3 ± 9.1	< 0.0001
BMI (kg/m^2)	23.3 ± 2.8	26.0 ± 2.7	< 0.0001	22.5 ± 2.9	26.2 ± 3.2	< 0.0001
Waist circumference (cm)	82.2 ± 7.9	91.2 ± 7.1	< 0.0001	76.3 ± 8.3	88.1 ± 7.9	< 0.0001
Systolic BP (mmHg)	114.6 ± 14	124.9 ± 15.2	< 0.0001	107.1 ± 13.7	126.2 ± 18.2	< 0.0001
Diastolic BP (mmHg)	75.6 ± 9.8	82.9 ± 10.9	< 0.0001	70.2 ± 9.7	79.3 ± 10.7	< 0.0001
Cholesterol (mg/dl)	183.4 ± 33.5	195.9 ± 35.8	< 0.0001	182.7 ± 33.7	200.3 ± 38.9	< 0.0001
HDL-cholesterol (mg/dl)	47.3 ± 9.6	39.8 ± 7.9	< 0.0001	52.9 ± 10.7	43.1 ± 8.4	< 0.0001
Triglyceride (mg/dl)	122.2 ± 77.7	247.9 ± 193.4	< 0.0001	90.8 ± 59.6	188.9 ± 114.5	< 0.0001
Fasting glucose (mg/dl)	93.9 ± 15.6	113.6 ± 29.8	< 0.0001	91.3 ± 14.8	112.2 ± 34.7	< 0.0001
Insulin (μIU/ml)	8.8 ± 4.4	11.6 ± 6	< 0.0001	9.0 ± 4.3	12.6 ± 10.2	< 0.0001
HOMA-IR	2.0 ± 1.2	3.2 ± 2	< 0.0001	2.0 ± 1.1	3.5 ± 3.2	< 0.0001
Education, N (%)						
Elementary	184 (14.4)	103 (19.1)	0.0003	410 (18.4)	371 (54)	< 0.0001
Middle	176 (13.7)	91 (16.9)		226 (10.1)	105 (15.3)	
High	478 (37.3)	210 (38.9)		900 (40.4)	167 (24.3)	
College	443 (34.6)	136 (25.2)		692 (31.2)	44 (6.4)	
Smoking, N (%)						
Smoker	595 (46.5)	232 (43)	0.004	129 (5.8)	38 (5.5)	0.247
Past-smoker	449 (35.1)	231 (42.8)		130 (5.8)	29 (4.2)	
Non-smoker	237 (18.5)	77 (14.3)		1,967 (88.4)	620 (90.3)	
Current drinker (%)	75.5	73.6	0.403	45.2	31.6	< 0.0001
Regular exerciser (%)	62.8	58.0	0.055	55.6	54.8	0.725
Multivitamin user (%)	15.3	17.4	0.319	24.8	18.6	0.003
Functional food use (%)	15.8	16.6	0.870	25.8	26.2	0.965
Energy (kcal/day)	2,174.3 ± 738.3[2)]	2,067.9 ± 694.7	0.004	1,636.6 ± 593.4	1,537.5 ± 545.5	< 0.0001
Carbohydrates (g/day)	340.3 ± 112.9	329.0 ± 104.5	0.046	279.7 ± 103.4	278.3 ± 99.8	0.782
Fat (g/day)	43.2 ± 29.5	36.2 ± 24.9	< 0.0001	32.3 ± 23.6	23.3 ± 17.8	< 0.0001
Protein (g/day)	78.3 ± 34.8	73.2 ± 33.1	0.004	58.2 ± 27.2	52.7 ± 25.7	< 0.0001
Fiber (g/day)	8.1 ± 4.8	8.0 ± 4.4	0.420	7.1 ± 4.8	7.0 ± 5.4	0.695
Vegetable (g/day)	410.1 ± 260.7	380.6 ± 225.1	0.022	318.4 ± 225.4	318.3 ± 210.9	0.994
Fruit (g/day)	152.5 ± 286.9	147.0 ± 296.2	0.713	202.8 ± 295.2	167.2 ± 265.3	0.005
Antocyanin (mg/day)	24.7 ± 41.4	28.3 ± 62.9	0.158	25.8 ± 47.3	26.6 ± 42.8	0.687
Flavan-3-ols (mg/day)	30.7 ± 105	28.3 ± 90.2	0.634	24.8 ± 74.2	14.9 ± 53.2	0.001
Catechin	4.43 ± 11.29	3.54 ± 9.45	0.106	3.91 ± 9.78	3.29 ± 10.28	0.148
Epigallocatechin	4.19 ± 17.89	3.99 ± 15.38	0.817	3.11 ± 11.96	1.63 ± 8.51	0.003
Epicatechin	5.62 ± 12.70	4.84 ± 10.45	0.213	6.21 ± 12.31	4.67 ± 11.23	0.004
Epicatechin 3-gallate	2.92 ± 13.02	2.78 ± 11.31	0.817	2.03 ± 8.73	1.11 ± 6.58	0.011
Epigallocatechin 3-gallate	12.74 ± 61.63	12.26 ± 53.18	0.875	8.36 ± 40.50	4.01 ± 29.17	0.009
Theaflavin	0.004 ± 0.05	0.004 ± 0.04	0.937	0.02 ± 0.31	0.001 ± 0.01	0.239
Thearubigins	0.43 ± 4.27	0.57 ± 4.65	0.552	0.97 ± 16.39	0.07 ± 0.58	0.169

[1)] BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment estimate of insulin resistance
[2)] Mean ± SD

potential confounders only in obese women. The present findings suggest that flavan3-ols intake may have beneficial effects on the risk of MetS by reducing hypertension risk, and the effects of flavan3-ols may be different depending on the presence or absence of obesity

Daily flavan-3-ols intake was estimated by 24-hr dietary recalls in the present study. The estimated means of daily flavan3-ols intake for men and women were 30.0 mg/d and 22.5 mg/d, respectively, which are lower than daily flavan3-ols intakes reported in other countries [25-27]. The main sources of flavan-

Table 2. Selected characteristics of subjects according to quintiles of flavan-3-ols intake

Variables	Male					*P*-for trend	Female					*P*-for trend
	Q1	Q2	Q3	Q4	Q5		Q1	Q2	Q3	Q4	Q5	
N	348	381	365	365	365		580	587	583	584	582	
Median	0	0.2	0.6	9.3	61.2		0	0.1	0.9	11.4	47.2	
Age (yrs)	46.3	47.5	45.5	46.5	45.4	0.159	46.9	44.7	45.4	44.3	44.9	0.0004
Height (cm)	169.2	168.8	169.3	169.7	170.5	0.0004	156.6	157.2	157.1	157.8	157.7	< 0.0001
Weight (kg)	69.0	68.6	69.0	69.1	71.1	0.0002	58	57.7	57.3	57.9	57.6	0.735
BMI (kg/m^2)	24.1	24.0	24.0	23.9	24.4	0.029	23.6	23.4	23.3	23.3	23.2	0.027
Current smoker (%)	42.1	51.2	55.4	39.5	39.7	0.483	7.1	6.3	5.5	4.6	5.2	0.333
Current drinker (%)	77.0	76.3	70.8	74.5	76.1	0.631	35.9	42.7	42.4	44.3	44.7	0.003
Regular exerciser (%)	69.3	58.8	56.4	61.1	61.9	0.150	56.0	56.4	54.2	54.6	55.8	0.741
Multivitamin user (%)	14.4	13.4	15.3	18.6	17.8	0.711	18.1	19.3	23.5	28.1	28.0	0.001
Functional food use (%)	10.3	13.9	15.6	18.4	21.9	0.010	21.6	23.0	28.3	29.3	27.3	0.224
Energy (kcal/day)	1,916.0	2,051.6	2,155.3	2,191.7	2,397.8	< 0.0001	1,418.1	1,527.8	1,649.9	1,622.1	1,850.9	< 0.0001
Carbohydrates, energy adjusted (g/day)	283.8	285.6	294.0	283.1	286.9	0.924	279.6	288.9	288.1	290.4	307.3	< 0.0001
Fat, energy adjusted (g/day)	28.8	28.5	30.8	29.6	27.5	0.016	29.3	30.6	34.2	32.4	30.4	0.251
Fiber, energy adjusted (g/day)	7.1	6.9	6.3	7.0	7.5	0.003	7.1	7.0	7.2	7.4	8.2	< 0.0001
Vegetable (g/day)	390.5	404.1	397.7	395.4	417.5	0.173	315.3	325.7	324.0	313.1	314.9	0.534
Fruit (g/day)	56.5	62.6	63.5	184.5	388.2	< 0.0001	67.0	66.2	133.7	231.8	474.3	< 0.0001

BMI, body mass index; Q, quintile

Table 3. Contribution of primary individual foods to favan-3-ols intake

N	Male (1,827)			Female (2,918)	
Food	% of intake[1)]	% of Acc[2)]	Food	% of intake	% of Acc
Green tea	67.02	67.02	Green tea	47.86	47.86
Grape	8.52	75.54	Apple	15.60	63.46
Apple	6.99	82.53	Grape	13.80	77.26
Beer	6.08	88.61	Pear	6.27	83.53
Pear	4.02	92.63	Peach	4.53	88.06
Peach	2.80	95.43	Black Tea	3.64	91.70
Black tea	0.89	96.32	Beer	2.96	94.66
Banana	0.84	97.16	Banana	1.28	95.94
Coffee	0.56	97.72	Strawberry	0.94	96.88
Strawberry	0.55	98.27	Wine	0.63	97.51

[1)] % of total flavan-3-ols intake
[2)] Acc stands for Accumulation

3-ols were green tea, apples, grapes, pears, beer, and peaches in the present study. Intakes of flavan-3-ols in Australia, Denmark, and the Netherlands were 422 mg/d, 148 mg/d, and 145 mg/d, respectively. The main sources of flavan-3-ols were black tea, fruits, and red wine in the three countries [25]. Estimated daily flavan-3-ols intakes in the U.S. and Spain were 158 mg/d and 32 mg/d, respectively [26,27]. Low tea and red wine consumption in Korean adults may be attributed to their low intakes of flavan-3-ols.

Flavan-3-ols intake was inversely associated with the risk of MetS in female subjects, particularly with respect to hypertension. Green tea is the main dietary source of catechins gallates, and gallocatechins. Several epidemiological studies have reported the protective effects of green tea consumption against cardiovascular disease risk [13-15]. Chronic human intervention trials reported vasodilation effects of green tea and green tea extract [28,29]. Green tea consumption for two weeks showed a significant improvement in flow-mediated dilatation (FMD) assessed vascular reactivity among twenty smokers [28]. In a study by Tinahones *et al*., a group who consumed green tea extract showed higher vasodilation effects than a placebo group [29]. Several animal studies have also reported the beneficial vascular functions of green tea extract and EGCG [30-32]. Fruits, red wine, cocoa, and black tea also have been reported to reduce the risk of MetS or MetS components in many research settings including cohort studies, clinical trials, and cross-sectional studies [16-19].

The possible mechanisms underlying the impact of flavan-3-ols on vascular function are explained as follows. EGCG activates endothelial NO synthase (eNOS) in rat aortic rings [33]. It was also proposed that catechins may help regulate NADPH oxidase activity by reducing O_2^- production, which results in the protection of NO from peroxynitrite formation [34]. Increased NO bioavailability may explain the improvements in endothelial function (blood pressure). Since insulin sensitivity is, at least in part, dependent on nitric oxide bioavailability, flavan-3-ols may simultaneously improve insulin sensitivity as well as vascular function. Catechins and theaflavins prevented hyperglycaemia by enhancing insulin sensitivity and by decreasing pancreatic β-cell damage in an animal study [35]. Another plausible mechanism is that EGCG increases prostacyclin (PGI_2) production which is known as a potent vasodilator. EGCG dose-dependently increased PGI_2 production in bovine endothelial cells [36]. Flavan-3-ols from fruits improved indices of MetS in animal models [37], but more studies examining flavan-3-ols from fruits are needed.

The effects of flavan-3-ols on MetS were different by obesity. In the male subjects, flavan-3-ols intake was inversely related to the risk of hypertension only in non-obese men. Among the

Table 4. Adjusted odd radios (ORs), and 95% confidence intervals (CIs) of MetS and MetS components by quintiles of flavan-3-ols intake

	Quintiles					*P*-for trend
	Q1	Q2	Q3	Q4	Q5	
Male[1)]						
Metabolic syndrome						
Model 1	1.00 (ref)	1.12 (0.78, 1.60)	0.92 (0.64, 1.33)	0.86 (0.60, 1.25)	0.86 (0.60, 1.24)	0.314
Model 2	1.00 (ref)	1.02 (0.71, 1.48)	0.85 (0.58, 1.25)	0.83 (0.57, 1.21)	0.84 (0.58, 1.22)	0.449
Model 3	1.00 (ref)	1.06 (0.73, 1.53)	0.90 (0.62, 1.32)	0.88 (0.60, 1.28)	0.92 (0.62, 1.34)	0.701
Components of the metabolic syndrome						
High blood pressure						
Model 1	1.00 (ref)	1.01 (0.73, 1.38)	0.71 (0.51, 0.99)	0.71 (0.51, 0.99)	0.74 (0.54, 1.03)	0.200
Model 2	1.00 (ref)	0.99 (0.72, 1.37)	0.71 (0.50, 0.99)	0.70 (0.50, 0.98)	0.73 (0.52, 1.02)	0.203
Model 3	1.00 (ref)	1.01 (0.73, 1.39)	0.73 (0.52, 1.02)	0.72 (0.51, 1.00)	0.75 (0.53, 1.06)	0.263
Hyperglycaemia						
Model 1	1.00 (ref)	0.97 (0.70, 1.35)	0.85 (0.61, 1.18)	0.81 (0.58, 1.13)	0.90 (0.65, 1.26)	0.852
Model 2	1.00 (ref)	0.89 (0.64, 1.24)	0.79 (0.56, 1.12)	0.76 (0.54, 1.07)	0.85 (0.60, 1.19)	0.813
Model 3	1.00 (ref)	0.89 (0.64, 1.24)	0.78 (0.55, 1.10)	0.75 (0.54, 1.06)	0.84 (0.59, 1.19)	0.835
Abdominal obesity						
Model 1	1.00 (ref)	1.27 (0.79, 2.06)	1.07 (0.66, 1.75)	1.13 (0.70, 1.84)	1.03 (0.64, 1.66)	0.660
Model 2	1.00 (ref)	1.16 (0.71, 1.90)	1.02 (0.62, 1.69)	1.13 (0.69, 1.85)	0.99 (0.61, 1.61)	0.670
Model 3	1.00 (ref)	1.18 (0.72, 1.93)	1.04 (0.62, 1.72)	1.14 (0.69, 1.87)	0.98 (0.59, 1.61)	0.587
Low HDL cholesterol						
Model 1	1.00 (ref)	1.02 (0.75, 1.40)	1.25 (0.91, 1.72)	1.23 (0.90, 1.69)	1.24 (0.90, 1.69)	0.360
Model 2	1.00 (ref)	1.02 (0.74, 1.40)	1.19 (0.86, 1.64)	1.23 (0.89, 1.69)	1.26 (0.91, 1.74)	0.247
Model 3	1.00 (ref)	1.05 (0.76, 1.44)	1.24 (0.90, 1.72)	1.30 (0.94, 1.80)	1.38 (0.99, 1.93)	0.113
Hypertriglyceridaemia						
Model 1	1.00 (ref)	1.18 (0.86, 1.60)	1.06 (0.77, 1.45)	1.15 (0.84, 1.57)	1.05 (0.77, 1.44)	0.808
Model 2	1.00 (ref)	1.10 (0.80, 1.50)	1.00 (0.72, 1.38)	1.12 (0.81, 1.54)	1.03 (0.75, 1.43)	0.950
Model 3	1.00 (ref)	1.11 (0.81, 1.52)	1.03 (0.74, 1.42)	1.14 (0.83, 1.58)	1.04 (0.75, 1.45)	0.895
Female[2)]						
Metabolic syndrome						
Model 1	1.00 (ref)	0.57 (0.41, 0.79)	0.60 (0.43, 0.83)	0.60 (0.43, 0.83)	0.58 (0.42, 0.81)	0.166
Model 2	1.00 (ref)	0.59 (0.43, 0.82)	0.63 (0.45, 0.88)	0.63 (0.45, 0.88)	0.62 (0.44, 0.87)	0.274
Model 3	1.00 (ref)	0.60 (0.43, 0.83)	0.65 (0.46, 0.91)	0.65 (0.46, 0.91)	0.64 (0.45, 0.91)	0.384
Components of the metabolic syndrome						
High blood pressure						
Model 1	1.00 (ref)	0.93 (0.69, 1.25)	0.81 (0.59, 1.10)	0.86 (0.63, 1.17)	0.55 (0.40, 0.76)	0.0003
Model 2	1.00 (ref)	0.94 (0.70, 1.28)	0.85 (0.62, 1.17)	0.90 (0.66, 1.23)	0.57 (0.41, 0.79)	0.0006
Model 3	1.00 (ref)	0.99 (0.73, 1.34)	0.92 (0.67, 1.26)	0.97 (0.70, 1.33)	0.64 (0.45, 0.90)	0.005
Hyperglycaemia						
Model 1	1.00 (ref)	0.82 (0.62, 1.10)	0.86 (0.64, 1.15)	0.87 (0.65, 1.16)	0.79 (0.59, 1.06)	0.334
Model 2	1.00 (ref)	0.83 (0.62, 1.10)	0.89 (0.66, 1.19)	0.90 (0.67, 1.21)	0.82 (0.61, 1.10)	0.428
Model 3	1.00 (ref)	0.84 (0.63, 1.12)	0.90 (0.67, 1.21)	0.92 (0.69, 1.24)	0.85 (0.63, 1.16)	0.616
Abdominal obesity						
Model 1	1.00 (ref)	1.10 (0.75, 1.61)	0.91 (0.61, 1.36)	0.99 (0.67, 1.49)	1.14 (0.77, 1.69)	0.436
Model 2	1.00 (ref)	1.12 (0.76, 1.64)	0.89 (0.60, 1.34)	1.01 (0.68, 1.51)	1.21 (0.81, 1.80)	0.274
Model 3	1.00 (ref)	1.13 (0.76, 1.66)	0.88 (0.59, 1.33)	1.01 (0.67, 1.52)	1.14 (0.75, 1.73)	0.466
Low HDL cholesterol						
Model 1	1.00 (ref)	0.96 (0.75, 1.22)	0.96 (0.75, 1.22)	0.84 (0.66, 1.06)	0.83 (0.66, 1.06)	0.129
Model 2	1.00 (ref)	0.99 (0.78, 1.26)	0.99 (0.78, 1.27)	0.88 (0.69, 1.13)	0.87 (0.68, 1.12)	0.202
Model 3	1.00 (ref)	0.99 (0.78, 1.26)	1.00 (0.78, 1.28)	0.88 (0.69, 1.13)	0.86 (0.67, 1.11)	0.169
Hypertriglyceridaemia						
Model 1	1.00 (ref)	0.72 (0.54, 0.96)	0.69 (0.51, 0.92)	0.71 (0.53, 0.94)	0.73 (0.55, 0.97)	0.442
Model 2	1.00 (ref)	0.73 (0.55, 0.96)	0.70 (0.53, 0.94)	0.71 (0.53, 0.95)	0.74 (0.55, 0.99)	0.475
Model 3	1.00 (ref)	0.73 (0.55, 0.97)	0.71 (0.53, 0.96)	0.72 (0.54, 0.97)	0.75 (0.56, 1.02)	0.612

Q, quintile; HDL, high-density lipoprotein

[1)] Model 1; adjusted for age, body mass index, Model 2; adjusted for all variables in model 1 plus education (elementary, middle, high, college), current smoking (yes/past/no), regular exercise (yes/no), functional food use (yes/no), Model 3; adjusted for all variables in model 2 plus intakes of total energy, fat, and fiber.

[2)] Model 1; adjusted for age, body mass index, Model 2; adjusted for all variables in model 1 plus education (elementary, middle, high, college), current drinking (more than once a month/none), vitamin/mineral supplement use (yes/no), functional food use (yes/no), Model 3; adjusted for all variables in model 2 plus intakes of total energy, fat, fiber, and carbohydrate

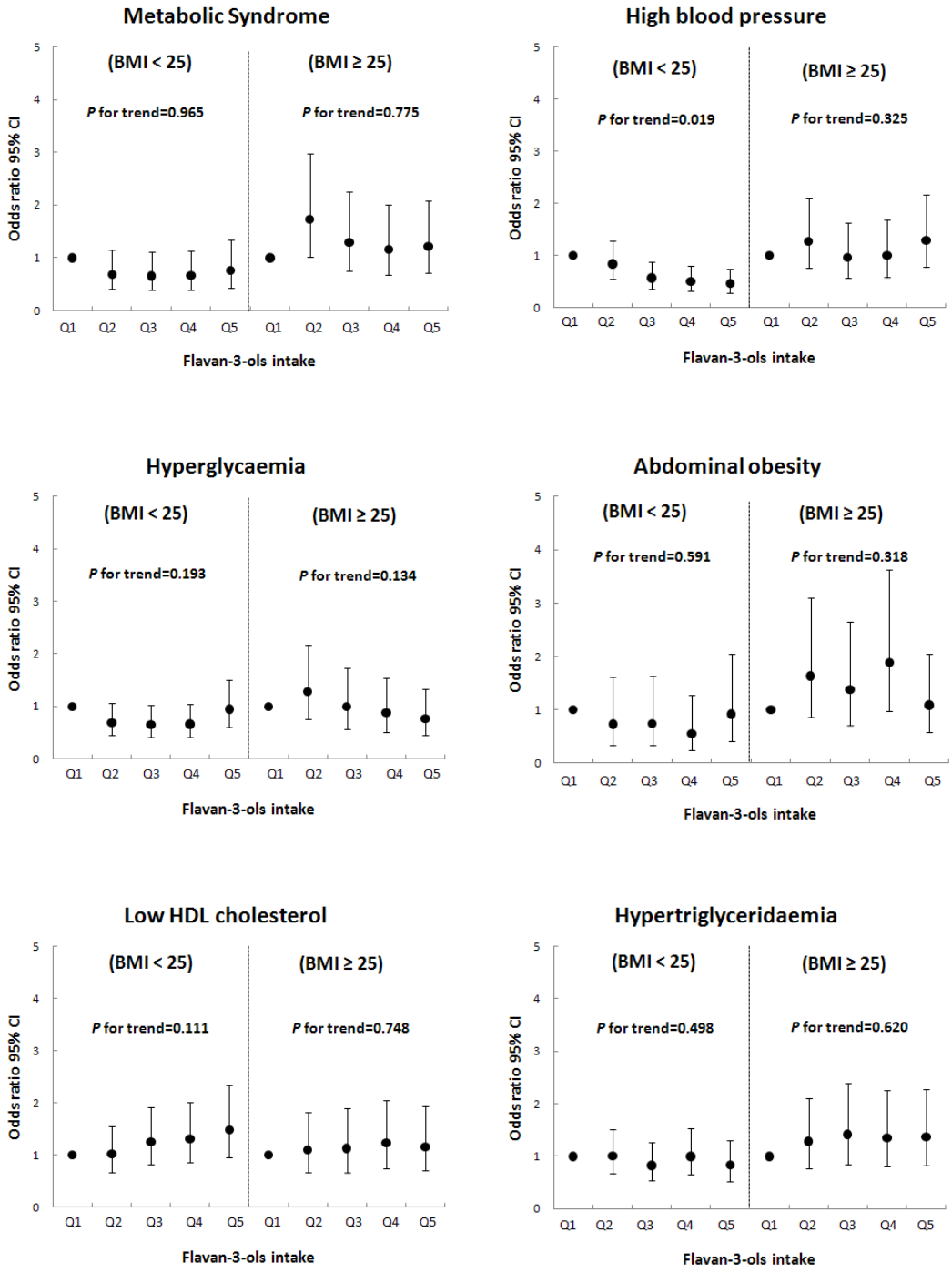

Fig. 1. Adjusted ORs and 95% CIs of MetS and MetS components by quintiles of flavan-3-ols in males according to obesity after adjusting for age, BMI, education (elementary, middle, high, college), current smoking (yes/past/no), regular exercise (yes/no), functional food use (yes/no), and intakes of total energy, fat, and fiber.

female subjects, the beneficial effects of flavan-3-ols on MetS were shown in only obese women. These results suggest that the effects of flavan-3-ols on MetS may be different depending on body fat composition. We could not find a previous study that compared the effects of flavan-3-ols by gender or weight status. Further studies on the effects of flavan-3-ols in normal, overweight, and obese subjects by gender are necessary.

The limitations of this study need to be considered when interpreting the findings. Since it was a cross-sectional study, we cannot conclude a causality of flavonoid intake and MetS. Due to large intra-individual variability in food and nutrient intakes of most people, a one-day 24 hr dietary recall is not

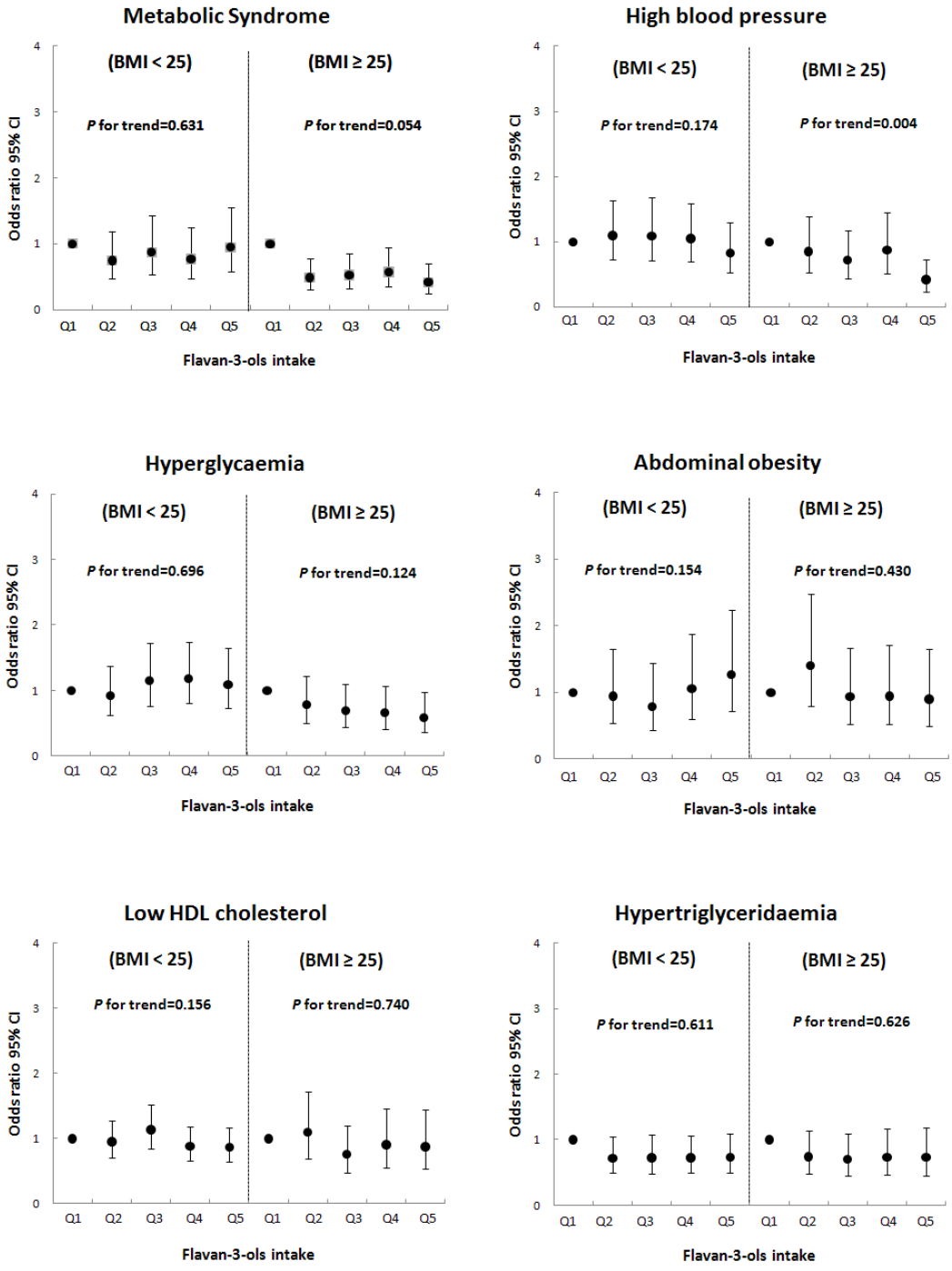

Fig. 2. Adjusted ORs and 95% CIs of MetS and MetS components by quintiles of flavan-3-ols in females according to obesity after adjusting for age, BMI, education (elementary, middle, high, college), current drinking (more than once a month/none), vitamin/mineral supplement use (yes/no), functional food use (yes/no), and intakes of total energy, fat, fiber, and carbohydrate.

sufficient to estimate usual daily flavan-3-ols intake. Since a national nutrient database on flavonoids is not available in Korea, we constructed a flavonoid database using the USDA Flavonoid Database [22], the Japan Functional Food Factor Database [23], and the Rural Development Administration Food Functional Composition Table [24], which covered 85% of plants foods and 96% of the most commonly consumed foods in the 2008 KNHANES. Missing flavan-3-ols values in the database would have decreased the estimation of flavan-3-ols intake. Moreover, there is large variability in the flavonoid content of foods

depending on cultivating season and methods, geographical origin, and processing; thus, the flavonoid contents of foods commonly consumed by Koreans need to be analyzed in further studies.

Despite these limitations, the results of this study suggest that flavan-3-ols intake may have beneficial effects on MetS, particularly by reducing the risk of hypertension. These beneficial effects may be different between non-obese and obese individuals. Further investigations including clinical trials and cohort studies are required to confirm these findings.

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