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ORIGINAL ARTICLE

Eating frequency is inversely associated with blood pressure and hypertension in Korean adults: analysis of the Third Korean National Health and Nutrition Examination Survey

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BACKGROUND/OBJECTIVES: A lower eating frequency (EF) has been suggested to be important in the development of cardiovascular risk factors such as obesity and hyperlipidemia. However, the association between EF and blood pressure (BP) remains unclear.

SUBJECTS/METHODS: The aim of this study was to explore the association of EF with BP and hypertension after adjusting for confounding variables, including body mass index (BMI) and waist circumference (WC). This cross-sectional study used data from the Third Korean National Health and Nutrition Examination Survey. A total of 4625 subjects aged ⩾19 years were included. To explore the association of EF with BP and hypertension, we performed multiple linear regression analyses and multiple logistic regression analyses for survey design, respectively.

RESULTS: EF was inversely associated with systolic BP (SBP) and diastolic BP (DBP). As EF increased from ⩽2 to 3, 4 and ⩾5 times per day, estimated adjusted means of both SBP and DBP decreased, showing a significant linear trend independent of obesity (SBP: 120.66, 120.23, 119.18 and 117.92 mm Hg, respectively; $P<0.001$; DBP: 78.36, 77.78, 77.25 and 76.50 mm Hg, respectively; $P=0.004$). The inverse association between EF and hypertension was gradually attenuated and significant after adjustment for confounding variables including BMI and WC ($P=0.040$).

CONCLUSIONS: This study suggests that lower EF is significantly associated with higher BP, which may be partially mediated by the effect of central obesity. Further prospective studies are needed to verify this causal relationship.

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INTRODUCTION

Hypertension, an important public health problem worldwide owing to its high prevalence, is a major preventable risk factor for cardiovascular disease and chronic renal disease.[1–5] Lifestyle modification is an effective tool for lowering blood pressure (BP).[1] Diet is a major lifestyle factor contributing to the development of hypertension and is modifiable if properly managed and educated.[1,6] The Dietary Approaches to Stop Hypertension (DASH) diet, which emphasizes fruit, vegetable and low-fat dairy product consumption and reduced sodium intake, is recommended to lower BP.[1,7,8] Two key aspects of dietary behavior are considered modifiable: what we eat and how often we eat.[9] Eating frequency (EF) is often reported as the sum of the number of meals and snacks consumed per day;[9,10] it is thought to be important in the development of obesity and other cardiometabolic risk factors. Increased EF was related to improved cholesterol profiles in some studies,[11–13] and a recent study reported that decreased EF is indicative of greater 10-year increases in body mass index (BMI) and waist circumference (WC).[14] Another cross-sectional study suggested that higher EF is associated with lower WC and reduced cardiometabolic risk factors, including fasting glucose, total cholesterol, low-density lipoprotein cholesterol and triglycerides, and that these associations are mediated by WC.[15]

As obesity and abdominal obesity are well-established risk factors for high BP,[16,17] EF is likely associated with BP; however, this association has not been extensively explored. A randomized crossover trial found that eating three meals per day led to approximately 6% lower systolic BP (SBP) and diastolic BP (DBP) after 8 weeks compared with consuming all daily energy needs in one large meal each day.[18] Another study investigating the relationship between meal frequency and plasma cholesterol level reported that the age- and sex-adjusted mean SBP for subjects who consumed four or more meals per day was significantly lower than that for those who consumed one or two meals per day.[12] However, no association between EF and BP was observed in other studies.[15,19,20]

In this study, we aimed to investigate the association of EF with BP and hypertension after adjusting for confounding variables, including BMI and WC, in a representative sample of Korean adults.

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SUBJECTS AND METHODS

Study population

This cross-sectional study was based on data from the Third Korean National Health and Nutrition Examination Survey (KNHANES III) conducted by the Korean Ministry of Health and Welfare in 2005. KNHANES III was a nationwide representative study for non-institutionalized civilians in the Republic of Korea using a stratified, multistage clustered probability sampling design.[21,22] Of the 9004 participants of the Nutrition Survey, we excluded 2420 subjects aged younger than 19 years. Subjects without records on current use of hypertension medications, data on BP and data on frequency of meals or snacks per day were also excluded. Of the remaining 4900 subjects, we excluded the 14 participants who answered that their meal frequency was zero and those with incomplete data on potential confounding variables including smoking status, smoking amount (pack-years), alcohol consumption frequency, nutrient intake per day and anthropometric values such as WC and BMI. Another 85 women who were pregnant or had missing data on pregnancy were also excluded. The final analysis included 4625 subjects. All participants signed an informed consent form.

Measurement of variables

Measurement of BP and confirmation of hypertension. BP was measured by trained medical staff using a standardized technique. A cuff size appropriate for the subject's arm circumference was chosen, and the subject sat in a chair for 5 min to relax before BP measurement. A sphygmomanometer (Baumanometer; WA Baum Co. Inc., Copiague, NY, USA) was used to measure BP three times. The average of the second and third BP measurements was used to identify hypertension,[1] defined by SBP $\geqslant$140 mm Hg or DBP $\geqslant$90 mm Hg according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) classification;[1] patients who reported taking antihypertensive medications were also considered to have hypertension.

EF and dietary measurements. Three measures of frequency of eating occasions were investigated: meal frequency, snack frequency and EF, which was defined as the sum of the number of meals and snacks eaten per day. Meal frequency was determined using the question 'Did you eat breakfast/lunch/dinner yesterday?' Snack frequency was estimated by the question 'How many times do you eat snacks per day?' The subjects were also asked about the types of snacks eaten frequently. The words 'meals' and 'snacks' were not further defined for the participants. Meal frequency was categorized as one, two and three meals per day; snack frequency was categorized as none, one, two and three or more snacks per day; and EF was categorized as two or less, three, four and five or more per day. Categories were determined by considering the distribution of each measure in the study population, ensuring adequate numbers in each group. Daily energy and nutrient intake, including intake of total calories (kcal per day), sodium (mg per day), potassium (mg per day) and calcium (mg per day), were assessed using a 24-h recall method by a well-trained nutritionist or interviewer for the Nutrition Survey. The 24-h recall method is a cost-effective and applicable dietary assessment for characterizing the average intake of a population.[23,24] The nutrient adequacy ratio (NAR) was calculated for each of nine nutrients (protein, calcium, phosphorus, iron, vitamin A, thiamin, riboflavin, niacin and vitamin C) using the formula: NAR = The subject's daily intake of a nutrient/recommended nutrition intake of that nutrient. The nine NAR values were then averaged to yield the mean adequacy ratio (MAR), which is an index of the overall diet quality.[25] The MAR provides an index of the overall diet quality. A high MAR score implies high-quality diet.[26]

Other potential confounding variables. Trained medical staff measured height and weight by 0.1 cm and 0.1 kg, respectively, following standardized procedures at mobile examination centers. BMI was calculated as weight divided by height squared (kg/m^2), and WC was measured, according to the World Health Organization guideline, at the midpoint between the inferior margin of the last rib and the crest of the ilium in a horizontal plane.[27] Data on age; sex; current medications for hypertension, diabetes and dyslipidemia; smoking status; smoking amount (pack-years); usual alcohol consumption frequency (per month); stress levels (rare, a little, much, too much); sleep sufficiency (very much sufficient, fairly sufficient, somewhat insufficient, definitely insufficient); exercise frequency (per week); and physical activity assessed by the score on the International Physical Activity Questionnaire (IPAQ)[28] were acquired by the Health Interview Survey. On the basis of the smoking status, participants were classified as never smokers, past smokers (had smoked $\geqslant$100 cigarettes during their lifetime but were not smoking currently) and current smokers (had smoked $\geqslant$100 cigarettes and were still smoking). Pack-years of smoking were calculated using answers to the questions about tobacco use, including assessment of the usual number of cigarettes smoked daily and the smoking duration.

Statistical analysis

All statistical analyses were conducted with Stata version 10.0 (Stata Corp. LP, College Station, TX, USA) using the survey data commands (svy) to account for cluster effects and sampling weights. All results are presented as weighted values. The baseline characteristics of the participants were compared according to EF group using the complex sample general linear model for continuous variables and Pearson's χ^2 test with Rao–Scott correction using F statistic for categorical variables. The nutritional characteristics of each EF group were presented as mean and s.e., and *P*-value for trend was obtained using complex sample general linear model after adjustment for age and sex. We explored the associations of EF, meal frequency and snack frequency with SBP and DBP using multiple linear regression analyses for survey design. We estimated the adjusted means and 95% confidence intervals (CIs) of SBP and DBP in each EF group and tested for linear trend across EF groups after adjusting for potential confounding variables including age, sex, smoking status, smoking amount (pack-years), usual alcohol consumption frequency (per month), exercise frequency (per week), IPAQ (metabolic equivalent of task-minutes per week), total calorie intake (kcal per day), sodium intake (mg per day), potassium intake (mg per day), calcium intake (mg per day), hypertension medication (yes or no), sleep sufficiency, stress levels, MAR, BMI and WC. In addition, the analyses were repeated, excluding subjects who reported taking medications for hypertension, diabetes or dyslipidemia. To investigate the association of EF, meal frequency and snack frequency with hypertension, we constructed three models and conducted analyses using the multiple logistic regression model for survey design to estimate the odds ratios (ORs) and 95% CIs for the presence of hypertension after adjusting for potential confounding variables. Model 1 was adjusted for age and sex. Smoking status, smoking amount, usual alcohol consumption frequency, exercise frequency, IPAQ, total calorie intake, sodium intake, potassium intake, calcium intake, sleep sufficiency, stress levels and MAR were added in model 2. To examine whether any associations were mediated by obesity, model 3 included additional adjustments for BMI and WC. Multiple logistic regression analyses were repeated for the subgroups stratified by the presence of abdominal obesity (WC $\geqslant$85 cm in women and $\geqslant$90 cm in men),[29] and by the diet quality index using the median of MAR as the cut-off point. Logistic regression was used in the tests for trend. We tested the interaction between WC and the categories of EF, snack frequency and meal frequency by including the interaction terms in the multiple logistic regression models. The same methods were also used to test interactions between diet quality and the categories of EF, snack frequency and meal frequency. All statistical significance was defined by a two-tailed *P*-value $<$0.05.

RESULTS

Baseline characteristics

EF was classified as 2 or less (9.28%), 3 (39.57%), 4 (35.37%) or 5 or more (15.78%) times per day. The (EF = 3) group had the highest mean SBP and DBP, whereas the high EF group (EF $\geqslant$5) had the lowest mean SBP and DBP, with significant differences between groups (120.27 ± 0.51 and 78.27 ± 0.32 mm Hg vs 114.92 ± 0.66 and 75.37 ± 0.49 mm Hg, $P<0.001$). Similar results were also observed when subjects taking antihypertensive medication were excluded. Hypertension prevalence was significantly lower in the high EF group (EF $\geqslant$5) than in the lower EF groups (19.04%, high EF group (EF $\geqslant$5); 28.64%, (EF = 3) group; 21.94%, low EF group (EF $\leqslant$2); $P<0.001$). The low EF group had a higher proportion of men and current smokers, and more frequent alcohol intake than the high EF group. Table 1 presents other baseline characteristics according to the EF groups.

Table 1. Baseline characteristics of the population according to the eating frequency

	EF⩽2		*EF = 3*		*EF = 4*		*EF⩾5*		*Total*		P-value
N (%)	*429 (9.28)*		*1830 (39.57)*		*1636 (35.37)*		*730 (15.78)*		*4625 (100)*		
	Value	*S.e.*	*Value*	*S.e.*	*Value*	*S.e.*	*Value*	*S.e.*	*Value*	*S.e.*	
Age (years)[a]	40.24	0.9	45.84	0.48	42.42	0.49	42.22	0.73	43.49	0.29	<0.001[b]
Sex[c] (%)											0.006[d]
Male	52.19	3.14	53.15	1.44	50	1.6	43.02	2.41	50.4	0.94	
Hypertension[c,e] (%)											<0.001[d]
Yes	21.94	2.38	28.64	1.26	21.51	1.22	19.04	1.68	23.95	0.74	
Hypertension medication[c] (%)											0.008[d]
Yes	7.8	1.28	12.48	0.86	9.32	0.78	10.27	1.24	10.53	0.49	
Smoking status[c] (%)											<0.001[d]
Never smoker	55.22	3.15	53.24	1.46	60.07	1.58	64.2	2.37	57.52	0.94	
Past smoker	13.13	1.98	19.06	1.14	15.51	1.09	13.82	1.57	16.37	0.67	
Current smoker	31.65	2.96	27.71	1.33	24.42	1.45	21.98	2.22	26.11	0.86	
Smoking amount (pack-year)[a]	4.59	0.71	5.33	0.34	3.58	0.24	3.79	0.43	4.4	0.19	<0.001[b]
Alcohol drinking frequency (per month)[a]	4.71	0.44	4.71	0.21	3.52	0.17	3.08	0.25	4.05	0.12	<0.001[b]
Stress level[c] (%)											0.018[d]
Rare	11.43	2.44	14.16	0.97	13.97	1.07	17.90	1.85	14.37	0.66	
A little	48.79	3.19	50.23	1.46	55.50	1.57	52.88	2.37	52.33	0.93	
Much	32.45	2.82	29.32	1.32	25.58	1.32	22.73	2.09	27.34	0.82	
Too much	7.33	1.45	6.28	0.67	4.96	0.61	6.49	1.20	5.96	0.42	
Sleep sufficiency[c] (%)											0.003[d]
Very much sufficient	8.12	2.09	5.26	0.63	7.54	1.08	5.69	0.99	6.44	0.53	
Fairly sufficient	45.11	3.11	60.15	1.42	57.68	1.59	60.52	2.28	57.71	0.93	
Somewhat insufficient	44.03	3.20	32.22	1.36	32.65	1.47	31.52	2.17	33.54	0.88	
Definitely insufficient	2.74	0.90	2.37	0.37	2.13	0.45	2.26	0.71	2.31	0.26	
Frequency of exercise (per week)[c] (%)											<0.001[d]
Not at all	63.53	3.07	52.01	1.45	48.78	1.6	51.68	2.37	52.07	0.93	
One time	8.39	2.3	7.91	0.81	8.3	0.98	6.49	1.14	7.88	0.55	
Two times	4.16	1.13	5.58	0.64	8.88	1.01	4.34	0.83	6.4	0.47	
Three times	6.34	1.55	8.6	0.84	9.54	0.92	10.37	1.28	8.96	0.53	
Four times	4.57	1.17	5.43	0.72	6.82	0.78	5.66	1.04	5.86	0.44	
Five or more times	13.02	1.82	20.47	1.11	17.68	1.11	21.46	2.15	18.84	0.7	
IPAQ (MET-minutes per week)[a]	666.74	82.85	860.53	47.81	847.07	45.19	847.24	72.69	832.87	28.16	0.214[b]
BMI (kg/m^2)[a]	23.46	0.21	23.68	0.1	23.66	0.1	23.33	0.15	23.6	0.06	0.212[b]
WC (cm)[a]	79.98	0.6	81.23	0.28	80.69	0.3	79.52	0.44	80.64	0.18	0.007[b]
SBP (mm Hg)[a]	118	0.87	120.27	0.51	117.1	0.48	114.92	0.66	118.1	0.29	<0.001[b]
DBP (mm Hg)[a]	77.97	0.61	78.27	0.32	76.94	0.32	75.37	0.49	77.33	0.19	<0.001[b]
N (%)	379 (9.44)		1549 (38.59)		1443 (35.95)		643 (16.02)		*N* = 4014		
SBP (mm Hg)[a,f]	116.31	0.88	117.83	0.51	115.41	0.49	112.87	0.64	116.04	0.29	<0.001[b]
DBP (mm Hg)[a,f]	77.34	0.63	77.50	0.34	76.41	0.33	74.56	0.51	76.65	0.20	<0.001[b]

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; EF, eating frequency; IPAQ, International Physical Activity Questionnaire; MET, metabolic equivalent of task; SBP, systolic blood pressure; WC, waist circumference. [a]Mean and its s.e. [b]*P*-values were calculated by complex sample general linear model. [c]Frequency and its s.e. [d]*P*-values were calculated by Pearson's χ^2 test with Rao–Scott correction using F statistic. [e]Hypertension is defined as SBP ⩾140 mm Hg or DBP ⩾90 mm Hg or as the use of antihypertensive medications. [f]Excluding subjects taking antihypertensive medications (*N* = 4014).

Nutritional characteristics of study participants

The mean values of total calorie, protein, fat, carbohydrate and crude fiber intake were significantly higher in the high EF group than in the low EF group. Further, water and mineral intake, including sodium, potassium and calcium, as well as vitamin intake, including vitamin A, carotene, retinol, thiamine, riboflavin and vitamin C, were significantly higher in the high EF group and lowest in the low EF group. MAR or the index of diet quality increased with increasing EF, showing a significant linear trend after adjusting for age and sex ($P<0.001$) (Table 2). In further analyses stratified by meal frequency (3 vs 1–2 times per day), frequent snack eaters consumed more potassium, retinol, thiamine and riboflavin regardless of the meal frequency. As snack frequency increased, MAR also showed a significant increasing trend in both groups stratified by meal frequency. However, sodium intake was not different between the groups stratified by snack frequency (Supplementary Table 1).

Association of EF, meal frequency and snack frequency with SBP and DBP

In multiple linear regression analyses for survey design after adjusting for covariates (Figure 1), the estimated adjusted mean

Table 2. Nutritional characteristics according to the eating frequency

	EF⩽2		*EF = 3*		*EF = 4*		*EF⩾5*		*Total*		P-value for trend
N (%)	*429 (9.28)*		*1830 (39.57)*		*1636 (35.37)*		*730 (15.78)*		*4625 (100)*		
	Value	*S.e.*	*Value*	*S.e.*	*Value*	*S.e.*	*Value*	*S.e.*	*Value*	*S.e.*	
Total calorie intake (kcal per day)[a]	1682.57	52.8	2032.79	25.51	2245.47	32.33	2288.19	40.35	2108.69	17.73	<0.001[b]
Proteins (g per day)[a]	62.67	2.16	76.47	1.22	87.08	1.5	85.44	1.87	80.08	0.82	<0.001[b]
Fat (g per day)[a]	38.29	2	41.75	0.98	48.41	1.26	52.42	2.1	45.34	0.71	<0.001[b]
Carbohydrates (g per day)[a]	244	6.7	311.02	3.49	344.41	4.48	354	6.09	322.08	2.48	<0.001[b]
Crude fiber (g per day)[a]	6.09	0.24	7.73	0.12	8.69	0.17	8.41	0.21	8	0.09	<0.001[b]
Sodium (mg per day)[a]	4708.23	182.73	5708.73	98.37	6141.07	121.03	6154.38	157.41	5820.71	65.66	<0.001[b]
Potassium (mg per day)[a]	2319.23	74.34	2884.49	37.53	3263.92	46.11	3293.18	68.06	3019.18	26.03	<0.001[b]
Calcium (mg per day)[a]	443.31	18.27	542.45	10.67	622.37	11.51	650.46	17.86	576.3	6.79	<0.001[b]
Phosphorus (mg per day)[a]	1012.93	29.07	1250.44	16.04	1419.52	20.1	1420.34	28	1310.15	11.1	<0.001[b]
Iron (mg per day)[a]	11.11	0.54	14.18	0.25	16.1	0.31	15.91	0.47	14.79	0.17	<0.001[b]
Vitamin A (μgRE per day)[a]	639.07	32.49	831.84	26.97	878.5	21.67	932.61	34.27	842.79	14.42	<0.001[b]
Carotene (μg per day)[a]	3297.92	186.88	4328.44	135.67	4565.99	125.11	4767.97	194.02	4367.73	77.51	<0.001[b]
Retinol (μg per day)[a]	57.67	3.99	73.2	3.48	87.53	3.38	101.93	9.73	80.94	2.38	<0.001[b]
Thiamin (vitamin B_1) (mg per day)[a]	1.1	0.04	1.27	0.02	1.44	0.03	1.48	0.04	1.34	0.02	<0.001[b]
Riboflavin (vitamin B_2) (mg per day)[a]	1	0.04	1.14	0.02	1.32	0.02	1.35	0.03	1.22	0.01	<0.001[b]
Niacin (mg per day)[a]	14.83	0.66	17.53	0.3	19.73	0.35	19.41	0.43	18.3	0.2	<0.001[b]
Vitamin C (mg per day)[a]	86.01	4.81	98.06	2.25	116.74	3.28	125.91	5	107.57	1.72	<0.001[b]
Water (g per day)[a]	759.53	34.32	825.75	17.46	944.94	20.96	972.41	27.52	882.85	11.49	<0.001[b]
MAR (%)[a,c]	76.00	1.12	84.24	0.41	88.42	0.38	89.25	0.51	85.58	0.26	< 0.001[b]
Types of snack[d]											<0.001[e]
No snack	86.97	2.48	69.07	1.39	0	0	0	0	36.19	0.89	
Carbohydrates	5.54	1.78	14.65	1.14	37.9	1.62	30.65	2.27	24.28	0.87	
Fruit and fruit juice	1.54	0.69	7.86	0.74	36.3	1.47	31.25	2.1	20.74	0.71	
Beverage	2.09	0.78	3.51	0.61	11.79	1.07	21.54	2.03	9.01	0.56	
Milk and dairy products	3.74	1.64	3.56	0.52	11.03	0.91	11.38	1.44	7.4	0.47	
Fried food	0	0	0.2	0.13	0.29	0.13	0.09	0.09	0.19	0.07	
Other	0.12	0.12	1.16	0.33	2.7	0.4	5.09	0.97	2.19	0.24	

Abbreviations: EF, eating frequency; MAR, mean adequacy ratio; NAR, nutrient adequacy ratio; RE, retinol equivalents; RNI, recommended nutrition intake. [a]Mean and its s.e. [b]*P*-value for trend was obtained using complex sample general linear model after adjustment for age and sex. [c]MAR: average of NAR for nine nutrients (protein, calcium, phosphorus, iron, vitamin A, thiamine, riboflavin, niacin, vitamin C). NAR = the subject's daily intake of a nutrient/Korean RNI of that nutrient. All NAR values are truncated at 1.0. [d]Frequency and its s.e. [e]*P*-values were calculated by Pearson's χ^2 test with Rao–Scott correction using F statistic.

SBP and DBP decreased as EF increased from 5 or more times per day, showing a significant linear trend (SBP: 120.66, 120.23, 119.18 and 117.92 mm Hg, respectively; *P*-value for trend <0.001; DBP: 78.36, 77.78, 77.25 and 76.50 mm Hg, respectively; *P*-value for trend = 0.004). As snack frequency increased from zero to three per day, estimated adjusted means of both SBP and DBP decreased, showing significant linear trends (SBP: 120.35, 119.5, 118.55 and 117.14 mm Hg, respectively; *P*-value for trend <0.001; DBP 77.93, 77.54, 76.56 and 75.94 mm Hg, respectively; *P*-value for trend = 0.003). However, the increasing trend of SBP or DBP with decreasing meal frequency was not statistically significant (Figure 1). Repeated analyses after excluding subjects taking medication for hypertension, diabetes or dyslipidemia showed similar results (Supplementary Table 2).

Association of EF, meal frequency and snack frequency with hypertension

In the multiple logistic regression analyses, after adjusting for covariates including BMI and WC, the adjusted ORs for hypertension were 1.046 (95% CI: 0.745–1.468), 0.856 (95% CI: 0.695–1.054) and 0.732 (95% CI: 0.555–0.965) in each EF group (EF = 2, EF = 4 and EF ⩾5, respectively) compared with the (EF = 3) group. As EF increased from 2 or less to 5 or more times per day, the ORs for hypertension decreased linearly in all models (*P*-value for trend: 0.016 in model 1, 0.021 in model 2 and 0.040 in model 3). The inverse association between EF and hypertension was gradually attenuated after adjustment for confounding variables including BMI and WC. Snack frequency was inversely related to the odds of hypertension. In the final model, the adjusted ORs for hypertension were 0.828 (95% CI: 0.672–1.020), 0.746 (95% CI: 0.552–1.007) and 0.618 (95% CI: 0.375–1.018) for the groups that had one, two and three snacks per day, respectively, compared with the group that had no snacks. Higher snack frequency also decreased the ORs for hypertension in all models, showing a linear trend (*P*-value for trend: 0.003 in model 1, 0.005 in model 2 and 0.009 in model 3). Eating one meal per day increased the ORs for hypertension compared to eating three meals per day; however, the associations were not statistically significant (Table 3).

The effect of EF on hypertension stratified by abdominal obesity and diet quality

A differential effect of EF and snack frequency on hypertension in terms of abdominal obesity was not observed (*P*-value for interaction = 0.518 and 0.762, respectively). However, in a stratified multiple logistic regression analysis according to abdominal obesity, EF and snack frequency were significantly associated with the odds of hypertension even after controlling for confounding variables such as BMI in the subgroup with abdominal obesity (*P*-value for trend: 0.02 and 0.009, respectively), but not in the subgroup without abdominal obesity. The

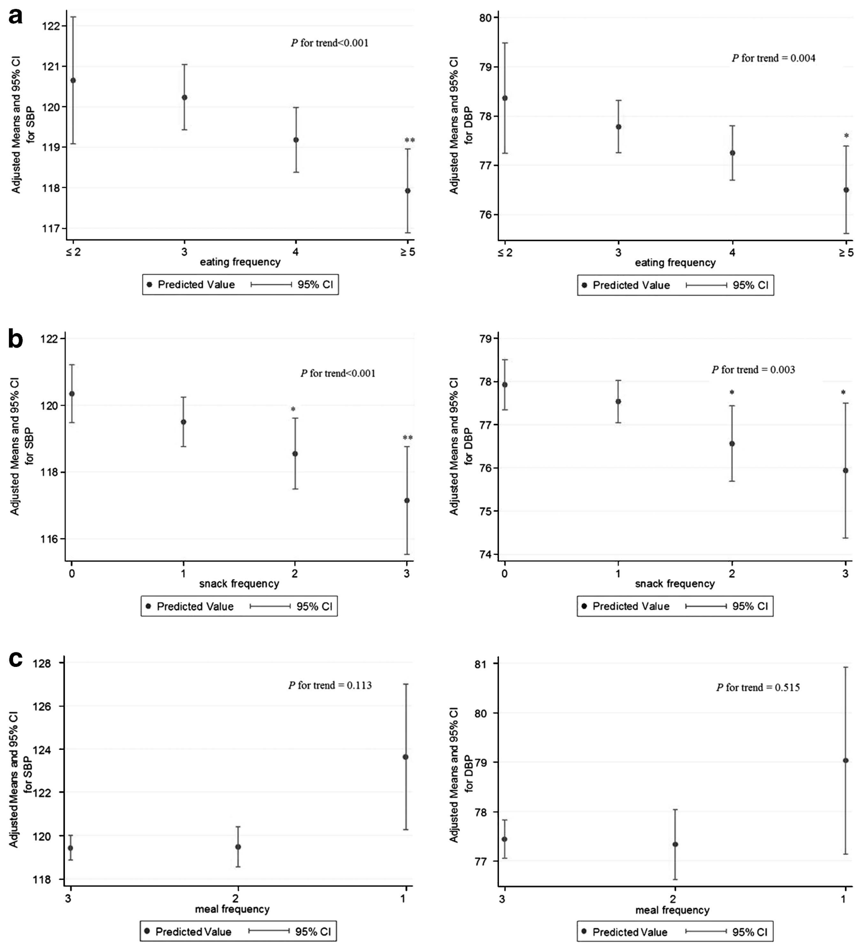

Figure 1. Adjusted mean (95% CIs) of SBP and DBP according to eating frequency using multiple linear regression analyses for survey design ($N = 4625$). The adjusted mean of each EF group was compared with that of the (EF = 3) group by the Wald test (**P*-value for trend <0.05, ***P*-value for trend <0.01). The adjusted mean of each snack frequency group was compared with that of the low snack frequency group (snack frequency = 0) by Wald test (**P*-value for trend <0.05, ***P*-value for trend <0.01). The adjusted mean of each meal frequency group was compared with that of the high meal frequency group (meal frequency = 3) by Wald test (**P*-value for trend <0.05, ***P*-value for trend <0.01). (**a**) Adjusted for age, sex, smoking status, smoking amount (pack-years), usual alcohol consumption frequency (per month), exercise frequency (per week), International Physical Activity Questionnaire score (metabolic equivalent of task (MET)-minutes per week), total calorie intake (kcal per day), sodium intake (mg per day), potassium intake (mg per day), calcium intake (mg per day), hypertension medication, sleep sufficiency, stress level, MAR, BMI and WC. (**b**) Plus additional adjustment for meal frequency. (**c**) Plus additional adjustment for snack frequency.

interaction of EF and snack frequency with diet quality was not significant (*P*-value for interaction = 0.461 and 0.817, respectively). However, in the stratified multiple logistic regression analysis according to diet quality, a marginally significant association between EF and the odds of hypertension and a significant relationship between snack frequency and the odds of hypertension were observed in the low diet quality group with MAR $<50\%$ (*P*-value for trend: 0.057 and 0.011, respectively), but not in the high diet quality group with MAR $\geqslant 50\%$ (Table 4).

DISCUSSION

In this study, we found that lower EF, after adjustment for total calorie intake, was associated with increased SBP and DBP independent of BMI and WC. Further, a statistically significant inverse relationship between EF and hypertension was observed. The high EF group (EF $\geqslant 5$) had an estimated lower level of SBP by 3 mm Hg and of DBP by 2 mm Hg than the low EF group (EF $\leqslant 2$). Participants who did not consume snacks had a higher level of SBP by 3 mm Hg and of DBP by 2 mm Hg than those who consumed snacks 3 or more times daily after controlling for total calorie intake. These effects are similar to those of moderate drinking or a low-salt diet for primary hypertension prevention.[1] Prospective studies reported that a 2 mm Hg decrease in the average DBP in the population would reduce the risk of hypertension by 17%; stroke by 14%; and coronary heart disease by 6%.[30] In addition, a 3 mm Hg decrement in SBP distribution would result in an 8% reduction in stroke risk, a 5% reduction in coronary heart disease risk and a 4% decrease in all-cause mortality.[31]

Previous studies have suggested an association between EF and cardiovascular risk factors such as lipid profile, obesity and glucose tolerance.[11–15] However, few studies have investigated the association between EF and BP. An 8-week randomized crossover study documented that eating three meals per day lowered SBP and DBP by 6% compared with eating one large meal, which corresponds to our study findings.[18] However, in that randomized crossover study, the BPs of subjects in the different meal frequency groups were measured at different times of day. Therefore, it is possible that an observed increase in BP in those who consumed one large meal per day may be owing to diurnal variation in BP. Another study reporting an observed inverse relationship between meal frequency and BP focused on the association of meal frequency with cholesterol level, suggesting

Table 3. Multiple logistic regression analyses for the odds of hypertension according to the eating frequency

	%	S.e.	Model 1[a]		Model 2[b]		Model 3[c]	
			aOR	95% CI	aOR	95% CI	aOR	95% CI
Eating frequency								
EF⩽2	10.78	0.64	1.046	0.745–1.468	1.068	0.756–1.508	1.022	0.717–1.456
EF = 3	38.83	0.9	1.000		1.000		1.000	
EF = 4	35.18	0.9	0.856	0.695–1.054	0.858	0.696–1.057	0.841	0.680–1.040
EF⩾5	15.21	0.66	0.732	0.555–0.965	0.745	0.563–0.987	0.763	0.570–1.022
P-value for trend			0.016		0.021		0.040	
Snack frequency[d]								
0	36.19	0.89	1.000		1.000		1.000	
1	43.85	0.93	0.830	0.677–1.018	0.832	0.678–1.021	0.828	0.672–1.020
2	14	0.64	0.726	0.546–0.965	0.734	0.548–1.021	0.746	0.552–1.007
3	5.96	0.48	0.594	0.370–0.951	0.611	0.380–0.982	0.618	0.375–1.018
P-value for trend			0.003		0.005		0.009	
Meal frequency[e]								
1	3.1	0.39	1.700	0.902–3.203	1.800	0.934–3.468	1.519	0.774–2.980
2	25.57	0.85	0.885	0.703–1.113	0.885	0.701–1.118	0.870	0.684–1.105
3	71.33	0.88	1.000		1.000		1.000	
P-value for trend			0.861		0.820		0.895	

Abbreviations: aOR, adjusted OR; BMI, body mass index; CI, confidence interval; EF, eating frequency; MAR, mean adequacy ratio; MET, metabolic equivalent of task; WC, waist circumference. [a]Model 1 adjusted for age and sex. [b]Model 2 adjusted for age, sex, smoking status, smoking amount (pack-years), usual alcohol consumption frequency (per month), exercise frequency (per week), International Physical Activity Questionnaire score (MET-minutes per week), total calorie intake (kcal per day), sodium intake (mg per day), potassium intake (mg per day), calcium intake (mg per day), sleep sufficiency, stress level and MAR. [c]Model 3 included additional adjustments for BMI and WC. [d]Plus additional adjustment for meal frequency. [e]Plus additional adjustment for snack frequency.

that potential confounding variables influencing measurement of BP may not have been sufficiently considered.[12] In this study, most of the participants (71.33%) had three meals per day; therefore, increases in EF appear to be attributed to increases in snack frequency. In the analyses of snack frequency and meal frequency, snack frequency but not meal frequency was negatively related to BP and hypertension. A previous study reported that participants who consumed three snacks per day had a greater decrease in BP than those who did not have a snack, although the difference was not significant, which may be owing to the small sample size.[19] Another study showed that the inverse association between daily eating frequency, especially snack frequency, and BP in school children depends on BMI and body fat mass.[32] Therefore, we performed further adjustment for BMI and WC, and the inverse association between EF and BP remained significant regardless of BMI and WC. The apparent discrepancy between the previous study in schoolchildren and our study may be owing to the different age groups studied.

The underlying mechanism of the association between EF and BP remains unclear, but may be partly mediated by obesity or central adiposity. Some studies have suggested that low EF is related to obesity, in particular central obesity.[9,10,33–35] A recent study reported that lower snack frequency and EF were related to greater 10-year changes in BMI and WC in adolescent girls.[14] Obesity is a well-known risk factor for hypertension.[16,36] In our study, the association between EF and hypertension attenuated after adjusting for BMI and WC. Furthermore, in subjects with abdominal obesity, a significant inverse association between EF and hypertension was observed, but these associations were not significant in subjects without abdominal obesity. These findings suggest that central adiposity is an important factor in the relationship between EF and hypertension. However, in the present study, the inverse association between EF and BP persisted even after controlling for BMI and WC; therefore, there may be another pathway independent of obesity.

Insulin resistance or hyperinsulinemia may also contribute to the association between EF and BP.[37] Increasing meal frequency while controlling the total calorie intake is related to lower insulin concentrations in type 2 diabetes patients.[38] In addition, a cross-sectional study showed that subjects who regularly eat three meals per day have a lower risk of metabolic syndrome and insulin resistance than irregular eaters who eat one or two meals per day.[39] Reduced insulin sensitivity in irregular eaters with decreased EF, which induces a higher insulin response to meals, is related to overactivation of the sympathetic nervous system, excess angiotensinogen secretion and renal sodium retention.[38–40] This effect could result in elevated BP and carry over to the fasting state, which may affect the risk of increased BP. These effects may be more prominent in obese subjects who are susceptible to insulin resistance. Taken together, data suggest that higher EF without a change in the total calorie intake may have a beneficial effect on insulin resistance and BP control.

In addition, other previous studies have found that subjects who ate more often were likely to select healthy foods, resulting in improved diet quality[15] and increased daily intakes of vitamins A, C and E and beta carotene.[41] In our study, the high EF group ate more fruits and vegetables, milk and dairy products and beverages such as coffee and tea, but less fried food than the lower EF group. They also consumed more potassium, calcium, vitamin A, carotene, retinol, thiamine, riboflavin and vitamin C than their counterparts. Eating more frequent snacks with the same meal frequency also increased daily intake of potassium, retinol, thiamine and riboflavin, but not of sodium (Supplementary Table 1). Hence, diet quality was improved with increasing EF or snack frequency. The inverse relationship between EF or snack frequency and hypertension was maintained in the group with low-diet quality, but not in the group with high-diet quality. Therefore, improved diet quality may also explain the relationship between higher EF or snack frequency and lower hypertension. However, the inverse association of EF or snack frequency with hypertension and BP was observed even after the adjustment for diet quality, suggesting that this relationship is independent of diet quality.

Table 4. Multiple logistic regression analyses for the odds of hypertension according to the eating frequency divided by the presence of abdominal obesity[a] and by the MAR[b]

	Group with abdominal obesity (N = 1151)				*Group without abdominal obesity (N = 3474)*				*P-value for interaction*
	%	*S.e.*	*aOR*	*95% CI*	*%*	*S.e.*	*aOR*	*95% CI*	
Eating frequency[c]									
EF⩽2	9.831	1.084	0.911	0.511–1.627	11.1	0.762	1.19	0.769–1.84	
EF = 3	42.96	1.768	1		37.6	1.042	1		
EF = 4	34.3	1.707	0.809	0.571–1.146	35.4	1.052	0.846	0.645–1.109	
EF⩾5	12.91	1.161	0.499	0.305–0.816	15.9	0.79	0.939	0.662–1.333	
P-value for trend			0.02				0.224		0.518
Snack frequency[d]									
0	42.43	1.758	1		34.3	1.021	1		
1	40.82	1.768	0.993	0.705–1.397	44.8	1.091	0.722	0.556–0.939	
2	11.36	1.085	0.491	0.297–0.811	14.8	0.764	0.888	0.619–1.274	
3	5.379	0.81	0.496	0.227–1.081	6.13	0.578	0.677	0.366–1.253	
P-value for trend			0.009				0.109		0.762
Meal frequency[e]									
1	3.217	0.658	1.467	0.513–4.193	3.07	0.463	1.837	0.767–4.396	
2	20.26	1.48	0.967	0.645–1.448	27.2	1.004	0.855	0.634–1.153	
3	76.52	1.56	1		69.8	1.043	1		
P-value for trend			0.771				0.993		0.568

	Group with MAR < 50% (N = 2354)				*Group with MAR ⩾ 50% (N = 2271)*				*P-value for interaction*
	%	*S.e.*	*aOR*	*95% CI*	*%*	*S.e.*	*aOR*	*95% CI*	
Eating frequency[f]									
EF⩽2	15.19	1.078	1.037	0.674–1.597	6.5	0.654	0.937	0.515–1.705	
EF = 3	42.19	1.294	1		35.6	1.264	1		
EF = 4	30.18	1.254	0.888	0.667–1.182	40.1	1.286	0.796	0.582–1.089	
EF⩾5	12.45	0.848	0.651	0.431–0.983	17.9	1.012	0.865	0.567–1.319	
P-value for trend			0.057				0.354		0.461
Snack frequency[g]									
0	41.04	1.288	1		31.5	1.217	1		
1	40.62	1.331	0.897	0.682–1.18	47	1.311	0.757	0.555–1.033	
2	13.27	0.904	0.706	0.458–1.087	14.7	0.902	0.789	0.516–1.205	
3	5.068	0.582	0.455	0.232–0.892	6.82	0.761	0.746	0.356–1.56	
P-value for trend			0.011				0.196		0.817
Meal frequency[h]									
1	5.022	0.681	1.341	0.638–2.816	1.23	0.366	1.796	0.442–7.29	
2	31.54	1.281	0.921	0.67–1.267	19.7	1.076	0.776	0.534–1.126	
3	63.44	1.322	1		79	1.112	1		
P-value for trend			0.88				0.49		0.369

Abbreviations: aOR, adjusted OR; BMI, body mass index; CI, confidence interval; EF, eating frequency; MAR, mean adequacy ratio; MET, metabolic equivalent of task; NAR, nutrient adequacy ratio; RNI, recommended nutrition intake; WC, waist circumference. [a]Abdominal obesity was defined as a WC ⩾85 cm in women and ⩾90 cm in men, proposed as the appropriate WC cutoffs for abdominal obesity by the Korean Society for the Study of Obesity.[29] [b]MAR: average of NAR for nine nutrients (protein, calcium, phosphorus, iron, vitamin A, thiamine, riboflavin, niacin, vitamin C). NAR = the subject's daily intake of a nutrient/Korean RNI of that nutrient. All NAR values are truncated at 1.0. [c]Adjusted for age, sex, smoking status, smoking amount (pack-years), usual alcohol consumption frequency (per month), exercise frequency (per week), International Physical Activity Questionnaire score (MET-minutes per week), total calorie intake (kcal per day), sodium intake (mg per day), potassium intake (mg per day), calcium intake (mg per day), sleep sufficiency, stress level, MAR and BMI. [d]Plus additional adjustment for meal frequency. [e]Plus additional adjustment for snack frequency. [f]Adjusted for age, sex, smoking status, smoking amount (pack-years), usual alcohol consumption frequency (per month), exercise frequency (per week), International Physical Activity Questionnaire score (MET-minute per week), total calorie intake (kcal per day), sodium intake (mg per day), potassium intake (mg per day), calcium intake (mg per day), sleep sufficiency, stress level, BMI and WC. [g]Plus additional adjustment for meal frequency. [h]Plus additional adjustment for snack frequency.

In the present study, dietary sodium intake, an important risk factor for hypertension,[42] increased with increasing EF. However, the inverse association of EF with BP or hypertension was maintained regardless of the adjustment for daily sodium intake. These results suggest that lower EF may be associated with high BP or the odds of hypertension, independent of sodium intake.

Although the influence of EF on total calorie intake remains unclear, the weighted mean daily calorie intake (± s.e.) and BMI (± s.e.) of the study subjects were 2108.7 (± 17.7) kcal per day and 23.6 (± 0.06) kg/m^2, respectively, and the daily total energy intake in the subjects with one or two meals per day with increasing snack frequency from 0 to 3 times was 1682.1 ± 52.2 and 2079.5 ± 167.6 kcal per day, respectively.[43]

In conclusion, these findings suggest that EF, especially snack frequency, and dietary components without changes in the total calorie intake may have an impact on hypertension.

This study has some limitations. First, this is a cross-sectional study, which limited its ability to reveal a causal relationship between EF and BP. Second, there was potential recall bias because diet and other lifestyle factors were based on information retrospectively collected by self-reported questionnaires. Third, antihypertensive medication was assessed by self-reported questionnaire, not confirmed by a physician, which could possibly affect the reported number of subjects with hypertension. Fourth, dietary variables were estimated by a single 24-h dietary recall instead of three 24-h dietary recalls. This might not reflect the true diet at the individual level, not considering day-to-day variation. Finally, the study participants were of single ethnic origin; therefore, the results must be generalized cautiously. However, to our knowledge, this is the first study to identify the association between EF and BP after adjusting for the effects of BMI and central obesity using a representative sample of the Korean population. Further prospective studies are needed to verify the causal relationship between EF and BP, and well-designed randomized clinical trials are needed to elucidate whether higher EF can improve BP control.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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