British Journal of Nutrition (2017), **117**, 315–324
doi:10.1017/S0007114517000046

Soft drink consumption is associated with increased incidence of the metabolic syndrome only in women

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(Submitted 6 August 2016 – Final revision received 9 December 2016 – Accepted 4 January 2017 – First published online 7 Febraury 2017)

Abstract

Prospective studies on the association between soft drink consumption and incident risk of the metabolic syndrome (MetS) have not been carried out in Asians. We explored the sex-specific association between soft drink consumption and incident risk of the MetS in Korean adults during 10 years of follow-up. A total of 5797 subjects who were free of the MetS at baseline were studied. Soft drink consumption was assessed using a semi-quantitative FFQ. Time-dependent Cox proportional hazard model was used to examine hazard ratios (HR) of incidence of the MetS and its components in relation to soft drink consumption. In women, the multivariable-adjusted HR for developing the MetS was 1·8-fold higher in frequent consumers of soft drinks (≥4 servings/week) compared with rare consumers (95 % CI 1·23, 2·64). The adjusted HR for elevated blood pressure increased by 2-fold (95 % CI 1·24, 3·14) and for hypertriacylglycerolaemia by 1·9-fold (95 % CI 1·19, 2·88) in frequent consumers of soft drinks compared with rare consumers. However, in men, there was no association between soft drink consumption and incident risk of the MetS or its components. Frequent soft drink consumption was associated with increased risk of developing the MetS and its components only in middle-aged Korean women, suggesting sex differences for the risk of the MetS related to diet.

Key words: Soft drink consumption: Metabolic syndrome: Sex differences: Korean adults

The consumption of sugar-sweetened beverages (SSB), which generally include soft drinks, fruit drinks and sports drinks, is increasing worldwide in youth and adults[1–3]. Many clinical studies have reported the link between high consumption of SSB and increased obesity and diabetes mellitus[4]. Recent epidemiological studies have shown that SSB consumption is associated with risk of the metabolic syndrome (MetS) in adults[5]. However, most studies on the association between soft drink consumption and the MetS have been performed in Western populations, although the prevalence of the MetS is rapidly increasing among Asian populations[6]. A few studies have been conducted in Asians[6,7], but their cross-sectional designs could not conclude a cause–effect relationship between soft drink consumption and the risk of developing the MetS.

In Korea, dietary habits have gradually changed from a traditional diet to more a Westernised diet including meat and sweet foods such as desserts and sugary beverages[8]. Soft drink consumption is increasing in the Korean population[9,10], although the amount is still lower than that in Western populations. The Korea National Health and Nutrition Examination Survey found that sweetened beverage consumption has doubled from 58 to 101 g over the past 3 years, and soft drinks are the major source of sugar intake from processed foods among Koreans[9]. Although soft drink consumption and the prevalence of the MetS are increasing among Koreans, no prospective study has been carried out on the relationship between soft drink consumption and incidence of the MetS.

Moreover, sex-specific associations between soft drink consumption and risk of incident MetS have not been examined, although sex difference has been suggested to play a role in the risk of chronic diseases including the MetS related to dietary factors[11].

Therefore, we evaluated the sex-specific association between soft drink consumption and risk of incident MetS and its components, considering the influence of multiple lifestyle factors using data from the Korean Genome and Epidemiology Study (KoGES), which is a large community-based cohort study.

Methods

Study subjects

The KoGES, a large-scale, community-based cohort study, was initiated in 2001. Initially, the target population consisted of 10 030 Korean adults aged 40–69 years and living in Ansan (urban) and Ansung (rural) areas. All participants responded

Abbreviations: BP, blood pressure; HR, hazard ratios; MET, metabolic equivalents; MetS, metabolic syndrome; SSB, sugar-sweetened beverages.

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to a baseline examination (2001–2002) with questionnaires including demographic information, socio-economic status, lifestyle, dietary intake, medical history, health examinations and biochemical measurements. Follow-up examinations were performed every 2 years over a 10-year period (2009–2010). The present study was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention (KCDC). Informed written consent was obtained from all participants.

Of the original 10 030 participants, participants without the MetS (*n* 7053) at baseline were included. We excluded participants who refused to participate in follow-up examinations (*n* 747), those who provided insufficient information (*n* 313), those who did not respond to dietary examination (*n* 59) and those who had CVD or cancer (*n* 137). After exclusion, a total of 5797 participants (3027 men and 2770 women) were included in the analysis during the 10-year period. A follow-up rate of 63·3 % was achieved, resulting in 33 269 person-years accrued. The average follow-up period was 5·7 years (68·8 months).

Dietary assessment

Trained dietitians examined dietary intake both at baseline and at the second follow-up examination (2005–2006) using a 103-item, semi-quantitative FFQ. The FFQ was developed and validated by the KCDC[12]. In the FFQ, participants reported the frequency and portion sizes of soft drink consumption during the past year. Soft drink consumption was estimated by the questions 'How often do you consume soft drinks (carbonated beverages, e.g., Cola and Sprite)?' for frequency and 'How much soft drink do you consume at once?' for portion size. The original responses for frequency included none or rarely, once/month, two to three times per month, one to two times per week, three to four times per week, five to six times per week, one to two times per d, three to four times per d and ≥5 times/d. The response options for portion size were as follows: 1/2 cup (100 ml), one cup (200 ml – one serving) and two or more cups (≥400 ml). For analysis, the nine response items were converted to frequency per week, and the serving per week was calculated on the basis of frequency and portion size (mean frequency/week × 0·5 for 1/2 cup, ×1·0 for one cup, ×2·0 for two or more cups) and then categorised into four groups: none or rarely, <1 serving/week, ≥1 serving/week to <4 servings/week and ≥4 servings/week. Nutrient intakes were measured using a database developed by the Rural Development and Administration.

Health examination

Trained professionals conducted a comprehensive health examination under the KCDC protocol. Height and body weight were measured to the nearest 0·1 cm and 0·1 kg, respectively, with no shoes and while wearing light clothing. BMI was defined as weight (kg)/height squared (m^2). Waist circumference (WC) measurements were repeated three times, and then averaged after measuring to the nearest 0·1 cm at the narrowest point between the lowest rib and the right iliac crest. Blood pressure (BP) was measured after participants had rested for more than 5 min in a sitting position (Baumanometer-Standby; W.A. Baum Co. Inc.)[13]. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated at Korotkoff phase I and Korotkoff phase V, respectively. Averaged values of left and right arms were measured a few times at 30-s intervals. Blood samples were collected to measure fasting blood glucose (FBG), TAG and HDL-cholesterol. The blood samples were collected after at least 8 h of fasting at baseline and during every follow-up examination. The concentrations of glucose, TAG and HDL-cholesterol in plasma were enzymatically measured using an autoanalyzer (ADVIA 1650; Bayer HealthCare)[14]. Incidence of the MetS was diagnosed at the follow-up examination by a physician.

Definition of the metabolic syndrome

The MetS was diagnosed using criteria based on the National Cholesterol Education Program Adult Treatment Panel III definition[15]. The MetS is defined as the presence of more than three of the following indicators: (1) abdominal obesity (WC ≥ 90 cm for men or ≥80 cm for women), (2) elevated BP (SBP ≥ 130 mmHg or DBP ≥ 85 mmHg), use of antihypertensive medication, hypertension diagnosis by a physician, (3) high blood glucose (FBG ≥ 5.6 mmol/l), current use of insulin or oral hypoglycaemic medication, diabetes diagnosis by a physician, (4) hypertriacylglycerolaemia (TAG ≥1.7 mmol/l) and (5) low HDL-cholesterol (HDL-cholesterol <1.0 mmol/l in men or <1.3 mmol/l in women).

Other measurements

Demographic characteristics, socio-economic status and lifestyle factors were examined from the baseline questionnaires. Income level was divided into four groups: <1 million KRW, 1–2 million KRW, 2–3 million KRW and ≥3 million KRW. Education level was categorised into three groups: ≤6 years (elementary school level), 7–12 years (middle/high school level) and >12 years (college level) of education. Smoking status was classified as follows: non-smoker, former smoker or current smoker. Alcohol intake was classified as follows: non-drinker, former drinker or current drinker. Physical activity was self-reported by a questionnaire. The questionnaire asked how many hours per day was spent performing physical activities according to its intensity (sedentary, very light, light, moderate, vigorous). Physical activities are presented as metabolic equivalents.

Statistical analysis

All the data were analysed using SAS software version 9.3 (SAS Institute). The results are expressed as percentages (categorical) or as means with their standard deviations (continuous). Differences in baseline characteristics by sex were examined by the χ^2 test for categorical variables or Student's *t* test for continuous variables. Differences in characteristics across soft drink consumption were evaluated by the χ^2 tests or a generalised linear model with *post hoc* Tukey's honestly significant difference test.

Time-dependent Cox proportional hazard models were used as a method of survival analysis to examine the hazard ratios (HR) and 95 % CI for the incident risk of the MetS and its individual components according to soft drink consumption. Survival analysis was performed separately in men and women. In multivariable adjusted models, model 1 was adjusted for age

and model 2 was adjusted for age, income level, education level, alcohol consumption, smoking status, physical activity, BMI, energy intake, percentage of fat from energy, fibre intake and the presence of diseases (diabetes and hypertension). For the selection of variables for adjustment in the multivariable model, potential confounders from the previously published scientific literature were taken into account with the statistical approach, such as stepwise procedures or comparing adjusted and unadjusted effect estimates[16]. Individuals with hypertension or diabetes at baseline were excluded from the survival analysis to examine the risk of incident elevated BP and high blood glucose, respectively.

The proportional hazards assumption was assessed graphically using log–log plots and statistically using Schoenfeld's residuals[17]. No violation of the proportional hazard assumption was detected. Tests for linear trends were performed on the basis of the median value of each category. All P values $< 0{\cdot}05$ were considered statistically significant.

Results

Characteristics of subjects at baseline

Among 5797 subjects, a total of 2129 (1046 men and 1083 women) developed the MetS. Table 1 shows the baseline characteristics of subjects by the presence of the MetS. Subjects with the MetS were older, more likely to be women, to live in the rural areas, to be exercisers, to have lower income and less likely to be educated compared with subjects without the MetS. In addition, subjects with the MetS had higher intakes of energy from carbohydrate as well as lower intakes of energy from fat compared with subjects without the MetS.

Characteristics of subjects according to soft drink consumption

Table 2 shows the characteristics of subjects according to soft drink consumption. Men consuming ≥4 servings/week of soft drinks were younger, more likely to have higher income, more likely to be educated and current smokers compared with rare consumers (none or rarely). Women consuming ≥4 servings/week of soft drinks were younger and more likely to have higher income, more likely to be educated and current drinkers compared with rare consumers. Regardless of sex, frequent consumers had higher intakes of energy, mostly energy from fat, along with lower intakes of energy from carbohydrates compared with rare consumers.

Association between soft drink consumption and incidence of the metabolic syndrome and its individual components

The relative risks for the MetS and its components according to soft drink consumption by sex are shown in Table 3. There was no association between soft drink consumption and risk of the MetS or its components in men. The risk of incident MetS increased significantly in women consuming ≥4 servings/week of soft drinks compared with rare consumers after adjustment for potential confounding factors such as age, income, education, smoking status, alcohol intake, physical activity, BMI, intakes of energy, percentage of fat, fibre intake and the presence of diseases (HR 1·82; 95 % CI 1·24, 2·68, $P_{\text{for trend}} = 0{\cdot}0005$). Women consuming ≥4 servings/week of soft drinks also had greater risks of elevated BP (HR 1·97; 95 % CI 1·23, 3·14, $P_{\text{for trend}} = 0{\cdot}0242$) and hypertriacylglycerolaemia (HR 1·90; 95 % CI 1·22, 2·96, $P_{\text{for trend}} = 0{\cdot}0030$) compared with rare consumers after adjustment for confounders.

The relative risks for the MetS and its components according to soft drink consumption and area of residence are shown in Table 4. There was no association between soft drink

Table 1. Characteristics of the study subjects at baseline (Numbers and percentages (categorised variables); mean values and standard deviations (continuous variables))

	MetS (*n* 2129)		Non-MetS (*n* 3668)		
	n	%	*n*	%	*P*
Age (years)					<0·0001
Mean	52·6		50·0		
SD	8·6		8·6		
No. of subjects (%)					0·0003
Men	1046	49·1	1981	54·0	
Women	1083	50·9	1685	46·0	
Area of residence (%)					<0·0001
Rural area (Ansung)	1211	56·9	1392	38·0	
Urban area (Ansan)	918	43·1	2276	62·1	
Income level (KRW/month) (%)					<0·0001
<1 million	791	37·2	959	26·2	
1–2 million	658	30·9	1121	30·6	
2–3 million	343	16·1	800	21·8	
≥3 million	337	15·8	788	21·5	
Educational level (%)					<0·0001
Elementary school (≤6 years)	732	34·4	854	23·3	
Middle/high school (7–12 years)	1118	52·5	2215	60·4	
College or higher (>12 years)	279	13·1	599	16·3	
Smoking status (%)					0·1520
Non-smokers	1216	57·1	2039	55·6	
Former smokers	323	15·2	628	17·1	
Current smokers	590	27·7	1001	27·3	
Alcohol consumption (%)					0·5305
Non-drinkers	914	42·9	1523	41·5	
Former drinkers	133	6·3	225	6·1	
Current drinkers	1082	50·8	1920	52·3	
Physical activity (MET/d)					<0·0001
Mean	24·4		22·8		
SD	15·4		14·6		
Total energy intake (kJ/d)					0·0715
Mean	8321·9		8175·5		
SD	3255·1		2769·8		
Total energy intake (kcal/d)					
Mean	1989·0		1954·2		
SD	778·5		662·4		
Percentage from energy					
Carbohydrate					<0·0001
Mean	71·9		71·0		
SD	7·5		7·0		
Protein					0·0624
Mean	13·6		13·7		
SD	2·4		2·3		
Fat					<0·0001
Mean	14·5		15·3		
SD	5·5		5·2		
BMI (kg/m^2)	24·9	2·8	23·1	2·7	<0·0001

MetS, metabolic syndrome.

Table 2. Characteristics of the study subjects according to soft drink consumption
(Numbers and percentages (categorised variables); mean values and standard deviations (continuous variables))

	Rarely or never		<1/week		≥1 to <4/week		≥4/week		
	n	%	*n*	%	*n*	%	*n*	%	*P*
Men									
No. of subjects (%)	1060	35	1180	39	671	22	116	3·8	
Age (years)									<0·0001
Mean	53·2[a]		51·2[b]		49·0[c]		48·9[c]		
SD	9·0		8·6		8·1		7·1		
Area of residence (%)									0·0020
Rural area (Ansung)	496	46·8	548	46·4	257	38·3	55	47·4	
Urban area (Ansan)	564	53·2	632	53·6	414	61·7	61	52·6	
Income level (KRW/month) (%)									<0·0001
<1 million	324	32·3	311	26·4	129	19·2	30	25·9	
1–2 million	309	29·2	368	31·2	222	33·1	32	27·6	
2–3 million	210	19·8	225	19·1	164	24·4	19	16·4	
≥3 million	199	18·8	276	23·4	156	23·3	35	30·2	
Educational level (%)									<0·0001
Elementary school (≤6 years)	265	25·0	222	18·8	90	13·4	15	12·9	
Middle/high school (7–12 years)	583	55·0	684	58·0	434	64·7	68	58·6	
College or higher (>12 years)	212	20·0	274	23·2	147	21·9	33	28·5	
Smoking status (%)									0·0017
Non-smokers	189	17·8	277	23·5	122	18·2	18	15·5	
Former smokers	328	30·9	368	31·2	194	28·9	31	26·7	
Current smokers	543	51·2	535	45·3	355	52·9	67	57·8	
Alcohol consumption (%)									0·5757
Non-drinkers	183	17·3	235	19·9	133	19·8	21	18·1	
Former drinkers	109	10·3	103	8·7	68	10·1	13	11·2	
Current drinkers	768	72·5	842	71·4	470	70·0	82	70·7	
Physical activity (MET/d)									0·3516
Mean	24·7		24·8		23·6		25·4		
SD	15·8		15·4		15·3		15·4		
Total energy intake (kJ/d)									<0·0001
Mean	8125·3		8129·5		9133·7		11 003·9		
SD	2640·1		2422·5		2849·3		5029·1		
Total energy intake (kcal/d)									
Mean	1942·9[a]		1943·7[a]		2183·3[b]		2630·9[c]		
SD	631·6		579·3		681·8		1202·1		
Percentage from energy									
Carbohydrate (%)									<0·0001
Mean	71·4[a]		71·3[a]		69·0[b]		67·0[c]		
SD	7·3		6·9		6·4		7·8		
Protein (%)									<0·0001
Mean	13·8[a]		13·5[a]		14·0[b]		14·2[c]		
SD	2·4		2·2		2·3		2·7		
Fat (%)									<0·0001
Mean	14·8[a]		15·2[a]		17·0[b]		18·8[c]		
SD	5·3		5·1		4·6		5·8		
BMI (kg/m^2)									0·0095
Mean	23·4[a]		23·6[a,b]		23·8[b]		23·8[a,b]		
SD	2·7		2·6		2·8		2·3		
Components of the metabolic syndrome									
Waist circumference (cm)									0·1260
Mean	81·4		81·5		81·7		83·0		
SD	6·8		6·8		6·9		6·4		
Systolic blood pressure (mmHg)									0·0086
Mean	120·2[a]		118·8[a,b]		117·5[b]		117·9[a,b]		
SD	16·6		15·9		16·0		14·3		
Diastolic blood pressure (mmHg)									0·1713
Mean	80·3		80·0		79·2		79·4		
SD	10·3		10·5		10·4		10·3		
Fasting blood glucose (mmol/l)									0·0150
Mean	5·1[a]		5·0[b]		5·0[b]		5·0[a,b]		
SD	1·2		0·9		0·8		0·8		
TAG (mmol/l)									0·4696
Mean	1·7		1·6		1·6		1·7		
SD	1·2		1·1		1·1		1·4		
HDL-cholesterol (mmol/l)									0·1198
Mean	1·3		1·3		1·3		1·3		
SD	0·3		0·3		0·3		0·3		
Women									
No. of subjects (%)	1404	51	996	36	315	11	55	2	
Age (years)									<0·0001
Mean	51·3[a]		50·1[b]		48·7[c]		48·7[c]		
SD	8·8		8·4		8·0		8·3		

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Table 2. *Continued*

	Rarely or never		<1/week		≥1 to <4/week		≥4/week		
	n	%	*n*	%	*n*	%	*n*	%	*P*
Area of residence (%)									0·0001
Rural area (Ansung)	613	43·7	479	48·1	119	37·8	36	65·5	
Urban area (Ansan)	791	56·3	517	51·9	196	62·2	19	34·6	
Income level (%)									0·0050
<1 million	499	35·5	337	33·8	80	25·4	22	40·0	
1–2 million	432	30·8	306	30·7	93	29·5	17	30·9	
2–3 million	251	17·9	190	19·1	80	25·4	4	7·3	
≥3 million	222	15·8	163	16·4	62	19·7	12	21·8	
Educational level (KRW/month) (%)									0·0175
Elementary school (≤6 years)	531	37·8	361	36·2	84	26·7	18	32·7	
Middle/high school (7–12 years)	771	54·9	555	55·7	207	65·7	31	56·4	
College or higher (>12 years)	102	7·3	80	8·0	24	7·6	6	10·9	
Smoking status (%)									
Non-smokers	1332	94·9	964	96·8	301	95·6	52	94·6	0·1932
Former smokers	15	1·1	10	1·0	5	1·6	0	0·0	
Current smokers	57	4·1	22	2·2	9	2·9	3	5·5	
Alcohol consumption (%)									<0·0001
Non-drinkers	992	70·7	671	67·4	173	54·9	29	52·7	
Former drinkers	36	2·6	17	1·7	11	3·5	1	1·8	
Current drinkers	376	26·8	308	30·9	131	41·6	25	45·5	
Physical activity (MET/d)									0·0009
Mean	21·9[a]		23·0[a]		19·6[b]		25·5[a]		
SD	13·8		14·6		13·3		18·7		
Total energy intake (kJ/d)									<0·0001
Mean	7740·4		7937.0		8744·7		10 108·5		
SD	3092·0		2962·2		2987·4		4217·5		
Total energy intake (kcal/d)									
Mean	1850·5[a]		1897·6[a]		2090·2[b]		2416·4[c]		
SD	739·1		708·6		714·4		1008·0		
Percentage from energy									
Carbohydrate (%)									<0·0001
Mean	72·6[a]		72·3[a]		69·9[b]		68·2[b]		
SD	7·2		7·1		6·4		10·6		
Protein (%)									<0·0001
Mean	13·6[a]		13·5[a]		13·9[b]		14·2[b]		
SD	2·3		2·3		2·1		3·4		
Fat (%)									<0·0001
Mean	13·7[a]		14·2[a]		16·2[b]		17·6[b]		
SD	5·3		5·2		4·8		7·7		
BMI (kg/m^2)									0·0175
Mean	23·8[a]		24·1[a,b]		24·3[a]		24·6[a,b]		
SD	3·0		3·0		3·1		2·9		
Component of the metabolic syndrome									
Waist circumference (cm)									0·1359
Mean	78·0		78·4		78·7		80·3		
SD	8·5		8·9		9·0		8·6		
Systolic blood pressure (mmHg)									0·0546
Mean	115·6		114·5		113·3		118·2		
SD	17·8		16·5		16·3		21·2		
Diastolic blood pressure (mmHg)									0·1413
Mean	75·8		75·2		75·1		77·9		
SD	10·8		10·3		10·6		11·6		
Fasting blood glucose (mmol/l)									0·1088
Mean	4·8		4·8		4·9		4·9		
SD	0·7		0·5		1·0		1·5		
TAG (mmol/l)									0·4205
Mean	1·2		1·2		1·2		1·1		
SD	0·5		0·7		0·6		0·5		
HDL-cholesterol (mmol/l)									0·5610
Mean	1·4		1·4		1·4		1·4		
SD	0·3		0·3		0·3		0·2		

[a,b,c] Multiple comparisons are given by *post hoc* Tukey's HSD test ($P<0·05$).

consumption and risk of the MetS or its components either in the rural area or in the urban area in men (data not shown). In addition, in women living in the rural area, there was no association between soft drink consumption and risk of the MetS and its components. However, in women living in the urban area, the risk of incident MetS increased significantly with consuming ≥4 servings/week of soft drinks compared with rare consumers after adjustment for potential confounding factors such as age, income, education, smoking status, alcohol intake, physical activity, BMI, intakes of energy, percentage of fat, fibre intake and the presence of diseases (HR 1·71; 95% CI 0·84, 3·47, $P_{\text{for trend}}=0·0021$). Women living in the urban area and

Table 3. Incidence of the metabolic syndrome (MetS) and its components according to soft drink consumption by sex* (Hazard ratios (HR) and 95 % confidence intervals)

	Rarely or never	<1/week		≥1/week to <4/week		≥4/week			
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$	$P_{for\ interaction}$
Total									
MetS	1·00	0·95	0·87, 1·05	1·18	1·04, 1·34	1·35	1·06, 1·71	0·5123	0·1041
Abdominal obesity	1·00	0·91	0·81, 1·02	1·11	0·96, 1·29	1·17	0·86, 1·60	0·3434	0·5079
Elevated blood pressure†	1·00	0·93	0·83, 1·04	1·28	1·12, 1·48	1·55	1·18, 2·03	0·0414	0·3769
High fasting blood glucose‡	1·00	0·86	0·78, 0·95	1·09	0·96, 1·24	1·20	0·94, 1·53	0·8967	0·8193
High TAG	1·00	0·89	0·80, 0·98	1·26	1·10, 1·43	1·20	0·91, 1·60	0·8682	0·5107
Low HDL–cholesterol	1·00	0·90	0·83, 0·98	1·05	0·94, 1·17	1·17	0·96, 1·44	0·9013	0·8797
Men									
MetS									
n	1060		1180		671		116		
No. of cases	385		382		234		45		
Model 1	1·00	0·81	0·70, 0·93	0·99	0·84, 1·17	1·08	0·79, 1·47	0·9808	
Model 2	1·00	0·86	0·74, 0·99	0·98	0·83, 1·16	1·09	0·79, 1·49	0·9531	
Abdominal obesity									
n	1127		1237		665		109		
No. of cases	278		273		167		28		
Model 1	1·00	0·84	0·71, 0·99	1·08	0·89, 1·31	1·11	0·75, 1·65	0·5280	
Model 2	1·00	0·87	0·73, 1·03	1·07	0·87, 1·31	1·11	0·74, 1·65	0·6012	
Elevated blood pressure									
n	710		813		510		89		
No. of cases	268		311		204		40		
Model 1†	1·00	0·97	0·82, 1·14	1·22	1·01, 1·47	1·36	0·98, 1·90	0·0159	
Model 2†	1·00	0·98	0·83, 1·16	1·22	1·01, 1·48	1·37	0·98, 1·93	0·0175	
High fasting blood glucose									
n	1042		1223		678		125		
No. of cases	416		443		264		58		
Model 1‡	1·00	0·80	0·70, 0·91	0·97	0·83, 1·14	1·20	0·91, 1·59	0·7706	
Model 2‡	1·00	0·80	0·70, 0·92	0·97	0·82, 1·13	1·12	0·85, 1·49	0·9527	
High TAG									
n	767		849		511		88		
No. of cases	298		292		223		33		
Model 1	1·00	0·76	0·64, 0·89	1·10	0·92, 1·31	0·84	0·58, 1·20	0·8361	
Model 2	1·00	0·78	0·66, 0·92	1·11	0·93, 1·33	0·90	0·62, 1·30	0·6592	
Low HDL-cholesterol									
n	1092		1127		658		123		
No. of cases	541		540		327		66		
Model 1	1·00	0·88	0·78, 0·99	1·03	0·89, 1·18	1·13	0·87, 1·46	0·5754	
Model 2	1·00	0·88	0·78, 0·99	1·02	0·89, 1·18	1·14	0·87, 1·18	0·6259	
Women									
MetS									
n	1404		996		315		55		
No. of cases	531		386		138		28		
Model 1	1·00	1·04	0·91, 1·18	1·40	1·16, 1·69	2·07	1·42, 3·03	<0·0001	
Model 2	1·00	1·01	0·89, 1·16	1·39	1·15, 1·69	1·82	1·24, 2·68	0·0005	
Abdominal obesity									
n	993		646		206		29		
No. of cases	405		254		82		15		
Model 1	1·00	0·96	0·82, 1·12	1·11	0·87, 1·41	1·78	1·06, 2·99	0·2532	
Model 2	1·00	0·95	0·81, 1·11	1·12	0·88, 1·43	1·32	0·78, 2·23	0·4387	
Elevated blood pressure									
n	1223		898		303		45		
No. of cases	382		253		112		19		
Model 1†	1·00	0·90	0·77, 1·06	1·37	1·11, 1·70	2·24	1·41, 3·56	0·0047	
Model 2†	1·00	0·88	0·75, 1·04	1·32	1·07, 1·64	1·97	1·23, 3·14	0·0242	
High fasting blood glucose									
n	1809		1319		407		57		
No. of cases	458		317		120		16		
Model 1‡	1·00	0·93	0·80, 1·07	1·33	1·08, 1·62	1·37	0·83, 2·26	0·0584	
Model 2‡	1·00	0·90	0·78, 1·04	1·23	1·00, 1·51	1·13	0·68, 1·86	0·3602	
High TAG									
n	1484		1063		331		51		
No. of cases	483		342		122		21		
Model 1	1·00	0·96	0·84, 1·11	1·33	1·09, 1·63	1·74	1·12, 2·69	0·0096	
Model 2	1·00	0·97	0·84, 1·11	1·40	1·14, 1·72	1·90	1·22, 2·96	0·0030	

Table 3. *Continued*

	Rarely or never	<1/week		≥1/week to <4/week		≥4/week			
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$	$P_{for\ interaction}$
Low HDL-cholesterol									
n	1120	672		261		58			
No. of cases	772	456		172		39			
Model 1	1·00	0·91	0·81, 1·02	1·02	0·87, 1·21	1·21	0·88, 1·67	0·8877	
Model 2	1·00	0·92	0·82, 1·03	1·08	0·91, 1·28	1·27	0·92, 1·28	0·4711	

* Model 1 was adjusted for age. Model 2 was adjusted for age, income level, education level, alcohol consumption, smoking status, physical activity, BMI, energy intake, percentage of fat, fibre intake and the presence of diseases.
† Excluded those who have hypertension at baseline from the analysis.
‡ Excluded those who have diabetes mellitus at baseline from the analysis.

consuming ≥4 servings/week of soft drinks also had greater risks of hypertriacylglycerolaemia (HR 1·76; 95 % CI 0·83, 3·74, $P_{for\ trend} = 0·0004$) compared with rare consumers after adjustment for confounders.

Discussion

We found that soft drink consumption was associated with a higher risk of the MetS only in women. In women, frequent consumption of soft drinks (≥4 servings/week) increased the risk of incident MetS by 80 % compared with rare consumers after adjustment for potential confounders. Frequent consumption of soft drinks also significantly increased the risks of incident elevated BP and hypertriacylglycerolaemia in women. In particular, a strong association between soft drink consumption and risk of the MetS or hypertriacylglycerolaemia was shown in women living in the urban area. However, in men, no association was found between soft drink consumption and risk of incident MetS or its components regardless of area of residence. These findings suggest sex differences in the associations between dietary factors and metabolic risks.

Our results are consistent with previous findings. In the Framingham Heart study, the incidence of the MetS was 44 % higher among middle-aged adults who consumed ≥1 soft drink/d compared with those who consumed <1 soft drink/d during 4 years of follow-up. In addition, frequent consumers of soft drinks had 25–32 % higher risk of incidence of abdominal obesity, impaired fasting glucose, hypertriacylglycerolaemia and low HDL-cholesterol compared with infrequent consumers[18]. Among young university graduates, participants in the highest quintile of SSB consumption had a 2-fold higher risk of developing the MetS compared with those in the lowest quintile during 6 years of follow-up. Increased intake of SSB was also associated with a greater risk of high BP, obesity and hypertriacylglycerolaemia[5].

Several mechanisms can explain the higher risk of the MetS associated with greater consumption of soft drinks. First, high consumption of added nutritive sweeteners such as high-fructose maize syrup (the primary sweetener in soft drinks) may be associated with metabolic traits. High-fructose maize syrup used in beverages contains about 55 % fructose. A human study showed that fructose over-feeding for 6 d led to stimulation of hepatic *de novo* lipogenesis and to a substantial increase in plasma TAG in young subjects[19]. High fructose intake in the form of added sugars (≥74 g/d) was associated with a 26–77 % higher risk of elevated BP in US adults[20].

The mechanism by which fructose causes elevated BP or hyperlipidaemia is not fully understood, but some possibilities have been suggested. Increased sympathetic nervous system activity, possibly triggered by insulin resistance, could lead to an increase in BP[21,22]. Another possibility includes increased activity of the renin–angiotensin system. A rat study showed that BP and TAG levels were significantly greater in fructose-fed rats than in control rats. The level of angiotensin II type 1 receptor mRNA was significantly higher in adipose tissue from fructose-fed rats than in tissue from control rats[23].

Second, dietary habits and lifestyle behaviours among individuals consuming soft drinks might be associated with the risk of the MetS. Frequent consumers of soft drinks had dietary habits characterised by greater intakes of energy content and fat with low intakes of dietary fibre, as well as unhealthy lifestyles including smoking and alcohol consumption. Although these dietary and lifestyle factors are adjusted for in the analysis, other factors not adjusted for in the present analysis, such as dietary pattern, might influence the incidence of the MetS and its individual components. Data from the National Health and Nutrition Examination Survey showed that adults who ate more snacks, high-fat foods and fast food had a higher possibility of drinking energetically sweetened beverages such as soda, fruit drinks and coffee[24].

Of particular interest, soft drink consumption was positively associated with the incident risk of the MetS, hypertriacylglycerolaemia and elevated BP in women only. Similarly, frequent consumption of soft drinks was related to a higher prevalence of the MetS, elevated BP and hypertriacylglycerolaemia in women only[6]. Sex might be a factor in determining the degree of association with the MetS or its components, particularly with hypertension and dyslipidaemia[25]. The sex difference may be associated with sex hormones[26]. Sex hormones such as oestrogen might participate in the activation pathway of protein kinase C, which might influence vascular smooth muscle contraction or relaxation by increasing nitric oxide release[27]. Oestrogen also affects the renin–angiotensin system, which might be regulated differently in men and women, with endogenous oestrogen suppressing angiotensin receptor type 1 expression and angiotensinogen synthesis[28]. Besides, oestrogen enhances fat transport and increases the levels of TAG and lipoprotein in the blood, whereas androgen has the opposite effect of oestrogen[29]. Therefore, lipid levels

Table 4. Incidence of the metabolic syndrome (MetS) and its components according to soft drink consumption by area of residence in women* (Hazard ratios (HR) and 95 % confidence intervals)

	Rarely or never	<1/week		≥1/week to <4/week		≥4/week		
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$
Rural area (Ansung)								
MetS								
n	613		479		119		36	
No. of cases	333		249		70		20	
Model 1	1·00	1·22	1·06, 1·40	1·52	1·19, 1·94	1·97	1·26, 3·08	0·1778
Model 2	1·00	1·05	0·90, 1·23	1·26	0·98, 1·63	1·79	1·14, 2·82	0·2234
Abdominal obesity								
n	333		227		51		14	
No. of cases	217		129		34		10	
Model 1	1·00	1·61	1·33, 1·95	2·26	1·60, 3·19	2·51	1·34, 4·70	0·6594
Model 2	1·00	1·40	1·13, 1·74	1·88	1·31, 2·69	2·27	1·20, 4·29	0·3007
Elevated blood pressure								
n	488		424		119		28	
No. of cases	229		170		62		15	
Model 1†	1·00	0·78	0·66, 0·93	1·10	0·85, 1·43	1·76	1·05, 2·94	0·3181
Model 2†	1·00	1·03	0·89, 1·20	1·24	0·98, 1·57	1·59	1·07, 2·36	0·8503
High fasting blood glucose								
n	892		732		187		39	
No. of cases	293		204		67		11	
Model 1‡	1·00	0·62	0·53, 0·72	0·86	0·67, 1·10	0·77	0·43, 1·40	0·6593
Model 2‡	1·00	0·73	0·61, 0·86	0·97	0·75, 1·25	0·85	0·47, 1·55	0·4517
High TAG								
n	726		582		142		34	
No. of cases	267		196		51		14	
Model 1	1·00	0·84	0·71, 0·98	0·97	0·73, 1·29	1·32	0·77, 2·24	0·7799
Model 2	1·00	0·90	0·76, 1·07	1·08	0·80, 1·46	1·56	0·91, 2·68	0·3870
Low HDL-cholesterol								
n	557		347		107		36	
No. of cases	426		247		80		26	
Model 1	1·00	1·32	1·15, 1·51	1·57	1·25, 1·97	1·77	1·20, 2·62	0·6176
Model 2	1·00	1·03	0·89, 1·20	1·24	0·98, 1·57	1·59	1·07, 2·36	0·8564
Urban area (Ansan)								
MetS								
n	791		517		196		19	
No. of cases	198		137		68		8	
Model 1	1·00	0·88	0·73, 1·05	1·34	1·04, 1·72	1·73	0·86, 2·48	<0·0001
Model 2	1·00	1·10	0·90, 1·35	1·61	1·24, 2·10	1·71	0·84, 3·47	0·0021
Abdominal obesity								
n	660		419		155		15	
No. of cases	188		125		48		5	
Model 1	1·00	1·50	1·23, 1·82	1·72	1·28, 2·32	2·09	0·87, 5·04	0·0749
Model 2	1·00	1·54	1·24, 1·92	1·77	1·29, 2·42	1·44	0·59, 3·51	0·3242
Elevated blood pressure								
n	735		474		184		17	
No. of cases	153		83		50		4	
Model 1†	1·00	0·59	0·46, 0·74	1·05	0·79, 1·41	1·00	0·37, 2·67	0·0345
Model 2†	1·00	1·11	0·95, 1·31	1·29	1·03, 1·61	1·38	0·80, 2·40	0·4012
High fasting blood glucose								
n	917		587		220		18	
No. of cases	165		113		53		5	
Model 1‡	1·00	0·61	0·50, 0·75	0·87	0·66, 1·15	0·91	0·38, 2·19	0·0024
Model 2‡	1·00	0·82	0·66, 1·01	1·05	0·78, 1·40	1·09	0·45, 2·65	0·0232
High TAG								
n	758		481		189		17	
No. of cases	216		146		71		7	
Model 1	1·00	0·80	0·67, 0·95	1·17	0·92, 1·50	1·41	0·67, 2·97	0·0005
Model 2	1·00	0·95	0·78, 1·15	1·38	1·06, 1·78	1·76	0·83, 3·73	0·0004
Low HDL-cholesterol								
n	563		325		154		22	
No. of cases	346		209		92		13	
Model 1	1·00	1·29	1·11, 1·49	1·42	1·14, 1·76	1·66	0·96, 2·87	0·6799
Model 2	1·00	1·11	0·95, 1·31	1·29	1·03, 1·61	1·38	0·80, 2·40	0·4094

* Model 1 was adjusted for age. Model 2 was adjusted for age, income level, education level, alcohol consumption, smoking status, physical activity, BMI, energy intake, % fat, fibre intake and the presence of diseases.
† Excluded those who have hypertension at baseline from the analysis.
‡ Excluded those who have diabetes mellitus at baseline from the analysis.

could be differently regulated between men and women. The levels of TAG and lipoproteins appear to be more sensitive to perturbations in dietary carbohydrates or fats in women than in men. Li *et al.* reported that a low-fat, high-carbohydrate diet for 6 weeks *v.* an average American diet increased TAG levels only in women[30]. In the present study, changes in lipid metabolism caused by sex hormones might have contributed to a greater association between soft drink consumption and hypertriacylglycerolaemia/MetS in women.

A positive association between soft drink consumption and risk of the MetS or hypertriacylglycerolaemia was stronger in women living in the urban area than those living in the rural area. The urban/rural differences may be due to the differences in dietary habits, physical activity and education of subjects[31]. If women living in the urban area had a healthy, balanced diet and a healthy lifestyle compared with those living in the rural area, frequent consumption of soft drinks as an unhealthy dietary habit would have had a greater impact on the MetS/hypertriacylglycerolaemia in women living in the urban area.

To the best of our knowledge, this is the first prospective study to investigate associations between soft drink consumption and incident MetS or its components in an Asian population. The study identified sex differences in the association between soft drink intake and risk of the MetS using data from a large-scale, cohort study, and the analysis considered multiple confounders including lifestyle factors and nutrient intakes. Despite these strengths, this study has some limitations. Confounding factors such as lifestyle or dietary patterns that were not considered in the analysis might affect the metabolic risks associated with soft drink consumption. The present study did not examine the consumption of diet soft drinks, which might have affected the metabolic risks. Our findings cannot be generalised to other age groups because the cohort comprised middle-aged Korean adults.

In conclusion, frequent soft drink consumption is associated with increased risk of developing the MetS and its components such as elevated BP and hypertriacylglycerolaemia in middle-aged Korean women living in the urban area. Further studies are required to determine the effect of sex on the metabolic risks related to dietary factors and to enable the most appropriate dietary intervention by sex for the prevention and management of the MetS.

Acknowledgements

Epidemiological data used in this study were obtained from the KoGES (4851–302) of Korea Centers for Disease Control and Prevention, Republic of Korea.

This study was supported by the Basic Science Research Program of the National Research Foundation of Korea (NRF), funded by the Ministry of Education, Science and Technology (NRF2016R1D1A1B03931307). The NRF had no role in the study design, data analysis or writing of this article.

Y. K. helped with data acquisition, analysis and interpretation of the data and wrote the paper; J. K. contributed to the study design, analysis and interpretation of the data, wrote the paper and had primary responsibility for the final content. All the authors read and approved the final manuscript.

The authors declare that they have no competing interests.

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British Journal of Nutrition