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**A DISSERTATION FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY IN HUMAN ECOLOGY**

**Dietary Determinants of Metabolic Syndrome
and Its Components in Korean Adults**

한국 성인에서 대사증후군 관련 식사 요인 연구

August, 2014

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ABSTRACT

Dietary Determinants of Metabolic Syndrome and Its Components in Korean Adults

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Metabolic syndrome is defined as a clustering of metabolic abnormalities, including abdominal obesity, dyslipidemia, elevated blood glucose, and hypertension. Metabolic syndrome is a strong predictor of type 2 diabetes and cardiovascular diseases. The prevalence of metabolic syndrome has been increasing in Korean adults. Diet, a key determinant of metabolic syndrome, is modifiable to prevent and improve metabolic syndrome. Nutritional epidemiologic studies in Western populations have found dietary determinants of metabolic syndrome at multiple levels: nutrients, food groups, and dietary patterns. Korean adults practice unique dietary patterns that are different from those of Western adults. This might cause differences in the susceptibility and the

mechanism of developing metabolic syndrome between Western and Korean adults. However, only a few studies have examined in Korean adults the dietary determinants of metabolic syndrome and of individual components of metabolic syndrome. Therefore, the aim of this study was to examine dietary determinants, such as nutrients, food groups, and dietary patterns of metabolic syndrome and its components in Korean adults based on data from the Korea National Health and Nutrition Examination Survey (KNHANES) and from patients of several outpatient clinics in and near Seoul.

Multiple cross-sectional studies were conducted based on three different datasets: 1) subjects from the Fourth KNHANES (2007–2009) were nationally representative adults who had no diabetes, dyslipidemia, and hypertension and had dietary intake data obtained from a single 24-hour recall and a food frequency questionnaire, 2) subjects recruited from four outpatient clinics in and near the Seoul metropolitan area between 2006 and 2012 were at a high risk of metabolic syndrome and had three days of dietary intake data from a combination of 24-hour recalls and dietary records, and 3) subjects recruited from the Health Examination Center or the Family Medicine Department in a general hospital in Seoul between 2010 and 2012 were disease-free at the time of study enrollment and had multiple days of dietary intake data from 24-hour recalls. Intakes of nutrients, alcohol, food groups, dietary glycemic index (DGI) and load (DGL) were evaluated and dietary patterns were identified using factor analysis and reduced rank regression for each subject based on their dietary intake data. Metabolic syndrome and its components were defined using the modified National Cholesterol Education Program Adult Treatment Panel III criteria and clustering patterns of metabolic syndrome components were derived from factor analysis.

In adults from the KNHANES data, high carbohydrate intake was a key determinant of metabolic syndrome and its components, such as insulin resistance and dyslipidemia. The percentage of energy from carbohydrates in men and intakes of refined grains and white rice in women were positively associated with the prevalence of metabolic syndrome (energy from carbohydrates Q5 vs. Q1: OR = 1.46, 95% CI = 1.07–2.01; refined grains Q5 vs. Q1: OR = 1.72, 95% CI = 1.24–2.40; white rice Q5 vs. Q1: OR = 1.74, 95% CI = 1.23–2.48). Among women without metabolic syndrome, subjects with insulin resistance had higher intakes of carbohydrates, DGI, and DGL than those without insulin resistance (58.8 vs. 57.9 for DGI; 171.4 vs. 164.5 for DGL). Of dietary patterns identified, the dietary pattern characterized by high intakes of whole grains and beans (low GI foods) was associated with a low prevalence of insulin resistance (pattern scores Q5 vs. Q1: OR = 0.80, 95% CI = 0.61–1.03, *P* for trend = 0.0134), whereas the rice-oriented dietary pattern characterized by a high intake of white rice but low intakes of vegetables, fruits, meat, milk and dairy products was positively associated with the risks for hypertriglyceridemia in men (pattern scores Q5 vs. Q1: OR = 1.58, 95% CI = 1.20–2.09) and low HDL-cholesterol in both men (Q5 vs. Q1: OR = 1.43, 95% CI = 1.12–1.82) and women (Q5 vs. Q1: OR = 1.29, 95% CI = 1.08–1.55).

Among adults of four outpatient clinics, men with metabolic syndrome had a higher intake of alcohol but a lower intake of fruits than those without metabolic syndrome (22.9 vs. 14.4 g for alcohol; 1.1 vs. 1.6 servings for fruits). Women with metabolic syndrome had a lower intake of milk and dairy products than those without metabolic syndrome (0.5 vs. 0.8 servings for milk and dairy products). Clustering patterns of metabolic syndrome components in adults from the general hospital were

differentially associated with dietary determinants. The high triglycerides and low HDL-cholesterol pattern was associated with low intakes of milk and dairy products (pattern scores T3 vs. T1 = 0.7 vs. 1.1 servings), calcium, and potassium but positively associated with DGI (T3 vs. T1 = 56.5 vs. 54.1) and DGL (T3 vs. T1 = 147.9 vs. 128.7). The high blood pressure pattern was associated with high alcohol intake (T3 vs. T1 = 19.5 vs. 5.6 g). The high total- and LDL-cholesterol pattern was associated with high intakes of fat and cholesterol and low intakes of vegetables (pattern scores T3 vs. T1 = 6.2 vs. 8.1 servings), dietary fiber, and iron.

In conclusion, diets low in DGI and DGL based on high intakes of whole grains rather than refined grains and white rice might have a protective effect on the development of metabolic syndrome and its components, such as insulin resistance and dyslipidemia in Korean adults. Lower intakes of beans, vegetables, fruits, milk and dairy products and heavy alcohol drinking may increase the risks for metabolic syndrome and its components. Findings from this study can be used to build nutrition intervention programs and specific dietary strategies for individuals and populations at high risk of metabolic syndrome in Asian regions.

Keywords: Metabolic syndrome, Carbohydrate, Alcohol, Food group, Dietary pattern, Korean adults

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LIST OF ABBREVIATIONS

ATP, Adult Treatment Panel

BMI, Body Mass Index

CI, Confidence Interval

DGI, Dietary Glycemic Index

DGL, Dietary Glycemic Load

FFQ, Food Frequency Questionnaire

GI, Glycemic Index

GL, Glycemic Load

GLM, General Linear Model

HDL, High-Density Lipoprotein

HOMA-IR, Homeostasis Model Assessment of Insulin Resistance

IDF, International Diabetes Federation

LDL, Low-Density Lipoprotein

KNHANES, Korea National Health and Nutrition Examination Survey

NCEP, National Cholesterol Education Program

NHANES, National Health and Nutrition Examination Survey

OR, Odds Ratio

RRR, Reduced Rank Regression

SAS, Statistical Analysis System

SD, Standard Deviation

SEM, Standard Error of the Mean

US, United States

WHO, World Health Organization

WHR, Waist-to-Hip Ratio

CHAPTER I. INTRODUCTION

1. Background

Metabolic syndrome is a state of having several metabolic abnormalities, including abdominal obesity, hyperglycemia, hypertension, hypertriglyceridemia, and low high-density lipoprotein (HDL) cholesterol (Grundy, SM *et al.* 2005). Metabolic syndrome is a strong predictor of overall morbidity and mortality of type 2 diabetes (Ford, ES *et al.* 2008) and cardiovascular diseases (Ford, ES 2005, Gami, AS *et al.* 2007). The early study reported that insulin resistance was a main underlying symptom of metabolic syndrome (Reaven, GM 1988), but recent studies have insisted that multiple pathophysiologic origins in the development of metabolic syndrome exist (Ferguson, TF *et al.* 2010, Shen, BJ *et al.* 2003).

The prevalence of metabolic syndrome has been increasing in the world (Grundy, SM 2008) and Asian countries (Cheung, BM 2005). In the United States (US), the prevalence of metabolic syndrome among adults was 24.0 % for men and 23.4 % for women between 1988 and 1994 based on the criteria from the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III (Ford, ES *et al.* 2002) to define metabolic syndrome. During the years 1999 to 2006, the prevalence was 34.9 % for men and 33.3 % for women using the revised diagnosis criteria from the American Heart Association and the NCEP ATP III (Mozumdar, A and Liguori, G 2011). In

Korean adults, the prevalence of metabolic syndrome increased from 24.9 % in 1998 to 31.3 % in 2007 (Lim, S *et al.* 2011). Because cardiovascular diseases and type 2 diabetes are main causes of death among the Korean population (KOSTAT 2014), metabolic syndrome is a major issue in public health. Therefore, the approaches to the prevention and management of metabolic syndrome is urgently needed to prevent chronic diseases during the early stages in Korean adults.

Genetic and racial factors, environmental factors, aging, endocrine disorders, and unhealthy lifestyle (e.g., heavy alcohol drinking, physical inactivity, and Western diet) have been known as determinants of metabolic syndrome and its components (Grundy, SM 2008, Grundy, SM *et al.* 2005). Among these determinants, diets play an important role in the development of metabolic syndrome and its components; it can be modifiable to reduce the risk of metabolic syndrome. Nutritional epidemiologic studies have found dietary determinants of metabolic syndrome at multiple levels: nutrients, food groups, and dietary patterns. Most studies about dietary determinants of metabolic syndrome and its components have been conducted in Western countries, and the results from these studies may not apply to the Korean adult population whose dietary patterns are different from those in Western countries.

In Western populations, it was suggested that a Western dietary pattern (Esmailzadeh, A *et al.* 2007, Lutsey, PL *et al.* 2008) and a diet high in potatoes, meat, and alcoholic beverages were positively associated with the risk of metabolic syndrome (Panagiotakos, DB *et al.* 2007, Wirfalt, E *et al.* 2001) whereas a diet rich in fruits and vegetables (Esmailzadeh, A *et al.* 2007) or milk and dairy products (Elwood, PC *et al.* 2007, Lutsey, PL *et al.* 2008, Ruidavets, JB *et al.* 2007, Wirfalt, E *et al.* 2001) were related to a reduced risk of metabolic syndrome. In addition, diets

with high glycemic index (GI) or glycemic load (GL) or those with low whole grains were positively associated with the risk of metabolic syndrome (McKeown, NM *et al.* 2004).

Korean adults who traditionally consume a high carbohydrate diet based on white rice as a staple food have different dietary practices from those of Western adult populations, which might lead to different metabolic pathways in the development of metabolic syndrome. In addition, heavy alcohol consumption is prevalent in Korean adult men (Lee, MY *et al.* 2010, Yoon, YS *et al.* 2004), but intake of milk and dairy products is lower in men and women compared to those of Western populations (Kwon, HT *et al.* 2010). Dietary pattern in Korean adults is unique, but only a few studies have examined various dietary determinants of metabolic syndrome and its components in Korean adults. Kim, K *et al.* (2008) reported that intakes of total carbohydrate, dietary glycemic index (DGI), and dietary glycemic load (DGL) were positively associated with the prevalence of metabolic syndrome in Korean women. Prospective (Baik, I and Shin, C 2008, Kim, BJ *et al.* 2012) and cross-sectional studies in Korean men (Lee, MY *et al.* 2010, Park, SH 2012, Shin, MH *et al.* 2013) showed that heavy alcohol drinking was positively associated with the risk of metabolic syndrome and its components, such as elevated blood pressure and high triglycerides. Diets high in fruits, vegetable, milk and dairy products were associated with a reduced risk of metabolic syndrome among Korean adults (Hong, S *et al.* 2012, Jung, HJ *et al.* 2011, Kwon, HT *et al.* 2010).

According to findings from previous studies in Western and Korean populations, dietary determinants have not been consistently associated with the components of metabolic syndrome. The role of diet in the development of metabolic syndrome

remains unclear but might be differentially associated with individual components of metabolic syndrome. To better understand the association between dietary determinants and the risk of metabolic syndrome, dietary determinants can be considered at multiple levels, including nutrients, food groups, and dietary patterns. In addition, dietary determinants associated with individual components of metabolic syndrome should be examined to provide specific nutritional strategies for the prevention and management of metabolic syndrome in Korean adults.

2. Goal and objectives

The overall goal of this study was to examine dietary determinants of metabolic syndrome and its components in Korean adults. To achieve the study goal, specific objectives were the followings:

- 1) To examine the association between dietary carbohydrate intake and risks for metabolic syndrome and its components,
- 2) To examine the association between alcohol intake and risks for metabolic syndrome and its components,
- 3) To examine the association between food group intake and risks for metabolic syndrome and its components, and
- 4) To examine the association between dietary patterns and risks for metabolic syndrome and its components.

3. Scope of the study

According to the goal and objectives of this study, multiple cross-sectional studies were conducted based on three different datasets. The overall scope of the study is presented in Table I - 1.

In chapter III, dietary determinants of metabolic syndrome and its components were evaluated in adults from the Fourth Korea National Health and Nutrition Examination Survey (KNHANES) data in 2007–2009. Subjects were large nationally representative samples who had no diagnosis and treatment for diabetes, hypertension, and dyslipidemia. Dietary intake was assessed by a single 24-hour recall and a FFQ in this subjects. Chapter III consists of four studies and specific aims of each study are as follows.

Study 1.

- To examine the association between the amounts of dietary carbohydrates and the prevalence of metabolic syndrome in men and women
- To examine the association between the sources of dietary carbohydrates and the prevalence of metabolic syndrome in men and women

Study 2.

- To examine the relationship between macronutrient intake and the presence of insulin resistance according to the number of symptoms of metabolic syndrome in men and women

- To examine the relationship between food group intake and the presence of insulin resistance according to the number of symptoms of metabolic syndrome in men and women

Study 3.

- To examine the association between dietary patterns and the prevalence of insulin resistance in adults

Study 4.

- To identify dietary patterns based on carbohydrate intake using the reduced rank regression (RRR) method in adults
- To examine the association of these dietary patterns with the prevalence of dyslipidemia and elevated blood glucose in men and women

In chapter IV, dietary determinants of metabolic syndrome and its components were evaluated in adults recruited in four outpatient clinics in and near the Seoul metropolitan area between 2006 and 2012. Subjects in this data were at high risk of metabolic syndrome and had three days of dietary intake data obtained from a combination of 24-hour recalls and dietary records. Chapter IV consists of two studies and specific aims of each study are as follows.

Study 5.

- To examine differences in intakes of nutrient and food group by the presence of metabolic syndrome in men and women

Study 6.

- To examine the association between alcohol consumption and the prevalence of metabolic syndrome and its components in men
- To examine the association between alcohol consumption and the prevalence of metabolic syndrome and its components by smoking status in men

In chapter V, clustering patterns of metabolic syndrome components and its association with dietary determinants were examined among adults who attended the Health Examination Center or the Family Medicine Department in Seoul National University Hospital between 2010 and 2012. Subjects were disease-free at the time of study enrollment and had no medication for chronic diseases. They had multiple days of dietary intake data obtained from 24-hour recalls through on-site and telephone interviews. Chapter V consists of two studies and specific aims of each study are as follows.

Study 7.

- To identify clustering patterns of metabolic syndrome components in adults
- To examine the association between these clustering patterns and dietary factors in adults

Study 8.

- To identify distinctive dyslipidemia patterns in adults
- To examine the association between dyslipidemia patterns and dietary factors in adults

Table I - 1. The overall scope of the study

Data and subjects	Study	Age	Sex (<i>n</i>)	Dietary assessment	Dietary determinants	Outcomes
Nationally representative adults who had no diabetes, dyslipidemia, and hypertension from the 4 th KNHANES data (2007–2009)	1	30–65y	M (2,631) W (4,214)	1d 24HR	Total CHO, energy from CHO, DGI, DGL, total grains, refined grains, & white rice	Prevalence of MetS
	2	30–65y	M (2,618) W (4,326)	1d 24HR	Macronutrients & food groups	Presence of IR
	3	30–65y	T (3,871)	FFQ with simple frequency	Dietary patterns from factor analysis	Prevalence of IR
	4	≥20y	M (3,795) W (5,930)	1d 24HR	Dietary patterns from RRR	Prevalence of dyslipidemia, IFG, & diabetes
Adults who were recruited in 4 outpatient clinics in and near Seoul (2006–2012) and at high risk of MetS	5	≥30y	M (413) W (255)	3d 24HRs & DRs within 2 weeks	Nutrients & food groups	Presence of MetS
	6	≥30y	M (413)	3d 24HRs & DRs within 2 weeks	Alcohol drinking (non-, moderate-, & heavy)	Prevalence of MetS & its components
Adults who attended the SNUH (2010–2012) and disease-free at the time of study enrollment	7	≥20y	T (141)	2–4d 24HRs over 4 months (interval of 3–4 months)	Nutrients, alcohol, DGI & DGL	Clustering patterns of MetS components
	8	≥20y	T (138)	3d 24HRs over 8 months (intervals of 3–4 months)	Nutrients, alcohol, DGI, DGL & food groups	Dyslipidemia patterns

CHO, Carbohydrate; DGI, Dietary glycemic index; DGL, Dietary glycemic load; DR, Dietary record; FFQ, Food frequency questionnaire; IFG, Impaired fasting glucose; IR, Insulin resistance; KNHANES, Korea National Health and Nutrition Examination Survey; M, Men; MetS, Metabolic syndrome; 24HR, 24-hour recall; SNUH, Seoul National University Hospital; T, Total; W, Women.

CHAPTER II. LITERATURE REVIEW

1. Definition and prevalence of metabolic syndrome

Definition of metabolic syndrome

The earliest definition of metabolic syndrome proposed by Reaven in 1988 included that insulin resistance and its compensatory hyperinsulinemia, which predisposed individuals to hypertension, dyslipidemia, and diabetes (Reaven, GM 1988). Since the Reaven's definition, a number of expert groups attempted to develop a unified definition of metabolic syndrome. In 1999, the World Health Organization (WHO) released the unified definition of metabolic syndrome (WHO 1999). In 2001, the NCEP published ATP III criteria for the clinical diagnosis of metabolic syndrome (Cleeman, JI *et al.* 2001). In 2005, the International Diabetes Federation (IDF) published a new criteria that modified the NCEP ATP III criteria (Alberti, KG *et al.* 2006). The specific criteria for diagnosis of metabolic syndrome by WHO, NCEP, and IDF are shown in Table II - 1.

Diagnosis of metabolic syndrome provides useful information to help in identifying individuals who are at high risks of chronic diseases in clinical settings. Because metabolic syndrome is a risk factor for chronic diseases, individuals with metabolic syndrome had higher risks for cardiovascular diseases (Ford, ES 2004,

Isomaa, B *et al.* 2001, Lakka, HM *et al.* 2002) and type 2 diabetes (Stern, MP *et al.* 2004) compared to those without metabolic syndrome.

Metabolic syndrome is consistently defined as a clustering of several metabolic abnormalities, such as insulin resistance, abdominal obesity, elevated fasting blood glucose, dyslipidemia, and high blood pressure (Grundy, SM *et al.* 2005). However, there are several limitations in definition of metabolic syndrome. Each definition has different components of metabolic syndrome with different cutoff points and methods for measuring them (Kahn, R *et al.* 2005). These different definitions of metabolic syndrome might lead to substantial confusion and absence of comparability between studies (Cameron, AJ *et al.* 2004). For example, microalbuminuria is included in the WHO criteria but not in the NCEP ATP III. Insulin resistance is related to the WHO criteria but not for the NCEP ATP III. Current definition of metabolic syndrome cannot evaluate the severity of symptom due to using dichotomous cutoff values (Simmons, RK *et al.* 2010). In addition, there are many possible combinations that will meet the definition of metabolic syndrome. Each combination would have different association with chronic diseases. Another issue of the current definitions of metabolic syndrome is that the NCEP ATP III and WHO definitions weigh each component equally, yet it is clear that some components included in the criteria have greater risks for cardiovascular diseases and type 2 diabetes than others. Metabolic syndrome does not include all known risk factors for cardiovascular diseases, such as LDL-cholesterol, age, physical activity, smoking, and family history.

Table II - 1. Specific criteria for diagnosis of metabolic syndrome

	WHO (1998)	NCEP ATP III (2001)	IDF (2005)
	IFG, IGT, diabetes, or IR plus any two of the following components	Three or more of the following five components	High waist circumference plus any two of the following components
Body weight	Waist-to-hip ratio M: > 0.90, W: 0.85 and/or BMI > 30 kg/m ²	Waist circumference M: > 102 cm, W: 88 cm	High waist circumference (population specific)
Triglycerides	≥ 150 mg/dL	≥ 150 mg/dL	≥ 150 mg/dL or using medication
HDL-cholesterol	M: < 35 mg/dL, W: < 39 mg/dL	M: < 40 mg/dL, W: < 50 mg/dL	M: < 40 mg/dL, W: < 50 mg/dL or using medication
Fasting blood glucose		≥ 110 mg/dL ^a (includes diabetes)	≥ 100 mg/dL (includes diabetes)
Blood pressure	≥ 140 mmHg systolic or ≥ 90 mmHg diastolic	≥ 130 mmHg systolic or ≥ 85 mmHg diastolic	≥ 130 mmHg systolic or ≥ 85 mmHg diastolic or using medication
Other	Urinary albumin excretion rate ≥ 20 µg/min or albumin to creatinine ratio ≥ 30 mg/g		

BMI, Body mass index; HDL, High-density lipoprotein; IDF, International Diabetes Federation; IFG, Impaired Fasting Glucose; IGT, Impaired Glucose Tolerance; IR, Insulin Resistance; M, Men; NCEP ATP, National Cholesterol Education Program Adult Treatment Panel; W, Women; WHO, World Health Organization

^a This was modified in 2004 to be ≥ 100 mg/dL.

Prevalence of metabolic syndrome

The prevalence of metabolic syndrome is increasing worldwide. According to data from the National Health and Nutrition Examination Survey (NHANES) III and NHANESs 1999–2006, the age-adjusted prevalence of metabolic syndrome increased from 29.2 % to 34.2 % in US (Mozumdar, A and Liguori, G 2011). A collaborative study of 11 large European cohorts reported that the age-standardized prevalence of metabolic syndrome was 15.7 % in men and 14.2 % in women (Hu, G *et al.* 2004). An elevated prevalence also has been observed in Asian countries (Nestel, P *et al.* 2007) although Asian populations have lower body mass index (BMI) compared with those of Western populations. The prevalence of metabolic syndrome in Korean adults increased from 24.9 % in 1998 to 31.3 % in 2007 in a previous study by (Lim, S *et al.* 2011). The prevalence was 28.4 % for men and 35.1 % for women in China (Xu, WH *et al.* 2010), 23–27 % for men and 15–19 % for women in Japan (Miyatake, N *et al.* 2006, Nishimura, R *et al.* 2007), and 31.6 % in Indian adults (Gupta, R *et al.* 2004).

Table II - 2 shows the prevalence of metabolic syndrome in Korean adults from the results of previous studies. It is difficult to directly compare the results across studies due to differences in criteria for diagnosis of metabolic syndrome, characteristics of the study subjects, and year of study conducted. Most studies used the NCEP ATP III criteria with the modified cutoff point of waist circumference for Asian or Korean adult populations.

The ranges of prevalence of metabolic syndrome were between 9.8 % and 37.1 % in men and 12.4 % and 34.6 % in women. Several studies showed a higher prevalence of metabolic syndrome in women than those in men (Kim, HM *et al.* 2007, Kim, K *et al.* 2008, Kim, MH *et al.* 2004, Lee, WY *et al.* 2004, Park, HS *et al.* 2006). Most

prevalent components of metabolic syndrome were high blood pressure and hypertriglyceridemia in men and low HDL-cholesterol in women.

In Korean adults, cardiovascular diseases and diabetes are major causes of morbidity and mortality. Increasing prevalence of metabolic syndrome is receiving a considerable attention from researchers and policy makers because metabolic syndrome is a strong predictor of chronic diseases in the early stages. Therefore, developing strategies for the prevention and management of metabolic syndrome is important in clinical and public health fields.

Table II - 2. The prevalence of metabolic syndrome in Korean adults

Author (year)	Study subjects (n, age)	Prevalence of MetS (%)	Criteria for definition of MetS	Most prevalent component of MetS
Oh, JY <i>et al.</i> (2004) ^a	774 (M: 269, W: 505), 30–80 y	M: 29.0, W: 16.8	NCEP ATP III	N/A
Kim, MH <i>et al.</i> (2004) ^a	6,147 (M: 2,731, W: 3,416), ≥ 25 y	M: 22.1, W: 27.8	NCEP ATP III	M: HBP (47.2 %), W: LHDL (49.0 %)
Lee, WY <i>et al.</i> (2004) ^a	40,698 (M: 26,528, W: 14,170), 20–82 y	M: 9.8, W: 12.4	NCEP ATP III	M: HTG (47.6 %), W: HBP (28.9 %)
Park, HS <i>et al.</i> (2006) ^b	6,824 (M: 3,057, W: 3,757), 20–80 y	M: 13.5, W: 15.0	IDF	M: HBP (44.2 %), W: LHDL (46.2 %)
Kim, HM <i>et al.</i> (2007) ^a	4,452 (M: 1,883, W: 2,569), ≥ 20 y	M: 24.6, W: 28.1 M: 16.5, W: 28.8	NCEP ATP III IDF	M: HBP (44.8 %), W: LHDL (58.9 %)
Kim, K <i>et al.</i> (2008) ^a	910 (M: 340, W: 570), ≥ 20 y	M: 23.3, W: 34.6	NCEP ATP III	M: HBP (49.4 %), W: AO (72.5 %)
Jung, HJ <i>et al.</i> (2011) ^b	596 (M: 256, W: 340), 30–59 y	M: 37.1, W: 13.8	NCEP ATP III	M: HTG (64.5 %), W: LHDL (30.3 %)
Ahn, Y <i>et al.</i> (2013) ^a	26,006 (M: 7,561, W: 18,445), 35–75 y	M: 19.4, W: 16.3	NCEP ATP III	N/A

AO, Abdominal obesity; HBP, High blood pressure; HTG, Hypertriglyceridemia; IDF, International Diabetes Federation; LHDL, Low HDL-cholesterol; M, Men; MetS, Metabolic syndrome; N/A, Not available; NCEP ATP, National Cholesterol Education Program Adult Treatment Panel; W, Women.

^a A cutoff point for high waist circumference is 90 cm for men and 80 cm for women.

^b A cutoff point for high waist circumference is 90 cm for men and 85 cm for women.

2. Clustering patterns of metabolic syndrome components

Concept of clustering patterns of metabolic syndrome components

Metabolic syndrome is defined as a co-existence of several metabolic abnormalities, such as abdominal obesity, insulin resistance, hypertension, hyperglycemia, and dyslipidemia (Grundy, SM *et al.* 2005). Insulin resistance was considered as one dominant origin of the development of metabolic syndrome and its components in the early study (Reaven, GM 1988). However, insulin resistance cannot explain the mechanisms of developing all the components of metabolic syndrome (Simmons, RK *et al.* 2010).

Recently, several researchers have examined the role of individual components in the development of metabolic syndrome separately through identifying clusters of individual metabolic syndrome components, which provides useful information to explain the pathophysiology of metabolic syndrome (Choi, KM *et al.* 2003, Gray, RS *et al.* 1998, Hanley, AJG *et al.* 2002a, Meigs, JB *et al.* 1997, Oh, JY *et al.* 2004, Park, YM *et al.* 2006, Yoon, JH *et al.* 2011). The major clustering patterns of metabolic syndrome components commonly reported in these previous studies are 1) the insulin resistance pattern characterized by high factor loadings of fasting blood glucose and insulin, 2) the obesity pattern characterized by high factor loadings of BMI and waist circumference, 3) the dyslipidemia pattern characterized by a high factor loading of triglycerides but a negative factor loading of HDL-cholesterol, and 4) the high blood pressure pattern. These clustering patterns of metabolic syndrome components explain that insulin resistance is not the only contributor to the development of metabolic

syndrome but multiple pathophysiologic origins exist in the development of metabolic syndrome.

Factor analysis has been applied to identify major clustering patterns of metabolic syndrome components. Edwards, KL *et al.* (1994) first used factor analysis to explore the clustering patterns of metabolic syndrome components. Factor analysis is a multivariate correlation statistical method that can reveal underlying patterns or structures among high inter-correlated individual components. Each pattern represents a set of components which are thought to act in combination as an underlying pathological factor of metabolic syndrome.

Clustering patterns of metabolic syndrome components in Western adults

Clustering patterns of metabolic syndrome components in Western populations have been examined by sex or ethnicity of the study population. Most studies used factor analysis to examine the clustering patterns among metabolic syndrome components. These studies usually found two to four clustering patterns of metabolic syndrome components: insulin resistance/hyperglycemia, dyslipidemia, hypertension, and obesity. Obesity loaded with one or more metabolic syndrome components, such as insulin resistance, hyperglycemia, or dyslipidemia (Table II - 3).

Meigs, JB (2000) summarized three common findings about clustering patterns of metabolic syndrome components by literature reviews of previous studies. First, there were at least two patterns and usually three or four patterns. Second, most studies reported the blood pressure pattern to be a separate pattern. Third, insulin resistance or obesity loaded one more clustering patterns.

Meigs, JB *et al.* (1997) examined clustering patterns of metabolic syndrome components in 2,458 non-diabetic subjects of the Framingham Offspring Study. Factor analysis of metabolic syndrome components included BMI, waist-to-hip ratio (WHR), systolic and diastolic blood pressure, HDL-cholesterol, triglycerides, fasting insulin, 2-h insulin, fasting glucose, and 2-h glucose. They found three clustering patterns: the first pattern was the central metabolic syndrome pattern, which was characterized by high factor loadings of BMI, WHR, triglycerides, HDL-cholesterol, fasting insulin, and 2-hour insulin. The second pattern was the impaired glucose tolerance pattern and the third pattern was the hypertension pattern. These patterns were consistently identified across sex, age, and smoking status subgroups.

Data from the Strong Heart Study of American Indians were used to examine the correlations among the components of metabolic syndrome (Gray, RS *et al.* 1998). In this study, factor analysis was used to assess clustering patterns of metabolic syndrome components, such as systolic and diastolic blood pressure, HDL-cholesterol, triglycerides, fasting glucose and insulin, and BMI, by the presence of diabetes. In non-diabetic subjects, glucose/obesity, blood pressure, and dyslipidemia patterns were observed. In diabetic subjects, blood pressure, glucose/dyslipidemia, and obesity/insulin resistance patterns were identified.

A previous study by Hanley, AJG *et al.* (2002a) investigated clustering patterns of metabolic syndrome components using factor analysis based on data from 1,087 non-diabetic subjects of the Insulin Resistance Atherosclerosis Study. They found two clustering patterns: the metabolic pattern and the blood pressure pattern. The metabolic pattern in this study was positively associated with BMI, waist circumference, fasting glucose, and 2-h glucose, but inversely associated with insulin sensitivity and HDL-

cholesterol. The blood pressure pattern was positively associated with systolic and diastolic blood pressure. These patterns were similar within sex or ethnicity subgroups.

Maison, P *et al.* (2001) conducted a prospective population-based cohort study of 937 subjects aged 40–65 years who had oral glucose tolerance testing on two occasions at 4.5 year intervals. Changes in the components of metabolic syndrome were included in factor analysis. This study identified three clustering patterns in men and women: the blood pressure pattern (systolic and diastolic blood pressure and BMI), the glucose/obesity pattern (fasting and 2-h glucose, BMI, WHR, and fasting insulin), and the lipid/obesity pattern (triglycerides, HDL-cholesterol, BMI, WHR, and fasting insulin). In women, an additional pattern was identified, which included BMI, WHR, and fasting insulin.

In 6,868 US adults from the Third NHANES data, three clustering patterns were identified in men and women, respectively. In men, BMI, WHR, waist circumference, fasting insulin, triglycerides, and HDL-cholesterol were consistently loaded together on the first pattern. The second and third patterns were blood pressure and glucose/albuminuria pattern. In women, obesity/insulin, blood pressure, and lipid/glucose patterns were identified (Ford, ES 2003).

Table II - 3. Clustering patterns of metabolic syndrome components in Western adults

Author (year)	Subjects (n, age)	Patterns in men	Patterns in women
Meigs, JB <i>et al.</i> (1997)	2,458, 26–82 y		1) Central metabolic syndrome 2) Impaired glucose tolerance 3) Hypertension
Gray, RS <i>et al.</i> (1998)	4,228, 45–74 y	In non-diabetic subjects, 1) Glucose/obesity 2) Blood pressure 3) Dyslipidemia In diabetic subjects, 1) Blood pressure 2) Glucose/dyslipidemia 3) Obesity/insulin resistance	
Hanley, AJG <i>et al.</i> (2002a)	1,087, 40–69 y		1) Metabolic 2) Blood pressure
Maison, P <i>et al.</i> (2001)	936 (M: 393, W: 543), 40–65 y	1) Blood pressure 2) Glucose/obesity 3) Lipid/obesity	1) Blood pressure 2) Glucose/obesity 3) Insulin/obesity 4) Lipid
Ford, ES (2003)	6,868 (M: 3,410, W: 3,458), ≥ 20 y	1) Lipid/obesity 2) Blood pressure 3) Glucose /albuminuria	1) Obesity/insulin 2) Blood pressure 3) Lipid/glucose

Clustering patterns of metabolic syndrome components in Korean adults

Previous studies have suggested that three or four clustering patterns were identified using several components of metabolic syndrome in Korean adults. Although minor differences in clustering patterns of metabolic syndrome components by sex, dominant patterns observed in Korean men and women were obesity related pattern and dyslipidemia pattern. In addition, glucose and insulin abnormalities pattern was prevalent among in Korean adults. High blood pressure pattern was consistently identified as a separate pattern. Although Korean adults have differences in the susceptibility and pathway of the development of metabolic syndrome from those of Western populations, these patterns observed in Korean adults were similar to those identified in Western populations (Table II - 4).

A previous study by Choi, KM *et al.* (2003) included 1,314 elderly Koreans aged 60 years or more to explore clustering patterns of metabolic syndrome components. They used 10 components of metabolic syndrome (e.g., BMI, WHR, systolic and diastolic blood pressure, HDL-cholesterol, triglycerides, fasting insulin, 2-h insulin, fasting glucose, and 2-h glucose) for factor analysis. Obesity/dyslipidemia, high blood pressure, glucose and insulin abnormalities patterns were identified as major patterns in men and women. Obesity and dyslipidemia were closely related and loaded on the same pattern in men and women, but blood pressure was not associated with other components of metabolic syndrome.

Oh, JY *et al.* (2004) examined clustering patterns of metabolic syndrome components in an urban Korean population of 206 men and 449 women. Clustering patterns were obtained from factor analysis with BMI, waist circumference, systolic and diastolic blood pressure, fasting glucose, postprandial glucose, fasting insulin,

triglycerides, and HDL-cholesterol. They reported four clustering patterns (e.g., obesity, glucose intolerance, hypertension, and dyslipidemia) in men and three clustering patterns (e.g., obesity/hypertension, glucose intolerance, and obesity/dyslipidemia) in women, respectively.

Among the 3,443 Korean adults who aged 40 years or more and lived in rural area, three clustering patterns of metabolic syndrome components were observed in men and women, respectively (Park, YM *et al.* 2006). Eight components of metabolic syndrome, including waist circumference, BMI, fasting glucose, fasting insulin, triglycerides, HDL-cholesterol, systolic and diastolic blood pressure, were used in factor analysis. They found obesity, hypertension, and dyslipidemia/insulin resistance patterns in men and obesity/insulin resistance, hypertension, and dyslipidemia patterns in women.

Yoon, JH *et al.* (2011) used factor analysis of 11 metabolic syndrome components, such as homeostasis model assessment of insulin resistance (HOMA-IR), fasting insulin, fasting glucose, systolic and diastolic blood pressure, HDL-cholesterol, triglycerides, waist circumference, BMI, high-sensitive C-reactive protein, and adiponectin to examine multiple pathophysiological origins among the Korean adult population. Four distinctive clustering patterns, including insulin resistance, obesity/inflammatory, blood pressure, and lipid metabolic patterns, were observed in this study.

Table II - 4. Clustering patterns of metabolic syndrome components in Korean adults

Author (year)	Subjects (n, age)	Patterns in men	Patterns in women
Choi, KM <i>et al.</i> (2003)	1,314 (M: 249, W: 1,065), 60–92 y	1) Obesity/lipid 2) Blood pressure 3) Fasting glucose /insulin 4) 2-h glucose/insulin	1) Blood pressure 2) Obesity/lipid 3) Insulin resistance /glucose 4) Obesity /insulin resistance
Oh, JY <i>et al.</i> (2004)	655 (M: 206, W: 449), 30–80 y	1) Obesity 2) Glucose intolerance 3) Hypertension 4) Dyslipidemia	1) Obesity/hypertension 2) Glucose intolerance 3) Obesity/dyslipidemia
Park, YM <i>et al.</i> (2006)	3,443 (M: 1,398, W: 2,045), ≥ 40 y	1) Obesity 2) Hypertension 3) Dyslipidemia /insulin resistance	1) Obesity /insulin resistance 2) Hypertension 3) Dyslipidemia
Yoon, JH <i>et al.</i> (2011)	1,374 (M: 947, W: 427), 53.7 y (mean)		1) Insulin resistance 2) Obesity /inflammatory 3) Blood pressure 4) Lipid metabolic

3. Multiple levels of dietary determinants of metabolic syndrome

Metabolic syndrome is highly prevalent in Western and Asian populations, and it confers high risks for cardiovascular diseases and diabetes. Therefore, it is a major problem in public health. Although the pathogenesis of metabolic syndrome is complex and poorly unknown, it is known that genetic, metabolic, environmental, and lifestyle factors, including diet, smoking, drinking, and physical activity, play important roles in the development of metabolic syndrome. Specifically, diet has been strongly linked with metabolic syndrome and its components. However, the role of diet in the etiology of metabolic syndrome is incompletely understood because diet has a complex structure and interacts with other lifestyle factors. Identifying dietary determinants of metabolic syndrome and understanding mechanisms of diet determinants-induced metabolic syndrome might provide strategies aimed to improve metabolic syndrome and its components.

Various dietary determinants of metabolic syndrome have been examined at multiple levels (e.g., nutrients, food groups, and dietary patterns) in epidemiologic and clinical intervention studies. Several studies have reported the role of nutrients in the development of metabolic syndrome. They found that macronutrients (e.g., carbohydrates and fats), vitamins (e.g., vitamin D), and minerals (e.g., calcium) were associated with metabolic syndrome and its components (Freire, RD *et al.* 2005, Liu, S *et al.* 2005, McKeown, NM *et al.* 2004). Recently, antioxidant nutrient, dietary fiber, monounsaturated and polyunsaturated fatty acids have been considered as important

nutritional components that can influence on the prevention and management of metabolic syndrome (Abete, I *et al.* 2011).

Previous studies have examined foods or food groups associated with the risk of metabolic syndrome. In the US adult population, high intakes of meat, fried foods, and soda were associated with an increased risk of metabolic syndrome (Lutsey, PL *et al.* 2008) but high intakes of dairy products, whole grains, fruits, and vegetables were inversely associated with the risk of metabolic syndrome (Esmailzadeh, A *et al.* 2006, Sahyoun, NR *et al.* 2006). Fruits and vegetables, whole grains, legumes, milk and dairy products contain many beneficial nutrients, such as calcium, magnesium, potassium, and dietary fiber. A Korean study (Jung, HJ *et al.* 2011) reported that subjects who consumed more milk and dairy products had a low probability of having metabolic syndrome. High intakes of oils, fats, and sugars were positively associated with elevated waist circumference and high intakes of meat, fish, eggs, and beans were positively associated with elevated fasting blood glucose. However, high intake of vegetables was negatively associated with elevated fasting blood glucose. A study of 7,081 Korean men aged 30 years and older reported that subjects with metabolic syndrome had significantly higher intakes of seaweeds and oily foods than those without metabolic syndrome (Shin, A *et al.* 2009).

Nutrients or foods are consumed in combination as a meal rather than single form and nutrients consumed have a highly correlations with each other (Newby, PK and Tucker, KL 2004). In addition, the relationship between diet and disease are complex. Therefore, recent epidemiologic studies have focused on dietary patterns as determinants of metabolic syndrome and its components (Panagiotakos, DB *et al.* 2007, Wirfalt, E *et al.* 2001). Dietary pattern analyses might capture the entire diet of

the population and enhance interpretation and translation of study outcomes into dietary guidelines. In nutritional epidemiologic studies, factor and cluster analysis are commonly used to derive dietary patterns from collected dietary intake data. Factor analysis reduces individual dietary variables into dietary patterns based on inter-correlations among dietary variables whereas cluster analysis divides individuals into different dietary patterns based on differences in mean intakes of dietary variables (Newby, PK and Tucker, KL 2004). Recently, RRR, a new approach to derive dietary patterns, which defines linear combinations of food group intakes that maximally explain response variables (e.g., disease related nutrients or intermediate markers) was suggested by Hoffmann, K *et al.* (2004). The analyses of dietary patterns have been used to investigate the association between diet patterns and the risk of metabolic syndrome among Western and Korean adult populations. These studies demonstrated that the “Western” or “meat and alcohol” dietary pattern was associated with a high risk for developing metabolic abnormalities (Denova-Gutierrez, E *et al.* 2010a, Esmailzadeh, A *et al.* 2007, Panagiotakos, DB *et al.* 2007, Wirfalt, E *et al.* 2001), while the “healthy” dietary pattern was related to a low risk for metabolic syndrome (Esmailzadeh, A *et al.* 2007, Hong, S *et al.* 2012, Panagiotakos, DB *et al.* 2007).

4. Dietary carbohydrate intake and metabolic syndrome

Concept of GI and GL

Carbohydrate is a macronutrient which provides energy in diet as a major source and supports organ functions. Especially, carbohydrate accounts for 60–70 % of total energy intake in Asian populations (Ahn, Y *et al.* 2013, Zuñiga, YL *et al.* 2014). Carbohydrate can be categorized according to a structural/chemical basis or a functional basis. Based on the degree of polymerization, carbohydrate is typically categorized into simple sugar and complex carbohydrates. Carbohydrate is also categorized according to their physiologic function as an ability to raise blood glucose (Jenkins, DJ *et al.* 1981).

The concept of GI was first suggested by Jenkins, DJ *et al.* (1981) to help individuals with diabetes improve their blood glucose control and manage their diabetes. The GI value of a food is defined as the incremental area under the blood glucose response curve of a 50 g carbohydrate portion from a test food expressed as a percent of the response to the same amount of carbohydrate from a reference food taken by the same subject (a scale from 0 to 100). A glucose solution or white bread is usually used as the reference food. The calculation of GL was based on the amounts of carbohydrate containing foods and total carbohydrate intake with the GI value of food (Liu, S and Willett, WC 2002). DGI is an indicator of carbohydrate quality in the diet and DGL is a measure of the quality and quantity of carbohydrate in the diet.

Foods with a high GI are rapidly digested and absorbed and result in a rapid increase of blood glucose concentrations in the early postprandial stage. It also

increases insulin secretion and inhibits fat oxidation. In the middle postprandial stage, there is a marked decrease in blood glucose concentration and a suppression of fat oxidation. In the late postprandial stage, counter regulatory hormones are activated and stimulate glucose production and fat oxidation (Du, H *et al.* 2006). In contrast, foods with a low GI are slowly digested and absorbed and produce gradual rises in blood glucose and insulin concentrations. The low GI diets have shown to improve both glucose and lipid and reduce insulin resistance.

According to the international tables of GI and GL values by Atkinson, FS *et al.* (2008), legumes, pasta, fruits, and dairy products are low GI foods ($GI \leq 55$ based on the glucose as the reference food). Bread, breakfast cereals, rice, and snack products are in both high ($GI \geq 70$ based on the glucose as the reference food) and low GI foods. Potatoes and white rice are high GI foods. Recent studies have shown that increasing GI and GL in diets may adversely affect blood lipid and lipoprotein concentrations, glucose metabolism, and insulin secretion (Ludwig, DDS 2002). Findings from previous studies have shown that a high GI or GL in diets is associated with metabolic syndrome and its components, such as elevated triglycerides, elevated blood glucose, and low HDL-cholesterol (Choi, H *et al.* 2012, Culbertson, A *et al.* 2009, Finley, CE *et al.* 2010, Ford, ES and Liu, S 2001, Kim, K *et al.* 2008, Levitan, EB *et al.* 2008, Liu, SM *et al.* 2001, Murakami, K *et al.* 2006, Nakashima, M *et al.* 2010). In addition, a high GI or GL in diets has been linked to increased risks for cardiovascular diseases and type 2 diabetes (Barclay, AW *et al.* 2008, DENOVA-GUTIERREZ, E *et al.* 2010b, Salmeron, J *et al.* 1997, Villegas, R *et al.* 2007). Therefore, this approach might provide a useful means to help individuals and populations select the most appropriate carbohydrate containing foods and reduce the risks of chronic diseases.

Mechanisms of developing metabolic syndrome

It is known that a diet plays an important role in the development and management of metabolic syndrome. Earlier studies have focused on the role of excessive intakes of energy and fat in the etiology of metabolic syndrome. In Asian diets, however, carbohydrates account for 60–70 % of total energy intake and grains and cereals are main staple foods. Therefore, high carbohydrate diet in Asian populations might affect the development of metabolic syndrome substantially. The mechanism of high carbohydrate intake in the development of metabolic syndrome is not fully understood.

Carbohydrate is the macronutrient that provides energy and can thus contribute to weight gain when consumed in excess of energy requirements. In addition, a high carbohydrate diet can result in an increase of insulin demand and hyperglycemia, depending on the amounts and sources of carbohydrates. An increased secretion of insulin leads to hyperinsulinemia and insulin resistance, which result in glucose intolerance and hyperglycemia. Insulin resistance also causes an excessive release of free fatty acids into the blood. In the liver, an increased flux of free fatty acids increases hepatic triglycerides synthesis (Liu, SM *et al.* 2001). On the other hand, a low carbohydrate diet results in less insulin secretion to maintain normal glucose concentration in blood, which may be beneficial in individuals who are resistant to insulin or have insulin secretion abnormalities. In Asian populations, high carbohydrate diets mainly derived from refined grains, such as white rice have been associated with high triglycerides and low HDL-cholesterol, and it probably contributes to the development of metabolic syndrome (Kim, K *et al.* 2008, Radhika, G *et al.* 2009). Therefore, both the amounts and the sources of carbohydrates are important determinants of metabolic syndrome and its components.

Association between dietary carbohydrate intake and metabolic syndrome in Western adults

Extensive studies on the association between dietary carbohydrate intake and the risk of metabolic syndrome have been conducted in Western populations. Dietary carbohydrate variables used in these studies were total carbohydrate, percentage of energy from carbohydrate intake, DGI, DGL, total grains, whole grains, and refined grains. Both the sources and the amounts of dietary carbohydrates have an effect on alteration of glucose and lipid metabolisms. Higher intakes of carbohydrate, including DGI and DGL, and refined grains, have resulted in elevated triglycerides (Liu, SM *et al.* 2001), blood glucose and insulin and decreased HDL-cholesterol (Ford, ES and Liu, S 2001, Frost, G *et al.* 1999). Several studies in western populations reported that diets with high GI or high GL increased risks of metabolic syndrome, diabetes, and cardiovascular diseases (Denova-Gutierrez, E *et al.* 2010b, Finley, CE *et al.* 2010, Hodge, AM *et al.* 2004, Schulze, MB *et al.* 2004). On the other hand, diets with high total grains or whole grains might help to prevent cardiovascular diseases and type 2 diabetes (Jacobs, DR *et al.* 1998, McKeown, NM *et al.* 2002, Ye, EQ *et al.* 2012). Therefore, the American Diabetes Association (ADA 2008) suggested dietary recommendations, including monitoring carbohydrate intake about both quantity and quality and choosing high fiber foods (e.g., whole grains, vegetables, legumes, and fruits). In addition, they emphasized the intake of low GI and GL foods to provide an additional benefit in the glycemic control.

Yang, EJ *et al.* (2003) found that percentage of energy from carbohydrate intake was positively associated with triglycerides in the US adult women ($n = 4,074$) from the Third NHANES. However, in men ($n = 3,754$), percentage of energy from

carbohydrate intake was inversely associated with BMI and total cholesterol. A cross-sectional study of US adults aged 20–79 years (Finley, CE *et al.* 2010) examined the association between DGI, DGL, and the prevalence of metabolic syndrome and its components. They found a positive association of DGI with metabolic syndrome, elevated triglycerides, and low HDL-cholesterol and an inverse association of DGI with elevated fasting blood glucose in men. McKeown, NM *et al.* (2004) examined a cross-sectional association between dietary carbohydrates intake, insulin resistance, and the prevalence of metabolic syndrome among 2,834 US adults from the Fifth examination of the Framingham Offspring Cohort. After adjustment for potential confounding variables, intakes of total dietary fiber, cereal fiber, fruit fiber, and whole grains were inversely associated, whereas DGI and DGL were positively associated with HOMA-IR. The prevalence of metabolic syndrome was significantly lower among subjects in the highest quintile of cereal fiber (Odds ratio (OR) = 0.62, 95% confidence interval (CI) = 0.45–0.86) and whole grains (OR = 0.67, 95% CI = 0.48–0.91) intakes compared to those in the lowest quintile. Conversely, the prevalence of metabolic syndrome was significantly higher among subjects in the highest quintile of DGI compared to those in the lowest quintile (OR = 1.41, 95% CI = 1.04–1.91). Intakes of total carbohydrate, dietary fiber, fruit fiber, vegetable fiber, legume fiber, DGL, and refined grains were not associated with the prevalence of metabolic syndrome. A cross-sectional study (Levitan, EB *et al.* 2008) of non-diabetic women from the Women’s Health Study showed that DGI was positively associated with low-density lipoprotein (LDL)-cholesterol, LDL/HDL-cholesterol ratio, and triglycerides but inversely associated with HDL-cholesterol. They also reported that DGL was inversely associated with HDL-cholesterol but positively associated with triglycerides

and LDL/HDL-cholesterol ratio. Liu, SM *et al.* (2001) reported that DGI and DGL were inversely associated with HDL-cholesterol and positively associated with triglycerides among 280 healthy postmenopausal women from the Nurses' Health Study, but they did not examine the association with metabolic syndrome. For the lowest and highest quintiles of DGL, the multivariate adjusted geometric mean of HDL-cholesterol were 58 and 52 mg/dL (P for trend < 0.05) whereas the geometric mean of triglycerides were 87 and 155 mg/dL (P for trend < 0.05), respectively. For the lowest and highest quintiles of DGI, the geometric mean of triglycerides were 103 and 120 mg/dL (P for trend < 0.05), respectively. For the lowest and highest quintiles of total carbohydrate intake, the geometric mean of triglycerides were 97 and 141 mg/dL (P for trend < 0.05), respectively. Culberson, A *et al.* (2009) found no association between metabolic syndrome and DGL but reported an inverse association between DGL and HDL-cholesterol based on data from the Third NHANES.

Overall, previous studies have shown consistent findings that both the quantity and quality of dietary carbohydrate intake were inversely associated with HDL-cholesterol and positively associated with triglycerides. In addition, these findings are consistent with findings from metabolic studies showing that high carbohydrate, low fat diets reduce HDL-cholesterol and increase triglycerides (Jeppesen, J *et al.* 1997, Knopp, RH *et al.* 1997, Mensink, RP and Katan, MB 1987). However, conflicting results on the association of high carbohydrate intake with waist circumference, blood pressure, and blood glucose were observed in previous studies. Furthermore, the association between carbohydrate intake and metabolic diseases was not consistent across previous studies.

Epidemiologic studies in Western populations have shown an inverse association between whole grain intake and the risk of metabolic syndrome, which is mediated by low insulin concentration or higher insulin sensitivity or low body weight (Kim, JY *et al.* 2008). Previous studies found that diets rich in whole grains might protect against cardiovascular diseases (Jacobs, DR *et al.* 1998, Jacobs, DR *et al.* 1999, Liu, SM *et al.* 1999), stroke (Liu, SM *et al.* 2000b), and type 2 diabetes (Liu, SM *et al.* 2000a, Meyer, KA *et al.* 2000). Whole grains contain many beneficial nutrients, such as dietary fiber, flavonoids, vitamin E, magnesium, folate, selenium, and zinc (Slavin, J *et al.* 1997, Slavin, JL *et al.* 1999), which may play important roles in the prevention of metabolic syndrome. Whole grains tend to be slowly digested and absorbed, and thus have low GI. In addition, diets high in whole grains tend to reflect an overall healthier lifestyle and dietary pattern (McKeown, NM *et al.* 2002).

Refined grains are more available today due to the development of food processing technology and the modern milling process. Refined grains contain lower amounts of vitamin E, dietary fiber, and magnesium than do whole grains (Slavin, JL *et al.* 2000) because refining process destroys the structure of grains and removes dietary fiber and other essential micronutrients in grains. High intakes of refined grains, including white rice, might induce high glycemic responses and has been associated with increased risks of metabolic syndrome, type 2 diabetes, and cardiovascular diseases (Sun, Q *et al.* 2010).

McKeown, NM *et al.* (2002) examined the association between diets rich in whole grains or refined grains and several metabolic syndrome components in the Framingham Offspring Study. This cross-sectional study of 2,941 US adults showed that whole grain intake was inversely associated with BMI, WHR, total cholesterol,

LDL-cholesterol, and fasting insulin. There were no significant trends in metabolic syndrome components across quintiles of refined grain intake. In the 535 healthy older adults aged 60–98 years, a significant inverse association between whole grain intake and metabolic syndrome was observed after adjustment for potential confounding variables (Sahyoun, NR *et al.* 2006). On the other hand, a high intake of refined grains was significantly associated with an elevated fasting blood glucose and a high prevalence of metabolic syndrome. Wirfalt, E *et al.* (2001) found that the refined bread food pattern was associated with hyperinsulinemia in women whereas the high-fiber bread food pattern was inversely associated with central obesity and dyslipidemia in men. An association between a high intake of white rice and an increased risk of type 2 diabetes was observed in the US population (Sun, Q *et al.* 2010).

Association between dietary carbohydrate intake and metabolic syndrome in Asian and Korean adults

Dietary carbohydrates account for a considerable part of daily energy intake in Asian populations compared to Western populations. High carbohydrate diets have been known to influence adverse effects in blood lipid and lipoprotein concentrations and also lead to glucose and insulin abnormalities. A different association of dietary carbohydrate intake with metabolic syndrome and its components might exist between Western and Asian populations. In Asian populations, white rice is the staple food that is a major contributor to total carbohydrate and energy intake in their diets, and a high consumption of refined grains, including white rice increases DGI and DGL. Therefore, it is important to understand the associations of quantity and quality of

dietary carbohydrates in diet with the risk of metabolic syndrome in order to develop public health recommendations among Asian populations.

A cross-sectional study by Murakami, K *et al.* (2006) examined the associations between DGI, DGL, and several metabolic syndrome components in 1,354 healthy Japanese women aged 20–78 years with traditional dietary habits. The mean DGI was 67 and the mean DGL (/1000 kcal) was 88 in this study population. White rice was the major contributor to DGI and DGL (58.5 %). After adjustment for potential confounding variables, DGI was positively associated with BMI, triglycerides, and fasting blood glucose. DGL was inversely associated with HDL-cholesterol but positively associated with triglycerides and fasting blood glucose. Amano, Y *et al.* (2004) also reported that DGI and DGL were positively associated with triglycerides but inversely associated with HDL-cholesterol among 32 Japanese women participated in a weight reduction program. In this study subjects, the mean DGI was 64 (Standard deviation (SD) = 6) and the mean DGL was 150 (SD = 37).

Although percentage of energy from carbohydrate in Korean diet has decreased in recent years, the percentage of energy from carbohydrate is about 66 %. Therefore, the amounts and the sources of dietary carbohydrate intake might play a significant role in the development of metabolic syndrome in Korean adults. Kim, K *et al.* (2008) examined the relationship between intakes of carbohydrate, DGI, and DGL and metabolic syndrome among Korean adults aged 20 years or more. In this study, they found that the quantity and quality of carbohydrates were positively associated with the risk of metabolic syndrome in women but not in men. In addition, the adverse effect of high carbohydrate intake on the risk of metabolic syndrome was observed in obese women but not in women with a normal weight. Among the components of metabolic

syndrome, elevated triglycerides and low HDL-cholesterol were positively associated with DGI and DGL in women. Choi, H *et al.* (2012) observed a significant inverse association between dietary carbohydrate variables and HDL-cholesterol concentration, except for DGI. The ORs for having low HDL-cholesterol in the highest quintile were 1.66 (95% CI = 1.24–2.22) for total carbohydrate, 1.34 (95% CI = 1.02–1.75) for percentage of energy from carbohydrate, and 1.54 (95% CI = 1.17–2.03) for DGL in men as compared with the second quintile as a reference. The ORs for having low HDL-cholesterol was 1.38 (95% CI = 1.12–1.71) for percentage of energy from carbohydrate in women. Other dietary carbohydrate variables were not associated with the prevalence of low HDL-cholesterol in women.

Park, SH *et al.* (2010) examined the association between excessive intakes of carbohydrates and risk factors for cardiovascular diseases in a representative sample of the Korean adult population from the Third KNHANES. The high carbohydrate diet (> 70 % of energy intake) was positively associated with BMI, blood pressure, fasting blood glucose, triglycerides, and LDL-cholesterol and negatively associated with HDL-cholesterol in women but not in men, except for systolic blood pressure. The women with a high carbohydrate diet had higher ORs for type 2 diabetes (OR = 2.53, 95% CI = 1.35–4.73, *P* for trend = 0.004) and low HDL-cholesterol (OR = 1.54, 95% CI = 1.26–1.87, *P* for trend < 0.0001) compared to those who consumed recommended level of carbohydrate (55–70 %). Choi, J *et al.* (2012) reported that a high carbohydrate diet (\geq 59.9 % of energy intake) was positively associated with the risk of metabolically obese normal weight compared to a low carbohydrate diet (< 59.9 %) in Korean women. In addition, the association between the high carbohydrate diet and the components of metabolically obese normal weight, such as elevated triglycerides and

low HDL-cholesterol was stronger in postmenopausal women than in premenopausal women. A cross-sectional study of 404 Korean elderly subjects aged 60 years or older (Kim, MH *et al.* 2007) showed that subjects with metabolic syndrome had a higher carbohydrate intake than those in the control group. In Korean women with type 2 diabetes, a higher OR for metabolic syndrome was found in the highest quartile of carbohydrate intake compared to those in the lowest quartile (OR = 3.0, 95% CI = 1.6–5.6) (Kim, WY *et al.* 2008).

Previous studies have shown that subjects with metabolic diseases had excessive intake of carbohydrate. A high carbohydrate diet in Korean adults is associated with excessive intake of white rice because white rice is the main staple food and a primary source of carbohydrate in Asian diet. For example, Korean adults consume rice two or three times a day as a staple food. Higher intake of refined grains, including white rice, has been associated with increased risks of metabolic diseases, such as metabolic syndrome (Radhika, G *et al.* 2009, Shi, ZM *et al.* 2012) and type 2 diabetes (Hu, EA *et al.* 2012, Nanri, A *et al.* 2010, Villegas, R *et al.* 2007) in Asian populations. The mechanism of this association is not fully understood. High consumption of white rice with high GI might lead to elevate a postprandial blood glucose and insulin. In addition, refined grains, such as white rice, contain low dietary fiber and other nutritional compounds that are associated with a reduced risk of metabolic diseases. Son, SH *et al.* (2013) insisted that higher percentages of energy from white rice were inversely associated with lower index of nutritional quality.

A cross-sectional study of 2,728 Singaporean Chinese adults (Zuñiga, YL *et al.* 2014) reported that intakes of refined grains (e.g., white rice and noodle) were associated with metabolic risk factors and intake of white rice was positively

associated with fasting blood glucose and HOMA-IR. The urban Asian Indian study (Radhika, G *et al.* 2009) found that high consumption of refined grains was associated with high body weight, waist circumference, fasting blood glucose, triglycerides, blood pressure, but low HDL-cholesterol after multivariate adjustment for potential confounding variables. The prevalence of metabolic syndrome was 36.5 % in the highest quartile of refined grain consumption but 13.9 % in the lowest quartile. The OR for having metabolic syndrome in the highest quartile of refined grain consumption was 7.83 (95% CI = 4.72–12.99) compared to the lowest quartile as a reference. A population based cross-sectional study of 827 Tehranian adults aged 18–74 years examined the relationship between whole grain consumption and the prevalence of metabolic syndrome and its components (Esmailzadeh, A *et al.* 2005). After adjustment for potential confounding variables, the quartiles of whole grains intake were significantly associated with the lower prevalences of abdominal obesity (Q4 vs. Q1: OR = 0.90, 95% CI = 0.79–0.96), hypertriglyceridemia (Q4 vs. Q1: OR = 0.53, 95% CI = 0.42–0.68), elevated blood pressure (Q4 vs. Q1: OR = 0.79, 95% CI = 0.70–0.85), abnormal glucose homeostasis (Q4 vs. Q1: OR = 0.75, 95% CI = 0.63–0.90) and metabolic syndrome (Q4 vs. Q1: OR = 0.68, 95% CI = 0.60–0.78) compared to the lowest quartile as a reference. A high consumption of refined grains was positively associated with the prevalences of hypertriglyceridemia (Q4 vs. Q1: OR = 2.23, 95% CI = 2.01–2.74), elevated blood pressure (Q4 vs. Q1: OR = 1.89, 95% CI = 1.41–2.33), and metabolic syndrome (Q4 vs. Q1: OR = 2.25, 95% CI = 1.80–2.84).

The Chinese study of 1,231 adults aged 20 years and older (Shi, ZM *et al.* 2012) examined a prospective association between rice intake and weight change and metabolic syndrome. The multivariate adjusted ORs for elevated fasting blood glucose

across rice intake (≤ 200 , 201–400, and ≥ 401 g/day) were 1.00, 1.96, and 2.50 (P for trend = 0.005), respectively. On the other hand, an inverse association between rice intake and the risk of high blood pressure was observed in this study (OR = 0.58, 95% CI = 0.36–0.93, P for trend = 0.009). Percentage of rice in staple food was positively associated with lower HDL-cholesterol. However, rice intake and percentage of rice in staple food were not associated with the risk of metabolic syndrome.

Ahn, Y *et al.* (2013) found various rice-eating patterns among 26,006 Korean adults with a carbohydrate based diet: 1) white rice, 2) rice with beans, 3) rice with multi-grains, and 4) mixed. These rice-eating patterns had different effects on the risk of metabolic syndrome. In men, the OR for elevated waist circumference was higher in the mixed group (OR = 1.18, 95% CI = 1.02–1.36) than the white rice group. In women, the ORs for elevated waist circumference and elevated fasting glucose were lower in the rice with beans group and elevated waist circumference in the rice with multi-grains group than those in the white rice group. In addition, ORs for elevated blood pressure and metabolic syndrome were lower in the mixed group than those in the white rice group.

In summary, an excessive intake of dietary carbohydrate or a rice-oriented dietary pattern low in other food groups was associated with an increased risk of metabolic syndrome in Korean adults. Therefore, adequate amounts of carbohydrate intake and substituting carbohydrate sources (for example, brown rice instead of white rice) to reduce DGI and DGL may prove a better strategy to decrease the risk of metabolic syndrome and its components in Asian populations whose total energy is primarily supplied through dietary carbohydrates.

5. Alcohol intake and metabolic syndrome

Mechanisms of developing metabolic syndrome

Alcohol drinking is an important lifestyle factor associated with the risks for several metabolic diseases, such as obesity, metabolic syndrome, type 2 diabetes, and cardiovascular diseases. Alcohol drinking is one of the most prevalent habit especially in men. Light to moderate alcohol consumption might have a protection effect on risks of metabolic syndrome (Freiberg, MS *et al.* 2004), type 2 diabetes (Koppes, LL *et al.* 2005), and cardiovascular diseases (Agarwal, DP 2002, Reynolds, K *et al.* 2003, Rimm, EB *et al.* 1999) through increasing insulin sensitivity (Bell, RA *et al.* 2000) and HDL-cholesterol (Rimm, EB *et al.* 1999). On the other hand, the harmful effect of heavy alcohol consumption on metabolic diseases have been suggested in previous studies. The harmful effect might be due to elevated triglycerides (Baik, I and Shin, C 2008, Jin, L *et al.* 2011, Wakabayashi, I 2010, Yoon, YS *et al.* 2004), elevated blood pressure (Jin, L *et al.* 2011, Sesso, HD *et al.* 2008, Xin, X *et al.* 2001), and glucose and insulin abnormalities (Baik, I and Shin, C 2008, Stoutenberg, M *et al.* 2013).

Alcohol drinking plays an important role in the development of metabolic syndrome, but previous studies have shown an inconsistent relationship between alcohol consumption and metabolic syndrome. Furthermore, the relationships differ by gender, ethnicity, or types of alcohol beverage. Some studies have shown a positive association (Wakabayashi, I 2010, Zhu, SK *et al.* 2004), whereas others have reported a negative association (Alkerwi, A *et al.* 2009, Stoutenberg, M *et al.* 2013) or no association (Kawada, T and Okada, K 2006, Santos, AC *et al.* 2007).

A meta-analysis (Alkerwi, A *et al.* 2009) of observational studies of Western and Asian populations concluded that light to moderate alcohol consumption was associated with a reduced prevalence of metabolic syndrome in men (< 40 g/day) and women (< 20 g/day). Another meta-analysis (Sun, K *et al.* 2013) including prospective studies showed that light drinkers had a lower risk of metabolic syndrome (RR = 0.86, 95% CI = 0.75–0.99) while heavy drinkers had a higher risk of metabolic syndrome (RR = 1.84, 95% CI = 1.34–2.52) compared with non-drinkers, respectively.

Association between alcohol intake and metabolic syndrome in Western adults

Epidemiologic and clinical studies in Western populations have shown that light to moderate alcohol drinking is associated with a reduced risk of metabolic syndrome. On the other hand, heavy alcohol consumption increases the risk of metabolic syndrome. Among the components of metabolic syndrome, consistent evidence on blood pressure elevated by moderate to heavy alcohol drinking has been reported.

Two prospective studies in the US adults showed inconsistent findings on the association between alcohol intake and the risk of metabolic syndrome: one study found no association (Carnethon, MR *et al.* 2004), but another study reported an inverse association (Stoutenberg, M *et al.* 2013). A cross-sectional analysis of data from the Third NHANES in the US population showed that mild to moderate alcohol consumption was associated with a low prevalence of metabolic syndrome (Freiberg, MS *et al.* 2004). After adjustment for age, sex, race/ethnicity, education, income, smoking, physical activity, and dietary variables, subjects who consumed 1 to 19 drinks and 20 drinks or more of alcohol per month had ORs for the prevalence of metabolic syndrome of 0.65 and 0.34, respectively, compared with current non-

drinkers. In addition, alcohol consumption was significantly associated with a reduced prevalence of metabolic syndrome components, such as low HDL-cholesterol, elevated triglycerides, elevated waist circumference, and hyperinsulinemia. Cross-sectional studies conducted in Canada (Gigleux, I *et al.* 2006) and Sweden (Lidfeldt, J *et al.* 2003) also reported that light and moderate alcohol consumption was negatively associated with the prevalence of metabolic syndrome. However, several cross-sectional studies have not found any association between alcohol consumption and metabolic syndrome in men and women (Santos, AC *et al.* 2007, Villegas, R *et al.* 2004a).

Association between alcohol intake and metabolic syndrome in Asian and Korean adults

The evidence about the relationship between alcohol consumption and metabolic syndrome in Asian populations is sparse. Among 22,892 Japanese men and women, a high alcohol intake (> 21.5 g/day) was significantly associated with an increased risk of metabolic syndrome after adjustment for sex and age (Urashima, M *et al.* 2005). A cross-sectional study of 2,358 Taiwanese men reported that heavy alcohol drinkers (\geq 50 g/day) had higher ORs for elevated triglycerides (OR = 1.74, 95% CI = 1.18–2.56) and elevated fasting blood glucose (OR = 1.72, 95% CI = 1.15–2.59), but a lower OR for low HDL-cholesterol (OR = 0.41, 95% CI = 0.28–0.60) compared to non-drinkers. However, there was no significant association between heavy drinking and metabolic syndrome.

Heavy alcohol consumption is prevalent in Korean adult men (Lee, MY *et al.* 2010, Yoon, YS *et al.* 2004) and the prevalence of metabolic syndrome is increasing in

this population (Lim, S *et al.* 2011). Therefore, examining the association between alcohol intake and the risk of metabolic syndrome and its components among the Korean adult population is necessary. The summary findings on the association between alcohol consumption and metabolic syndrome in Korean adults are shown in Table II - 5. Cross-sectional and prospective studies have shown that heavy alcohol consumption was associated with high risks for metabolic syndrome and its components, whereas the association between moderate alcohol consumption and the risk of metabolic syndrome was not consistent.

Two prospective studies (Baik, I and Shin, C 2008, Kim, BJ *et al.* 2012) showed that heavy drinking (30 g or more per day) was positively associated with risks for metabolic syndrome and its components, such as elevated blood pressure and elevated triglycerides. However, heavy alcohol consumption was inversely associated with the risk of low HDL-cholesterol. Cross-sectional studies in Korean men (Lee, MY *et al.* 2010, Park, SH 2012, Shin, MH *et al.* 2013) found that heavy alcohol consumption was associated with an increased prevalence of metabolic syndrome by elevated waist circumference, triglycerides, blood glucose, and blood pressure. However, two cross-sectional studies reported an inverse association between moderate alcohol consumption and the prevalence of metabolic syndrome (Park, SH 2012, Yoon, YS *et al.* 2004).

Overall, heavy alcohol consumption was associated with high waist circumference, high triglycerides, high fasting blood glucose, and high blood pressure, but inversely associated with low HDL-cholesterol. In a cross-sectional study of 27,030 Korean men (Sung, KC *et al.* 2007), heavy alcohol consumption (> 40 g/d) was positively associated with BMI, blood pressure, fasting blood glucose, and

triglycerides concentrations, but inversely associated with insulin and LDL-cholesterol concentrations.

It is difficult to directly compare the findings from previous studies due to differences in characteristics of study population and type of alcohol usually consumed. The accuracy of assessment of alcohol consumption is necessary to examine the association between alcohol intake and metabolic syndrome because heavy drinkers are more likely to underreport alcohol consumption or less likely to participate in the study.

Table II - 5. The association between alcohol consumption and metabolic syndrome in Korean adults

Author (year)	Study design	Assessment of alcohol consumption	Study subjects (prevalence or cases)	Alcohol consumption & MetS	Alcohol consumption & MetS components
Lee, MY <i>et al.</i> (2010)	Cross-sectional	Questionnaire (interviewer-administered) including drinking frequency and the average amount of alcohol they drank per week in the past 12 months	M: 4,089	0 g/d: 1.00 (Ref) > 40 g/d: 1.33 (1.11–1.59)	(+) HWC, HBP, HBG (-) LHDLD
Park, SH (2012)	Cross-sectional, using 2008 KNHANES	Questionnaire (interviewer-administered) including lifetime experience of drinking, frequency, usual quantity, and frequency of binge drinking in the past 12 months	M: 2,707 (23.2 %)	Lifetime abstainer: 1.00 (Ref) Ex-drinker: 3.15 (1.69–5.89) 0.1–39.9 g/d: 1.77 (1.00–3.13) ≥ 40 g/d: 2.06 (1.05–4.07)	(+) HBP, HBG (-) LHDLD
			W: 3,725 (24.4 %)	Lifetime abstainer and Ex-drinker: 1.00 (Ref) 0.1–19.9 g/d: 0.78 (0.62–0.98)	(+) HBP (-) LHDLD
Shin, MH <i>et al.</i> (2013)	Cross-sectional	Questionnaire (interviewer-administered) including lifetime experience of drinking, frequency, and usual quantity	M: 3,178 (38.3 %)	Lifetime abstainer: 1.00 (Ref) > 4.0 drinks/d: 1.63 (1.23–2.14)	(+) HWC, HTG, HBP, HBG (-) LHDLD
			W: 5,003 (49.5 %)		(+) HWC (-) LHDLD

Table II - 5. The association between alcohol consumption and metabolic syndrome in Korean adults (continued)

Author (year)	Study design	Assessment of alcohol consumption	Study subjects (prevalence or cases)	Alcohol consumption & MetS	Alcohol consumption & MetS components
Yoon, YS <i>et al.</i> (2004)	Cross-sectional, using 1998 KNHANES	Questionnaire (interviewer-administered) including average frequency (days/month) and amount (in mL) of alcoholic beverages ingested on a typical occasion or during a typical day	M: 3,597 (20.8 %)	0 g/d: 1.00 (Ref) 1–14.9 g/d: 0.71 (0.53–0.95)	(+) HWC, HBP, HTG (-) LHDLD
			W: 4,365 (26.9 %)	0 g/d: 1.00 (Ref) 1–14.9 g/d: 0.80 (0.65–0.98)	(+) HBG, HBP, HTG (-) LHDLD
Baik, I and Shin, C (2008)	Prospective, 4-year follow-up	Questionnaire (interviewer-administered) including drinking frequency, the average amount of 6 types of alcoholic beverages, and the volume of 1 standard drink for each type of alcoholic beverages	M & W: 3,383 (220 cases)	0 g/d: 1.00 (Ref) > 30 g/d: 1.63 (1.02–2.62)	(+) HWC, HTG, HBP, HBG (-) LHDLD
Kim, BJ <i>et al.</i> (2012)	Prospective, 3-year follow up	Questionnaire (self-reported) including drinking frequency and the average amount of alcohol per time	M: 4,505 (479 cases)	0 g/d: 1.00 (Ref) < 14.9 g/d: 1.51 (1.06–2.13) 15–29.9 g/d: 1.71 (1.14–2.55) ≥ 30.0 g/d: 2.11 (1.25–3.56)	(+) HBP, HTG (-) LHDLD

HBG, high blood glucose; HBP, high blood pressure; HTG, high triglycerides; HWC, high waist circumference; KNHANES, Korea National Health and Nutrition Examination Survey; LHDLD, low HDL-cholesterol; M, men; MetS, metabolic syndrome; Ref, reference group; W, women.

6. Food group intake and metabolic syndrome

Fruits and vegetables

According to previous studies, high intakes of fruits and vegetables have been associated with reduced risks for metabolic diseases, such as type 2 diabetes, cardiovascular diseases, and cancer (Genkinger, JM *et al.* 2004, Hung, HC *et al.* 2004, Liu, S *et al.* 2000, Liu, S *et al.* 2004). Fruits and vegetables are major sources of dietary fiber, vitamins, mineral, and other beneficial nutritional compounds. Studies examined the direct association between the consumption of fruits and vegetables and risks of metabolic syndrome and its components are limited. In addition, the mechanisms of a protective effect of fruits and vegetables on the development of metabolic syndrome have not been well established.

A cross-sectional study (Yoo, S *et al.* 2004) of young US adults aged 19–38 years was conducted to examine the relationship between dietary intakes and the risk of metabolic syndrome. Subjects of this study were divided into three groups according to the number of metabolic syndrome components (0, 1 or 2, and ≥ 3). After adjustment for age, total energy intake, BMI, and physical activity, mean intakes of fruits, fruit juice, and vegetables were significantly higher in subjects who had no component than in subjects who had 1 or 2 components (3.30 vs. 2.99 servings/day, P -value < 0.05). Among 468 Tehrani women aged 40–60 years, high intakes of fruits and vegetables were inversely associated with the risk of metabolic syndrome after adjustment for potential confounding variables (Esmailzadeh, A *et al.* 2006). Subjects in the highest quintile of fruits intake had a lower OR for metabolic syndrome (OR = 0.66, 95% CI =

0.54–0.80) than those in the lowest quintile. Subjects in the highest quintile of vegetables intake had a lower OR for metabolic syndrome (OR = 0.70, 95% CI = 0.61–0.84) than those in the lowest quintile. In addition, high intakes of fruits and vegetables were significantly associated with reduced risks for metabolic syndrome components, including elevated waist circumference, elevated triglycerides, elevated fasting blood glucose, and elevated blood pressure. In the Korean study of middle-aged men and women, a low intake of fruits was significantly associated with a high OR for elevated waist circumference (OR = 1.85, 95% CI = 1.03–3.33), but was not associated with other components of metabolic syndrome (Jung, HJ *et al.* 2011).

Milk and dairy products

Milk and dairy products are important dietary factors that might affect the development of metabolic syndrome. Previous epidemiologic and experimental studies in Western and Asian populations have suggested that milk and dairy products may have favorable effects on obesity and metabolic diseases, such as hypertension, cardiovascular diseases, and type 2 diabetes (Choi, HK *et al.* 2005, Liu, S *et al.* 2006, Wang, L *et al.* 2008) due to high content of beneficial nutrients, including calcium, potassium, and magnesium, in milk and dairy products.

Milk and dairy products are the main source of dietary calcium. There are evidences that calcium decrease LDL-cholesterol and triglycerides but increase HDL-cholesterol (van Meijl, LEC *et al.* 2008); inhibits fat absorption and increases fecal fat excretion (Tholstrup, T 2006); and reduces body weight and fat mass (Zemel, MB 2009). In addition, a possible effect of milk and dairy products on the development of

metabolic syndrome can be explained by healthy dietary patterns associated with intakes of milk and dairy products (e.g., low GI diet).

Prospective studies from Western populations have shown a consistent relationship between milk and dairy products consumption and reduced risks of metabolic syndrome and its components. The French epidemiologic study based on the metabolic syndrome patient cohort reported that a high consumption of dairy products was associated with a low incidence of metabolic syndrome and its components, such as impaired glucose tolerance and diabetes (Fumeron, F *et al.* 2011). The prospective effect of dairy products consumption on metabolic syndrome has also been reported from the Atherosclerosis Risk in Communities patient cohort (Lutsey, PL *et al.* 2008). A prospective study (Pereira, MA *et al.* 2002) of young US adults examined the association between dairy products consumption and the incidence of metabolic syndrome. Dairy products consumption was inversely associated with the incidence of hypertension, dyslipidemia, abnormal glucose homeostasis, and obesity among overweight subjects ($BMI \geq 25 \text{ kg/m}^2$) but not among normal weight subjects ($BMI < 25 \text{ kg/m}^2$). The multivariate adjusted OR for metabolic syndrome was 0.28 (95% CI = 0.14–0.58) among overweight subjects in the highest group of dairy products consumption compared with the lowest group. These findings from previous studies suggest that consumption of milk and dairy products is associated with a low prevalence of metabolic syndrome and its components. Elwood, PC *et al.* (2007) also showed an inverse relationship between milk consumption and the presence of metabolic syndrome. Men who drank one pint of milk or more per day had a lower OR for metabolic syndrome (OR = 0.38, 95% CI = 0.18–0.78) compared to men who drank little or no milk. In addition, many cross-sectional studies showed the same inverse

association between intakes of milk and dairy products and risks for metabolic syndrome and its components. A cross-sectional study (Ruidavets, JB *et al.* 2007) of 912 French men aged 45–64 years reported that a high consumption of dairy products was associated with a low prevalence of metabolic syndrome after adjustment for confounding variables (Q5: OR = 0.64, 95% CI = 0.37–1.09). A population based cross-sectional study (Azadbakht, L *et al.* 2005) of 827 Tehranian adults showed that high consumption of dairy products was inversely associated with the risk of having elevated waist circumference (Q4: OR = 0.80, 95% CI = 0.63–0.98), elevated blood pressure (Q4: OR = 0.83, 95% CI = 0.69–0.99), and metabolic syndrome (Q4: OR = 0.82, 95% CI = 0.63–0.99).

The results from Korean studies showed the inverse association between intakes of milk and dairy products and risks of metabolic syndrome and its components. Based on the Third KNHANES, Kwon, HT *et al.* (2010) examined the association between milk intake and the prevalence of metabolic syndrome among Korean adults. Overweight adults who drank milk more frequently (once a day or more) had a lower risk of metabolic syndrome compared with those who rarely consumed. Another study by Jung, HJ *et al.* (2011) showed that poor adherence to the recommendation intake for milk and dairy products was associated with a high risk of metabolic syndrome.

In the Korean population, a particularly low intake of milk and dairy products was observed, which applied to all age and sex. The overall milk and dairy products intake in adults aged 19 years and above was reported as having not consumed even half the recommended servings (Song, S *et al.* 2014). However, a few studies have examined the association between milk and dairy products consumption and risks of metabolic syndrome and its components among the Korean adult population.

Foods with high contents of fats and sugars

Foods with high contents of fats and sugars are a source of excessive energy intake, which may be associated with risks for obesity and chronic diseases (Cohen, DA *et al.* 2010, Malik, VS *et al.* 2010). Yoo, S *et al.* (2004) reported that the mean intake of sweetened beverages was lower in subjects who had no component of metabolic syndrome than in subjects who had 1 or 2 components or ≥ 3 components among white (1.45 compared with 1.77 and 2.22 servings/day in men, respectively; 1.26 compared with 1.62 and 1.78 servings/day in women, respectively) after adjustment for age, total energy intake, BMI, and physical activity. A total of 7,081 Korean men aged 30 years and older were included in the data analyses to evaluate the relationship between food group intake and the risk of metabolic syndrome (Shin, A *et al.* 2009). In this study, subjects who consumed oily foods more frequently had a higher OR for metabolic syndrome than those who consumed oily foods less frequently (OR = 1.28, 95% CI = 1.04–1.57).

7. Dietary patterns and metabolic syndrome

Dietary pattern methods in nutrition epidemiologic studies

Many nutritional epidemiologic studies have examined the effects of individual nutrients or foods on diseases, but these effects are too small to detect. Moreover, the complexity of diet and the high inter-correlations between intakes of foods and nutrients make it difficult to examine their separate effects. Dietary pattern methods

measure the total usual intake of food combinations in individuals and groups. In addition, assessment of dietary patterns can be used to examine the relationship between diet and diseases. Two most commonly used methods in dietary pattern studies are factor analysis and cluster analysis. Recently, RRR has been proposed and used (Hoffmann, K *et al.* 2004). Dietary pattern analysis uses intake of food groups, generally expressed as percent contribution to total energy intake or number of servings per day, as input variables and have different output information.

Factor analysis (principle components analysis) creates linear combinations of foods or food groups to explain the maximal amount of variance, whereas cluster analysis separates individuals into maximally different patterns based on the actual food intake of the population. RRR is similar to factor analysis, but it does not describe the actual food group intakes in the population. RRR uses intermediate (response) variables (e.g., disease related nutrients or biomarkers) to generate dietary patterns that explain the variance in a set of response variables. RRR may have useful applications to generate hypotheses about diet that may contribute to disease risk through specified causal pathways.

Dietary patterns associated with metabolic syndrome in Western adults

Western studies have examined two major dietary patterns, a “Western” characterized by high consumption of bread, meat, and fried foods, and a “prudent/healthy” characterized by high consumption of whole grains, legumes, vegetables, fruits, and dairy products. They found that the Western pattern was associated with increased risks for metabolic diseases, but the prudent/healthy pattern was associated with reduced risks for metabolic diseases (Fung, TT *et al.* 2004, Fung, TT *et al.* 2001b, Hu,

FB *et al.* 2000, Kerver, JM *et al.* 2003, van Dam, RM *et al.* 2002). Dietary patterns high in fruits and vegetables were found to be associated with a low prevalence of metabolic syndrome. Dietary patterns with high meat intake were frequently associated with impaired glucose intolerance. The dietary patterns that contain higher starch and refined grains were associated with dyslipidemia, but dietary patterns with a higher intake of whole grains rather than highly processed cereals appeared to have a protective effect against the components of metabolic syndrome.

In an urban Mexican population, three dietary patterns were identified by factor analysis: prudent, Western, and high protein/fat (Denova-Gutierrez, E *et al.* 2010a). Subjects in the highest tertile of the Western dietary pattern scores had higher ORs for elevated fasting blood glucose (OR = 1.67; 95% CI = 1.36–2.06), low HDL-cholesterol (OR = 1.55; 95% CI = 1.31–1.83), and metabolic syndrome (OR = 1.56; 95% CI = 1.31–1.88) compared to those in the lowest tertile. A non-diabetic Italian population-based cross-sectional study (Leite, ML and Nicolosi, A 2009) included 1,052 subjects and used cluster analysis to identify dietary patterns. Five dietary patterns were identified: common, animal products, starch, vegetal/fat, and vitamin/fibre. In subjects of the starch pattern, the prevalence of metabolic syndrome was the highest compared to those of the other patterns. On the other hand, subjects in the vegetal/fat pattern showed the lowest prevalence of metabolic syndrome. The starch pattern was associated with a high prevalence of dyslipidemia and the animal products pattern was associated with a high prevalence of elevated fasting blood glucose. A cross-sectional study of Greece population (Panagiotakos, DB *et al.* 2007) found six dietary patterns using factor analysis. The pattern 1 was characterized by the higher consumption of cereals, fish, legumes, vegetables, and fruits and it was inversely associated with the

prevalence of metabolic syndrome. On the other hand, the pattern 2 characterized by high intakes of potatoes and meat and the pattern 6 characterized by high consumption of alcohol were positively associated with the prevalence of metabolic syndrome. In two prospective studies of Western populations, Mediterranean style dietary pattern characterized by high in whole grains, fruits, vegetables, and omega-3 fatty acids, but low in refined grains, saturated fats, and trans fats had protective effects on metabolic syndrome (Rumawas, ME *et al.* 2009, Tortosa, A *et al.* 2007).

Dietary patterns associated with metabolic syndrome in Asian and Korean adults

The dietary patterns derived from Asian and Korean populations differ from those of Western populations, due to cultural differences in diet, foods mainly consumed in each population, and characteristics of study population. Most studies about dietary patterns associated with metabolic syndrome have been conducted in Western populations, but little is known about the associations in Asian populations. Therefore, it is necessary to identify dietary patterns associated with metabolic syndrome among Asian and Korean adult populations.

A previous study (Esmailzadeh, A *et al.* 2007) in Iranian women identified three major dietary patterns using factor analysis: healthy, Western, and traditional. The subjects in the highest quintile of the healthy dietary pattern scores showed a lower OR for metabolic syndrome (OR = 0.61, 95% CI = 0.30–0.79) compared to those in the lowest quintile. On the other hand, subjects in the highest quintile of the Western dietary pattern scores had a higher OR for metabolic syndrome (OR = 1.68, 95% CI = 1.10–1.95) compared to those in the lowest quintile. The healthy dietary pattern was inversely associated with the risks for all the components of metabolic syndrome, but

the Western dietary pattern was positively associated with the risks for all the components of metabolic syndrome.

Dietary patterns associated with metabolic syndrome and its components in Korean adults are summarized in Table II - 6. Previous studies in Korean adults used factor analysis or cluster analysis to identify dietary patterns based on dietary intake data obtained from food frequency questionnaire (FFQ) or 24-hour recall method. The traditional and Korean healthy dietary patterns were commonly identified and the meat and alcohol pattern and the Western pattern were also observed in this population. Overall, the healthy dietary pattern characterized by high intakes of fruits, vegetables, and dairy products was associated with low risks of metabolic syndrome and its components, but the dietary pattern with high intakes of meat and alcohol was associated with higher risks of metabolic syndrome and its components.

Table II - 6. Dietary patterns associated with metabolic syndrome and its components in Korean adults

Author (year)	Study subjects	Dietary assessment	Statistical methods	Dietary patterns	Outcome variables	Adjusted OR (95% CI)	Potential confounders
Ahn, Y <i>et al.</i> (2007)	6,873 (M: 3,429, W: 3,444), 40–70y	Semi-quantitative FFQ	Factor analysis, cluster analysis	1) Rice and Kimchi (REF) 2) Contented 3) Healthy and light	a) Hypertension b) Diabetes c) MetS d) Obesity	2)-b) 0.64 (0.45-0.92) 2)-c) 0.73 (0.61-0.88) 2)-d) 0.85 (0.73-0.99) 3)-a) 0.67 (0.49-0.91)	Age, sex
Kim, J and Jo, I (2011)	9,850, ≥ 19y	1d 24HR	Factor analysis	1) White rice and kimchi 2) Meat and alcohol 3) High fat, sweets, and coffee 4) Grains, vegetables and fish	a) AO b) HG c) HTG d) LHDLD e) HBP f) MetS	2)-c) 1.19 (1.05-1.34) 2)-e) 1.19 (1.05-1.35) 4)-c) 0.80 (0.72-0.90) 4)-f) 0.86 (0.76-0.98)	Age, sex, BMI, energy intake, alcohol intake, smoking, PA
Hong, S <i>et al.</i> (2012)	406 (M: 265, W: 141), 22–78y	1d 24HR & 3d DRs	Factor analysis	1) Korean traditional 2) Alcohol and meats 3) Sweets and fast foods 4) Fruit and dairy	a) IFG b) HBP c) LHDLD d) HTG e) AO f) MetS	1)-f) 2.03 (1.05-3.92) 2)-a) 0.46 (0.23-0.92) 4)-a) 0.42 (0.20-0.84) 4)-d) 0.39 (0.20-0.76) 4)-f) 0.46 (0.22-0.95)	Age, sex, taking medications, smoking, physical activity, BMI

Table II – 6. Dietary patterns associated with metabolic syndrome and its components in Korean adults (continued)

Author (year)	Study subjects	Dietary assessment	Statistical methods	Dietary patterns	Outcome variables	Adjusted OR (95% CI)	Potential confounders
Lee, JE <i>et al.</i> (2011)	M: 3,581, 40–69y	Semi-quantitative FFQ	Factor analysis	1) Animal-food 2) Rice-vegetable 3) Noodle-bread	a) Obesity b) AO c) Hypertension d) Hypercholesterolemia e) HTG	1)-a) 1.59 (1.24-2.04) 1)-d) 1.92 (1.33-2.78) 2)-c) 1.47 (1.05-2.07) 3)-b) 1.38 (1.05-1.81) 3)-d) 1.48 (1.07-2.05)	Age, occupation, income, education
Song, Y and Joung, H (2012)	4,731, ≥ 20y	1d 24HR	Cluster analysis	1) Traditional (REF) 2) Meat and alcohol 3) Korean healthy	a) AO b) HTG c) LHDLD d) HBP e) HG f) MetS	2)-b) 1.21 (1.00-1.47) 2)-c) 0.77 (0.65-0.92) 2)-e) 1.33 (1.01-1.75) 3)-c) 0.87 (0.76-1.00)	Age, sex, education, region, smoking, PA
Cho, YA <i>et al.</i> (2011)	W: 4,984, 30–79y	FFQ	Factor analysis	1) Western 2) Healthy 3) Traditional	a) MetS b) Obesity c) HBP d) HTG e) HG f) LHDLD	1)-f) 0.74 (0.61-0.90) 2)-a) 0.58 (0.50-0.91) 2)-b) 0.78 (0.64-0.94) 2)-c) 0.75 (0.62-0.91) 2)-d) 0.70 (0.53-0.93) 3)-f) 1.22 (1.01-1.46)	Age

Table II – 6. Dietary patterns associated with metabolic syndrome and its components in Korean adults (continued)

Author (year)	Study subjects	Dietary assessment	Statistical methods	Dietary patterns	Outcome variables	Adjusted OR (95% CI)	Potential confounders
Baik, I <i>et al.</i> (2013)	5,251, 40–69y	Semi-quantitative FFQ	Factor analysis	1) Healthy 2) Unhealthy	a) MetS b) AO c) HTG d) LHDLD e) HBP f) HG	1)-a) 0.76 (0.60-0.97) 1)-b) 0.61 (0.45-0.81) 1)-d) 0.73 (0.56-0.95) 1)-f) 0.67 (0.45-0.99) 2)-b) 1.48 (1.16-1.90)	Age, sex, income, occupation, education, smoking, alcohol intake, PA, FTO genotypes, energy intake

24HR, 24-hour recall; AO, Abdominal obesity; DR, Dietary record; FFQ, Food frequency questionnaire; FTO, Fat mass and obesity-associated gene; HBP, High blood pressure; HG, High fasting blood glucose; HTG, Hypertriglyceridemia; IFG, Impaired fasting glucose; LHDLD, Low HDL-cholesterol; M, Men; MetS, Metabolic syndrome; N/A, Not available; PA, Physical activity; REF, Reference group; W, Women.

**CHAPTER III. DIETARY DETERMINANTS OF
METABOLIC SYNDROME AND ITS COMPONENTS
IN KOREAN ADULTS OF THE KNHANES DATA**

STUDY 1. Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population¹

1. Introduction

Dietary carbohydrate intake has received considerable research attention because of proposed associations between diets with high GI or GL, or those with low whole grains, and increased risks of obesity, metabolic syndrome, diabetes, and coronary heart disease (Barclay, AW *et al.* 2008, Gaesser, GA 2007, McKeown, NM *et al.* 2004, Nettleton, JA *et al.* 2010). However, studies have produced conflicting evidence about the relationships between sources or types of dietary carbohydrates and metabolic disease. Several prospective studies (Liu, SM *et al.* 2000c, Meyer, KA *et al.* 2000, Oba, S *et al.* 2010) have shown that DGI or DGL were associated with high incidences of coronary heart disease, type 2 diabetes, and stroke. However, the results for total carbohydrate intake have been less clear (Liu, SM *et al.* 2000c, McKeown, NM *et al.* 2004). Extensive studies in Western populations have suggested that whole grains help

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to prevent diabetes, cardiovascular diseases, and metabolic syndrome (McKeown, NM *et al.* 2004, Ye, EQ *et al.* 2012).

Because Asians traditionally consume large amounts of rice as a staple food, dietary carbohydrate intake can play a substantial role in the development of metabolic disease in Asian populations. Diabetes and metabolic syndrome have recently become more prevalent in Asia, reaching levels similar to those in Western countries (Cheung, BM 2005, Hu, FB 2011). Positive associations between total carbohydrate or rice intake and the incidence of diabetes have been reported in Chinese (Villegas, R *et al.* 2007) and Japanese women (Nanri, A *et al.* 2010). Metabolic syndrome has been associated with total carbohydrate intake and GL in obese Korean women (Kim, K *et al.* 2008) and high refined-grain consumption in a south Indian population (Radhika, G *et al.* 2009). In addition, several studies have demonstrated stronger associations between dietary carbohydrate intake and metabolic disease in women than in men (Choi, J *et al.* 2012, Kim, K *et al.* 2008, Nanri, A *et al.* 2010, Park, SH *et al.* 2010).

However, few studies have examined the combined associations of all sources and types of dietary carbohydrates with metabolic syndrome in Asian populations. Dietary carbohydrates account for a considerable part of daily energy intake in Asian populations, and examination of the sources and types of dietary carbohydrates associated with metabolic syndrome is important. Metabolic syndrome is characterized by co-existence of abdominal obesity, high triglycerides and low HDL-cholesterol concentrations, high blood pressure, and high fasting blood glucose concentration. Assessment of the contributions of these metabolic syndrome components offers the opportunity to prevent the progression of chronic diseases, such as type 2 diabetes and cardiovascular diseases (Grundy, SM *et al.* 2005). We examined associations between

the sources and types of dietary carbohydrates and the prevalence of metabolic syndrome in Korean men and women using data from the KNHANES.

2. Methods

Study subjects

This study was based on data from the Fourth KNHANES, which was a cross sectional and nationally representative survey carried out by the Korea Centers for Disease Control and Prevention in 2007–2009. Among 10,618 eligible subjects aged 30 to 65 years, subjects were excluded if they had prior diagnoses and treatment for diabetes, hypertension, or dyslipidemia ($n = 2,257$). In addition, subjects who had incomplete information on sociodemographic, anthropometric, biochemical, or health-related variables ($n = 1,346$), reported implausible energy intakes (< 500 or $> 5,000$ kcal/day) ($n = 71$), or were pregnant or breastfeeding women ($n = 99$) were excluded. A total of 6,845 adults (2,631 men and 4,214 women) were included in the final data analyses. This study was approved by the Korea Centers for Disease Control and Prevention Institutional Review Board, and informed written consent was obtained from each subject.

Assessment of dietary intake

Dietary intake data were obtained through a single 24-hour recall. Energy and nutrient intakes for each subject were calculated using the seventh food composition table by Korean National Rural Resources Development Institute (2006).

The average DGI and DGL based on a glucose standard were calculated for each subject using the table of GI values for common Korean foods established in a previous study (Song, S *et al.* 2012). The GI values in this table were obtained from published estimates or inputted when necessary by matching similar foods based on calorie and carbohydrate content of each food. Among 653 food items in this table, 149 (22.8 %) were adapted from published data, 60 (9.2 %) were imputed from similar foods, and 444 (68.0 %) were assigned a zero. The DGL was calculated by multiplying the carbohydrate content of each food by its GI value, and this value was summed for all food items. The DGI was calculated by dividing the DGL by the total carbohydrate intake (Foster-Powell, K *et al.* 2002).

Refined grains were classified by the methods of Jacobs, DR *et al.* (1998) and Liu, SM *et al.* (1999). Refined grains included white rice, spaghetti, noodles, and white-flour products, such as cookies, biscuits, white bread, crackers, muffins, waffles, bagels, and pizza. Dietary carbohydrate intake variables included total carbohydrate (g/day), energy from carbohydrate (%), DGI, DGL, total grains (servings/day), refined grains (servings/ day), and white rice (servings/day). The food group database for common Korean foods was used to estimate the food group intake (in servings/day) (Song, S *et al.* 2014). The database provides a common serving size and number of servings per 100 grams of each food item.

Assessment of other variables

Sociodemographic variables such as age, living area, and education, and health-related variables such as smoking status, alcohol intake, physical activity, medical history, and medication use, were obtained by general questionnaire. Smoking status was categorized into the following groups: non-, ex-, or current-smokers. Current alcohol intake was assessed based on the average frequency of alcohol drinking during the last year. Vigorous physical activity was examined based on the frequency of high intensity exercise during the last week.

Height, weight, and waist circumference were measured using standardized techniques and calibrated equipment. BMI was calculated from the measured heights and weights (kg/m^2) of the subjects. Blood pressure was measured by standard methods three times, and the average value was used. Blood samples were collected after having fasted for at least 8 hours. Fasting blood glucose, triglyceride level, and HDL-cholesterol were analyzed in a certified clinical laboratory.

Assessment of metabolic syndrome

Metabolic syndrome was diagnosed based on the NCEP ATP III criteria (Grundy, SM *et al.* 2005) with a modified waist circumference cutoff for Korean adults (Lee, SY *et al.* 2007) if any three or more of the following components were present: high waist circumference, as defined by a waist circumference ≥ 90 cm in men and ≥ 85 cm in women; elevated triglycerides as defined by triglycerides level ≥ 150 mg/dL; low HDL-cholesterol as defined by HDL-cholesterol < 40 mg/dL in men and < 50 mg/dL in women; elevated fasting blood glucose as defined by fasting blood glucose ≥ 100

mg/dL; and elevated blood pressure as defined by systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg.

Statistical analyses

All statistical analyses were conducted using the Statistical Analysis System (SAS) statistical software package version 9.3 (2011, SAS Institute, Cary, NC, USA). All analyses accounted for the complex sampling design effect and appropriate sampling weights of the national survey using PROC SURVEY in SAS program.

Values of sociodemographic and health-related variables were expressed as mean and standard error of mean (SEM) for continuous variables or percentages for categorical variables; the *t*-test (for continuous variables) and the chi-square test (for categorical variables) were used to test differences by sex. All statistical analyses were conducted by sex because carbohydrate intakes, risk factors of metabolic syndrome, and prevalence of metabolic syndrome differed by sex.

Carbohydrate intake, including total carbohydrate (g/day), energy from carbohydrate (%), DGI, DGL, total grains (servings/day), refined grains (servings/day), and white rice (servings/day), were used as total energy adjusted values using the residual method (Willett, WC 2013) and were grouped into quintiles by sex. Food group intakes and metabolic syndrome components were expressed as mean and standard error of mean by quintiles of carbohydrate intake by sex. Tests for linear trend of these variables by quintiles of carbohydrate intake were conducted using a multivariate linear regression analysis.

A multivariate adjusted logistic regression analysis was performed to estimate ORs, 95% CIs, and *P* for trend for metabolic syndrome by quintiles of carbohydrate

intake, taking the lowest quintile group as the reference group, in men and women separately. Age (continuous), living area (urban or rural), education (elementary, junior high, senior high, or college or more), smoking status (non-, ex-, or current-smokers), current alcohol intake (never or rarely, less than once per month, once per month, two to four times per month, two to three times per week, or four or more times per week), vigorous physical activity (never or rarely, 1 to 2 days per week, 3 to 4 days per week, or 5 days or more per week), and total energy intake (continuous) were considered as potential confounding variables and were controlled in all models. All tests of significance were two-tailed, and P -values < 0.05 were considered significant.

3. Results

General characteristics of study subjects

Table III - 1 presents the general characteristics of the study subjects by sex. The study included 2,631 men and 4,214 women with mean ages of 43.2 (SEM = 0.2) and 43.9 (SEM = 0.2) years, respectively. Women were more likely to be older, live in an urban area, and to be less educated than men. The prevalence of obesity (BMI ≥ 25.0 kg/m²) was higher in men than in women. Men were more likely to be current smokers, drink alcohol frequently, and engage in vigorous physical activity than women. The prevalence of metabolic syndrome was 23 % in men and 13 % in women. Elevated triglycerides levels were prevalent in men (38 %) and low HDL-cholesterol levels were prevalent in women (51 %).

Table III - 1. General characteristics of the study subjects by sex (n = 6,845)^a

	Men (n = 2,631)	Women (n = 4,214)	P-value ^b
Age (Mean, SEM)			
Years	43.2, 0.2	43.9, 0.2	0.0035
Region (%)			
City	68.1	72.4	0.0001
Rural	31.9	27.6	
Education (%)			
Elementary	9.3	14.6	< 0.0001
Lower secondary	10.8	13.6	
Upper secondary	39.7	44.7	
College or more	40.2	27.2	
BMI (%)			
< 18.5 kg/m ²	2.8	4.8	< 0.0001
18.5–25.0 kg/m ²	61.9	72.5	
≥ 25.0 kg/m ²	35.2	22.7	
Smoking status (%)			
Current-smokers	49.2	5.7	< 0.0001
Ex-smokers	34.4	5.2	
Non-smokers	16.4	89.2	
Current alcohol intake ^c (%)			
Never or rarely	11.8	29.6	< 0.0001
< 1 time/month	11.3	25.4	
1 time/month	8.6	13.5	
2–4 times/month	29.4	20.4	
2–3 times/week	26.3	9.2	
≥ 4 times/week	12.6	1.9	
Vigorous physical activity ^d (%)			
Never or rarely	53.6	69.5	< 0.0001
1–2 days/week	25.7	14.3	
3–4 days/week	12.1	9.0	
≥ 5 days/week	8.6	7.1	
Prevalence of metabolic syndrome (%)			
Elevated waist circumference	23.4	18.5	< 0.0001
Elevated triglycerides	38.2	16.1	< 0.0001
Low HDL-cholesterol	33.7	50.5	< 0.0001
Elevated fasting blood glucose	26.1	16.0	< 0.0001
Elevated blood pressure	27.8	12.2	< 0.0001
Metabolic syndrome	22.7	12.5	< 0.0001

^a All analyses accounted for the complex sampling design effect and appropriate sampling weights of the national survey.

^b P-values were obtained from the *t*-test for continuous variables and the chi-square test for categorical variables.

^c Current alcohol intake was assessed based on the average frequency of alcohol drinking during the last year.

^d Vigorous physical activity was examined based on the frequency of high-intensity exercise during the last week.

Association between carbohydrate intake and metabolic syndrome in men and women

Table III - 2 presents the ORs for metabolic syndrome by quintiles of dietary carbohydrate intake in men. After adjusting for potential confounding variables, metabolic syndrome was more likely to be present among men in the highest quintile of percentage of energy from carbohydrates than among those in the lowest quintile (quintile 5: OR = 1.46, 95% CI = 1.07–2.01, *P* for trend = 0.0147). However, no association was observed between other types of carbohydrate intake and metabolic syndrome in men.

Table III - 3 shows the ORs for metabolic syndrome by quintiles of dietary carbohydrate intake in women. After adjusting for potential confounding variables, women in the highest quintiles of refined grains and white rice intakes were more likely to have metabolic syndrome than were women in the lowest quintiles (refined grains quintile 5: OR = 1.72, 95% CI = 1.24–2.40, *P* for trend = 0.0016; white rice quintile 5: OR = 1.74, 95% CI = 1.23–2.48, *P* for trend = 0.0078). However, no association was observed between other types of carbohydrate intake and metabolic syndrome in women.

Table III - 2. Multivariate adjusted ORs and 95% CIs for metabolic syndrome by quintiles of dietary carbohydrate intake in men ($n = 2,631$)^a

	Quintiles of dietary carbohydrate intake ^b					<i>P</i> for trend ^a
	Q1 ($n = 526$)	Q2 ($n = 526$)	Q3 ($n = 527$)	Q4 ($n = 526$)	Q5 ($n = 526$)	
Total carbohydrate (g/day)						
Median	255.8	326.6	361.8	394.3	448.0	
OR (95% CI)	1.00	0.90 (0.63–1.28)	0.94 (0.66–1.33)	1.18 (0.84–1.64)	1.18 (0.84–1.67)	0.1312
Energy from carbohydrate (%)						
Median	54.5	62.4	67.5	72.3	78.7	
OR (95% CI)	1.00	1.29 (0.93–1.80)	1.27 (0.92–1.76)	1.45 (1.03–2.04)	1.46 (1.07–2.01)	0.0147
Dietary glycemic index ^c						
Median	49.5	55.7	59.4	62.7	66.8	
OR (95% CI)	1.00	1.13 (0.84–1.51)	1.41 (1.05–1.91)	1.00 (0.73–1.36)	1.25 (0.90–1.72)	0.3445
Dietary glycemic load ^c						
Median	132.3	185.1	213.0	238.6	278.7	
OR (95% CI)	1.00	0.84 (0.59–1.18)	1.04 (0.75–1.44)	1.02 (0.73–1.42)	1.18 (0.86–1.62)	0.1973
Total grains (servings/day)						
Median	2.2	3.1	3.6	4.1	5.0	
OR (95% CI)	1.00	0.99 (0.70–1.41)	1.26 (0.88–1.79)	1.25 (0.88–1.76)	1.15 (0.82–1.61)	0.1564
Refined grains (servings/day)						
Median	1.7	2.7	3.2	3.7	4.5	
OR (95% CI)	1.00	0.87 (0.62–1.21)	1.12 (0.80–1.56)	1.21 (0.87–1.70)	1.02 (0.75–1.40)	0.2727
White rice (servings/day)						
Median	1.1	2.0	2.6	3.2	4.0	
OR (95% CI)	1.00	1.01 (0.72–1.43)	1.34 (0.97–1.86)	1.03 (0.75–1.43)	1.27 (0.91–1.77)	0.1716

^a All analyses accounted for the complex sampling design effect and appropriate sampling weights of the national survey. Multivariate adjusted logistic regression was used to estimate ORs (95% CIs) and *P* for trend after adjustment for age (continuous), living area (urban or rural), education (elementary, junior high, senior high, or college or more), smoking status (current-, ex-, or non-smokers), current alcohol intake (never or rarely, <1 time/mo, 1 time/mo, 2 to 4 times/mo, 2 to 3 times/wk, or ≥ 4 times/wk), vigorous physical activity (never or rarely, 1 to 2 days/wk, 3 to 4 days/wk, ≥ 5 days/wk), and total energy intake (continuous).

^b All dietary carbohydrate intake variables were energy adjusted using residual method and were categorized into quintiles.

^c Dietary glycemic index and load were calculated based on a glucose standard.

Table III - 3. Multivariate adjusted ORs and 95% CIs for metabolic syndrome by quintiles of dietary carbohydrate intake in women (n = 4,214)^a

	Quintiles of dietary carbohydrate intake ^b					P for trend ^a
	Q1 (n = 842)	Q2 (n = 843)	Q3 (n = 843)	Q4 (n = 843)	Q5 (n = 843)	
Total carbohydrate (g/day)						
Median	226.2	267.5	288.8	308.9	342.4	
OR (95% CI)	1.00	0.91 (0.64–1.30)	0.86 (0.61–1.21)	0.66 (0.46–0.96)	0.90 (0.64–1.29)	0.2511
Energy from carbohydrate (%)						
Median	56.2	65.1	70.4	75.2	81.6	
OR (95% CI)	1.00	1.20 (0.83–1.74)	1.12 (0.80–1.59)	0.96 (0.68–1.36)	1.09 (0.74–1.59)	0.8872
Dietary glycemic index ^c						
Median	49.6	55.8	59.3	62.8	67.4	
OR (95% CI)	1.00	1.17 (0.84–1.61)	0.92 (0.66–1.29)	1.19 (0.85–1.66)	1.17 (0.83–1.65)	0.4118
Dietary glycemic load ^c						
Median	120.3	151.8	169.9	187.7	216.7	
OR (95% CI)	1.00	0.72 (0.51–1.00)	0.72 (0.51–1.00)	0.71 (0.52–0.98)	0.88 (0.62–1.24)	0.5464
Total grains (servings/day)						
Median	1.9	2.5	2.9	3.3	3.9	
OR (95% CI)	1.00	0.88 (0.64–1.23)	1.00 (0.74–1.36)	0.83 (0.60–1.16)	1.18 (0.85–1.63)	0.4519
Refined grains (servings/day)						
Median	1.4	2.0	2.4	2.8	3.5	
OR (95% CI)	1.00	1.13 (0.80–1.60)	1.20 (0.86–1.69)	1.30 (0.93–1.81)	1.72 (1.24–2.40)	0.0016
White rice (servings/day)						
Median	0.7	1.4	1.8	2.3	3.1	
OR (95% CI)	1.00	1.38 (0.97–1.97)	1.20 (0.83–1.74)	1.30 (0.91–1.87)	1.74 (1.23–2.48)	0.0078

^a All analyses accounted for the complex sampling design effect and appropriate sampling weights of the national survey. Multivariate adjusted logistic regression was used to estimate ORs (95% CIs) and P for trend after adjustment for age (continuous), living area (urban or rural), education (elementary, junior high, senior high, or college or more), smoking status (current-, ex-, or non-smokers), current alcohol intake (never or rarely, <1 time/mo, 1 time/mo, 2 to 4 times/mo, 2 to 3 times/wk, or ≥ 4 times/wk), vigorous physical activity (never or rarely, 1 to 2 days/wk, 3 to 4 days/wk, ≥ 5 days/wk), and total energy intake (continuous).

^b All dietary carbohydrate intake variables were energy adjusted using residual method and were categorized into quintiles.

^c Dietary glycemic index and load were calculated based on a glucose standard.

Associations between carbohydrate intake and food group intakes

In men, the percentage of energy from carbohydrates was positively associated with the consumption of kimchi (a traditional fermented cabbage product) and fruits, but inversely associated with the consumption of meat, fish, vegetables, milk, and dairy products. Women in the highest quintile of white rice intake consumed more kimchi and less meat, fish, fruits, milk, and dairy products than did those in the lowest quintile (Table III - 4).

Table III - 4. Food group intakes by quintiles of dietary carbohydrate intake in men and women^a

	Quintiles of energy from carbohydrate ^b (%)										
	Q1 (n = 526)		Q2 (n = 526)		Q3 (n = 527)		Q4 (n = 526)		Q5 (n = 526)		P for trend ^c
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
Men (n = 2,631)											
Meat and its products (g/day)	200.4	8.9	115.0	6.0	85.5	5.6	69.0	4.4	37.0	3.7	< 0.0001
Fish (g/day)	96.0	5.6	86.6	5.7	75.5	3.8	67.1	3.7	51.0	4.1	< 0.0001
Vegetables (g/day)	237.7	7.7	237.1	9.1	262.9	11.2	226.9	8.6	221.6	13.8	0.0366
Kimchi ^d (g/day)	149.2	5.4	166.2	6.2	165.5	6.2	180.7	7.2	199.4	8.4	< 0.0001
Fruits (g/day)	81.0	8.0	141.8	14.4	143.0	12.7	183.4	14.3	298.4	24.8	< 0.0001
Milk and dairy products (g/day)	71.7	9.4	74.3	8.1	64.4	5.7	50.6	5.9	31.5	4.7	0.0003
	Quintiles of white rice intake ^b (servings/day)										
	Q1 (n = 842)		Q2 (n = 843)		Q3 (n = 843)		Q4 (n = 843)		Q5 (n = 843)		P for trend ^c
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
Women (n = 4,214)											
Meat and its products (g/day)	92.6	8.0	61.3	3.0	60.3	3.9	51.8	3.2	49.4	4.0	< 0.0001
Fish (g/day)	55.1	3.4	46.8	2.8	41.8	2.0	42.3	2.2	40.8	2.6	0.0032
Vegetables (g/day)	201.2	7.5	168.3	6.4	160.2	5.7	166.6	6.6	186.7	7.2	0.2298
Kimchi ^d (g/day)	99.4	4.4	109.7	4.0	129.2	4.5	134.8	4.8	157.2	5.6	< 0.0001
Fruits (g/day)	327.6	18.4	242.7	12.5	191.1	11.0	190.8	12.7	160.3	9.3	< 0.0001
Milk and dairy products (g/day)	112.8	6.6	84.3	6.1	67.4	4.6	48.9	4.3	41.8	5.3	< 0.0001

^a All analyses accounted for the complex sampling design effect and appropriate sampling weights of the national survey.

^b All dietary carbohydrate intake variables were energy adjusted using residual method and were categorized into quintiles.

^c P for trend was obtained from a multivariate linear regression analysis after adjustment for age (continuous), living area (urban or rural), education (elementary, junior high, senior high, or college or more), smoking status (current, ex-, or nonsmokers), current alcohol intake (never or rarely, < 1 time/mo, 1 time/mo, 2 to 4 times/mo, 2 to 3 times/wk, or ≥ 4 times/wk), vigorous physical activity (never or rarely, 1 to 2 days/wk, 3 to 4 days/wk, ≥ 5 days/wk), and total energy intake (continuous).

^d Traditional fermented cabbage product.

Associations between carbohydrate intake and metabolic syndrome components

In men, diastolic blood pressure and HDL-cholesterol level decreased and triglycerides and fasting blood glucose levels increased across quintiles of the percentage of energy obtained from carbohydrates. High systolic blood pressure, fasting blood glucose and triglycerides levels, and low HDL-cholesterol level were associated with white rice intake in women (Table III - 5).

Table III - 5. Metabolic syndrome components by quintiles of dietary carbohydrate intake in men and women^a

	Quintiles of energy from carbohydrate ^b (%)										<i>P</i> for trend ^c
	Q1 (<i>n</i> = 526)		Q2 (<i>n</i> = 526)		Q3 (<i>n</i> = 527)		Q4 (<i>n</i> = 526)		Q5 (<i>n</i> = 526)		
Men (<i>n</i> = 2,631)	Mean	<i>SEM</i>	Mean	<i>SEM</i>	Mean	<i>SEM</i>	Mean	<i>SEM</i>	Mean	<i>SEM</i>	
Waist circumference (cm)	83.8	0.4	85.4	0.4	84.0	0.4	83.3	0.4	83.8	0.4	0.0655
Triglycerides (mg/dL)	146.0	4.4	164.0	7.2	161.0	5.5	153.9	5.3	159.2	6.1	0.0277
HDL-cholesterol (mg/dL)	46.6	0.5	44.8	0.4	45.2	0.4	45.3	0.5	45.1	0.5	0.0477
Fasting blood glucose (mg/dL)	94.5	0.7	94.2	0.6	94.8	0.8	97.5	1.1	97.2	0.9	0.0035
Systolic blood pressure (mmHg)	114.9	0.5	116.0	0.6	115.3	0.6	115.9	0.8	116.1	0.7	0.8147
Diastolic blood pressure (mmHg)	78.8	0.5	79.3	0.5	78.0	0.5	77.5	0.6	77.8	0.5	0.0441

	Quintiles of white rice intake ^b (servings/day)										<i>P</i> for trend ^c
	Q1 (<i>n</i> = 842)		Q2 (<i>n</i> = 843)		Q3 (<i>n</i> = 843)		Q4 (<i>n</i> = 843)		Q5 (<i>n</i> = 843)		
Women (<i>n</i> = 4,214)	Mean	<i>SEM</i>	Mean	<i>SEM</i>	Mean	<i>SEM</i>	Mean	<i>SEM</i>	Mean	<i>SEM</i>	
Waist circumference (cm)	76.5	0.4	77.2	0.4	76.7	0.3	77.2	0.4	79.0	0.4	0.4316
Triglycerides (mg/dL)	96.9	2.3	102.9	2.4	102.0	2.9	108.6	3.2	109.1	2.6	0.0530
HDL-cholesterol (mg/dL)	52.4	0.5	50.8	0.4	51.1	0.4	50.1	0.4	49.2	0.4	0.0024
Fasting blood glucose (mg/dL)	91.1	0.4	92.0	0.4	92.5	0.5	92.9	0.5	93.4	0.7	0.0591
Systolic blood pressure (mmHg)	107.6	0.5	108.3	0.5	109.3	0.6	109.4	0.5	112.2	0.6	0.0098
Diastolic blood pressure (mmHg)	71.8	0.4	71.9	0.4	71.9	0.4	72.3	0.4	73.5	0.4	0.1051

^a All analyses accounted for the complex sampling design effect and appropriate sampling weights of the national survey.

^b All dietary carbohydrate intake variables were energy adjusted using residual method and were categorized into quintiles.

^c *P* for trend was obtained from a multivariate linear regression analysis after adjustment for age (continuous), living area (urban or rural), education (elementary, junior high, senior high, or college or more), smoking status (current, ex-, or nonsmokers), current alcohol intake (never or rarely, <1 time/mo, 1 time/mo, 2 to 4 times/mo, 2 to 3 times/wk, or ≥ 4 times/wk), vigorous physical activity (never or rarely, 1 to 2 days/wk, 3 to 4 days/wk, ≥ 5 days/wk), total energy intake (continuous), and body mass index (continuous, exception for waist circumference).

4. Discussion and conclusions

We found that dietary carbohydrate intakes were positively related to the prevalence of metabolic syndrome, and the sources and types of dietary carbohydrates were differentially associated with metabolic syndrome according to sex, in the Korean adult population. Metabolic syndrome was significantly associated with the percentage of energy from carbohydrates in men and with refined grains and white rice intakes in women.

The mechanism underlying the carbohydrate-induced risk for metabolic syndrome remains unclear. However, Hu, FB (2011) indicated that Asian populations tend to develop diabetes at younger ages and lower BMI than white populations, which can be attributed to high intakes of refined carbohydrates, including white rice. Cheung, BM (2005) reported that obesity and insulin resistance, which are mechanisms underlying metabolic disease, are not caused by excessive dietary fat intake, but by carbohydrate intake that exceeds energy needs.

Our analysis of metabolic syndrome components revealed that elevated triglycerides and blood glucose levels in combination with reduced HDL-cholesterol level were associated with high dietary carbohydrate intake in men and women. These findings are in agreement with those of previous studies demonstrating that high carbohydrate intake increases the triglycerides level and reduces the HDL-cholesterol level (Choi, H *et al.* 2012, Parks, EJ and Hellerstein, MK 2000). In addition, high refined-grain consumption was significantly associated with elevated triglycerides and

fasting blood glucose levels and reduced HDL-cholesterol level in an Asian Indian population (Radhika, G *et al.* 2009).

We found that metabolic syndrome was positively associated with carbohydrate intake (percentage of energy) in men and refined-grain consumption in women. Several other studies of Asian populations have found that carbohydrate consumption was associated more strongly with metabolic syndrome abnormalities in women than in men (Choi, J *et al.* 2012, Kim, K *et al.* 2008, Nanri, A *et al.* 2010, Park, SH *et al.* 2010). A recent study of Korean adolescents (Kim, HA *et al.* 2013) also reported a sex difference characterized by the associations of insulin resistance with large waist circumference, high triglycerides level, and low HDL-cholesterol level in girls, but not in boys.

In our study sample, men in the highest quintile of carbohydrate intake (percentage of energy) consumed less meat, fish, vegetables, milk, and dairy products, but more fruits and kimchi, and women in the highest quintile of white rice intake consumed less meat, fish, fruits, milk, and dairy products, but more kimchi, compared with those in the lowest quintiles. These findings suggest that sex differences in dietary practices among those consuming high carbohydrate diets can have differential effects on metabolic syndrome or its components. In other words, the sources and types of dietary carbohydrates might differentially optimize metabolic features according to sex. Additional studies are needed to elucidate the mechanisms underlying the association between high carbohydrate intake and metabolic syndrome by sex, and prospective studies are needed to confirm our results.

Several limitations of this study should be considered to correctly interpret our findings. First, the cross-sectional design of the study prevented the identification of

any causal relationship based on the associations observed. Second, evidence related to DGI and DGL conflicted much more than that related to other sources and types of dietary carbohydrates. DGI and DGL calculations were based on a database that we established in a previous study (Song, S *et al.* 2012), and most values were taken from international tables (Atkinson, FS *et al.* 2008). The lack of GI values for some Asian foods, particularly Korean foods, in the GI database might have altered the results and compromised the precision of data. In addition, considerable debate has been generated about the use and interpretation of the DGI and DGL (Jones, J 2012). These measures should be validated to increase the precision of estimates, particularly for Asian populations. Finally, we used recalled dietary data from a single 24-hour period for each subject, which might have affected estimates of actual intake at the individual level. However, we grouped dietary carbohydrate intakes into quintiles and evaluated their effects at the population level, but the possibility of error or misclassification remains a concern. In addition, variation in the intakes of macronutrients, such as carbohydrates (typically providing 60 to 70 % of daily energy), is smaller than that for other nutrients (Willett, WC 2013).

Despite these limitations, this study used data from a nationally representative Korean adult population and was the first large population study in Asia to examine the associations between all sources and types of dietary carbohydrates and metabolic syndrome by sex. Because disease can alter dietary habits, we excluded subjects who had been previously diagnosed or treated for diabetes, dyslipidemia, or hypertension. Our results are useful for the prevention of metabolic syndrome in healthy Korean adults. Future studies should continue to explore the wide range of evidence for the effect of dietary carbohydrate intake on metabolic disease in Asian populations.

The sources and types of dietary carbohydrates were differentially associated with metabolic syndrome according to sex in this large population study of 6,845 Korean men and women. Among men, the percentage of energy from carbohydrates was positively associated with the prevalence of metabolic syndrome and its components. Sources of carbohydrates, such as refined grains and white rice, were strongly associated with metabolic syndrome in women, which was characterized by elevated triglycerides and fasting blood glucose levels and systolic blood pressure, as well as reduced HDL-cholesterol level. Further studies are needed to examine the mechanism underlying the association between the sources and types of dietary carbohydrates and metabolic syndrome in this population.

STUDY 2. Intakes of macronutrients and food groups are associated with insulin resistance in the Korean adult population²

1. Introduction

Recently, the prevalence of metabolic syndrome has been increased in Asian countries, including Korea, due to changing socioeconomic environment and adopting the Western dietary pattern (Grundy, SM 2008, Lim, S *et al.* 2011). Metabolic syndrome is characterized by a clustering of metabolic abnormalities, such as abdominal obesity, insulin resistance, hyperlipidemia, hyperglycemia, and hypertension, and it increases risks of cardiovascular diseases and type 2 diabetes (Grundy, SM *et al.* 2005). Insulin resistance is a physiological state in which cells fail to respond to the normal actions of the hormone insulin. Insulin resistance is considered as an underlying risk factor of several metabolic diseases, such as metabolic syndrome, hypertension, and cardiovascular diseases (Grundy, SM 1999, Mikhail, N 2009, Reaven, GM 1988).

HOMA-IR is a reliable indicator of insulin resistance, which is used in the clinical settings and large scaled human studies in which only a fasting blood sample is

² This study was published in the Korean Journal of Nutrition vol. 46, no. 1, pages 61-71 in 2013.

available to assess insulin resistance due to the lack of time and cost. A previous study showed a strong correlation between clamp-measured total glucose disposal, the reference method, and HOMA-IR estimated insulin sensitivity (Bonora, E *et al.* 2000). Therefore, HOMA-IR can be used as the most accurate surrogate measure of insulin resistance.

Previous studies have reported that HOMA-IR can predict the risk of metabolic syndrome. The Framingham Offspring Cohort Study of 2,834 US adults found that the prevalence of metabolic syndrome was 2 % in the lowest quintile of HOMA-IR but was 59 % in the highest quintile (McKeown, NM *et al.* 2004). The Korean study of 1,091 adults aged 30–79 years showed that the prevalence of metabolic syndrome was 1.1 % in the lowest tertile of HOMA-IR but was 48.1 % in the highest tertile (Lee, S *et al.* 2002).

The Framingham Offspring Cohort Study (McKeown, NM *et al.* 2004) showed that DGI and DGL were positively associated with HOMA-IR whereas intakes of total dietary fiber and whole grains were inversely associated with HOMA-IR. However, total carbohydrate intake was not associated with HOMA-IR. The Inter 99 study (Lau, C *et al.* 2005) of non-diabetic Danish men and women aged 30–60 years reported that intakes of DGL, glucose, total dietary fiber, and total carbohydrate were inversely associated with HOMA-IR, and no significant association was observed between DGI and HOMA-IR. In the Australian study (O'Sullivan, TA *et al.* 2010) of 329 women aged 42–81 years, insulin resistance group (HOMA-IR > 3.99) had a significantly higher DGL than those in non-insulin resistance group. These studies reported inconsistent findings on the relationships between dietary factors and insulin resistance and the role of dietary factors in the development of insulin resistance is not fully

understood. Because insulin resistance is closely linked with the risk of metabolic syndrome, dietary factors associated with insulin resistance need to be examined according to symptoms of metabolic syndrome.

Metabolic syndrome is a concept of complex multifactorial health problems, such as dyslipidemia, glucose intolerance, hypertension, and abdominal obesity. Despite the importance of diagnosis of metabolic syndrome, metabolic syndrome has a limited utility in clinical settings and epidemiologic studies due to the inconsistent definitions of metabolic syndrome. Metabolic syndrome can be considered as a pre-morbid condition rather than a clinical symptom, and thus individuals who were diagnosed for diabetes or cardiovascular diseases should be excluded for the diagnosis of metabolic syndrome (Simmons, RK *et al.* 2010). There have been few studies on the relationship between insulin resistance and dietary factors in Korean adults who traditionally consume a high carbohydrate diet, including white rice and other grains as staple foods. Therefore, the aim of this study was to examine the relationship between dietary variables (e.g., macronutrients and food groups) and the prevalence of insulin resistance according to symptoms of metabolic syndrome in the middle-aged Korean adults who had no prior diagnoses and treatment for diabetes, hypertension, or dyslipidemia using data from the 2007–2009 KNHANES.

2. Methods

Study subjects

This study was conducted based on data from the Fourth KNHANES in 2007–2009. The KNHANES is a cross-sectional and nationally representative survey carried out by the Korea Centers for Disease Control and Prevention using the stratified, multistage probability sampling design. It consists of three survey sections, including the health interview survey, the health examination survey, and the nutrition survey.

Among 10,618 eligible subjects aged 30–65 years, subjects were excluded if they had prior diagnoses and treatment for diabetes, hypertension, or dyslipidemia ($n = 2,257$). In addition, subjects who had incomplete information on sociodemographic, anthropometric, biochemical, or health-related variables ($n = 1,346$) or reported implausible energy intakes (< 500 or $> 5,000$ kcal/day) ($n = 71$) were excluded. A total of 6,944 adults (2,618 men and 4,326 women) were included in the final data analyses. This study was approved by the Korea Centers for Disease Control and Prevention Institutional Review Board, and informed written consent was obtained from each subject.

Because insulin resistance is closely linked with metabolic syndrome, subjects were divided into three groups according to symptoms of metabolic syndrome: 1) the ‘normal group’ without any symptoms of metabolic symptoms ($n = 2,085$), 2) the ‘risk group’ with one or two symptoms of metabolic syndrome ($n = 3,699$), and 3) the ‘metabolic syndrome (MetS) group’ with three or more symptoms of metabolic

syndrome ($n = 1,160$). Figure III - 1 shows the procedure of the study subjects selection and categorization of subjects according to symptoms of metabolic syndrome.

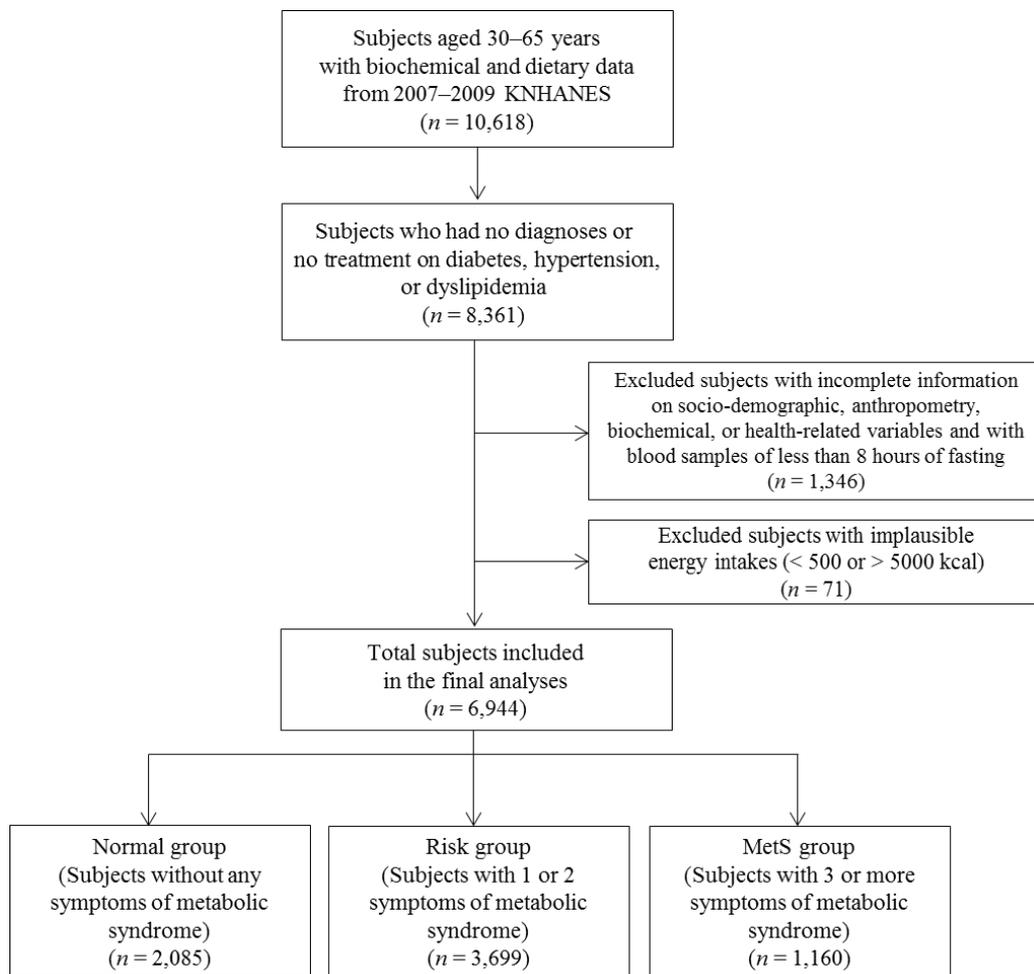


Figure III - 1. Flow chart of the study subjects selection

Dietary variables

Dietary intake data were obtained through a single 24-hour recall. Energy and nutrient intakes for each subject were calculated based on the Seventh Food Composition Table by Korean National Rural Resources Development Institute (RDA 2006). Average DGI and DGL based on a glucose standard (GI for glucose = 100) were calculated for each subject using a table of GI values for common Korean foods established in a previous study (Song, S *et al.* 2012). DGI was calculated by multiplying the percentage contribution of each food to the amount of carbohydrates consumed by the food's GI value, and then this value was summed for all food items. DGL was calculated by multiplying the amount of carbohydrates consumed from each food by the food's GI value, and then this value was summed for all food items (dividing by 100) (Foster-Powell, K *et al.* 2002). Therefore, DGI represents the quality of total carbohydrate intake and DGL reflects the overall quantity and quality of total carbohydrate intake.

To calculate the number of servings consumed for six food groups (e.g., Grains; Meat, fish, eggs and Beans; Vegetables; Fruits; Milk and dairy products; Fats, oils, and sugars) by each subject, the total amount of foods (in grams) that each subject consumed as reported in the 24-hour recall data were converted to number of servings using a food group database of 4,370 common Korean foods (Song, S *et al.* 2014). The database provides number of servings per 100 grams of each food item for six food groups based on the Korean Food Guidance System (KNS 2010), Korean dish recipes, and other references (KDA 1999, RDA 2009). The amount of food items consumed were divided by weights of food group servings of the food items, and then summed across each food group.

Sociodemographic and lifestyle variables

Sociodemographic variables (e.g., age, education, and household income) and lifestyle variables (e.g., smoking, alcohol use, physical activity, medical history, and medication use) were obtained by a general questionnaire. Education level was categorized into the following groups: elementary, lower secondary, upper secondary, or college or more. Household income was divided into four groups according to the quartiles of household income level. Current alcohol use was assigned “yes” if a subject drank a glass of alcohol or more per month over the previous year. Physical activity was assigned “yes” if a subject engaged in physical activity at high intensity more than 20 minutes at least 3 days or more per week over the previous week.

Anthropometric and biochemical variables

Height, weight, and waist circumference were measured using standardized techniques and calibrated equipment. Height was measured to the nearest 0.1 cm using a portable stadiometer (SECA 225, SECA Deutschland, Hamburg, Germany). Weight was measured to the nearest 0.1 kg using an electronic scale (GL-6000-20, CAS Korea, Seoul, Korea). Waist circumference was measured to the nearest 0.1 cm with a measuring tape (SECA 200, SECA Deutschland, Hamburg, Germany). BMI was calculated from the measured heights and weights (kg/m^2) of the subjects. Blood pressure was measured three times using a mercury sphygmomanometer (Baumanometer, WA Baum Co., New York, USA) after at least 5 minutes of rest in the sitting position, and the average of the last two values was used.

Venous blood samples were collected from each subject after having fasted for at least 8 hours and were analyzed in a certified clinical laboratory. Blood glucose,

triglycerides, and HDL-cholesterol were measured using an ADVIA 1650 automatic analyzer (Siemens, Washington, DC, USA) in 2007 and a Hitachi automatic analyzer 7600 (Hitachi, Tokyo, Japan) in 2008 and 2009 by the enzymatic method. Fasting insulin was measured using a 1470 WIZARD gamma counter (Perkin-Elmer, Turku, Finland) by the radioimmunoassay method. HOMA-IR, a surrogate measure of insulin resistance, was calculated according to the formula: fasting glucose (mmol/L) \times fasting insulin (μ U/mL) / 22.5 (Matthews, DR *et al.* 1985).

Metabolic syndrome and insulin resistance

Metabolic syndrome was defined according to the NCEP ATP III criteria (Grundy, SM *et al.* 2005) with a modified waist circumference cutoff for Korean adults (Lee, SY *et al.* 2007) if any three or more of the following components were present: 1) elevated waist circumference (≥ 90 cm in men and ≥ 85 cm in women); 2) elevated triglycerides (≥ 150 mg/dL); 3) low HDL-cholesterol (< 40 mg/dL in men and < 50 mg/dL in women); 4) elevated fasting blood glucose (≥ 100 mg/dL); and 5) elevated blood pressure (systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg). Insulin resistance was defined according to elevated HOMA-IR (> 2.0) (Eslam, M *et al.* 2011, Schwimmer, JB *et al.* 2003).

Statistical analyses

All statistical analyses were conducted using the SAS statistical software package version 9.2 (SAS Institute, Cary, NC, USA). Values of sociodemographic, lifestyle, anthropometric, biochemical, and dietary variables were expressed as adjusted mean and standard error for continuous variables or percentages for categorical variables by

the presence of insulin resistance in the normal, risk, and MetS groups. The general linear model (GLM) for continuous variables and the chi-square test for categorical variables were used to test differences in these variables by the presence of insulin resistance. Adjusted means, standard errors, and *P*-values were obtained from the GLM after adjustment for potential confounding variables. All tests of significance were two-tailed, and *P*-values < 0.05 were considered significant.

3. Results

Comparison of characteristics by the presence of insulin resistance in the normal, risk, and MetS groups

Figure III - 2 shows the prevalence of insulin resistance by symptoms of metabolic syndrome. The prevalence of insulin resistance was 26.7 % in the normal group, 46.8 % in the risk group, and 77.0 % in the MetS group (*P*-value < 0.0001).

Characteristics of the study subjects by the presence of insulin resistance in the normal, risk, and MetS group are provided in Table III - 6. To identify potential confounding variables of the relationship between insulin resistance and diet, differences in characteristics (e.g., socioeconomic, lifestyle, and biochemical variables) by the presence of insulin resistance according to the symptoms of metabolic syndrome were examined. Subjects with insulin resistance were younger than non-insulin resistance subjects in all three groups. Subjects with insulin resistance in the normal group had a higher income level and were less physically active than non-insulin resistance

subjects. In the risk group, subjects with insulin resistance had a lower prevalence of smoking and drinking and were less physically active compared with non-insulin resistance subjects. In the MetS group, subjects with insulin resistance were more educated and had a lower prevalence of smoking and drinking compared with non-insulin resistance subjects.

BMI was associated with insulin resistance in the normal, risk, and MetS groups. In the normal group, the prevalence of obesity ($BMI \geq 25 \text{ kg/m}^2$) was 12.8 % in the insulin resistance subjects, but 6.7 % in the non-insulin resistance subjects. In the risk group, the prevalence of obesity was 36.5 % in the insulin resistance subjects, but 18.0 % in the non-insulin resistance subjects. In the MetS group, the prevalence of obesity was 70.4 % in the insulin resistance subjects, but 53.6 % in the non-insulin resistance subjects. Subjects with insulin resistance had a significantly higher waist circumference compared to subjects without insulin resistance in the normal group, but there was no difference by the presence of insulin resistance in the risk and MetS groups. Subjects with insulin resistance had a lower HDL-cholesterol than subjects without insulin resistance in the normal, risk, and MetS groups and subjects with insulin resistance had a higher triglycerides than subjects without insulin resistance in the normal and risk groups. In addition, fasting blood glucose and blood pressure were higher in the insulin resistance group than the non-insulin resistance group for the normal group.

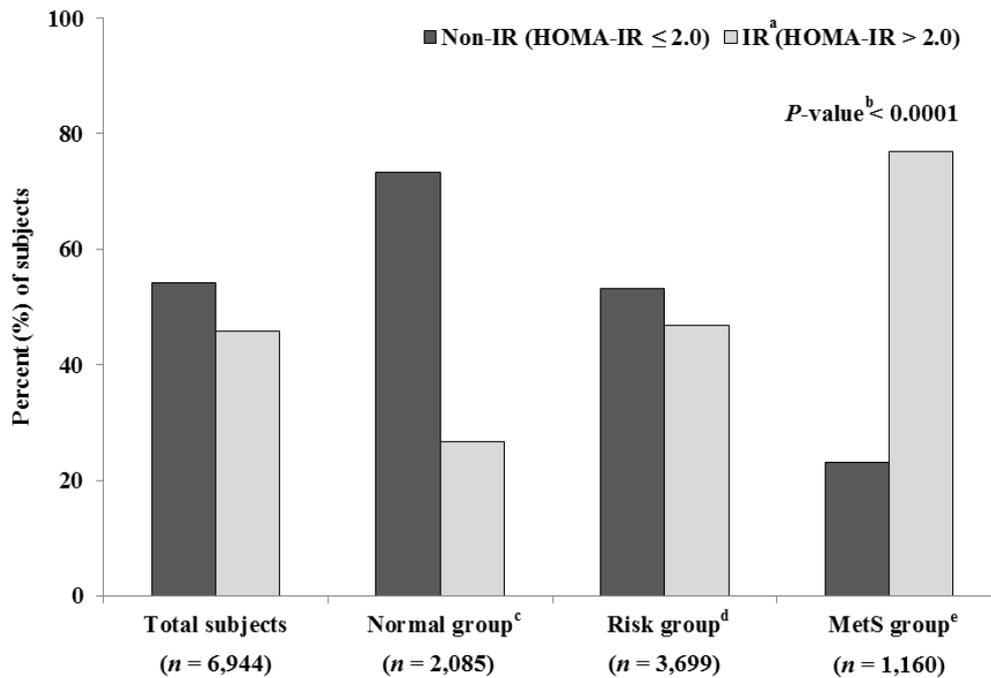


Figure III - 2. Prevalence of insulin resistance by symptoms of metabolic syndrome

^a Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μIU/mL)] / 22.5.

^b P-value was obtained from the chi-square test.

^c Subjects without any symptoms of metabolic syndrome were defined as the normal group.

^d Subjects with 1 or 2 symptoms of metabolic syndrome were defined as the risk group.

^e Subjects with 3 or more symptoms of metabolic syndrome were defined as the metabolic syndrome (MetS) group.

Table III - 6. Comparison of general characteristics by the presence of insulin resistance^a in the normal, risk, and metabolic syndrome group

Characteristics	Normal group ^b (n = 2,085)			Risk group ^c (n = 3,699)			MetS group ^d (n = 1,160)		
	Non-IR (n = 1,529)	IR (n = 556)	P-value ^e	Non-IR (n = 1,968)	IR (n = 1,731)	P-value ^e	Non-IR (n = 267)	IR (n = 893)	P-value ^e
Sex (%)									
Men	34.9	31.8	0.1974	35.6	34.5	0.4720	59.6	50.5	0.0094
Education (%)									
Elementary	9.7	8.1	0.0700	17.0	15.8	0.2394	30.0	22.5	0.0245
Lower secondary	10.6	9.2		14.1	13.1		15.7	15.3	
Upper secondary	42.4	41.7		39.3	40.8		32.2	38.2	
College or more	37.3	41.0		29.6	30.3		22.1	24.0	
Income (%)									
Lowest	8.5	6.3	0.0304	11.3	10.3	0.5092	18.0	12.7	0.3997
Medium-low	21.2	20.9		23.2	25.8		24.0	28.2	
Medium-high	33.4	30.4		33.1	33.2		30.7	32.3	
Highest	37.0	42.5		32.3	30.7		27.3	26.9	
BMI (%)									
< 18.5 kg/m ²	9.9	2.9	< 0.0001	4.2	1.6	< 0.0001	0.8	0.1	< 0.0001
18.5–25.0 kg/m ²	83.4	84.4		77.8	61.9		45.7	29.5	
≥ 25.0 kg/m ²	6.7	12.8		18.0	36.5		53.6	70.4	
Current smoking (%)									
Yes	20.5	16.7	0.0562	20.6	17.2	0.0081	34.8	26.8	0.0105
Current alcohol use ^f (%)									
Yes	56.9	55.2	0.4928	55.6	52.1	0.0341	65.5	57.9	0.0254
Physical activity ^g (%)									
Yes	19.0	15.1	0.0423	19.3	15.5	0.0026	16.5	17.3	0.7704

Table III - 6. Comparison of general characteristics by the presence of insulin resistance^a in the normal, risk, and metabolic syndrome group (continued)

	Normal group					Risk group					MetS group (n = 1,160)				
	Non-IR		IR		P-value	Non-IR		IR		P-value	Non-IR		IR		P-value
	Mean	SE	Mean	SE		Mean	SE	Mean	SE		Mean	SE	Mean	SE	
Age (year)	43.0	0.2 ^h	40.8	0.4	< 0.0001	45.7	0.2	44.5	0.2	0.0002	49.2	0.6	47.1	0.3	0.0009
Waist circumference (cm)	75.3	0.1	75.9	0.2	0.0031	80.8	0.1	81.1	0.1	0.0870	89.0	0.3	89.4	0.2	0.2324
Fasting blood glucose (mg/dL)	87.5	0.2	91.0	0.3	< 0.0001	90.2	0.2	96.5	0.2	< 0.0001	96.5	1.5	108.1	0.8	< 0.0001
Fasting blood insulin (μIU/mL)	6.7	0.05	11.1	0.08	< 0.0001	6.9	0.1	11.7	0.1	< 0.0001	7.3	0.5	13.7	0.3	< 0.0001
HOMA-IR	1.4	0.01	2.5	0.02	< 0.0001	1.5	0.02	2.8	0.02	< 0.0001	1.7	0.1	3.6	0.1	< 0.0001
Triglycerides (mg/dL)	76.7	0.7	84.4	1.2	< 0.0001	122.2	1.7	132.2	1.9	< 0.0001	213.5	8.8	225.7	4.7	0.2269
HDL-cholesterol (mg/dL)	55.6	0.2	54.4	0.3	0.0026	46.6	0.2	46.0	0.2	0.0395	41.8	0.5	40.4	0.2	0.0095
Systolic blood pressure (mmHg)	105.9	0.2	107.0	0.4	0.0200	112.8	0.3	113.1	0.3	0.4904	123.9	1.0	123.6	0.5	0.7217
Diastolic blood pressure (mmHg)	70.1	0.2	70.9	0.3	0.0183	74.9	0.2	75.3	0.2	0.2078	82.9	0.6	82.1	0.3	0.2942

^a Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μIU/mL)] / 22.5.

^b Subjects without any symptoms of metabolic syndrome were defined as the normal group.

^c Subjects with 1 or 2 symptoms of metabolic syndrome were defined as the risk group.

^d Subjects with 3 or more symptoms of metabolic syndrome were defined as the metabolic syndrome (MetS) group.

^e P-values were obtained from the chi-square test for categorical variables and from the general linear model (GLM) for continuous variables after adjustment for sex (men or women), age (continuous), and BMI (continuous).

^f Current alcohol use was assigned “yes” if a subject drank a glass of alcohol or more per month over the previous year.

^g Physical activity was assigned “yes” if a subject engaged in physical activity at high intensity more than 20 minutes at least 3 days or more per week over the previous week.

^h Mean and standard error were obtained from the GLM after adjustment for sex (men or women), age (continuous), and BMI (continuous).

Comparison of nutrient and food group intakes by the presence of insulin resistance in the normal group

Men with insulin resistance in the normal group had a tendency to consume more oils and sugars than non-insulin resistance men (Insulin resistance vs. non-insulin resistance: 7.7 vs. 6.5 servings, P -value = 0.0075). Other nutrient or food group intakes showed no significant differences between non-insulin resistance and insulin resistance men in the normal group (Table III - 7). Women with insulin resistance in the same group had higher intakes of total carbohydrate, energy from carbohydrate, DGI, and DGL but lower intakes of total fat and energy from fat than non-insulin resistance women (P -values < 0.05). DGI and DGL in women with insulin resistance were 58.8 and 171.4, but DGI and DGL in women without insulin resistance were 57.9 and 164.5 (Table III - 8).

Table III - 7. Comparison of adjusted^a mean intake of nutrient and food groups by the presence of insulin resistance in the normal group men^b (*n* = 710)

	Non-IR (<i>n</i> = 533)		IR ^c (<i>n</i> = 177)		<i>P</i> -value ^d
	Mean	<i>SE</i>	Mean	<i>SE</i>	
Macronutrients					
Total energy (kcal)	2310	32.1	2181	56.7	0.0510
Carbohydrate (g)	360.8	3.5	355.5	6.2	0.4639
Fat (g)	45.7	0.9	47.6	1.6	0.2971
Protein (g)	81.8	0.9	84.0	1.6	0.2310
Energy from carbohydrate (%)	66.5	0.4	66.0	0.7	0.5699
Energy from fat (%)	18.5	0.3	18.7	0.6	0.7039
Energy from protein (%)	15.0	0.2	15.3	0.3	0.5479
Dietary glycemic index ^e	58.4	0.3	57.8	0.5	0.3243
Dietary glycemic load ^e	211.8	2.6	206.4	4.6	0.3081
Food groups (serving)					
Grains	3.7	0.0	3.5	0.1	0.0610
Meat, fish, eggs, and beans	4.6	0.1	4.8	0.2	0.5179
Vegetables	10.5	0.2	10.1	0.4	0.3346
Fruits	1.5	0.1	1.9	0.2	0.1310
Milk and dairy products	0.4	0.0	0.4	0.1	0.9956
Fats, oils, and sugars	6.5	0.2	7.7	0.4	0.0075

^a All values were adjusted for age (continuous), BMI (continuous), and total energy intake (continuous).

^b Subjects without any symptoms of metabolic syndrome were defined as the normal group.

^c Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μU/mL)] / 22.5.

^d *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

^e Dietary glycemic index and dietary glycemic load were calculated using glucose as the reference food.

Table III - 8. Comparison of adjusted^a mean intake of nutrient and food groups by the presence of insulin resistance in the normal group women^b (n = 1,375)

	Non-IR (n = 996)		IR ^c (n = 379)		P-value ^d
	Mean	SE	Mean	SE	
Macronutrients					
Total energy (kcal)	1657	19.4	1694	31.8	0.3282
Carbohydrate (g)	282.4	1.6	290.2	2.7	0.0146
Fat (g)	33.9	0.5	31.7	0.9	0.0316
Protein (g)	59.7	0.5	58.7	0.9	0.3249
Energy from carbohydrate (%)	67.8	0.3	69.1	0.5	0.0317
Energy from fat (%)	17.8	0.3	16.7	0.4	0.0270
Energy from protein (%)	14.3	0.1	14.1	0.2	0.3287
Dietary glycemic index ^e	57.9	0.2	58.8	0.4	0.0312
Dietary glycemic load ^e	164.5	1.3	171.4	2.1	0.0064
Food groups (serving)					
Grains	2.8	0.0	2.9	0.0	0.2217
Meat, fish, eggs, and beans	3.1	0.1	2.9	0.1	0.1371
Vegetables	7.7	0.1	7.7	0.2	0.8633
Fruits	2.1	0.1	2.4	0.2	0.1506
Milk and dairy products	0.5	0.0	0.5	0.0	0.9610
Fats, oils, and sugars	4.5	0.1	4.6	0.2	0.5481

^a All values were adjusted for age (continuous), BMI (continuous), and energy intake (continuous).

^b Subjects without any symptoms of metabolic syndrome were defined as the normal group.

^c Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μU/mL)] / 22.5.

^d P-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

^e Dietary glycemic index and dietary glycemic load were calculated using glucose as the reference food.

Comparison of nutrient and food group intakes by the presence of insulin resistance in the risk group

In men of the risk group, no difference in nutrient and food group intakes was observed by the presence of insulin resistance (Table III - 9). Women with insulin resistance in the risk group had lower energy intake but higher intakes of oils and sugars than non-insulin resistance women (Insulin resistance vs. non-insulin resistance: 4.2 vs. 3.9 servings, P -value = 0.0394) (Table III - 10).

Table III - 9. Comparison of adjusted^a mean intake of nutrient and food groups by the presence of insulin resistance in the risk group men^b (*n* = 1,298)

	Non-IR (<i>n</i> = 701)		IR ^c (<i>n</i> = 597)		<i>P</i> -value ^d
	Mean	<i>SE</i>	Mean	<i>SE</i>	
Macronutrients					
Total energy (kcal)	2320	29.6	2258	32.2	0.1687
Carbohydrate (g)	355.9	3.1	356.2	3.3	0.9456
Fat (g)	43.2	0.8	45.4	0.8	0.0595
Protein (g)	82.4	0.9	82.9	1.0	0.7123
Energy from carbohydrate (%)	67.1	0.4	66.7	0.4	0.5151
Energy from fat (%)	17.5	0.3	18.0	0.3	0.2283
Energy from protein (%)	15.4	0.2	15.3	0.2	0.5342
Dietary glycemic index ^e	59.0	0.3	58.6	0.3	0.3027
Dietary glycemic load ^e	210.7	2.3	209.2	2.5	0.6651
Food groups (serving)					
Grains	3.7	0.0	3.6	0.0	0.4276
Meat, fish, eggs, and beans	4.7	0.1	4.8	0.1	0.4724
Vegetables	10.7	0.2	10.7	0.2	0.9553
Fruits	1.5	0.1	1.7	0.1	0.1271
Milk and dairy products	0.3	0.0	0.4	0.0	0.1272
Fats, oils, and sugars	6.2	0.2	6.2	0.2	0.9869

^a All values were adjusted for age (continuous), BMI (continuous), and energy intake (continuous).

^b Subjects with 1 or 2 symptoms of metabolic syndrome were defined as the risk group.

^c Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μU/mL)] / 22.5.

^d *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

^e Dietary glycemic index and dietary glycemic load were calculated using glucose as the reference food.

Table III - 10. Comparison of adjusted^a mean intake of nutrient and food groups by the presence of insulin resistance in the risk group women^b (*n* = 2,401)

	Non-IR		IR ^c		<i>P</i> -value ^d
	<i>(n</i> = 1,267)		<i>(n</i> = 1,134)		
	Mean	<i>SE</i>	Mean	<i>SE</i>	
Macronutrients					
Total energy (kcal)	1691	16.8	1641	17.7	0.0441
Carbohydrate (g)	290.4	1.4	290.3	1.5	0.9805
Fat (g)	30.6	0.5	30.9	0.5	0.7004
Protein (g)	59.6	0.5	59.0	0.5	0.3460
Energy from carbohydrate (%)	69.8	0.3	69.7	0.3	0.7699
Energy from fat (%)	16.0	0.2	16.2	0.2	0.5069
Energy from protein (%)	14.2	0.1	14.1	0.1	0.5824
Dietary glycemic index ^e	58.9	0.2	59.0	0.2	0.5925
Dietary glycemic load ^e	171.8	1.1	171.7	1.2	0.9331
Food groups (serving)					
Grains	3.0	0.0	2.9	0.0	0.0923
Meat, fish, eggs, and beans	3.0	0.1	3.0	0.1	0.9773
Vegetables	8.0	0.1	8.0	0.1	0.8265
Fruits	2.2	0.1	2.4	0.1	0.0789
Milk and dairy products	0.4	0.0	0.4	0.0	0.6374
Fats, oils, and sugars	3.9	0.1	4.2	0.1	0.0394

^a All values were adjusted for age (continuous), BMI (continuous), and energy intake (continuous).

^b Subjects with 1 or 2 symptoms of metabolic syndrome were defined as the risk group.

^c Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μU/mL)] / 22.5.

^d *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

^e Dietary glycemic index and dietary glycemic load were calculated using glucose as the reference food.

Comparison of nutrient and food group intakes by the presence of insulin resistance in the MetS group

Men with insulin resistance in the MetS group had lower energy intake but higher intake of fruits than non-insulin resistance men (Table III - 11). In women, consumption of fruits was higher in subjects with insulin resistance than in subjects without insulin resistance (Insulin resistance vs. non-insulin resistance: 1.9 vs. 1.3 servings, P -value = 0.0358). Other nutrient or food group intakes showed no significant differences between non-insulin resistance and insulin resistance subjects in the MetS group (Table III - 12).

Table III - 11. Comparison of adjusted^a mean intake of nutrient and food groups by the presence of insulin resistance in men of the metabolic syndrome group^b (*n* = 610)

	Non-IR (<i>n</i> = 159)		IR ^c (<i>n</i> = 451)		<i>P</i> -value ^d
	Mean	<i>SE</i>	Mean	<i>SE</i>	
Macronutrients					
Total energy (kcal)	2373	60.0	2224	35.2	0.0344
Carbohydrate (g)	352.0	6.6	355.5	3.9	0.6470
Fat (g)	41.3	1.5	42.2	0.9	0.6011
Protein (g)	77.4	1.8	80.3	1.1	0.1704
Energy from carbohydrate (%)	67.7	0.8	67.7	0.4	0.9880
Energy from fat (%)	17.6	0.6	17.2	0.4	0.6192
Energy from protein (%)	14.8	0.3	15.1	0.2	0.3836
Dietary glycemic index ^e	59.6	0.6	58.7	0.3	0.2262
Dietary glycemic load ^e	211.1	4.9	209.1	2.9	0.7240
Food groups (serving)					
Grains	3.6	0.1	3.6	0.1	0.7650
Meat, fish, eggs, and beans	4.3	0.2	4.4	0.1	0.5827
Vegetables	10.6	0.5	10.6	0.3	0.8826
Fruits	1.2	0.2	1.7	0.1	0.0502
Milk and dairy products	0.3	0.1	0.3	0.0	0.9856
Fats, oils, and sugars	6.0	0.4	6.0	0.2	0.9771

^a All values were adjusted for age (continuous), BMI (continuous), and energy intake (continuous).

^b Subjects with 3 or more symptoms of metabolic syndrome were defined as the MetS group.

^c Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μIU/mL)] / 22.5.

^d *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

^e Dietary glycemic index and dietary glycemic load were calculated using glucose as the reference food.

Table III - 12. Comparison of adjusted^a mean intake of nutrient and food groups by the presence of insulin resistance in women of the metabolic syndrome group^b (*n* = 550)

	Non-IR (<i>n</i> = 108)		IR ^c (<i>n</i> = 442)		<i>P</i> -value ^d
	Mean	<i>SE</i>	Mean	<i>SE</i>	
Macronutrients					
Total energy (kcal)	1648	58.5	1586	28.5	0.3455
Carbohydrate (g)	279.2	4.7	280.7	2.3	0.7683
Fat (g)	25.7	1.4	27.2	0.7	0.3471
Protein (g)	53.3	1.6	55.7	0.8	0.1860
Energy from carbohydrate (%)	72.3	0.9	71.1	0.4	0.2207
Energy from fat (%)	14.2	0.7	14.9	0.3	0.3968
Energy from protein (%)	13.4	0.4	14.0	0.2	0.1991
Dietary glycemic index ^e	60.4	0.7	59.8	0.4	0.4192
Dietary glycemic load ^e	169.4	3.9	168.6	1.9	0.8512
Food groups (serving)					
Grains	3.0	0.1	2.9	0.0	0.0695
Meat, fish, eggs, and beans	2.5	0.2	2.8	0.1	0.1975
Vegetables	7.0	0.5	8.0	0.2	0.0607
Fruits	1.3	0.3	1.9	0.1	0.0358
Milk and dairy products	0.3	0.1	0.3	0.0	0.6225
Fats, oils, and sugars	3.1	0.3	3.5	0.2	0.2919

^a All values were adjusted for age (continuous), BMI (continuous), and energy intake (continuous).

^b Subjects with 3 or more symptoms of metabolic syndrome were defined as the MetS group.

^c Insulin resistance (IR) was defined as HOMA-IR > 2.0. Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μIU/mL)] / 22.5.

^d *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

^e Dietary glycemic index and dietary glycemic load were calculated using glucose as the reference food.

4. Discussion and conclusions

We examined the relationship between intakes of nutrient and food group and insulin resistance according to symptom of metabolic syndrome in the middle-aged Korean adults using data from the Fourth KNHANES in 2007–2009. The prevalence of insulin resistance significantly increased across symptom of metabolic syndrome: 26.7 % in the normal group, 46.8 % in the risk group, and 77.0 % in the MetS group. We found that subjects with insulin resistance in the normal group had higher BMI, waist circumference, fasting blood glucose, triglycerides, and blood pressure, but lower HDL-cholesterol than those without insulin resistance in the same group. Although subjects in the normal group had no symptom of metabolic syndrome, subjects with insulin resistance in this group had a higher risk for metabolic syndrome than subjects without insulin resistance.

The prevalence of obesity ($\text{BMI} \geq 25.0 \text{ kg/m}^2$) was higher in subjects with insulin resistance than subjects without insulin resistance in the normal, risk, and Mets group, and waist circumference was higher in subjects with insulin resistance than subjects without insulin resistance in the normal group. In addition, subjects with insulin resistance in the normal and risk groups had lower level of physical activity than subjects without insulin resistance in these groups. These findings of our study were consistent with those from previous studies which reported that higher BMI and lower physical activity level were key determinants of insulin resistance and metabolic syndrome (McAuley, KA *et al.* 2002, Meigs, JB *et al.* 1997, Miyatake, N *et al.* 2002, Park, HS *et al.* 2004, Reaven, GM 2000).

Our most interesting finding was that women with insulin resistance in the normal group had a higher intake of dietary carbohydrates, including DGI and DGL, than women without insulin resistance in the same group. High carbohydrate diet increase postprandial blood glucose and insulin secretion and high DGI or DGL diet have a greater adverse effect on postprandial response of blood glucose and insulin. These response due to high carbohydrate diet result in inappropriate metabolism of blood glucose, insulin, serum lipid, and lipoprotein concentrations and consequently increases risk of metabolic syndrome (Choi, H *et al.* 2012, Finley, CE *et al.* 2010, Kim, K *et al.* 2008, Levitan, EB *et al.* 2008, Murakami, K *et al.* 2006).

Previous studies in Korean adults reported a positive association between carbohydrate intake and metabolic abnormalities, and these associations were stronger in women than in men. Kim, K *et al.* (2008) found that DGL was positively associated with a higher risk of low HDL-cholesterol in men and total carbohydrate, DGI, and DGL were positively associated with higher risks of low HDL-cholesterol and metabolic syndrome in women. Another Korean study (Park, SH *et al.* 2010) showed that a high carbohydrate diet (> 70 % of energy from carbohydrate) was associated with higher risks of diabetes and low HDL-cholesterol in women while it was not in men. In the present study, women consumed less amount of dietary carbohydrate than men but percentage of energy from carbohydrate in the diet is higher in women than in men. In addition, higher DGI and DGL were significantly associated with insulin resistance in women of the Normal group. Therefore, both quantity and quality of carbohydrate in their diet seemed to be a contributing factor for insulin resistance. Western population studies also reported that DGI or DGL were related to a higher HOMA-IR (McKeown, NM *et al.* 2004, O'Sullivan, TA *et al.* 2010). In addition,

Cheung, BM (2005) insisted that insulin resistance in Asian populations might be not caused by excessive intake of fat but by excessive intake of carbohydrate in their diet.

Men with insulin resistance in the normal group and women with insulin resistance in the risk group had higher intakes of fats, oils, and sugars than subjects without insulin resistance in the same group, respectively. Men with insulin resistance in the normal group consumed 7.7 serving of fats, oils and sugars per day, and it was above the recommended number of servings (5 servings per day) according to the Dietary Reference Intakes for Koreans (KNS 2010). In addition, men in the risk and MetS groups consumed higher intakes of fats, oils and sugars in excess of the recommended servings, regardless of the presence of insulin resistance. This finding suggests the need for a public health policy or a nutritional education program that emphasizes the benefits of a diet low in fats, oils, and sugars. Fats and oils group includes vegetable oils, mayonnaise, salad dressing, and fried foods and sugars group includes candy, chocolate, jam, and sugar sweetened beverages. Foods with higher contents of sugars and fats include high energy and low nutrients and thus are associated with obesity and metabolic syndrome (Jung, HJ *et al.* 2011, Lutsey, PL *et al.* 2008, Shin, A *et al.* 2009, Yoo, S *et al.* 2004).

Although our study showed a positive association between fruits intake and insulin resistance, subjects in the MetS group consumed lower fruits than the normal or risk groups and did not meet the recommended level of fruits consumption. Previous studies have found that fruits intake has a protective effect on metabolic diseases, such as metabolic syndrome, cardiovascular diseases, and type 2 diabetes (Ford, ES *et al.* 2003). In the Bogalusa Heart Study, low consumption of fruits and vegetables and high

consumption of sugar sweetened beverages were independently associated with the prevalence of metabolic syndrome (Yoo, S *et al.* 2004).

Our study has several limitations. The KNHANES does not include a questionnaire about the previous diagnosis and treatment for metabolic syndrome, so we did not obtain the information on subjects' recognition on metabolic syndrome. The recognition of metabolic syndrome could affect and change their diet. In addition, the cross-sectional design limits the inference of causal relationship for the association between diet and insulin resistance. We used a single 24-hour recall dietary data, which might have affected estimates of usual intake. Regardless of these limitations, our study included a relatively large representative sample of Korean adults. In addition, we excluded subjects who had been previously diagnosed or treated for diabetes, dyslipidemia, or hypertension to reduce the effects of these diseases on their lifestyle and diet.

In conclusion, findings of this study suggest that dietary carbohydrate intake, including DGI and DGL, might be associated with insulin resistance in healthy women. Further research in prospective cohort studies in order to examine the association of dietary carbohydrate intake with an incidence of insulin resistance will be necessary among Korean adults.

STUDY 3. High intake of whole grains and beans pattern is inversely associated with insulin resistance in the Korean adult population³

1. Introduction

Insulin resistance is defined as the condition in which cells do not respond to the normal actions of the hormone insulin. As a result, insulin resistance can lead to a variety of chronic diseases. Insulin resistance is associated with risks for type 2 diabetes, cardiovascular diseases, and metabolic syndrome (Hanley, AJG *et al.* 2002b, McNaughton, SA *et al.* 2008). The HOMA-IR score is calculated from fasting blood glucose and insulin concentrations to assess insulin resistance in the clinical setting of large scaled populations (Bonora, E *et al.* 2000).

Recently, many researchers have applied dietary pattern analysis in epidemiologic studies about diet and disease because it provides a picture about the overall quality of diet instead of focusing on specific nutrients or foods. In previous studies of Western populations, two major dietary patterns were identified: the Western and the healthy/prudent patterns (Fung, TT *et al.* 2001b, Hu, FB *et al.* 2000, van Dam, RM *et*

³ This study was published in the Diabetes Research and Clinical Practice vol. 98, no. 3, pages E28-E31 in 2012.

al. 2002). The Western dietary pattern characterized by higher intakes of bread, potatoes, meat, soft drinks, sweets and dessert has been associated with increased risks for metabolic diseases, such as diabetes, cardiovascular disease, and metabolic syndrome (Denova-Gutierrez, E *et al.* 2010a, Fung, TT *et al.* 2004, Fung, TT *et al.* 2001b, Hu, FB *et al.* 2000). On the other hand, the healthy/prudent dietary pattern characterized by higher intakes of fruits, vegetables, legumes, and whole grains has been lined with reduced risks for metabolic diseases (Esmailzadeh, A *et al.* 2007, Fung, TT *et al.* 2001b, Panagiotakos, DB *et al.* 2007, van Dam, RM *et al.* 2002).

Insulin resistance is one component of metabolic syndrome and a strong predictor of chronic diseases (Grundy, SM 1999, Reaven, GM 1988). Therefore, investigation of dietary patterns associated with insulin resistance is important to prevent and attenuate the risk for chronic diseases. Several studies in Western populations reported that dietary patterns with higher consumption of fruits, vegetables, and whole grains were associated with a reduced risk of insulin resistance (Anderson, AL *et al.* 2012, Esmailzadeh, A *et al.* 2007, Villegas, R *et al.* 2004b). However, only a few studies have examined the relationship between dietary patterns and insulin resistance among Asian populations. Among non-diabetic Chinese adults, the Western dietary pattern was positively associated with the risk of insulin resistance but the Hedonic dietary pattern was inversely associated with the risk of insulin resistance (Zuo, H *et al.* 2013). The aim of this study was to explore the association between dietary patterns and insulin resistance in the Korean adult population.

2. Methods

Study subjects

Subjects of this study were selected among adults participated in the 2007–2008 KNHANES, which was a cross-sectional and nationally representative survey. The design of KNHANES is described in detail elsewhere (Choi, HS *et al.* 2011). Out of 6,084 individuals aged between 30 and 65 years, 1,098 were excluded for missing information or implausible energy intake (< 500 or > 5000 kcal) and 1,115 were excluded due to a history or treatment of diabetes, hypertension, or dyslipidemia to avoid the effects of preexisting disease condition. A total of 3,871 individuals were included in the final analysis.

Data variables

Information on sociodemographic and lifestyle variables was collected using a structured questionnaire in the health interview survey. The covariates used in this study were age, sex, education, income, BMI, current smoking, current alcohol use, and physical activity. Fasting blood glucose and insulin levels were determined from the health examination. Insulin resistance was defined as the upper quartile of the HOMA-IR scores (Esmailzadeh, A *et al.* 2007, Villegas, R *et al.* 2004b). HOMA-IR was calculated according to the formula: fasting glucose (mmol/L) × fasting insulin (μ IU/mL) / 22.5 (Matthews, DR *et al.* 1985). In the nutrition survey of the KNHANES, dietary intake data for individuals were collected using a FFQ and a single 24-hour recall. In this study, to determine dietary patterns based on the usual intake of this

population, dietary intake data obtained from the FFQ was used. The FFQ was developed to assess usual nutrient intake and included 63 food items with simple frequency (Choi, MK *et al.* 2011).

Statistical analyses

All statistical analyses were performed using the SAS statistical software package, version 9.2 (SAS Institute, Cary, NC, USA). Dietary pattern analysis was conducted by factor analysis using FACTOR PROCEDURE and varimax rotation function in SAS. For the dietary pattern analysis, all food items in the FFQ were quantified as daily frequency and aggregated into 24 food groups based on similarity. Food groupings used in the dietary pattern analysis are shown in Table III - 13. To determine the number of patterns to retain, eigenvalues, the Scree test, and interpretability were considered (Newby, PK and Tucker, KL 2004). Multivariate adjusted logistic regression analysis was conducted to calculate the ORs and 95% CIs for insulin resistance across quintiles of dietary pattern scores.

Table III - 13. Food groupings used in the factor analysis

Food or food group	Food items in a food frequency questionnaire of the KNHANES
White rice	White rice
Grains	Other grains
Noodle	Instant noodle, Udong, Chinese noodle, Wheat noodle, Vermicelli
Bread & Snack	Bread, Rice cakes, Crackers, Cookies, Biscuit, Snack
Soy products	Tofu, Soybean milk
Beans	Beans, Bean-mixed rice, Beans cooked in soy sauce
Potatoes	Potatoes, Sweet potatoes
Meat	Beef, Poultry, Pork
Processed meats	Ham, Bacon, Sausage, Hot dogs
Eggs	Eggs
Fishes	Mackerel, Tuna, Yellow corvina, Pollack, Anchovy, Fish paste, Squid, Clam, Salted fish (including dried fish)
Kimchi	Traditional fermented cabbage product
Vegetables	White radish and leaves, Bean sprouts, Spinach, Cucumber, Pepper, Carrot, Pumpkin, Cabbage
Tomatoes	Tomatoes, including fresh and tomato juice
Mushrooms	Mushrooms
Seaweeds	Seaweeds, Laver
Fruits	Tangerines, Persimmons, Pears, Watermelon, Melon, Strawberries, Grapes, Peaches, Apples, Bananas, Oranges (including fruit juice and canned fruits)
Milk & Dairy products	Milk, Yogurt, Ice-cream
High energy drinks	Colas, Sodas
Coffee	Coffee
Tea	Green tea
Alcohols	Beer, Soju, Makgeolli (traditional unrefined rice wine)
Hamburger & Pizza	Hamburger, Pizza
Fried foods	Fried foods

3. Results

Dietary patterns by factor analysis

Five dietary patterns were identified by factor analysis and were labeled as follows: 1) Diverse diet, 2) Western diet, 3) Whole grains and beans, 4) White rice and kimchi (traditional fermented cabbage), and 5) Alcohol and coffee based on the food groups showing high loadings by each dietary pattern (Table III - 14). The diverse diet pattern was characterized by higher intakes of many food groups, including eggs, fish, vegetables, mushrooms, seaweeds, potatoes, fruits, and soy product. The Western pattern included high loadings of bread and snacks, meat, soft drinks, hamburger, pizza, and fried foods. The whole grains and beans pattern was characterized by higher intakes of whole grain, beans, tomatoes, fruits, and tea. The white rice and kimchi pattern was positively associated with white rice and kimchi, but inversely associated with tomatoes, milk and dairy products, and tea. The alcohol and coffee pattern was characterized by higher intakes of noodle, coffee, tea, and alcoholic beverages. Five patterns accounted for 42.1 % of the total variance in the dietary data.

Table III - 14. Factor loading matrix for five dietary patterns^{a,b}

	Pattern 1	Pattern 2	Pattern 3	Pattern 4	Pattern 5
Food or food groups	Diverse diet	Western diet	Whole grains & beans	White rice & kimchi	Alcohol & coffee
White rice			0.23	0.73	
Other grain			0.75	0.25	
Noodle		0.36			0.36
Bread & Snack	0.23	0.54			
Soy products	0.50				
Beans			0.74		
Potatoes	0.52				
Meat	0.39	0.45			0.23
Processed meats		0.64			
Eggs	0.50	0.27			
Fishes	0.65				
Kimchi ^c				0.74	
Vegetables	0.66				0.22
Tomatoes	0.39		0.34	-0.29	
Mushrooms	0.56				
Seaweeds	0.61				
Fruits	0.51		0.30		
Milk & Dairy products	0.42	0.27		-0.22	
High energy drinks		0.50			0.28
Coffee					0.50
Tea			0.30	-0.20	0.43
Alcohols					0.68
Hamburger & Pizza		0.70			
Fried foods		0.59			
Variance explained (%)	13.3	10.0	6.7	6.3	5.8

^a Factor loading values < |0.20| were excluded for simplicity.

^b The patterns were identified by factor analysis with the daily frequency of food groups.

^c Traditional fermented cabbage product.

Characteristics across quintiles of dietary pattern scores

Table III - 15 presents general characteristics of the study subjects across quintiles of dietary pattern scores. The diverse and the Western patterns were inversely associated with age but the whole grains and beans and the white rice and kimchi patterns were positively associated with age. Subjects in the highest quintile of the diverse and the whole grains and beans patterns scores were more likely to be women whereas subjects in the highest quintile of the white rice and kimchi and the alcohol and coffee patterns scores were more likely to be men. The diverse and the Western patterns scores were positively associated with education levels but the white rice and kimchi and the alcohol and coffee patterns scores were negatively associated with education levels. Scores of all the dietary patterns were positively associated with household income levels, except for the white rice and kimchi pattern. Subjects in the highest quintile of the white rice and kimchi and the alcohol and coffee patterns scores were more likely to be obese compared to those in the lowest quintile. The Western and the alcohol and coffee patterns were positively associated with the prevalences of current smoking and alcohol use, but the whole grains and beans pattern were inversely linked with the prevalences of current smoking and alcohol use.

Table III - 15. General characteristics of the study subjects across quintiles of dietary pattern scores (n = 3,871)

	Pattern 1: Diverse diet			Pattern 2: Western diet			Pattern 3: Whole grains & beans			Pattern 4: White rice & kimchi			Pattern 5: Alcohol & coffee		
	Q1	Q5	<i>P</i> -value ^a	Q1	Q5	<i>P</i> -value	Q1	Q5	<i>P</i> -value	Q1	Q5	<i>P</i> -value	Q1	Q5	<i>P</i> -value
Age (Mean, <i>SD</i>)															
Year	47.7, 10.3	42.3, 8.3	0.0031	50.2, 8.9	38.5, 7.0	< 0.0001	44.1, 9.8	46.8, 9.9	< 0.0001	42.7, 9.2	45.5, 9.7	0.0019	43.8, 10.5	44.0, 8.7	0.8381
Sex (%)															
Men	42.6	30.4	< 0.0001	36.4	42.4	0.1378	47.7	23.4	< 0.0001	28.8	45.0	< 0.0001	13.1	69.5	< 0.0001
Education (%)															
Elementary	30.5	6.1	< 0.0001	29.5	2.8	< 0.0001	20.4	17.7	0.8920	9.4	20.7	< 0.0001	17.1	10.3	0.0184
Secondary	47.9	52.5		53.5	47.7		53.8	53.1		50.4	53.6		48.2	57.2	
College or more	21.6	41.5		17.1	49.5		25.8	29.2		40.2	25.7		34.8	32.4	
Income (%)															
Low	19.9	4.5	< 0.0001	16.5	3.4	< 0.0001	13.2	10.6	< 0.0001	7.9	15.4	< 0.0001	11.2	8.5	0.0040
Medium	57.0	56.3		55.6	58.4		60.5	52.7		53.1	57.8		58.4	56.2	
High	23.1	39.2		27.9	38.2		26.4	36.7		39.0	26.9		30.4	35.3	
BMI (%)															
< 18.5 kg/m ²	4.9	3.6	0.0449	4.3	4.1	0.0903	4.9	3.5	0.9113	5.6	3.4	0.0118	6.5	2.6	< 0.0001
18.5-24.9 kg/m ²	65.9	72.6		67.3	68.5		66.4	68.4		68.5	66.4		72.0	64.3	
≥ 25.0kg/m ²	29.2	23.8		28.4	27.4		28.7	28.2		26.0	30.2		21.6	33.1	
Current smoking (%)															
Yes	21.2	16.7	0.0071	18.0	26.2	< 0.0001	31.3	8.8	< 0.0001	17.2	23.8	0.1292	4.0	41.9	< 0.0001
Alcohol use (%)															
Yes	54.0	53.8	0.8192	55.3	59.2	0.0080	61.9	45.1	< 0.0001	56.6	60.6	0.6150	26.5	87.2	< 0.0001
Physical activity (%)															
Yes	16.0	18.6	0.1174	20.2	15.1	0.0105	16.5	20.2	0.1322	16.4	16.4	0.8331	16.0	21.2	0.0038

^a *P*-value was obtained from the chi-square test for categorical variable and the general linear model for continuous variable.

Nutrient intake across quintiles of dietary pattern scores

Table III - 16 shows macronutrient intake of the study subjects across quintiles of dietary pattern scores. The diverse pattern scores were positively associated with intakes of total energy, fat (g, % energy), and protein (g, % energy) but inversely associated with percentage of energy from carbohydrate, DGI, and DGL. The Western pattern scores were positively associated with intakes of total energy, fat (g, % energy), and protein (% energy) but negatively associated with percentage of energy from carbohydrate. The whole grains and beans pattern scores were positively associated with intakes of carbohydrate (g) and protein (g) but inversely associated with total energy intake and DGI. The white rice and kimchi pattern scores were positively associated with intakes of total energy, carbohydrate (g, % energy), DGI, and DGL but negatively associated with intake of fat (g, % energy). The alcohol and coffee pattern scores were positively associated with intakes of carbohydrate (g), fat (% energy), protein (% energy), and DGL but inversely associated with intakes of carbohydrate (% energy) and DGI.

Table III - 16. Macronutrient intake of the study subjects across quintiles of dietary pattern scores

	Q1 (n = 774)		Q2 (n = 774)		Q3 (n = 775)		Q4 (n = 774)		Q5 (n = 774)		P for trend ^a
	Mean	SD									
Pattern 1: Diverse diet											
Total energy (kcal)	1798	699.7	1874	697.9	1911	714.3	1929	758.8	1894	723.2	< 0.0001
Carbohydrate (g)	307.9	116.2	312.2	113.0	318.7	117.5	317.7	120.3	309.6	118.4	0.1220
Fat (g)	29.8	22.2	35.1	24.0	36.3	24.7	38.0	27.4	37.9	26.5	0.0204
Protein (g)	60.7	30.6	67.3	32.2	67.8	32.0	70.1	34.1	70.0	32.3	< 0.0001
Energy from carbohydrate (%)	71.5	10.0	68.8	10.0	68.6	10.0	67.8	10.1	67.0	10.0	< 0.0001
Energy from fat (%)	14.7	7.9	16.6	7.8	16.9	8.0	17.4	8.0	17.9	7.8	0.0035
Energy from protein (%)	13.8	3.9	14.6	4.3	14.5	4.2	14.8	4.0	15.1	4.1	< 0.0001
Dietary glycemic index	60.4	7.1	59.1	7.5	58.6	7.1	57.8	7.5	57.3	7.4	< 0.0001
Dietary glycemic load	186.6	74.7	185.7	73.4	187.9	74.6	184.2	73.7	178.3	72.8	0.0005
Pattern 2: Western diet											
Total energy (kcal)	1776	729.5	1832	651.6	1866	683.4	1898	724.9	2033	780.7	< 0.0001
Carbohydrate (g)	302.5	121.6	315.3	107.6	312.8	113.2	310.3	114.4	325.4	127.1	0.7742
Fat (g)	28.7	21.5	31.3	21.2	34.4	23.9	38.6	27.8	44.1	27.9	< 0.0001
Protein (g)	62.6	31.8	64.8	29.9	66.3	29.6	68.8	33.5	73.6	35.8	0.7379
Energy from carbohydrate (%)	71.0	10.4	70.6	9.4	69.1	10.0	67.3	9.9	65.7	9.8	0.0029
Energy from fat (%)	14.5	7.5	15.1	7.3	16.4	7.8	18.0	8.0	19.6	8.2	< 0.0001
Energy from protein (%)	14.5	4.4	14.3	3.9	14.5	4.0	14.7	4.2	14.7	3.9	0.0298
Dietary glycemic index	59.8	7.9	59.5	6.9	58.9	7.3	57.7	7.1	57.4	7.6	0.1423
Dietary glycemic load	181.2	76.6	188.6	69.9	185.0	71.6	180.1	72.1	187.7	78.6	0.6702
Pattern 3: Whole grains & beans											
Total energy (kcal)	1894	744.2	1956	771.1	1836	681.9	1871	698.8	1848	696.5	0.0067
Carbohydrate (g)	309.5	115.5	317.8	118.0	303.6	110.8	315.2	118.5	320.1	122.1	0.0052
Fat (g)	34.5	24.6	38.9	28.4	36.0	26.6	34.8	23.3	32.9	22.3	0.5346
Protein (g)	65.9	32.4	69.3	35.5	66.1	31.0	67.3	30.8	67.3	32.1	0.0009
Energy from carbohydrate (%)	69.0	10.4	67.9	10.4	68.1	10.4	68.9	9.6	69.8	9.6	0.9737
Energy from fat (%)	16.5	8.0	17.6	8.4	17.3	8.4	16.5	7.4	15.7	7.5	0.2706
Energy from protein (%)	14.5	4.5	14.5	4.1	14.6	3.8	14.6	4.1	14.6	3.9	0.0543
Dietary glycemic index	59.7	8.0	58.3	7.1	58.6	7.2	58.2	7.6	58.4	6.9	< 0.0001
Dietary glycemic load	186.1	76.6	186.2	74.2	178.5	69.1	184.4	73.7	187.4	75.6	0.9374

Table III - 16. Macronutrient intake of the study subjects across quintiles of dietary pattern scores (continued)

	Q1 (n = 774)		Q2 (n = 774)		Q3 (n = 775)		Q4 (n = 774)		Q5 (n = 774)		P for trend ^a
	Mean	SD									
Pattern 4: White rice & kimchi											
Total energy (kcal)	1776	758.7	1844	730.0	1923	719.6	1950	685.9	1912	692.2	< 0.0001
Carbohydrate (g)	285.7	115.8	303.3	119.2	322.4	118.0	333.7	113.5	321.0	113.2	< 0.0001
Fat (g)	37.7	28.7	36.1	24.9	35.4	24.4	34.2	25.4	33.7	22.1	< 0.0001
Protein (g)	64.2	32.5	66.0	32.3	69.2	32.0	69.4	33.2	67.2	31.9	0.5963
Energy from carbohydrate (%)	66.7	10.8	67.9	10.4	69.0	9.5	70.4	9.8	69.7	9.5	< 0.0001
Energy from fat (%)	18.6	8.6	17.4	8.3	16.4	7.5	15.3	7.5	15.9	7.5	< 0.0001
Energy from protein (%)	14.8	4.4	14.7	4.3	14.6	4.1	14.3	3.9	14.4	3.8	0.1390
Dietary glycemic index	56.7	8.0	58.0	7.8	58.9	6.9	60.1	6.4	59.6	7.3	< 0.0001
Dietary glycemic load	162.5	70.1	176.7	75.1	190.5	73.4	201.1	73.0	191.8	71.6	< 0.0001
Pattern 5: Alcohol & coffee											
Total energy (kcal)	1744	627.5	1779	665.3	1794	687.4	1933	711.1	2155	816.5	0.1941
Carbohydrate (g)	308.1	114.0	310.7	119.4	304.4	113.9	315.5	116.2	327.6	121.0	< 0.0001
Fat (g)	32.1	22.2	31.9	22.0	33.6	27.2	37.4	25.3	42.0	27.5	0.3081
Protein (g)	61.3	27.6	63.3	29.1	64.1	33.5	69.1	31.6	78.1	36.7	0.3613
Energy from carbohydrate (%)	70.2	9.7	70.1	9.8	69.4	10.4	67.9	10.1	66.2	10.0	0.0012
Energy from fat (%)	15.9	7.6	15.7	7.6	16.3	8.4	17.4	8.0	18.2	7.9	0.0123
Energy from protein (%)	13.9	4.0	14.2	3.9	14.3	3.9	14.8	4.2	15.6	4.4	0.0030
Dietary glycemic index	60.0	6.8	59.7	7.3	58.7	7.1	58.0	7.1	57.0	8.3	< 0.0001
Dietary glycemic load	185.1	70.4	186.2	76.3	179.5	71.7	184.3	75.3	187.6	75.4	< 0.0001

^a P for trend was obtained from the general linear model (GLM) after adjustment for age (continuous), sex (men or women), education (elementary, secondary, or college or higher), income (low, medium, or high), BMI (continuous), current smoking (yes or no), current alcohol use (yes or no), physical activity (yes or no), and total energy intake (continuous).

The association between dietary patterns and insulin resistance

Table III - 17 shows mean values of fasting blood glucose, insulin, and HOMA-IR across quintiles of dietary pattern scores. The whole grains and beans pattern scores were inversely associated with fasting blood glucose, insulin, and HOMA-IR. The alcohol and coffee pattern scores were positively associated with fasting blood glucose. Other dietary patterns scores were not associated with fasting blood glucose, insulin, and HOMA-IR.

The ORs and 95% CIs for insulin resistance across quintiles of dietary pattern scores are presented in Table III - 18. After adjusting for potential confounding variables, subjects in the highest quintile of the whole grains and beans pattern had a 20 % reduced prevalence of insulin resistance than those in the lowest quintile and displayed a significant trend (OR for highest quintile = 0.80, 95% CI = 0.61–1.03, *P* for trend = 0.0134). No association was observed between other dietary patterns and insulin resistance.

Table III - 17. Fasting blood glucose, insulin, and HOMA-IR across quintiles of dietary pattern scores

	Q1 (n = 774)		Q2 (n = 774)		Q3 (n = 775)		Q4 (n = 774)		Q5 (n = 774)		P for trend ^a
	Mean	SD									
Pattern 1: Diverse diet											
Glucose (mg/dL)	94.0	14.1	93.3	12.2	93.9	14.5	92.6	13.1	91.8	11.6	0.3612
Insulin (μIU/ml)	9.1	3.7	9.3	3.5	9.1	3.6	9.0	3.5	9.3	3.6	0.9862
HOMA-IR ^b	2.13	1.00	2.15	0.88	2.14	0.99	2.09	0.91	2.12	0.93	0.7776
Pattern 2: Western diet											
Glucose (mg/dL)	93.8	11.7	94.5	14.7	93.2	14.6	91.7	11.2	92.3	13.1	0.6565
Insulin (μIU/ml)	8.8	3.6	9.2	3.8	9.1	3.4	9.2	3.3	9.5	3.7	0.2801
HOMA-IR	2.06	0.94	2.17	1.03	2.11	0.91	2.10	0.86	2.19	0.97	0.2645
Pattern 3: Whole grains & beans											
Glucose (mg/dL)	93.7	13.8	93.2	12.1	93.5	14.4	92.7	13.3	92.5	12.1	0.0317
Insulin (μIU/ml)	9.2	3.7	9.2	3.8	9.4	3.6	9.0	3.6	8.9	3.1	0.0262
HOMA-IR	2.16	1.00	2.15	0.98	2.18	0.93	2.08	0.92	2.06	0.87	0.0054
Pattern 4: White rice & kimchi											
Glucose (mg/dL)	92.2	10.6	93.6	14.3	92.1	11.6	94.0	14.0	93.7	14.8	0.8038
Insulin (μIU/ml)	9.2	3.5	9.4	3.7	9.0	3.4	9.1	3.8	9.1	3.5	0.5055
HOMA-IR	2.11	0.91	2.18	0.96	2.08	0.92	2.13	1.00	2.12	0.92	0.5702
Pattern 5: Alcohol & coffee											
Glucose (mg/dL)	90.8	9.2	92.8	14.0	92.8	12.8	93.5	13.3	95.6	15.3	0.0001
Insulin (μIU/ml)	9.3	3.6	9.3	3.6	9.2	3.5	9.1	3.6	8.9	3.6	0.1037
HOMA-IR	2.10	0.92	2.15	0.99	2.13	0.91	2.13	0.95	2.11	0.95	0.6721

^a P for trend was obtained from the general linear model (GLM) after adjustment for age (continuous), sex (men or women), education (elementary, secondary, or college or higher), income (low, medium, or high), BMI (continuous), current smoking (yes or no), current alcohol use (yes or no), physical activity (yes or no), total energy intake (continuous), and dietary pattern scores (continuous).

^b Insulin resistance was defined as the upper quartile of the homeostasis model assessment of insulin resistance (HOMA-IR) scores.

Table III - 18. Multivariate adjusted^a ORs and 95% CIs for insulin resistance^b across quintiles of dietary pattern scores

Q1 (<i>n</i> = 774)	Q2 (<i>n</i> = 774)	Q3 (<i>n</i> = 775)	Q4 (<i>n</i> = 774)	Q5 (<i>n</i> = 774)	<i>P</i> for trend
Pattern 1: Diverse diet					
1.00	1.16 (0.91–1.48)	1.05 (0.82–1.35)	0.89 (0.69–1.15)	1.09 (0.84–1.41)	0.7269
Pattern 2: Western diet					
1.00	1.31 (1.02–1.69)	1.13 (0.87–1.48)	1.21 (0.93–1.59)	1.17 (0.89–1.55)	0.4938
Pattern 3: Whole grains & beans					
1.00	1.12 (0.87–1.43)	1.12 (0.87–1.42)	0.84 (0.65–1.08)	0.80 (0.61–1.03)	0.0134
Pattern 4: White rice & kimchi					
1.00	1.15 (0.90–1.46)	0.86 (0.66–1.10)	1.07 (0.84–1.38)	0.92 (0.71–1.18)	0.3977
Pattern 5: Alcohol & coffee					
1.00	1.28 (0.99–1.64)	1.29 (1.00–1.67)	1.09 (0.83–1.43)	1.01 (0.75–1.35)	0.7472

^a Adjusted for age (continuous), sex (men or women), education (elementary, secondary, or college or higher), income (low, medium, or high), BMI (continuous), current smoking (yes or no), current alcohol use (yes or no), physical activity (yes or no), total energy intake (continuous), and dietary pattern scores (continuous).

^b Insulin resistance was defined as the upper quartile of the homeostasis model assessment of insulin resistance (HOMA-IR) scores.

4. Discussion and conclusions

In this study of dietary patterns associated with insulin resistance in the Korean adult population, we found that the whole grains and beans pattern was inversely associated with insulin resistance. The whole grains and beans pattern identified in this study included high loadings of whole grains and beans as well as tomatoes and fruits. All these components, including dietary fiber (Lau, C *et al.* 2005), phytoestrogens (Bhathena, SJ and Velasquez, MT 2002), vitamin C (Paolisso, G *et al.* 1994), vitamin E (Manning, PJ *et al.* 2004), and magnesium (McKeown, NM *et al.* 2002), have been reported to have an association in reducing risk of insulin resistance.

With regard to studies on applied dietary patterns, our findings are consistent with other observational studies. The healthy dietary pattern, characterized by high consumption of fruits, tomatoes, legumes, vegetables, and whole grains was associated with a lower risk of insulin resistance in Tehrani women (Esmailzadeh, A *et al.* 2007), and the prudent dietary pattern, characterized by higher intakes of fruits, vegetables, whole grains, and poultry was associated with lower fasting insulin concentration (Fung, TT *et al.* 2001a). In older adults from the Health, Aging, and Body Composition study, subjects in the healthy foods pattern obtained from cluster analysis had lower fasting insulin, fasting glucose, and HOMA-IR than those in other patterns (Anderson, AL *et al.* 2012). Even though it is difficult to compare the results of dietary pattern studies due to different methods and different populations with unique dietary cultures (Hu, FB 2002), it suggests that a diet rich in whole grains, beans, and fruits are inversely associated with insulin resistance.

Recently, Asian countries have been experiencing a rapid increase in diabetes. According to Hu, FB (2011), one of contributing dietary factor for this increase in the Asian population is a large shift from consumption of coarse grains to polished rice and refined wheat. Our findings about the whole grains and beans pattern may support this claim. Further investigations on dietary patterns and insulin resistance are needed to confirm in intervention or prospective studies among Asian population. Our study has several limitations. First, the cross-sectional design does not allow inference of a causal relationship between dietary patterns and insulin resistance. Thus, the association between these dietary patterns and insulin resistance remains to be confirmed in prospective studies. Second, HOMA-IR can be used as a surrogate measure of insulin resistance at the population level, but it is perhaps less useful on an individual basis. However, this study was based on a large nationally representative sample and we targeted a population without disease condition such as diabetes or hypertension so that our findings would be used to develop a dietary strategy in preventing diabetes applicable to this population. In conclusion, our study indicates that a dietary pattern characterized by high consumption of whole grains, beans, and fruits is inversely associated with insulin resistance in healthy Korean adults.

STUDY 4. Dietary patterns based on carbohydrate nutrition are associated with the risk for diabetes and dyslipidemia in the Korean adult population⁴

1. Introduction

Dietary pattern analysis has drawn considerable attention in studies to examine the relationships between diet and disease, as it measures the effect of the overall diet beyond that of single foods or nutrients. Among large-scaled prospective studies, Hu, FB *et al.* (2000) identified a Western vs. a prudent pattern in the US population and reported that the Western pattern was associated with increased risks and that the prudent pattern was associated with decreased risks for cardiovascular disease (Fung, TT *et al.* 2001b, Hu, FB *et al.* 2000) and diabetes (van Dam, RM *et al.* 2002). Along with that study, several other Western studies (Amini, M *et al.* 2010, Denova-Gutierrez, E *et al.* 2010a, Esmailzadeh, A *et al.* 2007, Panagiotakos, DB *et al.* 2007) have focused on Western and prudent/healthy dietary patterns associated with risks for diabetes, cardiovascular disease, and metabolic syndrome.

⁴ This study was published in the Nutrition Research and Practice vol. 6, no. 4, pages 349-356 in 2012.

However, Asian countries have a different dietary culture, although the Western pattern has emerged in the Asian population, yet it differs from that of the Western population because staple foods such as rice are still major sources in the diet. With rapid economic growth, Western patterns among Asian populations, characterized by increased consumption of animal food including meat, bread, and butter as well as sweet desserts, have shown inconsistent relationships with metabolic risk factors, although it is difficult to compare studies due to different dietary pattern analysis methodologies. A Western pattern was associated with higher total, HDL-, and LDL-cholesterol in the Japanese population (Sadakane, A *et al.* 2008) and a meat-rich pattern was associated with an increased risk for diabetes in the Chinese population (Cai, H *et al.* 2007). A meat and alcohol pattern was associated with elevated fasting glucose and serum triglycerides in the Korean population (Song, Y and Joung, H 2012). In contrast, a westernized breakfast pattern was associated with a reduced risk for elevated glycated hemoglobin concentrations ($\geq 5.5\%$) in the Japanese population (Nanri, A *et al.* 2008) and a Western pattern was associated with reduced risks for elevated fasting blood glucose and low HDL-cholesterol in Korean women (Cho, YA *et al.* 2011).

Among these inconsistent findings, the quantity and quality of carbohydrate intake contributes to metabolic abnormalities, as the Asian diet is typically a high carbohydrate diet, which can raise fasting glucose and triglycerides but reduce HDL-cholesterol. Among several studies on dietary carbohydrates, the GI was reportedly associated with metabolic risk factors in Asian populations (Kim, K *et al.* 2008, Murakami, K *et al.* 2006, Park, SH *et al.* 2010), but no study has been conducted on dietary patterns based on carbohydrate nutrition. A recently proposed method of

dietary pattern analysis is RRR, which uses intermediary information that best explains the variance in a set of response variables selected with prior knowledge (Hoffmann, K *et al.* 2004, Tucker, KL 2010). The RRR identifies dietary patterns that explain a combined set of known risk factors and the findings on the association between dietary patterns identified and chronic disease risk provides important information for a disease prevention strategy. Hoffmann, K *et al.* (2005) derived dietary patterns using percentages of energy from saturated fat, polyunsaturated fat, protein, and carbohydrate as response variables, and those patterns were associated with all-cause mortality. McNaughton, SA *et al.* (2008) identified a dietary pattern using fasting glucose and fasting insulin as response variables and that pattern was associated with type 2 diabetes.

Thus, we applied RRR to identify specific dietary patterns in an Asian population. The aim of this study was to identify dietary patterns that explain the maximal variation in carbohydrate quantity and quality and to examine the relationship between dietary patterns and metabolic risks for dyslipidemia and diabetes among the Korean adult population.

2. Methods

Study subjects

This study was based on data from the Fourth KNHANES in 2007–2009. Among 24,871 eligible subjects who participated in the survey, those who were aged at least 20 years old were included in data analyses. We excluded subjects with incomplete information on sociodemographic and health-related variables, blood samples, and dietary intake. Subjects who had extreme energy intakes (< 500 or > 5,000 kcal/day) were also excluded. In addition, we excluded subjects with previous diagnoses of diabetes, hypertension, or dyslipidemia and those who had taken medications to lower serum lipids, blood glucose, or blood pressure to avoid the effects of treatment or intervention by related disease, as they were considered to have made changes in their diet. The remaining 9,725 subjects (3,795 men and 5,930 women) were included in the final analyses. This study protocol was approved by the Ministry of Health and Welfare in Korea. All subjects in the survey participated voluntarily, and written informed consent was obtained from all subjects.

Definition of impaired fasting glucose, diabetes, and dyslipidemia

Blood glucose and lipid indicators were chosen as the metabolic risk factors. Blood samples were collected in the morning after fasting for at least 8 hours. Fasting blood glucose, total cholesterol, triglycerides, and HDL-cholesterol were analyzed in a central, certified laboratory.

Impaired fasting glucose was defined as fasting blood glucose of 100–125 mg/dL and diabetes as fasting blood glucose \geq 126 mg/dL by the American Diabetes Association (ADA 2011). The definition of dyslipidemia provided by the NCEP was used: 1) hypercholesterolemia as total cholesterol \geq 240 mg/dL, 2) hypertriglyceridemia as triglycerides \geq 200 mg/dL, 3) low HDL-cholesterol as HDL-cholesterol $<$ 40 mg/dL in men and $<$ 50 mg/dL in women (NCEP 2002).

Measurement of dietary intake

Dietary intake information was obtained through a 24-hour recall method. The food items appearing in this study were categorized into 18 common food groups based on a Korean nutrient database. However, the grain group was further divided into four subgroups to examine types of staple foods in detail: 1) white rice, 2) other grains, 3) bread and snacks, and 4) noodles and dumplings. Kimchi (traditional fermented cabbage) in the vegetable group was separated into a single food group, as it is traditionally served as a single side dish (Song, Y *et al.* 2005), resulting in 22 food groups (Table III - 19).

GI values were obtained from published values or imputed when necessary by matching similar foods based on calories, carbohydrate, and dietary fiber content to evaluate carbohydrate quality. Among 662 (total of 1,088) food items appearing in this study, the GI values for 209 food items (31.6 %) were estimated from international GI tables (Atkinson, FS *et al.* 2008, Foster-Powell, K *et al.* 2002). The other four food items (0.6 %) were estimated from data based on Asian foods (Chen, YJ *et al.* 2010, Murakami, K *et al.* 2006). The remaining 449 (67.8 %) food items had no GI values, because these foods contain little or no carbohydrates, and thus the GI values of these

foods was assigned zero. The reference for the GI values was glucose. The GL is an indicator that reflects both the quantity and quality of carbohydrates (Salmeron, J *et al.* 1997). GL was calculated by multiplying the GI value of the food by the amount of carbohydrate consumed, and then dividing by 100 (Foster-Powell, K *et al.* 2002).

Assessment of dietary patterns

Dietary patterns were generated by RRR, which identifies linear combinations of predictor variables that explain as much response variables variation as possible, whereas factor analysis determines linear functions of predictor variables by maximizing the explained variation of all predictor variables (Hoffmann, K *et al.* 2004, Tucker, KL 2010). We used standardized daily intake of the 22 food groups as predictor variables and selected four dietary factors: 1) total energy intake (kcal/day), 2) total carbohydrate intake (g/day), 3) percentage (%) of energy from carbohydrate, and 4) GI, as the set of response variables. The response variables were based on dietary variables representing carbohydrate quantity (e.g., total carbohydrate intake and percentage of energy from carbohydrate) and quality (e.g., GI). Additionally, total energy intake, which represents the entire diet quantity, was added to the response variables to obtain dietary patterns that would explain the variation in energy intake, which is highly composed of and correlated with carbohydrate intake in the Korean diet. We considered the proportion of variance explained by each dietary pattern to determine the number of patterns to retain. The four patterns obtained from RRR explained 41.7 %, 24.6 %, 4.3 %, and 0.008 % of the total variation of a set of all four response variables, respectively, and, therefore, the first two patterns were retained.

Table III - 19. Food groupings used in the reduced rank regression

Food group	Examples of food items included in each food group
White rice	
Other grain	Whole grain parched powder, Corn, Chestnuts
Bread and snack	Bread, Pizza, Hamburger, Cereals
Noodle and dumpling	Wheat flour, Instant noodles (Ramyon)
Potatoes	Sweet potato starch vermicelli
Sugars and sweets	
Legumes	
Nuts	
Vegetables	
Kimchi	Salted and fermented vegetables
Mushrooms	
Fruits	
Meat and its products	
Eggs	
Fishes	
Seaweeds	
Milk and dairy products	
Oils	
Beverages	Coffee, Tea
Alcohols	
Seasonings	

Measurements of other variables

Information about sociodemographic (e.g., sex, age, household income, and education) and health-related variables (e.g., history of disease, medication use, smoking status, alcohol use, and physical activity) were obtained through a health interview survey. Age was divided into groups of 20–29, 30–49, 50–64, and ≥ 65 years. Household income was divided into low, medium, and high groups. Education was categorized as elementary, secondary, and college or more. Smoking status was classified as never smoked, past smoker, or current smoker. Current alcohol use was assigned “yes” if a subject drank a glass of alcohol or more per month over the previous year. Physical activity was assigned “yes” if a subject engaged in physical activity at least 3 days or more per week at high intensity over the previous week. Height and weight were obtained using standardized techniques and calibrated equipment. BMI was calculated as body weight (kg) divided by squared body height (m²).

Statistical analyses

All statistical analyses were performed using the SAS statistical software package version 9.1 (SAS Institute, Cary, NC, USA). RRR was employed using the PLS procedure in SAS to derive the dietary patterns. The application of this method for a dietary pattern analysis was described in detail elsewhere (Hoffmann, K *et al.* 2004). The dietary pattern scores were calculated for all subjects and divided into quintiles.

Distribution (%) of sociodemographic and health-related variables across quintiles of dietary pattern scores were tested using the Mantel-Haenszel chi-square test. The GLM was used to test for significant trends in mean nutrient intake across quintiles of dietary pattern scores. Multivariate logistic regression was performed to estimate the

ORs and 95% CIs for diabetes and dyslipidemia across quintiles of dietary pattern scores, taking the lowest quintile group as the reference group. Age (continuous), household income (low, medium, or high), education (elementary, secondary, or college or more), BMI (continuous), smoking status (never, past, or current), current alcohol use (yes or no), and physical activity (yes or no) were considered potential confounding variables, so these were adjusted in all models. Subsequently, scores of two dietary patterns were mutually adjusted in multivariate logistic regression models, because one could explain the association for the other pattern.

3. Results

Dietary patterns

The factor loadings of the food groups by dietary patterns are provided in Table III - 20. The most important contributor was white rice in the two dietary patterns (factor loading was 0.43 in the balanced pattern; 0.52 in the rice-oriented pattern). The first pattern was characterized by high positive loading for bread, noodles, vegetables, fruits, meat, eggs, and oils and was named the “balanced pattern”. The second pattern had only white rice with a positive loading and others items such as vegetables, meat, eggs, fish, and dairy products were inversely correlated with the pattern scores, so it was named the “rice-oriented pattern”.

Table III - 20. Factor loading matrix for the two dietary patterns^a

Food groups	Dietary patterns	
	Balanced	Rice-oriented
White rice	0.43	0.52
Other grains		
Bread and Snacks	0.25	
Noodles and Dumpling	0.21	
Potatoes		
Sugar and Sweets	0.23	
Legumes		
Nuts		
Vegetables	0.34	-0.21
Kimchi (Traditional fermented cabbage)	0.22	
Mushrooms		
Fruits	0.28	
Meat and Its products	0.21	-0.39
Eggs	0.20	-0.20
Fish		-0.24
Seaweeds		
Milk and Dairy products		-0.23
Oils	0.29	-0.35
Beverages		
Alcohol		-0.30
Seasonings	0.29	-0.26
Explained variation (%) of all four response variables	41.7	24.6

^a Factor loadings < |0.20| are not shown for simplicity.

Characteristics across quintiles of dietary patterns

The sociodemographic and health-related variables of the study subjects across quintiles of dietary pattern scores are described in Table III - 21 and Table III - 22. In both men and women, subjects with a higher score for the balanced pattern were more likely to be younger, have a higher income, be more educated, and smoke less. The balanced pattern was also associated positively with BMI and physical activity in men and inversely with alcohol use in women. Men with a higher score for the rice-oriented pattern were more likely to be older, have a lower income, be less educated, be less obese, and drink less, whereas women with a higher score for the rice-oriented pattern were more likely to be older, have a lower income, be less educated, more obese, smoke less, drink less, and be less physically active.

Table III - 21. Sociodemographic and health-related variables across quintiles of the balanced pattern scores

	Men (<i>n</i> = 3,795)					<i>P</i> -value ^a	Women (<i>n</i> = 5,930)					<i>P</i> -value ^a
	Q1	Q2	Q3	Q4	Q5		Q1	Q2	Q3	Q4	Q5	
Age group (%)												
20–29 y	17.8	15.0	12.9	12.9	17.8	< 0.0001	17.4	15.7	14.6	13.2	15.2	0.0004
30–49 y	34.8	43.1	46.6	50.9	56.1		46.0	50.6	51.8	56.2	54.2	
50–64 y	21.0	19.8	24.0	25.3	19.2		20.0	17.5	21.3	20.7	23.1	
65 y or more	26.5	22.1	16.5	10.9	6.9		16.6	16.2	12.4	10.0	7.5	
Income (%)												
Low	24.9	20.2	17.0	13.8	9.4	< 0.0001	20.2	17.6	16.4	15.2	11.2	< 0.0001
Medium	51.1	52.3	54.7	51.8	57.7		53.5	52.4	55.1	53.6	55.1	
High	24.0	27.5	28.3	34.4	32.9		26.2	30.0	28.4	31.2	33.6	
Education (%)												
Elementary	25.2	20.7	18.8	13.3	10.7	< 0.0001	29.3	25.1	25.2	20.2	17.4	< 0.0001
Secondary	48.4	49.9	48.6	49.9	53.4		49.2	48.7	47.1	48.1	48.3	
College or more	26.5	29.4	32.5	36.8	36.0		21.4	26.2	27.7	31.8	34.3	
BMI (%)												
< 18.5 kg/m ²	7.8	3.6	4.4	2.9	3.0	< 0.0001	6.8	7.3	6.9	5.7	5.7	0.7891
18.5–25.0 kg/m ²	65.6	66.9	62.7	63.5	65.2		68.3	71.5	70.6	71.4	72.6	
≥ 25.0 kg/m ²	26.6	29.5	32.9	33.6	31.8		25.0	21.2	22.5	22.9	21.7	
Current smoking (%)												
Yes	48.6	46.6	43.0	42.2	47.3	0.0325	8.9	5.3	5.3	4.6	4.3	< 0.0001
Current alcohol use ^b (%)												
Yes	75.1	71.8	74.3	73.9	73.3	0.7545	45.9	43.9	42.6	42.0	39.6	0.0015
Physical activity ^c (%)												
Yes	14.9	19.6	20.6	21.6	24.8	< 0.0001	15.5	13.9	14.9	16.4	14.8	0.7389

Q, quintiles of dietary pattern scores.

^a *P*-value was obtained from the Mantel-Haenszel chi-square test.

^b Current alcohol use was assigned “yes” if subjects drank a glass of alcohol or more per month over the previous year.

^c Physical activity was assigned “yes” if subjects engaged in physical activity at least 3 days or more per week at high intensity over the previous week.

Table III - 22. Sociodemographic and health-related variables across quintiles of the rice-oriented pattern scores

	Men (<i>n</i> = 3,795)					<i>P</i> -value ^a	Women (<i>n</i> = 5,930)					<i>P</i> -value ^a
	Q1	Q2	Q3	Q4	Q5		Q1	Q2	Q3	Q4	Q5	
Age group (%)												
20–29 y	22.7	18.1	15.6	12.8	7.4	< 0.0001	25.4	20.8	13.4	9.7	5.3	< 0.0001
30–49 y	58.2	54.6	48.4	37.7	32.7		58.8	57.5	56.3	52.1	34.4	
50–64 y	13.8	18.5	22.1	27.3	27.5		12.7	17.0	21.3	23.1	29.8	
65 y or more	5.3	9.0	14.0	22.3	32.4		3.2	4.6	8.9	15.1	30.5	
Income (%)												
Low	8.0	9.4	13.6	22.7	31.6	< 0.0001	7.0	9.8	12.1	20.5	31.3	< 0.0001
Medium	51.5	56.5	54.7	54.3	50.6		55.5	54.3	55.4	54.1	50.5	
High	40.5	34.1	31.8	23.1	17.8		37.5	35.9	32.5	25.4	18.2	
Education (%)												
Elementary	5.9	9.8	14.4	23.9	34.8	< 0.0001	7.2	11.8	19.1	28.2	51.0	< 0.0001
Secondary	51.7	49.8	51.8	49.1	47.8		52.8	50.3	53.3	48.2	36.8	
College or more	42.4	40.5	33.9	27.0	17.4		40.1	37.9	27.7	23.6	12.2	
BMI (%)												
< 18.5 kg/m ²	3.3	2.8	4.6	4.7	6.2	< 0.0001	6.3	8.1	7.0	5.4	5.7	< 0.0001
18.5–25.0 kg/m ²	60.6	63.9	64.2	66.4	68.9		73.0	72.4	70.7	70.9	67.3	
≥ 25.0 kg/m ²	36.1	33.3	31.2	28.9	24.9		20.7	19.5	22.3	23.7	27.1	
Current smoking (%)												
Yes	52.8	47.7	47.3	40.7	39.1	0.2297	9.0	5.6	5.3	4.8	3.7	< 0.0001
Current alcohol use ^b (%)												
Yes	84.5	77.9	72.9	71.0	62.2	< 0.0001	55.5	50.6	42.5	36.5	28.9	< 0.0001
Physical activity ^c (%)												
Yes	21.3	21.9	19.6	19.9	18.7	0.1165	17.7	15.2	15.6	14.2	12.9	0.0012

Q, quintiles of dietary pattern scores.

^a *P*-value was obtained from the Mantel-Haenszel chi-square test.

^b Current alcohol use was assigned “yes” if subjects drank a glass of alcohol or more per month over the previous year.

^c Physical activity was assigned “yes” if subjects engaged in physical activity at least 3 days or more per week at high intensity over the previous week.

Nutrient intakes across quintiles of dietary patterns

The mean energy and macronutrient intake of the study subjects across quintiles of dietary pattern scores are presented in Table III - 23 and Table III - 24. Energy intake increased but GI decreased when total carbohydrate (g/day) and GL increased across quintiles of scores in the balanced pattern. In contrast, GI increased when total carbohydrate (g/day) and GL increased across quintiles of scores in the rice-oriented pattern. The percentages of energy from carbohydrates, fat, and protein in the highest quintile of the balanced pattern were 66.3 %, 18.7 %, and 14.9 % in men and 69.7 %, 16.5 %, and 13.8 % in women, respectively. However, the percentages of energy from carbohydrates, fat, and protein in the highest quintile of the rice-oriented pattern were 78.2 %, 10.1 %, and 11.6 % in men and 80.0 %, 8.9 %, and 11.1 % in women, respectively.

Table III - 23. Mean energy and macronutrient intake across quintiles of the balanced pattern scores

	Q1		Q2		Q3		Q4		Q5		<i>P</i> for trend ^a
	Mean	<i>SD</i>									
Men (<i>n</i> = 3,795)											
Total energy (kcal)	1392	432.1	1836	396.6	2152	435.1	2492	477.1	3162	666.0	< 0.0001
Carbohydrate (g)	213.5	46.9	288.1	43.2	335.7	45.2	389.9	57.3	505.5	105.3	< 0.0001
Fat (g)	24.4	17.6	33.1	20.3	41.1	24.1	49.7	28.7	66.0	36.9	< 0.0001
Protein (g)	47.7	20.1	63.1	21.7	76.6	25.4	90.0	28.4	115.3	40.3	< 0.0001
Energy from carbohydrate (%)	68.6	11.7	68.4	10.9	67.3	10.3	66.7	10.4	66.3	9.9	0.5705
Energy from fat (%)	16.5	9.2	16.9	8.6	17.6	8.2	18.2	8.4	18.7	8.0	0.1309
Energy from protein (%)	14.9	4.9	14.7	4.2	15.1	4.1	15.1	3.9	14.9	4.0	0.1379
Dietary glycemic index ^b	60.1	9.1	59.8	7.7	59.3	7.2	58.9	6.6	57.8	7.2	0.0008
Dietary glycemic load	129.4	36.7	173.6	38.6	200.3	40.5	230.7	46.0	293.4	76.3	< 0.0001
Women (<i>n</i> = 5,930)											
Total energy (kcal)	969	233.6	1323	216.2	1568	240.3	1862	293.8	2452	553.1	< 0.0001
Carbohydrate (g)	162.4	37.9	226.4	35.6	271.2	39.1	321.7	49.4	427.6	97.7	< 0.0001
Fat (g)	18.5	13.6	24.9	16.3	29.1	17.8	35.5	22.8	46.8	29.3	< 0.0001
Protein (g)	34.4	14.1	47.1	16.4	55.1	18.3	65.5	20.9	85.4	31.1	< 0.0001
Energy from carbohydrate (%)	68.9	11.8	69.5	10.9	69.9	10.3	69.5	10.2	69.7	10.1	< 0.0001
Energy from fat (%)	16.7	9.4	16.3	8.6	16.1	8.3	16.5	8.3	16.5	8.2	0.0032
Energy from protein (%)	14.4	4.5	14.2	4.1	14.0	3.8	13.9	3.6	13.8	3.7	< 0.0001
Dietary glycemic index ^b	59.4	8.7	59.5	7.7	59.6	7.1	58.8	7.2	58.4	6.9	0.0493
Dietary glycemic load	97.4	29.1	135.7	31.5	162.6	33.9	190.1	41.4	250.7	67.6	< 0.0001

Q, quintiles of dietary pattern scores.

^a *P* for trend from the general linear model (GLM) across quintiles of dietary pattern scores was adjusted for age (continuous), income (low, medium, or high), education (elementary, secondary, or college or more), body mass index (continuous), smoking (never, past, or current), alcohol use (yes or no), and physical activity (yes or no).

^b Glycemic index for glucose = 100.

Table III - 24. Mean energy and macronutrient intake across quintiles of the rice-oriented pattern scores

	Q1		Q2		Q3		Q4		Q5		<i>P</i> for trend ^a
	Mean	<i>SD</i>									
Men (<i>n</i> = 3,795)											
Total energy (kcal)	2762	831.0	2193	719.2	2013	694.0	1923	652.4	2142	678.0	< 0.0001
Carbohydrate (g)	332.4	116.1	324.4	108.6	331.3	115.0	337.6	105.1	407.1	121.3	< 0.0001
Fat (g)	71.3	37.6	48.8	24.5	38.5	21.5	30.3	19.4	25.3	18.2	< 0.0001
Protein (g)	111.7	43.5	83.9	30.8	71.5	28.3	63.8	26.5	61.9	24.9	< 0.0001
Energy from carbohydrate (%)	55.3	9.2	62.8	7.0	68.2	6.8	72.8	6.3	78.2	6.3	< 0.0001
Energy from fat (%)	25.9	8.5	20.9	6.7	17.2	6.2	13.8	5.6	10.1	5.2	< 0.0001
Energy from protein (%)	18.7	4.9	16.4	3.9	14.6	3.0	13.4	2.7	11.6	2.3	< 0.0001
Dietary glycemic index ^b	51.2	8.1	57.3	5.7	59.8	4.7	62.6	4.7	65.1	5.6	< 0.0001
Dietary glycemic load	172.3	69.4	185.5	62.9	197.0	66.0	209.5	61.8	263.2	75.9	< 0.0001
Women (<i>n</i> = 5,930)											
Total energy (kcal)	1870	691.1	1554	566.1	1481	565.2	1534	532.4	1736	556.0	0.9407
Carbohydrate (g)	262.3	103.5	252.2	95.7	261.2	97.6	286.6	96.6	347.0	108.9	< 0.0001
Fat (g)	51.6	29.5	34.6	18.3	27.2	17.7	23.2	15.3	18.2	13.6	< 0.0001
Protein (g)	79.3	33.4	59.1	24.4	51.5	22.6	49.0	20.7	48.7	19.4	< 0.0001
Energy from carbohydrate (%)	57.5	9.4	64.9	7.4	70.5	6.8	74.7	6.3	80.0	6.1	< 0.0001
Energy from fat (%)	24.9	8.8	19.8	6.8	15.7	6.1	12.8	5.4	8.9	4.9	< 0.0001
Energy from protein (%)	17.6	4.7	15.3	3.4	13.8	2.9	12.5	2.5	11.1	2.2	< 0.0001
Dietary glycemic index ^b	51.8	7.5	56.7	5.4	59.5	5.2	62.1	5.5	65.5	5.7	< 0.0001
Dietary glycemic load	137.3	59.7	143.1	56.5	154.2	56.2	176.5	55.7	225.4	67.3	< 0.0001

Q, quintiles of dietary pattern scores.

^a *P* for trend from the general linear model (GLM) across quintiles of dietary pattern scores was adjusted for age (continuous), income (low, medium, or high), education (elementary, secondary, or college or more), body mass index (continuous), smoking (never, past, or current), alcohol use (yes or no), and physical activity (yes or no).

^b Glycemic index for glucose = 100.

Association of dietary patterns with diabetes and dyslipidemia

The multivariate adjusted ORs (95% CIs) for diabetes and dyslipidemia across quintiles of dietary pattern scores are presented in Table III - 25 and Table III - 26. After adjusting for potential confounding variables, the rice-oriented pattern was significantly associated with a higher prevalence of hypertriglyceridemia in men (OR for highest quintile = 1.58, 95% CI = 1.20–2.09, *P* for trend = 0.0042) and low HDL-cholesterol in men (OR for highest quintile = 1.43, 95% CI = 1.12–1.82, *P* for trend = 0.0015) and women (OR for highest quintile = 1.29, 95% CI = 1.08–1.55, *P* for trend = 0.0020). The balanced pattern was not associated with diabetes or dyslipidemia after adjusting for potential confounding variables. However, men with an median energy intake level of $\geq 2,089$ kcal showed a significantly reduced prevalence of diabetes across quintiles of the balanced pattern scores (OR for highest quintile = 0.29; 95% CI = 0.10–0.83). No association was observed when energy intake was below the median level in men (Table III - 27). In the rice-oriented pattern, men with an energy intake below the median level had a significantly increased trend of prevalence for diabetes (*P* for trend = 0.0110). The two dietary patterns were not associated with diabetes by energy intake level in women.

Table III - 25. Multivariate adjusted ORs and 95% CIs for diabetes and dyslipidemia across quintiles of the balanced pattern scores

	Q1		Q2		Q3		Q4		Q5				<i>P</i> for trend ^a	
	OR	OR	95% <i>CI</i>		OR	95% <i>CI</i>		OR	95% <i>CI</i>					
Men (<i>n</i> = 3,795)														
Impaired fasting glucose														
100 ≤ FBG < 126 mg/dL	1.00	1.11	0.86	1.43	1.15	0.90	1.49	0.97	0.75	1.26	1.12	0.87	1.46	0.7450
Diabetes mellitus														
FBG ≥ 126 mg/dL	1.00	1.29	0.71	2.32	0.96	0.51	1.82	1.02	0.54	1.91	0.55	0.26	1.20	0.1360
Dyslipidemia														
Total chol. ≥ 240 mg/dL	1.00	1.02	0.67	1.55	1.00	0.66	1.52	1.07	0.70	1.62	0.92	0.60	1.42	0.8229
TG ≥ 200 mg/dL	1.00	0.99	0.76	1.29	1.13	0.87	1.47	1.15	0.88	1.49	0.89	0.68	1.17	0.8165
HDL-chol. < 40 mg/dL	1.00	0.86	0.68	1.08	1.05	0.84	1.31	1.07	0.85	1.34	1.04	0.83	1.31	0.2588
Women (<i>n</i> = 5,930)														
Impaired fasting glucose														
100 ≤ FBG < 126 mg/dL	1.00	1.13	0.89	1.44	1.20	0.95	1.53	1.16	0.91	1.48	0.99	0.77	1.27	0.9794
Diabetes mellitus														
FBG ≥ 126 mg/dL	1.00	1.13	0.54	2.39	0.87	0.39	1.93	1.34	0.64	2.80	1.33	0.63	2.78	0.3988
Dyslipidemia														
Total chol. ≥ 240 mg/dL	1.00	0.79	0.56	1.11	1.14	0.83	1.56	0.98	0.70	1.37	0.98	0.70	1.37	0.6940
TG ≥ 200 mg/dL	1.00	1.12	0.83	1.50	0.80	0.59	1.10	0.91	0.67	1.25	0.91	0.66	1.24	0.2569
HDL-chol. < 50 mg/dL	1.00	1.19	1.01	1.41	0.95	0.80	1.13	1.04	0.88	1.23	0.99	0.83	1.17	0.4002

Q, quintiles of dietary pattern scores; FBG, fasting blood glucose; Chol., cholesterol; TG, triglycerides; HDL-chol., high-density lipoprotein cholesterol.

^a *P* for trend from logistic regression analysis across quintiles of dietary pattern scores was adjusted for age (continuous), income (low, medium, or high), education (elementary, secondary, or college or more), body mass index (continuous), smoking (never, past, or current), alcohol use (yes or no), physical activity (yes or no), and dietary pattern scores (continuous).

Table III - 26. Multivariate adjusted ORs and 95% CIs for diabetes and dyslipidemia across quintiles of the rice-oriented pattern scores

	Q1		Q2		Q3		Q4		Q5					
	OR	OR	95% CI		P for trend ^a									
Men (n = 3,795)														
Impaired fasting glucose														
100 ≤ FBG < 126 mg/dL	1.00	1.08	0.83	1.41	1.12	0.86	1.45	1.20	0.92	1.57	1.00	0.76	1.32	0.7383
Diabetes mellitus														
FBG ≥ 126 mg/dL	1.00	0.64	0.30	1.37	1.09	0.56	2.13	1.03	0.52	2.05	1.28	0.65	2.52	0.2291
Dyslipidemia														
Total chol. ≥ 240 mg/dL	1.00	1.00	0.67	1.49	0.75	0.49	1.16	0.73	0.46	1.13	1.00	0.65	1.54	0.5391
TG ≥ 200 mg/dL	1.00	1.18	0.90	1.54	1.33	1.01	1.73	1.19	0.90	1.57	1.58	1.20	2.09	0.0042
HDL-chol. < 40 mg/dL	1.00	1.12	0.89	1.41	1.26	1.00	1.58	1.33	1.05	1.69	1.43	1.12	1.82	0.0015
Women (n = 5,930)														
Impaired fasting glucose														
100 ≤ FBG < 126 mg/dL	1.00	0.83	0.64	1.08	0.84	0.65	1.08	0.89	0.69	1.14	0.85	0.66	1.11	0.4050
Diabetes mellitus														
FBG ≥ 126 mg/dL	1.00	1.97	0.87	4.49	0.87	0.34	2.21	1.34	0.57	3.13	0.79	0.32	1.95	0.2782
Dyslipidemia														
Total chol. ≥ 240 mg/dL	1.00	1.38	0.96	1.97	1.16	0.80	1.66	0.94	0.65	1.36	0.76	0.52	1.12	0.0220
TG ≥ 200 mg/dL	1.00	0.83	0.58	1.19	1.23	0.89	1.70	0.86	0.61	1.22	1.10	0.78	1.55	0.5806
HDL-chol. < 50 mg/dL	1.00	1.02	0.86	1.21	1.04	0.88	1.23	1.19	1.00	1.41	1.29	1.08	1.55	0.0020

Q, quintiles of dietary pattern scores; FBG, fasting blood glucose; Chol., cholesterol; TG, triglycerides; HDL-chol., high-density lipoprotein cholesterol.

^a P for trend from logistic regression analysis across quintiles of dietary pattern scores was adjusted for age (continuous), income (low, medium, or high), education (elementary, secondary, or college or more), body mass index (continuous), smoking (never, past, or current), alcohol use (yes or no), physical activity (yes or no), and dietary pattern scores (continuous).

Table III - 27. Multivariate adjusted ORs and 95% CIs for diabetes (fasting blood glucose \geq 126 mg/dL) across quintiles of dietary pattern scores by energy intake level^a

	Q1		Q2		Q3		Q4		Q5		<i>P</i> for trend ^b			
	OR	OR	95% CI											
The balanced pattern														
Men (<i>n</i> = 3,795)														
< median	1.00	1.02	0.40	2.60	1.79	0.76	4.22	0.66	0.24	1.85	0.93	0.35	2.44	0.6121
\geq median	1.00	0.26	0.10	0.69	0.38	0.16	0.89	0.27	0.10	0.72	0.29	0.10	0.83	0.0116
Women (<i>n</i> = 5,930)														
< median	1.00	2.56	0.86	7.59	1.15	0.30	4.44	1.99	0.63	6.30	1.78	0.54	5.79	0.5793
\geq median	1.00	1.31	0.38	4.47	1.67	0.52	5.36	2.40	0.80	7.21	1.07	0.30	3.89	0.4908
The rice-oriented pattern														
Men (<i>n</i> = 3,795)														
< median	1.00	0.32	0.06	1.62	2.54	0.94	6.82	2.70	1.00	7.25	2.21	0.78	6.26	0.0110
\geq median	1.00	0.67	0.25	1.78	0.74	0.28	1.95	0.63	0.23	1.70	0.97	0.36	2.60	0.9062
Women (<i>n</i> = 5,930)														
< median	1.00	1.10	0.39	3.12	0.63	0.19	2.08	0.72	0.24	2.16	0.56	0.18	1.76	0.2368
\geq median	1.00	1.82	0.56	5.89	0.61	0.16	2.39	1.12	0.33	3.76	1.11	0.32	3.79	0.7894

Q, quintiles of dietary pattern scores.

^a The median value for total energy intake was 2,089 kcal in men and 1,555 kcal in women.

^b *P* for trend from logistic regression analysis across quintiles of dietary pattern scores was adjusted for age (continuous), income (low, medium, or high), education (elementary, secondary, or college or more), body mass index (continuous), smoking (never, past, or current), alcohol use (yes or no), physical activity (yes or no), and dietary pattern scores (continuous).

4. Discussion and conclusions

In this study, two dietary patterns, termed balanced and rice-oriented, were identified using RRR. The rice-oriented pattern was significantly associated with an increased prevalence of dyslipidemia in both men and women. In men, the balanced pattern was associated with reduced prevalence of diabetes when energy intake was above the median, whereas the rice-oriented pattern was associated with increased prevalence of diabetes when energy intake was below the median.

Different from previous studies of dietary patterns for Asian populations, we derived dietary patterns focusing on carbohydrate nutrition. White rice was a major contributor in both patterns, although with different carbohydrate quantity and quality, reflecting the Asian diet quite well. Our most interesting finding was that men in the highest quintile of the rice-oriented pattern, characterized by high white rice intake and low intake of other foods, had a 58 % increased prevalence of hypertriglyceridemia and a 43 % increased prevalence of low HDL-cholesterol compared to those in the lowest quintile, whereas the balanced pattern, characterized by high intake of various kinds of foods, was not associated with dyslipidemia. Women with a higher score for the rice-oriented pattern were also positively associated with low HDL-cholesterol.

White rice is associated with an increased risk for diabetes in Japanese (Nanri, A *et al.* 2010) and US individuals (Sun, Q *et al.* 2010), and ischemic stroke in Chinese adults (Liang, W *et al.* 2010). Given that white rice was the highest loading in both patterns, meal composition would be more influential than white rice intake itself. In the Korean diet, rice, soup, and side dishes are a typical meal, and the type of food in

these side dishes would be a core factor for diet variation. The balanced pattern included vegetables, fruits, and dairy products, which beneficial for health, whereas the rice-oriented pattern had low consumption of these foods. Several prospective studies (Baxter, AJ *et al.* 2006, Ford, ES and Mokdad, AH 2001, Pereira, MA *et al.* 2002) have suggested that intake of vegetables, fruits, and dairy products are inversely related to risks for metabolic abnormalities such as diabetes, dyslipidemia, and metabolic syndrome.

In our study, the two dietary patterns differed in carbohydrate quantity and quality. Subjects in the highest quintile of the rice-oriented pattern showed lower energy and total carbohydrate intake but higher GI and percentage of energy from carbohydrate than those in the highest quintile of the balanced pattern. High carbohydrate intake or a high GI diet has adverse effects on serum lipid levels and glucose metabolism (Ford, ES and Liu, S 2001, Levitan, EB *et al.* 2008, McKeown, NM *et al.* 2009, Murakami, K *et al.* 2006, Park, SH *et al.* 2010), which are likely due to increase risks for metabolic abnormalities such as diabetes (Hodge, AM *et al.* 2004, Schulze, MB *et al.* 2004) and cardiovascular disease (Denova-Gutierrez, E *et al.* 2010b). Although many studies have reported a positive association between GI and diabetes, two large cohort studies (Meyer, KA *et al.* 2000, Stevens, J *et al.* 2002) did not find any association between GI and diabetes incidence. Considering that GI alone cannot fully explain the effects of diet on metabolic abnormalities, dietary pattern, which captures the overall quality of the diet, would be more important than solely a high carbohydrate diet or a high GI diet.

We also found that the balanced pattern was associated with a reduced prevalence of diabetes under high energy intake, whereas the rice-oriented pattern was associated

with an increased prevalence of diabetes under low energy intake in men. We have no clear answer for the favorable effects of the balanced pattern when energy intake was only above the median. The protective effect of the balanced pattern on diabetes may represent the beneficial effects of a variety of nourishing foods and a low GI diet on glucose metabolism. A possible explanation is that if energy intake is low, it represents that overall nutrition status is poor. According to Choi, MJ and Kim, MK (1995), total energy and intake of particular micronutrients were significantly lower among diabetic patients than non-diabetic patients in the Korean population. Another study (Kim, WK and Lee, KA 1999) showed significantly low intakes of energy, carbohydrate, potassium, riboflavin, niacin, and dietary fiber among hyperinsulinemic individuals. Slabber, M *et al.* (2003) concluded that optimal nutrition might play an important role in the prevention of diabetes. This supports the notion that the balanced pattern would be effective to reduce risk of diabetes if proper energy intake is provided.

This study had several limitations. First, the cross-sectional design made it difficult to examine the causal relationships between dietary patterns and metabolic abnormalities. Rather, this study represents more of a hypothesis-generating approach. Second, we used dietary data from a single 24-hour recall, which might not represent usual intake. Third, the GI calculation was based on international tables in which most foods were derived from Western countries. The development or validation of GI values for Korean foods is necessary in the near future.

Regardless of these limitations, to our knowledge, this is the first study to derive dietary patterns using the RRR method based on carbohydrate-related dietary factors in an Asian population. Factor analysis derives dietary patterns by maximizing the explained variation of all predictor variables, whereas RRR provides linear functions of

predictor variables that explain as much of the variation in response variables (e.g., biomarkers or nutrients) as possible (Hoffmann, K *et al.* 2004). The RRR method has an advantage to combine dietary information with prior knowledge about the pathway from diet to disease. Thus, the RRR method may be a useful tool for identifying dietary patterns related to the risk for diabetes or dyslipidemia. This study also included a relatively large representative sample of the Korean population, so it captured an entire spectrum of carbohydrate intake and serum indicators. Additionally, we excluded subjects who had been previously diagnosed or treated for diabetes, dyslipidemia, or hypertension, so that our results would be meaningful to provide proper nutrition information for healthy adults to prevent chronic disease.

In conclusion, we derived two dietary patterns based on carbohydrate quantity and quality among the Korean adult population. The rice-oriented pattern was associated with an increased risk for dyslipidemia whereas the balanced pattern was associated with a reduced risk for diabetes when energy intake was adequate. Our findings imply that dietary patterns based on carbohydrate nutrition should be considered together with other foods consumed rather than considering the sole effect of a single food item, such as white rice. Further prospective or intervention studies are necessary to confirm our findings.

**CHAPTER IV. DIETARY DETERMINANTS OF
METABOLIC SYNDROME AND ITS COMPONENTS
IN KOREAN ADULTS OF OUTPATIENT CLINICS**

STUDY 5. Low intakes of fruits and milk·dairy products are associated with metabolic syndrome in Korean men and women

1. Introduction

Metabolic syndrome is defined as a clustering of metabolic abnormalities, including abdominal obesity, dyslipidemia, elevated fasting blood glucose, and hypertension (Grundy, SM *et al.* 2005). Metabolic syndrome is a strong predictor for type 2 diabetes and cardiovascular diseases. Several determinants of metabolic syndrome include genetic, environmental, socioeconomic, dietary and lifestyle factors (Ford, ES *et al.* 2008, Gami, AS *et al.* 2007, McKeown, NM *et al.* 2009). Among those determinants, diet is one of the determinants can be modifiable to prevent and improve metabolic syndrome (Magkos, F *et al.* 2009).

Although the mechanism of diet in the development of metabolic syndrome is not fully understood, prospective and cross-sectional studies in Western populations have reported that the risk of metabolic syndrome are inversely associated with intakes of fruits (Yoo, S *et al.* 2004), milk·dairy products (Elwood, PC *et al.* 2007, Fumeron, F *et al.* 2011, Liu, S *et al.* 2005, Pereira, MA *et al.* 2002) and several nutrients that are predominant in these foods (Aleixandre, A and Miguel, M 2008, Beydoun, MA *et al.* 2008, Ford, ES *et al.* 2003, Lopez-Legarrea, P *et al.* 2013, Puchau, B *et al.* 2010).

The typical Korean meal consist of rice and side dishes made from animal foods and vegetables (Park, MH *et al.* 2003). Among food groups, grains, meat·fish·eggs·beans, and vegetables are consumed daily as staple food whereas fruits and milk·dairy products are consumed on a less frequent basis as between-meal snacks. According to a previous study, poor adherences to the recommended amounts for fruits and milk·dairy products were observed in Korean adults (Song, S *et al.* 2014).

Dietary determinants of metabolic syndrome in Korean adults have also been reported. Among Korean adult men and women aged 30 to 59 years, poor adherence to the recommended amount for milk ·dairy products was associated with a high prevalence of metabolic syndrome, whereas fruits intake was positively associated with a prevalence of abdominal obesity (Jung, HJ *et al.* 2011). Additional studies have suggested that milk ·dairy products have been associated with a low prevalence of metabolic syndrome (Kim, J 2013, Kwon, HT *et al.* 2010, Lee, CJ and Joung, H 2012). Shin, A *et al.* (2009) showed that men with metabolic syndrome had higher intakes of seaweeds and oily foods than those without metabolic syndrome. However, these previous studies focused on the association of single food group (e.g., milk ·dairy products) with metabolic syndrome or examined the association only in men. Limited data exist regarding the overall evaluation of dietary intake associated with metabolic syndrome among Korean adults.

A recent study reported that the prevalence of metabolic syndrome in Korean adults has been increasing (Lim, S *et al.* 2011). Furthermore, type 2 diabetes and cardiovascular diseases are one of the main causes of mortality in Korean (KOSTAT 2014). Therefore, investigation of dietary determinants of metabolic syndrome is important to prevent chronic diseases during the early stages. The aim of this study was

to identify dietary determinants of metabolic syndrome by examining differences in intakes of nutrients and food groups according to the presence of metabolic syndrome among Korean men and women recruited from outpatient clinics in and near Seoul.

2. Methods

Study subjects

The data used in this cross-sectional study were from those subjects who attended health examination centers, internal medicine or family medicine departments of four outpatient clinics in and near the Seoul metropolitan area of South Korea between 2006 and 2012. Of the records of 782 subjects who gave written informed consent to the current study, we excluded subjects who were younger than 30 years of age ($n = 17$), had less than three days of dietary intake data ($n = 91$), or had incomplete information on anthropometric or biochemical variables ($n = 6$). A total of 668 subjects (413 men and 255 women) were included in the data analysis. This study was approved by the Institutional Review Boards at the Seoul Medical Center, Bundang Jesaeng General Hospital, and Seoul National University Hospital.

Assessment of dietary intake

Three days of dietary intake data were obtained from a combination of 24-hour recalls and dietary records. Mean daily energy and nutrient intakes were calculated from three days of dietary intake data using the Diet Evaluation System (The Human Nutrition

Lab., Seoul National University, Seoul, South Korea), a validated web-based computer program for dietary assessment (Jung, HJ *et al.* 2013). Mean daily food group intake in numbers of servings from each subject was calculated based on the newly-developed food group database (Song, S *et al.* 2014). The database consisted of 4,370 foods and provided common serving size and number of food group servings per 100 grams of each food for six food groups (e.g., Grains, Meat·fish·eggs·beans, Vegetables, Fruits, Milk·dairy products, and Oils·fats·sugars). To evaluate food group intake, percentage of servings recommended in the Korean Food Guidance System (KNS 2010) were calculated according to sex and age group. The Korean Food Guidance System recommended specific patterns of food group intake in numbers of serving for individuals within their energy and nutrients requirements assuming a sedentary activity level according to sex and age group. Mean daily alcohol consumption from three days of dietary intake data was calculated as grams per day using a Korean food composition table that included the specific alcohol content of each type of alcoholic beverage (RDA 2006).

Assessment of lifestyle, anthropometric, and biochemical variables

Information on demographic and lifestyle variables was obtained through questionnaires. Smoking status was categorized into current-, ex-, and non-smoker. Regular physical activity was determined by asking whether the subjects participated in exercise regularly during the last month. Height, weight, and waist circumference were obtained using standardized techniques and calibrated equipment. BMI was calculated as weight (kg) / height (m²). Blood pressure was measured with a standardized sphygmomanometer. Blood samples were collected after the subjects had

fasted for at least 8 hours. Fasting blood glucose, triglycerides, and HDL-cholesterol were analyzed at certified clinical laboratories.

Definition of metabolic syndrome

Metabolic syndrome was diagnosed using the NCEP ATP III criteria (Grundy, SM *et al.* 2005) with a modified waist circumference cutoff for Koreans (Lee, SY *et al.* 2007). Metabolic syndrome was defined as having three or more of the following components: 1) elevated waist circumference (≥ 90 cm in men and ≥ 85 cm in women), 2) elevated triglycerides (≥ 150 mg/dL or using medication for hyperlipidemia), 3) low HDL-cholesterol (< 40 mg/dL in men and < 50 mg/dL in women), 4) elevated fasting blood glucose (≥ 100 mg/dL or using medication for diabetes), and 5) elevated blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or using medication for hypertension).

Statistical analyses

All statistical analyses were conducted using the SAS statistical software package version 9.3 (SAS Institute, Cary, NC, USA). Continuous variables were expressed as means and SD and categorical variables as percentages by the presence of metabolic syndrome in men and women. The GLM or the *t*-test (for continuous variables) and the chi-square test (for categorical variables) were performed to examine the differences in variables by the presence of metabolic syndrome. Sex, age, BMI, regular physical activity, smoking status, and total energy intake were considered as potential confounding variables and were controlled in the model. All statistical tests were two-sided and a *P*-value of < 0.05 represented statistical significance.

3. Results

Characteristics of the study subjects by the presence of metabolic syndrome

The prevalence of metabolic syndrome in this study population was 50 % (55.4 % in men and 41.2 % in women). Elevated triglycerides in men (66.1 %) and low HDL-cholesterol in women (51.8 %) were the most prevalent component of metabolic syndrome. Characteristics of the study subjects by the presence of metabolic syndrome are shown in Table IV - 1. Subjects with metabolic syndrome were likely to be men, more obese, and current- or ex-smokers. According to the stratified analysis by sex (Table IV - 2), men with metabolic syndrome were likely to be older, more obese, current- or ex-smokers, and less physically active than subjects without metabolic syndrome whereas women with metabolic syndrome were likely to be older and more obese.

Table IV - 1. Characteristics of the study subjects by the presence of metabolic syndrome

	Total (<i>n</i> = 668)				<i>P</i> -value ^a
	Non-MetS (<i>n</i> = 334)		MetS (<i>n</i> = 334)		
	<i>n</i>	%	<i>n</i>	%	
Sex					
Men	184	55.1	229	68.6	0.0003
Women	150	44.9	105	31.4	
Age (Mean, SD)					
Year	50.7	10.2	52.1	10.6	0.0666
BMI (Mean, SD)					
kg/m ²	24.3	2.6	26.5	2.9	< 0.0001
Smoking status					
Current-smokers	63	18.9	97	29.0	< 0.0001
Ex-smokers	74	22.2	101	30.2	
Non-smoker	197	59.0	136	40.7	
Regular physical activity					
Yes	236	70.7	230	68.9	0.6132
No	98	29.3	104	31.1	
Prevalence of MetS					
Elevated waist circumference	85	25.5	252	75.5	< 0.0001
Elevated triglycerides	120	35.9	266	79.6	< 0.0001
Low HDL-cholesterol	84	25.2	184	55.1	< 0.0001
Elevated fasting blood glucose	88	26.4	217	65.0	< 0.0001
Elevated blood pressure	114	34.1	279	83.5	< 0.0001

MetS, Metabolic syndrome.

^a *P*-value was obtained from the chi-square test for categorical variables and the *t*-test for continuous variables.

Table IV - 2. Characteristics of the study subjects by sex and the presence of metabolic syndrome

	Men (<i>n</i> = 413)					Women (<i>n</i> = 255)				
	Non-MetS (<i>n</i> = 184)		MetS (<i>n</i> = 229)		<i>P</i> -value ^a	Non-MetS (<i>n</i> = 150)		MetS (<i>n</i> = 105)		<i>P</i> -value ^a
Age (Mean, SD)										
Year	48.0	9.8	50.1	10.6	0.0408	54.0	9.7	56.7	8.9	0.0240
BMI (Mean, SD)										
kg/m ²	24.9	2.4	26.6	2.7	< 0.0001	23.6	2.6	26.3	3.4	< 0.0001
Smoking status (n, %)										
Current-smokers	59	32.1	92	40.2	0.0052	4	2.7	5	4.8	0.3888
Ex-smokers	70	38.0	98	42.8		4	2.7	3	2.9	
Non-smoker	55	29.9	39	17.0		142	94.7	97	92.4	
Regular physical activity (n, %)										
Yes	141	76.6	154	67.3	0.0359	95	63.3	76	72.4	0.1303
No	43	23.4	75	32.8		55	36.7	29	27.6	
Prevalence of MetS (n, %)										
Elevated waist circumference	55	29.9	176	76.9	< 0.0001	30	20.0	76	72.4	< 0.0001
Elevated triglycerides	77	41.9	196	85.6	< 0.0001	43	28.7	70	66.7	< 0.0001
Low HDL-cholesterol	34	18.5	102	44.5	< 0.0001	50	33.3	82	78.1	< 0.0001
Elevated fasting blood glucose	56	30.4	152	66.4	< 0.0001	32	21.3	65	61.9	< 0.0001
Elevated blood pressure	64	34.8	191	83.4	< 0.0001	50	33.3	88	83.8	< 0.0001

MetS, Metabolic syndrome.

^a *P*-value was obtained from the chi-square test for categorical variables and the *t*-test for continuous variables.

Mean daily energy and nutrient intake of the study subjects by the presence of metabolic syndrome

Mean daily energy and nutrient intake of the study subjects by the presence of metabolic syndrome are presented in Table IV - 3. Intakes of thiamin and alcohol had a significant difference by the presence of metabolic syndrome. Among dietary factors, alcohol consumption had only significant difference between non-metabolic syndrome men and metabolic syndrome men (14.4 g/day in men without metabolic syndrome vs. 22.9 g/day in men with metabolic syndrome). Other nutrient intake was not different between non-metabolic syndrome men and metabolic syndrome men (Table IV - 4). In women, mean daily energy and nutrient intake was not associated with the presence of metabolic syndrome (Table IV - 5).

Table IV - 3. Mean daily energy and nutrient intake of the study subjects by the presence of metabolic syndrome

	Total (<i>n</i> = 668)				
	Non-MetS (<i>n</i> = 334)		MetS (<i>n</i> = 334)		<i>P</i> -value ^a
	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1747	425.5	1814	465.3	0.3144
Energy from carbohydrate (%)	60.0	8.7	59.0	9.7	0.5985
Energy from fat (%)	20.9	5.7	20.1	5.2	0.1882
Energy from protein (%)	16.0	2.6	15.8	2.9	0.2253
Energy from alcohol (%)	3.1	6.3	5.1	9.2	0.0472
Nutrients					
Carbohydrate (g)	268.0	59.0	272.5	63.8	0.6636
Fat (g)	43.1	18.9	42.5	16.8	0.4541
Protein (g)	72.7	22.1	74.6	22.8	0.8869
Dietary fiber (g)	21.5	6.3	22.8	7.7	0.0903
Vitamin A (µg RE)	743.7	356.8	730.5	373.8	0.9353
Vitamin E (mg)	10.73	3.17	10.68	3.32	0.6070
Thiamin (mg)	1.1	0.4	1.2	0.4	0.0205
Riboflavin (mg)	1.12	0.4	1.11	0.4	0.7258
Niacin (mg)	14.9	5.1	15.5	5.8	0.7852
Vitamin C (mg)	97.6	46.2	96.5	47.2	0.9697
Calcium (mg)	515.1	197.1	505.2	197.9	0.4194
Phosphorus (mg)	1062	302.0	1087	305.5	0.8114
Sodium (mg)	4259	1433	4565	1553	0.1219
Potassium (mg)	2804	816.4	2846	851.5	0.5835
Iron (mg)	14.9	4.6	15.8	5.9	0.2193
Cholesterol (mg)	275.7	155.4	267.7	136.3	0.2861
Alcohol (g)	9.2	19.5	16.7	35.5	0.0249

MetS, Metabolic syndrome.

^a *P*-value was obtained from the general linear model (GLM) after adjustment for sex (men or women), age (continuous), BMI (continuous), and smoking status (current, past, or never).

Table IV - 4. Mean daily energy and nutrient intake by the presence of metabolic syndrome in men

	Men (<i>n</i> = 413)				
	Non-MetS (<i>n</i> = 184)		MetS (<i>n</i> = 229)		<i>P</i> -value ^a
	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1899	431.9	1930	466.9	0.3332
Energy from carbohydrate (%)	58.3	9.4	57.1	9.9	0.3314
Energy from fat (%)	21.0	6.0	20.2	5.2	0.3075
Energy from protein (%)	16.0	2.7	15.9	2.9	0.3915
Energy from alcohol (%)	4.7	7.6	6.8	10.4	0.0644
Nutrients					
Carbohydrate (g)	282.5	60.3	281.2	65.2	0.7634
Fat (g)	47.2	20.8	45.3	17.4	0.6159
Protein (g)	79.3	23.5	79.3	22.3	0.9342
Dietary fiber (g)	22.2	6.7	23.0	8.1	0.3485
Vitamin A (µg RE)	756.3	309.4	723.8	372.2	0.7657
Vitamin E (mg)	11.2	3.3	10.8	3.3	0.2906
Thiamin (mg)	1.18	0.4	1.24	0.4	0.0673
Riboflavin (mg)	1.19	0.4	1.16	0.4	0.7944
Niacin (mg)	16.3	5.5	16.5	6.0	0.8851
Vitamin C (mg)	94.9	41.3	95.0	49.3	0.8862
Calcium (mg)	526.7	201.7	519.0	200.5	0.8636
Phosphorus (mg)	1126	329.0	1131	302.2	0.8753
Sodium (mg)	4692	1424	4841	1607	0.5201
Potassium (mg)	2901	823.2	2880	821.5	0.9057
Iron (mg)	15.9	4.8	16.4	5.9	0.3927
Cholesterol (mg)	306.7	165.0	289.3	140.0	0.3355
Alcohol (g)	14.4	23.8	22.9	40.9	0.0411

MetS, Metabolic syndrome.

^a *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), smoking status (current, past, or never), and regular physical activity (yes or no).

Table IV - 5. Mean daily energy and nutrient intake by the presence of metabolic syndrome in women

	Women (<i>n</i> = 255)				
	Non-MetS (<i>n</i> = 150)		MetS (<i>n</i> = 105)		<i>P</i> -value ^a
	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1560	334.1	1560	347.3	0.7738
Energy from carbohydrate (%)	62.2	7.4	63.3	7.7	0.5218
Energy from fat (%)	20.8	5.4	19.8	5.3	0.4022
Energy from protein (%)	15.9	2.4	15.7	2.8	0.5561
Energy from alcohol (%)	1.14	3.32	1.14	3.22	0.7112
Nutrients					
Carbohydrate (g)	250.3	52.5	253.5	56.3	0.6668
Fat (g)	38.1	15.0	36.2	13.5	0.5444
Protein (g)	64.7	17.2	64.3	20.4	0.9829
Dietary fiber (g)	20.7	5.8	22.4	7.0	0.0624
Vitamin A (µg RE)	728.2	408.1	745.1	378.6	0.4245
Vitamin E (mg)	10.1	2.9	10.3	3.4	0.4662
Thiamin (mg)	1.00	0.3	1.03	0.3	0.1740
Riboflavin (mg)	1.04	0.3	1.00	0.3	0.9329
Niacin (mg)	13.3	3.9	13.4	4.6	0.8728
Vitamin C (mg)	100.9	51.5	99.8	42.2	0.7974
Calcium (mg)	500.8	191.0	475.1	189.6	0.2985
Phosphorus (mg)	984	244.4	990	291.1	0.8426
Sodium (mg)	3729	1259	3964	1239	0.0729
Potassium (mg)	2685	794.7	2770	913.0	0.1911
Iron (mg)	13.6	4.0	14.5	5.6	0.2997
Cholesterol (mg)	237.7	133.8	220.5	115.0	0.6577
Alcohol (g)	2.9	9.0	3.0	9.2	0.6261

MetS, Metabolic syndrome.

^a *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous) and BMI (continuous).

Mean daily food group intake of the study subjects by the presence of metabolic syndrome

Mean daily food group intake of the study subjects by the presence of metabolic syndrome are shown in Table IV - 6. Subjects with metabolic syndrome had a significantly lower intake of fruits, milk·dairy products, and oils·fats·sugars than subjects without metabolic syndrome. Men with metabolic syndrome had a significantly lower intake of fruits and oils·fats·sugars than men without metabolic syndrome (Table IV - 7) while women with metabolic syndrome had a significantly lower intake of milk·dairy products than women without metabolic syndrome (Table IV - 8).

Table IV - 6. Mean daily food group intake of the study subjects by the presence of metabolic syndrome

	Total (<i>n</i> = 668)				
	Non-MetS (<i>n</i> = 334)		MetS (<i>n</i> = 334)		<i>P</i> -value ^a
	Mean	<i>SD</i>	Mean	<i>SD</i>	
Food groups (servings)					
Grains	2.7	0.7	2.8	0.7	0.0781
Meat·fish·eggs·beans	4.5	1.9	4.8	2.0	0.9773
Vegetables	7.1	2.7	7.6	3.1	0.2772
Fruits	1.8	1.5	1.3	1.4	0.0004
Milk·dairy products	0.7	0.8	0.5	0.6	0.0007
Oils·fats·sugars	5.1	3.0	4.7	2.6	0.0017
Food groups (% recommended servings)					
Grains	77.0	20.9	78.1	20.9	0.0735
Meat·fish·eggs·beans	101.5	43.2	107.1	50.2	0.8622
Vegetables	103.8	39.7	110.6	44.5	0.2767
Fruits	85.1	88.8	67.6	89.8	0.0070
Milk·dairy products	67.2	76.8	45.6	59.0	0.0007
Oils·fats·sugars	115.1	64.3	103.3	54.0	0.0011

MetS, Metabolic syndrome.

^a *P*-value was obtained from the general linear model (GLM) after adjustment for sex (men or women), age (continuous), BMI (continuous), smoking status (current, past, or never) and total energy intake (continuous).

Table IV - 7. Mean daily food group intake by the presence of metabolic syndrome in men

	Men (<i>n</i> = 413)				
	Non-MetS (<i>n</i> = 184)		MetS (<i>n</i> = 229)		<i>P</i> -value ^a
	Mean	<i>SD</i>	Mean	<i>SD</i>	
Food groups (servings)					
Grains	2.9	0.7	2.9	0.7	0.2904
Meat·fish·eggs·beans	4.9	2.1	5.1	1.9	0.7101
Vegetables	7.6	2.7	7.8	3.2	0.5442
Fruits	1.6	1.5	1.1	1.4	0.0006
Milk·dairy products	0.6	0.7	0.4	0.6	0.0745
Oils·fats·sugars	5.8	3.4	5.0	2.8	0.0113
Food groups (% recommended servings)					
Grains	72.3	17.6	74.4	18.6	0.2822
Meat·fish·eggs·beans	99.7	43.1	104.4	39.5	0.7733
Vegetables	108.8	37.9	111.8	45.2	0.5442
Fruits	63.5	86.9	49.5	80.3	0.0109
Milk·dairy products	58.0	74.1	44.2	61.7	0.0745
Oils·fats·sugars	116.4	69.1	102.2	56.4	0.0106

MetS, Metabolic syndrome.

^a *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), smoking status (current, past, or never), regular physical activity (yes or no), and total energy intake (continuous).

Table IV - 8. Mean daily food group intake by the presence of metabolic syndrome in women

	Women (<i>n</i> = 255)				
	Non-MetS		MetS		<i>P</i> -value ^a
	<i>(n</i> = 150)		<i>(n</i> = 105)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	
Food groups (servings)					
Grains	2.5	0.7	2.6	0.7	0.1527
Meat·fish·eggs·beans	3.9	1.5	4.0	2.0	0.5763
Vegetables	6.5	2.7	7.1	2.8	0.1680
Fruits	2.0	1.5	1.8	1.4	0.3026
Milk·dairy products	0.8	0.8	0.5	0.5	0.0023
Oils·fats·sugars	4.4	2.3	4.0	1.9	0.0786
Food groups (% recommended servings)					
Grains	82.8	23.0	86.2	23.3	0.1527
Meat·fish·eggs·beans	103.7	43.4	112.9	67.7	0.5139
Vegetables	97.7	41.0	108.0	42.9	0.1532
Fruits	111.7	84.0	107.1	96.9	0.3770
Milk·dairy products	78.6	78.8	48.9	52.6	0.0023
Oils·fats·sugars	113.5	58.2	105.8	48.3	0.0596

MetS, Metabolic syndrome.

^a *P*-value was obtained from the general linear model (GLM) after adjustment for age (continuous), BMI (continuous), and total energy intake (continuous).

4. Discussion and conclusions

In the study of Korean adults from outpatient clinics, fruits consumption in men and milk-dairy products consumption in women were dietary determinants of metabolic syndrome. Men with metabolic syndrome had a lower intake of fruits and oils-fats-sugars compared to those without metabolic syndrome. Women with metabolic syndrome had a lower intake of milk-dairy products compared to those without metabolic syndrome.

Our findings are consistent with those from previous epidemiologic studies. A higher intake of milk-dairy products was consistently associated with lower risks for metabolic syndrome and its components in Western (Elwood, PC *et al.* 2007, Liu, S *et al.* 2005, Lutsey, PL *et al.* 2008, Ruidavets, JB *et al.* 2007) and Asian populations (Azadbakht, L *et al.* 2005, Kim, J 2013, Kwon, HT *et al.* 2010). Although the types of dairy products were not considered to examine the association with metabolic syndrome in this study, several studies have shown different associations with metabolic syndrome according to the types of dairy products. Liu, S *et al.* (2005) divided total dairy products into high-fat dairy products and low-fat dairy products and examined the associations with metabolic syndrome by the types of dairy products among US women. They found the inverse association of high-fat dairy products with metabolic syndrome only. In another study, the associations between several types of milk-dairy products, such as whole milk, low fat milk, skim milk, cheese, and yogurt and the risk of metabolic syndrome were evaluated (Beydoun, MA *et al.* 2008) based on data from the NHANES in 1999–2004.

Milk-dairy products are major sources of calcium, vitamin D, potassium, and magnesium, which are inversely associated with individual components of metabolic syndrome, including elevated fasting blood glucose, elevated blood pressure, elevated triglycerides, and obesity (Beydoun, MA *et al.* 2008, Fumeron, F *et al.* 2011, Liu, S *et al.* 2005). Tehranian study by Azadbakht, L *et al.* (2005) indicated that the association between dairy consumption and metabolic syndrome became weaker after adjustment for calcium intake. Therefore, the inverse relationship between dairy consumption and metabolic syndrome might be explained by the effect of calcium on metabolic syndrome components, such as blood pressure, adiposity, and insulin sensitivity. However, beneficial nutrients in such foods are highly correlated so that it is difficult to completely separate the independent effects of these nutrients on risks for metabolic syndrome and its components. Further mechanism studies need to determine what nutrients are responsible for the potential beneficial effects of these foods on the development of metabolic syndrome.

Higher intakes of fruits may reduce the risk of metabolic syndrome through their beneficial compounds, such as fruits fiber (Hosseinpour-Niazi, S *et al.* 2011) and antioxidants (Ford, ES *et al.* 2003). An inverse association between fruits consumption and metabolic syndrome was observed but there was no association between vegetables consumption and metabolic syndrome. A previous study found the combined effects of fruits and vegetables on the development of metabolic syndrome (Yoo, S *et al.* 2004). However, the association between vegetables consumption and metabolic syndrome might be different depending on specific subgroups of vegetables.

In addition, an inverse relationship between healthy foods (e.g., fruits and milk-dairy products) and the risk of metabolic syndrome may be attributed to the

healthy lifestyle behaviors associated with higher intakes of these foods. People who consume higher amounts of healthy foods show a tendency of having healthier dietary practice. Dietary patterns characterized by higher intakes of fruits and milk-dairy products have shown beneficial effects on metabolic syndrome (Esmailzadeh, A *et al.* 2007, Hong, S *et al.* 2012, Williams, DEM *et al.* 2000, Wirfalt, E *et al.* 2001).

Several limitations should be considered to correctly interpret findings from this study. Cross-sectional design cannot define the causal relationship between diet and the risk of metabolic syndrome. According to the results from the KNHANES data, in Korean adult, daily intakes of fruits and milk-dairy products are relatively low compared to the recommended amounts for these food groups (Song, S *et al.* 2014). Therefore, consumption of fruits and milk-dairy products might be key determinants of metabolic syndrome in Korean adults. The subjects of this study were recruited at outpatient clinics, so our findings may not be directly generalized to the general Korean adult population. In addition, we could not examine the associations between various subtypes of foods and the risk of metabolic syndrome. However, dietary determinants of metabolic syndrome were examined using three days of dietary intake data that could closely estimate the usual intake of nutrients and food groups in this population.

In this cross-sectional study, low intakes of fruits and milk-dairy products are associated with having metabolic syndrome in Korean adults. Prospective and intervention studies are needed to confirm the cause-effect association between the specific dietary attributes and metabolic syndrome. Dietary recommendations for individuals and populations who are at high risk of metabolic syndrome can be suggested based on the results of this study. In addition, findings of the present study

can be used to extend the knowledge about the mechanism of dietary determinants related to the development of metabolic syndrome and its components.

STUDY 6. Heavy alcohol drinking is a determinant of metabolic syndrome in Korean current-smokers

1. Introduction

Metabolic syndrome, a cluster of abdominal obesity, dyslipidemia, high blood pressure, and elevated blood glucose, is associated with increased risks of diabetes and cardiovascular disease (Grundy, SM *et al.* 2005). Although the mechanism underlying the development of metabolic syndrome is not fully elucidated, several lifestyle factors, such as diet, alcohol drinking, smoking, and physical activity have been identified as determinants of metabolic syndrome (Lee, WY *et al.* 2005, Magkos, F *et al.* 2009, Minehira, K and Tappy, L 2002).

Previous studies have examined relationships between alcohol consumption and metabolic syndrome but have reported inconsistent findings. Overall, light to moderate alcohol drinking was associated with a low prevalence of metabolic syndrome in the US (Freiberg, MS *et al.* 2004, Stoutenberg, M *et al.* 2013) and Japanese populations (Wakabayashi, I 2010) while heavy alcohol drinking was associated with an increased risk of metabolic syndrome (Wakabayashi, I 2010). However, other studies in Japanese and Portuguese men reported no significant associations between alcohol consumption and metabolic syndrome (Kawada, T and Okada, K 2006, Santos, AC *et al.* 2007).

A high prevalence of heavy alcohol consumption among Korean men has been reported (Lee, MY *et al.* 2010, Yoon, YS *et al.* 2004), and a recent study showed increasing prevalence of metabolic syndrome from 1998 to 2007 in Korean men over 30 years of age (Lim, S *et al.* 2011). A prospective study of middle-aged Korean adults reported that heavy alcohol drinking was associated with an increased risk of metabolic syndrome (Baik, I and Shin, C 2008) and cross-sectional studies reported a positive (Lee, MY *et al.* 2010, Yoon, YS *et al.* 2004) or no (Lee, WY *et al.* 2005) associations between alcohol consumption and metabolic syndrome in Korean adults.

Alcohol consumption is highly correlated with other lifestyle factors, especially smoking (Donahue, RP *et al.* 1999, Gulliver, SB *et al.* 2000). However, only a few studies have examined alcohol drinking, smoking status, and metabolic syndrome together. Therefore, we examined the association between alcohol consumption and the prevalence of metabolic syndrome in relation to smoking status among Korean men.

2. Methods

Study subjects

Among the subjects of STUDY 5, only 413 men were included in the data analyses because in Korean women of this study, the prevalences of consuming alcohol any amount over three-day period (43 %), more than one drink over three-day period (6 %) and smoking (4 %) were low.

Data collection

Three days of dietary intake data were obtained from a combination of 24-hour recalls and dietary records. Mean daily energy and nutrient intakes were calculated from three days of dietary intake data using the Diet Evaluation System (The Human Nutrition Lab., Seoul National University, Seoul, South Korea), a validated web-based computer program for dietary assessment (Jung, HJ *et al.* 2013). Mean daily alcohol consumption from three days of dietary intake data was calculated as grams per day using a Korean food composition table that included the specific alcohol content of each type of alcoholic beverage (RDA 2006). Based on the maximum daily recommended amount of alcohol consumption for men (two drinks, one drink equals 15 g of alcohol) (Paik, HY *et al.* 2008), the subjects were categorized into three alcohol drinking groups: 1) non- (0 g/day), 2) moderate- (≤ 30 g/day), and 3) heavy- (> 30 g/day) drinkers.

Height, weight, and waist circumference were obtained using standardized techniques and calibrated equipment. BMI was calculated as weight (kg) / height (m²). Blood pressure was measured with a standardized sphygmomanometer. Blood samples were collected after the subjects had fasted for at least 8 hours. Fasting blood glucose, triglycerides, and HDL-cholesterol were analyzed at certified clinical laboratories.

Metabolic syndrome was diagnosed using the NCEP ATP III criteria (Grundy, SM *et al.* 2005) with a modified waist circumference cutoff for Koreans (Lee, SY *et al.* 2007). Metabolic syndrome was defined as having three or more of the following components: 1) elevated waist circumference (≥ 90 cm), 2) elevated triglycerides (≥ 150 mg/dL or using medication for hyperlipidemia), 3) low HDL-cholesterol (< 40 mg/dL), 4) elevated fasting blood glucose (≥ 100 mg/dL or using medication for

diabetes), and 5) elevated blood pressure (systolic \geq 130 mmHg or diastolic \geq 85 mmHg or using medication for hypertension).

Information on demographic and lifestyle variables was obtained through questionnaires. Smoking status was categorized into current-, ex-, and non-smoker. Regular physical activity was determined by asking whether the subjects participated in exercise regularly during the last month.

Statistical analyses

All statistical analyses were conducted using the SAS statistical software package version 9.3 (SAS Institute, Cary, NC, USA). Continuous variables were expressed as means and SD and categorical variables as percentages (%) by alcohol drinking groups. The general linear model (for continuous variables) and the chi-square test (for categorical variables) were performed to examine the differences in variables by alcohol drinking groups.

A multivariate logistic regression was performed to estimate ORs (95% CIs) and *P* for trend of metabolic syndrome and its components by alcohol drinking groups and smoking status, taking non-drinkers as the reference group. Age, BMI, regular physical activity, and total energy intake were considered as potential confounding variables and were controlled in the model. All statistical tests were two-sided and a *P*-value of < 0.05 represented statistical significance.

3. Results

Characteristics of the study subjects by alcohol drinking groups

Characteristics of the study subjects by alcohol drinking groups are presented in Table IV - 9. Heavy-drinkers (> 30 g/day) were more likely to be young and current-smokers than non- drinkers. Heavy-drinkers had a significantly higher intake of total energy, fat, protein, thiamin, riboflavin, phosphorus, and sodium, but lower intake of energy from carbohydrate, energy from fat, energy from protein, total carbohydrate, dietary fiber, vitamin A, vitamin C, calcium, and potassium than non-drinkers. Other characteristics were not associated with alcohol drinking groups.

Table IV - 9. Characteristics of the study subjects by alcohol drinking groups^a in men (*n* = 413)

Characteristics	Non -drinkers (<i>n</i> = 149)		Moderate -drinkers (<i>n</i> = 172)		Heavy -drinkers (<i>n</i> = 92)		<i>P</i> for trend ^b
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Age (years)	51.2	10.7	47.5	10.1	48.8	9.5	0.0338
Body mass index (kg/m ²)	25.8	2.7	25.8	2.8	26.0	2.6	0.9193
Smoking status (%)							
Current-smokers	33.6		33.1		47.8		0.0484
Ex-smokers	44.3		38.4		39.1		
Non-smokers	22.2		28.5		13.0		
Regular physical activity (%)							
Yes	66.4		76.2		70.7		0.3309
No	33.6		23.8		29.4		
Prevalence of metabolic syndrome and its components (%)							
Elevated waist circumference	55.7		57.0		54.4		0.8828
Elevated triglycerides	64.4		61.6		77.2		0.0798
Low HDL-cholesterol	36.9		33.1		26.1		0.0887
Elevated fasting blood glucose	48.3		48.8		56.5		0.2546
Elevated blood pressure	57.1		62.2		68.5		0.0758
Metabolic syndrome	53.0		52.9		64.1		0.1267
Energy and nutrient intake (/day)							
Total energy (kcal)	1830	406.0	1981	463.0	2283	489.5	< 0.0001
Energy from carbohydrate (%)	63.0	7.5	58.9	7.2	46.6	7.9	< 0.0001
Energy from fat (%)	20.9	6.0	21.4	5.2	18.3	5.1	< 0.0001
Energy from protein (%)	16.1	2.9	16.6	2.5	14.5	2.6	0.0001
Energy from alcohol (%)	0.0	0.0	3.2	3.4	20.6	9.1	< 0.0001
Carbohydrate (g)	285.3	60.5	289.2	67.1	261.9	55.0	< 0.0001
Fat (g)	43.7	19.3	47.9	19.6	46.8	16.9	< 0.0001
Protein (g)	73.7	21.3	82.4	23.8	82.7	21.7	0.0080
Dietary fiber (g)	23.1	7.0	23.0	8.2	21.1	6.6	< 0.0001
Vitamin A (µg RE)	732.1	346.2	763.4	336.7	701.5	360.9	0.0133
Thiamin (mg)	1.19	0.38	1.23	0.38	1.24	0.44	< 0.0001
Riboflavin (mg)	1.12	0.37	1.22	0.40	1.18	0.37	< 0.0001
Niacin (mg)	14.9	5.6	17.0	5.6	17.7	6.1	0.4936
Vitamin C (mg)	97.9	45.5	99.5	51.2	81.7	31.6	< 0.0001
Calcium (mg)	529.2	202.6	532.5	212.9	492.7	171.8	< 0.0001
Phosphorus (mg)	1074	295.2	1171	333.4	1140	295.8	< 0.0001
Sodium (mg)	4706	1536	4789	1524	4856	1535	0.0107
Potassium (mg)	2810	799.3	3006	889.3	2800	696.3	< 0.0001
Iron (mg)	15.7	4.5	16.4	5.6	16.6	6.7	0.0993
Cholesterol (mg)	252.8	143.0	324.5	153.5	317.5	146.9	0.5229
Alcohol (g)	0.0	0.0	9.0	9.5	69.1	43.9	< 0.0001

^a The study subjects were categorized into three alcohol drinking groups according to their mean daily alcohol consumption: 1) non- (0 g/day), 2) moderate- (≤ 30 g/day), and 3) heavy- (> 30 g/day) drinkers.

^b *P* for trend was obtained from the Mantel-Haenszel chi-square test for categorical variables and the general linear model for continuous variables. *P* for trend for BMI and total energy intake was adjusted for age, smoking status, and regular physical activity, and *P* for trend for nutrient intake was adjusted for age, smoking status, regular physical activity, and total energy intake.

The association between alcohol drinking and metabolic syndrome

Multivariate ORs for metabolic syndrome and its components by alcohol drinking groups are shown in Table IV - 10. Heavy-drinkers had significantly higher OR for elevated blood pressure (OR = 0.53, 95% CI = 0.29–0.98) but lower OR for low HDL-cholesterol (OR = 2.00, 95% CI = 1.09–3.65) compared with non-drinkers after adjusting for potential confounding variables.

Multivariate ORs for metabolic syndrome and its components by alcohol drinking groups and smoking status are shown in Table IV - 11. Among current-smokers, heavy-drinkers had significantly higher ORs for metabolic syndrome (OR = 3.26, 95% CI = 1.16–9.17) compared with non-drinkers after adjusting for age, BMI, physical activity, and total energy intake. However, there was no association between alcohol consumption and the prevalence of metabolic syndrome in ex- or non-smokers. Heavy alcohol drinking was positively associated with an elevated blood pressure in current-smokers whereas inversely associated with a low HDL-cholesterol in ex- or non-smokers.

Table IV - 10. Multivariate ORs and 95% CIs^a for metabolic syndrome and its components by alcohol drinking groups^b (*n* = 413)

	Non		Moderate		Heavy		
	-drinkers		-drinkers		-drinkers		
	OR	OR	95% CI	95% CI	OR	95% CI	
Elevated waist circumference	1.00	1.09	0.69	1.72	0.86	0.49	1.51
Elevated triglycerides	1.00	0.85	0.53	1.36	1.63	0.86	3.08
Low HDL-cholesterol	1.00	0.77	0.48	1.24	0.53*	0.29	0.98
Elevated fasting blood glucose	1.00	1.13	0.72	1.78	1.53	0.87	2.70
Elevated blood pressure	1.00	1.51	0.94	2.42	2.00*	1.09	3.65
Metabolic syndrome	1.00	1.10	0.70	1.74	1.47	0.82	2.63

^a Multivariate adjusted logistic regression analysis was performed to estimate ORs and 95% CIs for metabolic syndrome and its components after adjustment for age, smoking status, and total energy intake.

^b The subjects were categorized into three alcohol drinking groups according to their mean daily alcohol consumption: 1) non- (0 g/day), 2) moderate- (≤ 30 g/day), and 3) heavy- (> 30 g/day) drinkers.

* $P < 0.05$

Table IV - 11. Multivariate ORs and 95% CIs^a for metabolic syndrome^b and its components by alcohol drinking groups and smoking status (*n* = 413)^c

	Non-drinkers	Moderate-drinkers	Heavy-drinkers
	OR	OR (95% CI)	OR (95% CI)
In current-smokers	(<i>n</i> = 50)	(<i>n</i> = 57)	(<i>n</i> = 44)
Elevated waist circumference	1.00	1.76 (0.63–4.93)	0.91 (0.29–2.86)
Elevated triglycerides	1.00	1.15 (0.45–2.94)	2.12 (0.64–6.99)
Low HDL-cholesterol	1.00	0.86 (0.37–2.00)	0.78 (0.30–2.03)
Elevated blood glucose	1.00	1.58 (0.69–3.62)	2.50 (0.96–6.51)
Elevated blood pressure	1.00	3.33 (1.39–8.00)*	4.09 (1.46–11.47)*
MetS	1.00	2.49 (1.03–6.00)*	3.26 (1.16–9.17)*
In ex- or non-smokers	(<i>n</i> = 99)	(<i>n</i> = 115)	(<i>n</i> = 48)
Elevated waist circumference	1.00	1.11 (0.56–2.20)	0.66 (0.27–1.60)
Elevated triglycerides	1.00	0.81 (0.46–1.43)	1.52 (0.70–3.32)
Low HDL-cholesterol	1.00	0.80 (0.44–1.43)	0.33 (0.14–0.83)*
Elevated blood glucose	1.00	1.06 (0.61–1.85)	1.26 (0.60–2.63)
Elevated blood pressure	1.00	1.09 (0.60–1.97)	1.35 (0.61–3.00)
MetS	1.00	0.83 (0.46–1.50)	0.96 (0.44–2.10)

^a A multivariate logistic regression was performed to estimate ORs and 95% CIs for metabolic syndrome after adjustment for age, BMI, regular physical activity, and total energy intake.

^b Metabolic syndrome was diagnosed using the National Cholesterol Education Program Adult Treatment Panel III criteria with a modified waist circumference cutoff for Koreans. Metabolic syndrome was defined as presenting three or more of the following components: 1) elevated waist circumference (≥ 90 cm), 2) elevated triglycerides (≥ 150 mg/dL or using medication for hyperlipidemia), 3) low HDL-cholesterol (< 40 mg/dL), 4) elevated fasting blood glucose (≥ 100 mg/dL or using medication for diabetes), and 5) elevated blood pressure (systolic ≥ 130 mmHg or diastolic ≥ 85 mmHg or using medication for hypertension).

^c The subjects were categorized into three alcohol drinking groups according to their mean daily alcohol consumption: 1) non- (0 g/day), 2) moderate- (≤ 30 g/day), and 3) heavy- (> 30 g/day) drinkers.

* $P < 0.05$

4. Discussion and conclusions

We found that the relationship between alcohol consumption and the prevalence of metabolic syndrome differed by smoking status. Men who were heavy-drinkers and also smokers had a higher prevalence of metabolic syndrome. However, no association between alcohol consumption and the prevalence of metabolic syndrome was observed in ex- or non-smokers.

Previous studies showed that the association between heavy alcohol consumption and risk of metabolic syndrome was not consistent. One meta-analysis of prospective studies reported that heavy alcohol consumption was associated with an increased risk of metabolic syndrome (Sun, K *et al.* 2013), but another meta-analysis of cross-sectional studies showed no association between heavy drinking and the prevalence of metabolic syndrome (Alkerwi, A *et al.* 2009). The stronger relationship between heavy drinking and metabolic syndrome was observed in Asian populations than in Western populations (Sun, K *et al.* 2013). In addition, Korean adults studies showed the consistent relationship between heavy drinking and metabolic syndrome in men, but not in women (Park, SH 2012, Shin, MH *et al.* 2013).

In the stratified analysis by smoking status, for Japanese men, alcohol consumption had J- and U-shaped relationships with the prevalence of metabolic syndrome in non-smokers and current-smokers, respectively (Wakabayashi, I 2010). Another Japanese study, however, showed no relationship between alcohol drinking and the prevalence of metabolic syndrome in current-smokers (Takeuchi, T *et al.* 2009). These inconsistent findings may be partly explained by differences in the study

design, the characteristics of study populations, such as sex and ethnicity, the methods of alcohol consumption assessment, and the types of alcoholic beverages consumed. In addition, the prevalence of metabolic syndrome in the subjects of this study was much higher than in those of other studies. Therefore, these factors should be considered to correctly interpret our findings.

Among the metabolic syndrome components, elevated blood pressure seems to be a main contributor to the positive association between heavy alcohol consumption and metabolic syndrome in current-smokers. Previous studies have consistently shown elevated blood pressure by heavy alcohol drinking in the Asian adult men population (Jin, L *et al.* 2011, Wakabayashi, I 2010, Yoon, YS *et al.* 2004). Although we found no significant differences in prevalence of other metabolic syndrome components according to alcohol drinking groups, other studies reported positive associations between heavy alcohol drinking and other metabolic syndrome components, such as elevated waist circumference (Baik, I and Shin, C 2008, Lee, WY *et al.* 2005, Yoon, YS *et al.* 2004), elevated triglycerides (Baik, I and Shin, C 2008, Jin, L *et al.* 2011, Wakabayashi, I 2010, Yoon, YS *et al.* 2004), and elevated fasting blood glucose (Baik, I and Shin, C 2008, Stoutenberg, M *et al.* 2013).

This study has several limitations and strengths. First, the cross-sectional design made it difficult to examine a causal relationship between alcohol consumption and the risk of metabolic syndrome. Second, this study population may not fully represent the general Korean adult men population. Third, we could not examine the effects of various types of alcohols or the frequency and duration of drinking on the prevalence of metabolic syndrome. However, this study used three days of dietary intake data, which were collected all year round and on all days of the week, so that it provided

detailed, quantitative estimates of daily alcohol consumption. Although there were possibilities of under reporting and misclassification of alcohol consumption, the mean daily alcohol consumption for each subject might represent their usual intake for a long time. The current study provides important information about the effect of smoking on the association between alcohol drinking and the prevalence of metabolic syndrome through the stratified analysis by smoking status.

In conclusion, our cross-sectional study of Korean men found that heavy alcohol drinking was linked to a higher prevalence and severity of metabolic syndrome in current-smokers than in ex- or non-smokers. Advice on reducing heavy drinking is needed to prevent and attenuate the risk of metabolic syndrome, especially for current-smokers. Further prospective studies are necessary to confirm our findings.

**CHAPTER V. CLUSTERING PATTERNS OF
METABOLIC SYNDROME COMPONENTS AND THEIR
ASSOCIATIONS WITH DIETARY FACTORS IN
KOREAN ADULTS USING REPEATED DIETARY DATA**

STUDY 7. Three distinct clustering patterns in metabolic syndrome abnormalities are differentially associated with dietary factors in Korean adults⁵

1. Introduction

Metabolic syndrome refers to a clustering of metabolic abnormalities and is associated with increased risk of cardiovascular diseases or type 2 diabetes (Grundy, SM *et al.* 2005). The prevalence of metabolic syndrome is increasing worldwide, and an alarming increase has been observed in Asian countries (Nestel, P *et al.* 2007). The prevalence of metabolic syndrome in Korean adults increased from 24.9 % in 1998 to 31.3 % in 2007 (Miyatake, N *et al.* 2002), and these rates are comparable with the 34.2 % prevalence reported in the US (Sadakane, A *et al.* 2008).

The rapid increase in the prevalence of metabolic syndrome in Asian countries has been attributed to a Westernized diet and sedentary lifestyles. Several studies have examined the associations between a Western dietary pattern, characterized by high intake of animal-based foods, and metabolic syndrome in Asian adult populations (Akter, S *et al.* 2013, Cho, YA *et al.* 2011, Lee, JE *et al.* 2011, Song, Y and Joung, H 2012). However, these studies have not shown a strong consistent association between

⁵ This study was published in the Nutrition Research vol. 34, no. 5, pages 383–390 in 2014.

Western dietary patterns and metabolic syndrome. Rather, some individual abnormalities of metabolic syndrome have shown a different association with diet. The Westernized pattern, including a high consumption of meat, was associated with an increased risk of glucose tolerance abnormalities in Korean (Song, Y and Joung, H 2012) and Chinese adult populations (He, YN *et al.* 2009), while the Westernized breakfast pattern or the Western dietary pattern was associated with a reduced risk of high blood pressure in the Japanese working population (Akter, S *et al.* 2013) and low HDL-cholesterol in Korean women (Cho, YA *et al.* 2011), respectively. The role of diet in the development of metabolic syndrome remains unclear but may differentially influence individual components of metabolic syndrome.

Recent studies have questioned whether a single metabolic risk factor underlies metabolic syndrome. Although the underlying pathophysiology is thought to be related to insulin resistance, several studies have modeled the structure of metabolic syndrome with various metabolic syndrome components (Ferguson, TF *et al.* 2010, Pladevall, M *et al.* 2006, Shen, BJ *et al.* 2003). From these studies, some types of models, including three- or four-factor models, were proposed with good fit of data, and their major proposed factors included insulin resistance, obesity, dyslipidemia, or high blood pressure. However, studies on the association of these models with dietary factors have not been conducted.

To understand the role of diet in the development of metabolic syndrome, identifying the underlying risk factors of metabolic syndrome and exploring the association of dietary factors with these underlying risk factors is essential. In this cross-sectional study, we hypothesized that distinct clustering patterns exist in metabolic syndrome abnormalities and that those patterns are differentially associated

with dietary factors. To test this hypothesis, we examined the distinct clustering patterns of metabolic syndrome abnormalities and the association between clustering patterns of metabolic syndrome abnormalities and dietary factors in the urban Korean adult population.

2. Methods

Study subjects

Subjects in this study were recruited through the Health Examination Center or the Family Medicine Division of Seoul National University Hospital in the Seoul metropolitan area in South Korea, from September 2010 to December 2012.

Individuals were considered eligible if they were 20 years of age or older and were disease-free at the time of study enrollment. Among the 182 eligible subjects, subjects with incomplete data regarding general characteristics ($n = 9$) or biochemical variables ($n = 17$) were excluded. In addition, subjects who took medications to lower serum lipids, blood glucose, or blood pressure ($n = 15$) to avoid related disease treatment effects were excluded as they were considered to have made dietary changes. A total of 141 subjects (44 men and 97 women) were included in the present cross-sectional analyses. This study protocol was approved by the Institutional Review Board at the Seoul National University Hospital, and written informed consent was obtained from each subject.

Subjects were considered to have metabolic syndrome according to the NCEP ATP III criteria (Grundy, SM *et al.* 2005) with a modified waist circumference cutoff for Asian populations provided by the IDF (Alberti, KG *et al.* 2005). Metabolic syndrome was defined as subjects presenting with three or more of the following components: 1) elevated waist circumference ≥ 90 cm in men and ≥ 80 cm in women, 2) elevated triglycerides ≥ 150 mg/dL, 3) reduced HDL-cholesterol < 40 mg/dL in men and < 50 mg/dL in women, 4) elevated blood glucose ≥ 100 mg/dL or a diagnosis of diabetes, and 5) elevated systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or a diagnosis of hypertension.

Assessment of dietary factors

Dietary intake data were obtained from multiple 24-hour recalls. All subjects in this study had 2–4 days of dietary data. Two days of dietary data were obtained through on-site interviews for all subjects, and an additional 1–2 days of dietary data were collected by telephone interviews with available subjects (average 2.8 days of dietary data: 55 subjects (39.0 %) with 2 days, 58 subjects (41.1 %) with 3 days, and 28 subjects (19.9 %) with 4 days of dietary data). Trained dietitians interviewed the subjects when they visited the hospital following a multiple three-step procedure (Kang, H *et al.* 2009) regarding their dietary intake during the previous 24-hour period. Briefly, in the first step, the subject quickly reported food items eaten during the previous day. Second, the subject was questioned in detail concerning the food reported in the first step. Lastly, a subject was asked about any forgotten food items. The telephone interview was conducted using the same protocol as the on-site interview within 2 weeks from the day of the on-site interview.

Mean daily energy and nutrient intake for each subject was calculated from the 2–4 days of dietary intake data using the Diet Evaluation System (Human Nutrition Lab, Seoul National University, Seoul, South Korea), which is a web-based computer program for dietary assessment (Jung, HJ *et al.* 2013). Mean daily alcohol intake was estimated in grams per day for each subject based on their dietary intake data. We evaluated the specific alcohol content of each type of alcoholic beverage according to the Korean food composition table (RDA 2006).

Average DGI and DGL based on a glucose standard were calculated for each subject using a table of GI values for common Korean foods established in a previous study (Song, S *et al.* 2012). The GI values in this table were obtained from the international tables of GI and GL values (Atkinson, FS *et al.* 2008, Foster-Powell, K *et al.* 2002) and from additional publications (Chen, YJ *et al.* 2010, Kim, EK *et al.* 2009, Kim, HY *et al.* 2007, Murakami, K *et al.* 2008, Murakami, K *et al.* 2006). For foods without a specific published GI value, we matched a food with similar energy and carbohydrate content and assigned that value. The GI values of foods with lower carbohydrate content were assigned a value of zero. DGI was calculated by multiplying the percentage contribution of each food to the amount of consumed carbohydrates by the food's GI value, and this value was then summed for all food items. DGL was calculated by multiplying the amount of carbohydrates consumed from each food by the food's GI value, and this value was then summed for all food items (dividing by 100) (Foster-Powell, K *et al.* 2002).

Assessment of anthropometric and biochemical variables

Anthropometric and biochemical variables were measured in all subjects. Height and weight were measured in subjects while wearing light clothing and no shoes using an automatic height and weight scale (BSM330, Biospace, Seoul, South Korea) to the nearest 0.1 cm and 0.1 kg, respectively. BMI was calculated as weight (in kg) divided by height squared (in m²). Waist circumference was measured at the narrowest part of the waist over light clothing using a tape measure (Lim, S *et al.* 2011). Systolic and diastolic blood pressure was measured using an automatic sphygmomanometer (EASY X 800 R/L, Jawon Medical, Kungsan, South Korea) after subjects rested for 10 minutes in the sitting position.

Blood samples were collected from each subject after fasting for at least 8 hours and analyzed using an automatic analyzer (Toshiba 200 FR, Toshiba, Tokyo, Japan) in the clinical laboratory of Seoul National University Hospital. Blood glucose was measured using the oxidase method, triglycerides using enzymatic methods, and HDL-cholesterol using the elimination method.

Assessment of sociodemographic and lifestyle variables

Information on sociodemographic (e.g., sex, age, and education) and lifestyle variables (e.g., history of disease, medication use, smoking status, and physical activity) was collected through a combination of self-administered and interviewer-administered questionnaires. Education was categorized as elementary, secondary, and college or more. Smoking status was classified into three categories: current-, ex-, or non-smoker. Physical activity level was assessed based on how many days per week subjects exercised for 30 minutes or more over the previous 6 months.

Statistical analyses

All statistical analyses were performed using the SAS software, version 9.3 (SAS Institute, Cary, NC, USA). To identify clustering patterns of metabolic syndrome abnormalities, factor analysis with varimax rotation (PROC FACTOR and VARIMAX options in SAS) was conducted for six metabolic syndrome components, including waist circumference, systolic and diastolic blood pressure, blood glucose, triglycerides, and HDL-cholesterol. Because blood glucose, triglycerides, and HDL-cholesterol showed skewed distributions, these variables were included in the factor analysis after log transformation. To determine which patterns to retain, the eigenvalue, scree test, and interpretability were considered (Newby, PK and Tucker, KL 2004). The derived patterns were interpreted and named according to metabolic syndrome components with higher factor loadings ($\geq |0.4|$). Each subject had a pattern score for each identified pattern, and subjects were categorized by tertiles of pattern scores for each pattern.

Characteristics (e.g., sociodemographic, lifestyle, biochemical variables, and prevalence of metabolic syndrome and its components) and mean daily energy and nutrient intake across tertiles of clustering pattern scores were presented as means and SD for continuous variables and as percentages (%) for categorical variables. Characteristics and dietary factors across tertiles of pattern scores were compared using the general linear model for continuous variables and the Mantel-Haenszel chi-square test for categorical variables. Sex (men or women), age (continuous), BMI (continuous), smoking status (current-, ex-, or non-smoker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and total energy intake (continuous) were considered potential confounding variables and, thus, were adjusted

in all models. The *P*-values for the trends were obtained from the log transformed data of blood glucose, triglycerides, and HDL-cholesterol, but the means of these variables were presented as untransformed data. All statistical tests were two-sided and a *P*-value of < 0.05 represented statistical significance.

3. Results

General, biochemical, and dietary characteristics of the study subjects by sex

Table V - 1 shows general characteristics of the study subjects by sex. Women were more likely to be older, be less educated, and smoke less than men. The prevalence of metabolic syndrome was 27.3 % in men and 28.9 % in women. The most prevalent component of metabolic syndrome was elevated blood pressure in men (40.9 %) and elevated waist circumference in women (56.7 %). The prevalence of elevated waist circumference was significantly higher in women than in men. Biochemical characteristics of the study subjects by sex are presented in Table V - 2. Waist circumference was significantly higher in men than in women whereas total-, HDL-, and LDL-cholesterol concentrations were significantly higher in women than in men. Other biochemical variables were not different by sex. Dietary characteristics of the study subjects by sex are shown in Table V - 3. Men had higher intakes of total energy, alcohol (g, % energy), fat (g), and vitamin E than those in women. Women had a higher percentage of energy from carbohydrate than those in men (61.5 vs. 55.2 %).

Table V - 1. General characteristics of the study subjects by sex

	Total		Men		Women		<i>P</i> -value ^a
	(<i>n</i> = 141)		(<i>n</i> = 44)		(<i>n</i> = 97)		
Sex (<i>n</i>, %)							
Men	44	31.2					
Women	97	68.8					
Age (mean, <i>SD</i>)							
Years	57.3	9.7	53.7	11.6	59.0	8.2	0.0077
Education (<i>n</i>, %)							
Elementary	7	5.0	1	2.3	6	6.2	0.0511
Secondary	64	45.4	16	36.4	48	49.5	
College or more	70	49.7	27	61.4	43	44.3	
Smoking status (<i>n</i>, %)							
Current-smokers	15	10.6	13	29.6	2	2.1	< 0.0001
Ex-smokers	22	15.6	20	45.5	2	2.1	
Non-smoker	104	73.8	11	25.0	93	95.9	
Physical activity (<i>n</i>, %)							
Never or rarely	30	21.3	8	18.2	22	22.7	0.6158
1–2 days/week	26	18.4	12	27.3	14	14.4	
3–4 days/week	47	33.3	14	31.8	33	34.0	
≥ 5 days/week	38	27.0	10	22.7	28	28.9	
Metabolic syndrome (<i>n</i>, %)							
Elevated waist circumference	69	48.9	14	31.8	55	56.7	0.0068
Elevated triglycerides	45	31.9	15	34.1	30	30.9	0.7018
Reduced HDL-cholesterol	33	23.4	7	15.9	26	26.8	0.1995
Elevated fasting glucose	37	26.2	16	36.4	21	21.7	0.0973
Elevated blood pressure	48	34.0	18	40.9	30	30.9	0.2564
Metabolic syndrome	40	28.4	12	27.3	28	28.9	0.8458

^a *P*-value was obtained from the *t*-test for continuous variables and the chi-square test for categorical variables.

Table V - 2. Biochemical characteristics of the study subjects by sex

	Total		Men		Women		<i>P</i> -value ^a
	<i>(n</i> = 141)		<i>(n</i> = 44)		<i>(n</i> = 97)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Body mass index (kg/m ²)	24.5	2.6	25.2	2.4	24.1	2.7	0.1117
Waist circumference (cm)	83.1	7.2	86.8	6.9	81.3	6.7	0.0040
Systolic blood pressure (mmHg)	123.2	14.4	126.0	13.9	121.9	14.5	0.8651
Diastolic blood pressure (mmHg)	74.4	9.7	76.7	8.2	73.4	10.2	0.5298
Fasting blood insulin (μIU/mL) (<i>n</i> = 136)	7.3	4.3	7.6	4.0	7.2	4.4	0.2471
Fasting blood glucose (mg/dL)	95.0	12.6	98.6	14.4	93.3	11.3	0.2056
HOMA-IR ^b (<i>n</i> = 136)	1.7	1.1	1.9	1.0	1.7	1.1	0.2671
Total cholesterol (mg/dL)	220.4	35.5	204.7	33.4	227.5	34.3	0.0061
Triglycerides (mg/dL)	146.2	82.2	152.6	82.0	143.3	82.5	0.8109
HDL-cholesterol (mg/dL)	56.0	13.0	51.8	12.3	57.9	12.9	0.0419
LDL-cholesterol (mg/dL) (<i>n</i> = 140)	140.7	31.7	132.0	33.4	144.7	30.3	0.0360

^a *P*-value was obtained from the general linear model after adjustment for age, smoking status, and BMI.

^b Homeostasis model assessment of insulin resistance (HOMA-IR), a surrogate measure of IR, was calculated by the following formula; [fasting plasma glucose (mmol/L) × fasting plasma insulin (μIU/mL)] / 22.5.

Table V - 3. Dietary characteristics of the study subjects by sex

	Total (<i>n</i> = 141)		Men (<i>n</i> = 44)		Women (<i>n</i> = 97)		<i>P</i> -value ^a
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1626	420.0	1936	472.4	1486	305.6	0.0019
Energy from carbohydrate (%)	59.6	9.3	55.2	10.1	61.5	8.2	0.0357
Energy from fat (%)	21.0	6.2	20.3	6.0	21.3	6.3	0.2701
Energy from protein (%)	16.1	2.7	16.0	2.4	16.2	2.9	0.4801
Energy from alcohol (%)	3.4	7.5	8.5	11.1	1.1	3.1	0.0004
Nutrients							
Carbohydrate (g)	251.0	54.7	277.3	53.5	239.0	51.1	0.3325
Fat (g)	40.7	19.0	47.5	21.1	37.7	17.3	0.0162
Protein (g)	68.6	18.4	81.0	17.2	62.9	16.1	0.1676
Dietary fiber (g)	20.9	6.1	21.3	5.1	20.7	6.5	0.3992
Vitamin A (μg RE)	713.6	364.8	733.0	360.7	704.8	368.2	0.5698
Vitamin E (mg)	10.7	3.2	11.0	3.0	10.6	3.3	0.0321
Thiamin (mg)	1.0	0.3	1.1	0.3	0.9	0.3	0.6675
Riboflavin (mg)	1.1	0.3	1.2	0.3	1.1	0.3	0.2612
Niacin (mg)	14.1	5.0	17.1	5.4	12.8	4.2	0.8447
Vitamin C (mg)	87.4	40.7	78.2	30.2	91.5	44.1	0.2192
Calcium (mg)	528.5	198.2	514.2	180.6	535.0	206.3	0.2218
Phosphorus (mg)	1004	249.6	1080	233.7	969	249.9	0.2037
Sodium (mg)	3767	1183	4330	1043	3512	1159	0.3046
Potassium (mg)	2579	739.7	2646	612.6	2549	791.8	0.0647
Iron (mg)	14.6	5.4	15.3	3.8	14.4	6.0	0.5024
Cholesterol (mg)	255.9	147.7	297.0	173.8	237.2	131.0	0.2776
Alcohol (g)	10.7	25.7	29.0	39.1	2.4	7.5	0.0041
Dietary glycemic index	55.2	3.9	55.6	3.9	55.1	4.0	0.4141
Dietary glycemic load	139.7	34.0	154.6	32.6	132.9	32.6	0.5081

^a *P*-value was obtained from the general linear model after adjustment for age, smoking status, BMI, and total energy intake.

Three distinct clustering patterns of metabolic syndrome abnormalities

Table V - 4 shows the factor loading matrix for three distinct clustering patterns of metabolic syndrome abnormalities identified by factor analysis with six metabolic syndrome components. Three patterns accounted for 77.7 % of the total variance in the dataset. The first pattern was closely associated with systolic and diastolic blood pressure and was named the “high blood pressure” pattern. The second pattern was characterized by high factor loadings for waist circumference and triglycerides, but a lower factor loading for HDL-cholesterol and was named the “dyslipidemia” pattern. The first and second patterns accounted for 30.9 % and 29.4 % of the total variance, respectively. The third pattern, the “high blood glucose” pattern, was characterized by a high factor loading for fasting blood glucose and accounted for 17.4 % of the total variance.

Table V - 4. Factor loading matrix for three distinct clustering patterns of metabolic syndrome abnormalities^a

	Pattern 1: High blood pressure	Pattern 2: Dyslipidemia with abdominal obesity	Pattern 3: High blood glucose
Waist circumference	0.31	0.61	0.28
Systolic blood pressure	0.92	0.20	0.05
Diastolic blood pressure	0.95	0.08	0.01
Fasting blood glucose	0.02	0.09	0.98
Triglycerides	0.13	0.80	0.06
HDL-cholesterol	- 0.02	- 0.84	0.03
Variance explained (%)	30.9	29.4	17.4

^aThe patterns were identified by factor analysis with six metabolic syndrome abnormalities. Because fasting blood glucose, triglycerides, and HDL-cholesterol showed skewed distributions, factor analysis included these variables after log transformed.

Characteristics of the study subjects by tertiles of three pattern scores

Characteristics of the study subjects across tertiles of the three pattern scores are presented in Table V - 5. Subjects in the highest tertile of the dyslipidemia pattern scores tended to be men and have lower levels of physical activity than those in the lowest tertile. Subjects in the highest tertile of the high blood glucose pattern scores were more likely to be men and be current- or ex-smokers. All three pattern scores were positively associated with BMI and waist circumference. The high blood pressure pattern scores were positively associated with systolic and diastolic blood pressure, but they were not associated with other biochemical variables. Subjects in the highest tertile of the high blood pressure pattern scores had a higher prevalence of elevated blood pressure and metabolic syndrome compared with those in the lowest tertile. The dyslipidemia pattern scores were positively associated with triglycerides but inversely associated with HDL-cholesterol. The prevalence of metabolic syndrome and its components increased across tertiles of the dyslipidemia pattern scores except for the prevalence of elevated blood pressure. The high blood glucose pattern scores had significantly positive associations with blood glucose and HDL-cholesterol. Subjects in the highest tertile of the high blood glucose pattern scores had a higher prevalence of elevated blood glucose compared with those in the lowest tertile. The prevalence of metabolic syndrome in the study subjects was 28.4 %. The highest prevalence of metabolic syndrome was observed in the highest tertile of the dyslipidemia pattern scores (61.7 %), compared with those in the highest tertile of the high blood pressure pattern scores (44.7 %) or the high blood glucose pattern scores (40.4 %).

Table V - 5. Characteristics of the study subjects across tertiles of the three clustering pattern scores of metabolic syndrome abnormalities

	High blood pressure pattern			Dyslipidemia pattern			High blood glucose pattern		
	T1 (<i>n</i> = 47)	T3 (<i>n</i> = 47)	<i>P</i> for trend ^a	T1 (<i>n</i> = 47)	T3 (<i>n</i> = 47)	<i>P</i> for trend ^a	T1 (<i>n</i> = 47)	T3 (<i>n</i> = 47)	<i>P</i> for trend ^a
General characteristics									
Sex (%)									
Men	23.4	38.3	0.1205	21.3	46.8	0.0078	19.2	44.7	0.0078
Women	76.6	61.7		78.7	53.2		80.9	55.3	
Age ^b (mean, <i>SD</i>)									
Years	59.1, 8.3	56.1, 11.4	0.2592	57.5, 8.5	56.8, 10.7	0.6943	57.4, 9.1	56.9, 10.1	0.6286
Education (%)									
Elementary	6.4	6.4	0.8614	0.0	8.5	0.1625	4.3	6.4	0.6004
Secondary	46.8	44.7		40.4	40.4		53.2	42.6	
College or more	46.8	48.9		59.6	51.1		42.6	51.1	
Smoking status (%)									
Current-smoker	8.5	14.9	0.2180	6.4	14.9	0.0903	10.6	19.2	0.0209
Ex-smoker	10.6	14.9		12.8	19.2		8.5	23.4	
Non-smoker	80.9	70.2		80.9	66.0		80.9	57.5	
Physical activity ^c (%)									
Never or rarely	14.9	21.3	0.7774	12.8	31.9	0.0109	21.3	19.2	0.9249
1–2 days/week	23.4	14.9		17.0	14.9		12.8	19.2	
3–4 days/week	36.2	40.4		29.8	34.0		38.3	34.0	
≥ 5 days/week	25.5	23.4		40.4	19.2		27.7	27.7	
Biochemical variables^d (mean, <i>SD</i>)									
BMI ^d (kg/m ²)	23.7, 2.3	25.5, 2.8	0.0079	23.0, 1.9	25.7, 2.5	< 0.0001	23.9, 2.4	25.6, 2.8	0.0076
WC ^d (cm)	81.0, 7.3	86.1, 7.3	0.0043	77.7, 5.0	87.6, 6.0	< 0.0001	81.3, 6.7	86.5, 7.0	0.0070
SBP ^e (mmHg)	108.1, 7.2	138.6, 8.2	< 0.0001	120.1, 12.9	125.4, 14.9	0.8702	122.5, 13.5	125.3, 15.2	0.5000
DBP ^e (mmHg)	64.4, 4.7	85.1, 5.4	< 0.0001	73.9, 9.2	74.9, 10.3	0.2827	74.0, 9.2	75.4, 10.3	0.6804
FBG ^e (mg/dL)	95.2, 15.2	95.1, 10.8	0.3005	91.5, 8.7	96.6, 14.9	0.6427	84.1, 5.2	107.6, 12.5	< 0.0001
TG ^e (mg/dL)	139.1, 87.6	166.1, 90.7	0.5290	90.0, 24.0	221.8, 94.8	< 0.0001	157.1, 96.9	155.3, 78.1	0.5628
HDL-cholesterol ^e (mg/dL)	57.0, 14.1	53.8, 10.9	0.8868	68.4, 10.8	44.1, 6.3	< 0.0001	53.6, 12.4	55.9, 12.6	0.0167

Table V - 5. Characteristics of the study subjects across tertiles of the three clustering pattern scores of metabolic syndrome abnormalities (continued)

	High blood pressure pattern			Dyslipidemia pattern			High blood glucose pattern		
	T1 (n = 47)	T3 (n = 47)	P for trend ^a	T1 (n = 47)	T3 (n = 47)	P for trend ^a	T1 (n = 47)	T3 (n = 47)	P for trend ^a
Prevalence of MetS and its components (%)									
Elevated WC	44.7	53.2	0.4109	19.2	63.8	< 0.0001	51.1	57.5	0.5374
Elevated TG	29.8	40.4	0.2703	2.1	74.5	< 0.0001	31.9	36.2	0.6592
Reduced HDL-chol.	23.4	21.3	0.8082	2.1	55.3	< 0.0001	34.0	17.0	0.0521
Elevated FBG	23.4	25.5	0.8153	10.6	31.9	0.0195	0.0	76.6	< 0.0001
Elevated BP	0.0	91.5	< 0.0001	25.5	38.3	0.1931	31.9	38.3	0.5153
MetS	12.8	44.7	0.0006	2.1	61.7	< 0.0001	25.5	40.4	0.1105

T, tertiles of pattern scores; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TG, triglycerides; HDL-chol., high-density lipoprotein cholesterol; MetS, metabolic syndrome.

^a P for trend was obtained using the Mantel-Haenszel chi-square test for categorical variables and the general linear model for continuous variables.

^b P for trend was obtained using the general linear model after adjustment for sex (men or women).

^c Physical activity level was assessed based on how many days per week subjects exercised for 30 minutes or more over the previous 6 months.

^d P for trend was obtained using the general linear model after adjustment for sex (men or women), age (continuous), smoking status (current-, ex-, or non-smoker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and daily alcohol intake (continuous).

^e P for trend was obtained using the general linear model after adjustment for sex (men or women), age (continuous), BMI (continuous), smoking status (current-, ex-, or non-smoker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and daily alcohol intake (continuous). P for trend was obtained from the log transformed data of FBG, TG, and HDL-chol., but means of these variables were presented as untransformed data.

Associations between the three patterns of metabolic syndrome abnormalities and dietary factors

Mean daily energy and nutrient intake across tertiles of each pattern score are shown in Table V - 6, Table V - 7, and Table V - 8, respectively. After adjustment for confounding variables, the high blood pressure pattern scores were positively associated with higher alcohol intake (T1 vs. T3: 5.6 vs. 19.5 g, P for trend = 0.0455) but inversely associated with carbohydrate intake, such as total carbohydrates, percentage of energy from carbohydrates and DGI. In the dyslipidemia pattern, DGI and DGL significantly increased across tertiles of the scores (T1 vs. T3: 54.1 vs. 56.5, P for trend = 0.0026 for DGI; T1 vs. T3: 128.7 vs. 147.9, P for trend = 0.0257 for DGL). The high blood glucose pattern scores were positively associated with percentage of energy from alcohol intake (T1 vs. T3: 0.9 vs. 5.7 %, P for trend = 0.0380) but inversely associated with carbohydrate intake, including total carbohydrates, percentage of energy from carbohydrates, DGI, and DGL.

Table V - 6. Mean daily energy and nutrient intake across tertiles of the high blood pressure pattern scores

	High blood pressure pattern						<i>P</i> for trend ^a
	T1 (<i>n</i> = 47)		T2 (<i>n</i> = 47)		T3 (<i>n</i> = 47)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1567	368.4	1645	323.3	1666	539.6	0.9335
Energy from carbohydrate (%)	61.2	7.5	60.8	9.7	56.6	9.9	0.0324
Energy from fat (%)	20.8	6.0	20.7	6.6	21.4	6.1	0.5112
Energy from protein (%)	16.0	2.8	16.2	2.6	16.2	2.8	0.4836
Energy from alcohol (%)	2.0	6.3	2.3	4.6	5.8	10.1	0.0706
Nutrients							
Carbohydrate (g)	249.2	51.3	261.0	49.3	242.6	62.2	0.0377
Fat (g)	39.1	17.2	41.0	19.9	42.1	20.0	0.7123
Protein (g)	65.3	17.2	70.2	17.0	70.1	20.7	0.4924
Dietary fiber (g)	21.2	5.9	22.0	7.5	19.4	4.3	0.1642
Vitamin A (µg RE)	696.8	383.7	773.0	362.1	671.0	347.9	0.8089
Vitamin E (mg)	10.7	3.0	11.1	3.2	10.4	3.4	0.2131
Thiamin (mg)	0.9	0.3	1.0	0.3	1.0	0.3	0.7677
Riboflavin (mg)	1.1	0.3	1.1	0.2	1.1	0.3	0.6889
Niacin (mg)	13.1	4.0	14.0	4.2	15.3	6.3	0.0820
Vitamin C (mg)	91.8	42.9	88.8	39.5	81.4	39.6	0.4997
Calcium (mg)	526.8	210.1	540.8	180.4	517.9	206.5	0.7837
Phosphorus (mg)	974.2	251.8	1027	236.1	1010	262.5	0.6729
Sodium (mg)	3802	1242	3744	1168	3756	1162	0.4091
Potassium (mg)	2586	750.9	2668	798.9	2483	667.7	0.5845
Iron (mg)	14.4	4.1	14.8	4.3	14.8	7.3	0.9275
Cholesterol (mg)	230.4	112.9	256.1	133.0	281.1	186.1	0.3145
Alcohol (g)	5.6	17.7	6.9	15.0	19.5	36.8	0.0455
Dietary glycemic index ^b	55.8	3.7	55.5	3.9	54.5	4.2	0.0582
Dietary glycemic load ^b	139.5	31.2	146.2	32.1	133.3	37.8	0.0281

^a *P* for trend was obtained using the general linear model after adjustment for sex (men or women), age (continuous), BMI (continuous), smoking status (current-, ex-, or non-smoker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and total energy intake (continuous).

^b Average dietary glycemic index and dietary glycemic load based on a glucose standard were calculated for each subject using a table of glycemic index values for common Korean foods.

Table V - 7. Mean daily energy and nutrient intake across tertiles of the dyslipidemia pattern scores

	Dyslipidemia pattern						<i>P</i> for trend ^a
	T1 (<i>n</i> = 47)		T2 (<i>n</i> = 47)		T3 (<i>n</i> = 47)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1519	334.7	1666	395.6	1694	500.4	0.1404
Energy from carbohydrate (%)	59.7	9.3	59.4	9.5	59.6	9.3	0.1790
Energy from fat (%)	21.3	6.8	21.5	5.6	20.1	6.3	0.4136
Energy from protein (%)	16.0	2.8	16.0	2.7	16.3	2.7	0.4261
Energy from alcohol (%)	2.9	6.5	3.1	6.9	4.1	9.0	0.1948
Nutrients							
Carbohydrate (g)	236.4	46.7	256.2	56.6	260.3	58.2	0.1946
Fat (g)	39.1	19.8	42.2	15.6	41.0	21.5	0.4617
Protein (g)	64.0	15.8	70.0	19.8	71.7	18.9	0.5986
Dietary fiber (g)	20.4	6.3	21.8	7.2	20.4	4.6	0.6846
Vitamin A (µg RE)	750.3	397.3	706.8	378.8	683.7	318.5	0.4301
Vitamin E (mg)	10.2	2.6	11.5	3.9	10.5	2.8	0.5729
Thiamin (mg)	0.9	0.3	1.0	0.3	1.0	0.3	0.8137
Riboflavin (mg)	1.1	0.3	1.2	0.3	1.0	0.3	0.1162
Niacin (mg)	13.2	4.0	14.8	5.1	14.4	5.7	0.1704
Vitamin C (mg)	90.7	36.0	95.2	46.5	76.2	37.0	0.3276
Calcium (mg)	514.1	178.8	568.9	229.9	502.5	179.5	0.5816
Phosphorus (mg)	967	222.5	1054	275.8	990	244.5	0.2906
Sodium (mg)	3544	962.7	3709	1343	4049	1181	0.3629
Potassium (mg)	2625	599.9	2709	982.2	2403	538.3	0.1341
Iron (mg)	13.2	3.2	15.6	7.5	15.2	4.4	0.4783
Cholesterol (mg)	218.1	97.7	270.8	157.8	278.7	172.4	0.3117
Alcohol (g)	8.1	18.3	10.3	26.0	13.6	31.4	0.1806
Dietary glycemic index ^b	54.1	3.9	55.2	4.1	56.5	3.5	0.0026
Dietary glycemic load ^b	128.7	27.7	142.4	35.6	147.9	35.9	0.0257

^a *P* for trend was obtained using the general linear model after adjustment for sex (men or women), age (continuous), BMI (continuous), smoking status (current-, ex-, or non-smoker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and total energy intake (continuous).

^b Average dietary glycemic index and dietary glycemic load based on a glucose standard were calculated for each subject using a table of glycemic index values for common Korean foods.

Table V - 8. Mean daily energy and nutrient intake across tertiles of the high blood glucose pattern scores

	High blood glucose pattern						<i>P</i> for trend ^a
	T1 (<i>n</i> = 47)		T2 (<i>n</i> = 47)		T3 (<i>n</i> = 47)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1549	301.6	1639	457.9	1691	475.1	0.9869
Energy from carbohydrate (%)	63.0	9.1	59.2	8.2	56.6	9.6	0.0040
Energy from fat (%)	20.4	6.1	21.1	6.5	21.4	6.0	0.2536
Energy from protein (%)	15.8	3.2	16.1	2.4	16.3	2.6	0.2380
Energy from alcohol (%)	0.9	2.6	3.6	8.1	5.7	9.3	0.0380
Nutrients							
Carbohydrate (g)	254.6	55.1	248.8	48.8	249.4	60.5	0.0122
Fat (g)	37.2	14.8	41.3	21.1	43.7	20.4	0.1440
Protein (g)	64.1	17.5	68.9	18.0	72.6	19.1	0.1634
Dietary fiber (g)	20.6	5.8	20.5	5.0	21.5	7.3	0.5639
Vitamin A (µg RE)	669.9	341.6	751.7	411.3	719.1	340.4	0.4509
Vitamin E (mg)	10.4	3.0	10.7	3.4	11.1	3.2	0.4592
Thiamin (mg)	0.9	0.3	1.0	0.3	1.0	0.3	0.9929
Riboflavin (mg)	1.0	0.3	1.1	0.3	1.1	0.3	0.4435
Niacin (mg)	12.9	3.9	14.3	5.3	15.2	5.5	0.0993
Vitamin C (mg)	98.1	48.2	82.3	35.6	81.7	35.6	0.2087
Calcium (mg)	495.8	159.0	554.2	238.1	535.5	189.1	0.2631
Phosphorus (mg)	943	205.1	1047	281.8	1022	249.2	0.2251
Sodium (mg)	3662	1116	3595	1071	4046	1321	0.4773
Potassium (mg)	2616	858.3	2578	690.5	2543	670.2	0.6710
Iron (mg)	15.0	7.0	14.3	4.0	14.6	4.8	0.3872
Cholesterol (mg)	231.2	140.8	261.7	123.8	274.7	173.8	0.5615
Alcohol (g)	2.5	7.9	12.1	29.4	17.4	31.1	0.0912
Dietary glycemic index ^b	56.4	3.3	55.0	3.9	54.4	4.3	0.0082
Dietary glycemic load ^b	144.8	35.0	137.5	29.4	136.7	37.2	0.0026

^a *P* for trend was obtained using the general linear model after adjustment for sex (men or women), age (continuous), BMI (continuous), smoking status (current-, ex-, or non-smoker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and total energy intake (continuous).

^b Average dietary glycemic index and dietary glycemic load based on a glucose standard were calculated for each subject using a table of glycemic index values for common Korean foods.

4. Discussion and conclusions

In this study, three distinct clustering patterns of metabolic syndrome abnormalities were identified and differentially associated with dietary factors, thus supporting the study hypothesis. The high blood pressure pattern scores were strongly associated with high alcohol intake. The dyslipidemia pattern was positively associated with DGI and DGL, while the other two patterns were inversely associated with carbohydrate intake.

Previous studies have consistently shown a relationship between high alcohol intake and elevated blood pressure in Korean adult populations (Baik, I and Shin, C 2008, Yoon, YS *et al.* 2004). In particular, a positive association between alcohol intake and blood pressure was frequently observed in Korean adult men (Lee, MY *et al.* 2010, Sung, KC *et al.* 2007). According to a meta-analysis of 12 cohort studies, gender differences and a dose-response linear relationship between alcohol intake and high blood pressure were observed (Taylor, B *et al.* 2009). This study also reported that Asian populations have a higher risk of hypertension with alcohol intake compared with non-Asian populations. Conversely, no association has been established between alcohol intake and high blood pressure in prospective and cross-sectional studies of the US populations (Freiberg, MS *et al.* 2004, Stoutenberg, M *et al.* 2013). Based on our study results, the high blood pressure pattern was not significantly associated with either dyslipidemia or glucose abnormalities. Although the three patterns shared the same traits of elevated BMI and waist circumference, each pattern was characterized by their own dominant components, suggesting that the subjects with metabolic

syndrome in the study developed the metabolic abnormalities by different underlying traits.

Carbohydrate intake was differentially associated with the three clustering patterns. The dyslipidemia pattern was significantly associated with high DGI and DGL, while the other two patterns were associated with low carbohydrate intake. High carbohydrate intake, including DGI or DGL, was consistently related to elevated triglycerides and reduced HDL-cholesterol (Choi, H *et al.* 2012, McKeown, NM *et al.* 2009, Murakami, K *et al.* 2006). The Asian diet, which is usually rice-based and high in carbohydrates, was suggested to cause abdominal obesity and lead to metabolic syndrome (Cheung, BM 2005).

However, in this study, dominant traits such as high blood pressure or high blood glucose were inversely associated with carbohydrate intake. We could not explain these findings clearly, particularly for glucose abnormalities, but assumed that people with high blood pressure as a dominant trait were more likely to consume alcohol, which had a greater effect than carbohydrate intake. This was in agreement with a previous study from the NHANES III reporting that systolic blood pressure was inversely associated with carbohydrate intake (as a percentage of energy) in the US adult men (Yang, EJ *et al.* 2003).

Current epidemiologic and intervention studies have shown that consumption of different types of fatty acids (Ebbesson, SO *et al.* 2005, Melanson, EL *et al.* 2009, Noel, SE *et al.* 2010) and antioxidants (Babio, N *et al.* 2009, Li, YR *et al.* 2013, Lopez-Legarrea, P *et al.* 2013, Puchau, B *et al.* 2010) was associated with metabolic syndrome. Antioxidant nutrients and antioxidant-rich foods, such as vegetables, fruits, legumes, and nuts, have been suggested for the prevention and management of

metabolic syndrome because of their potential beneficial effects against oxidative stress related to obesity, hypertension, dyslipidemia, and type 2 diabetes (Abete, I *et al.* 2011). Higher intake of monounsaturated and polyunsaturated fatty acids may reduce risks of inflammation-related diseases, such as obesity, insulin resistance, dyslipidemia, and metabolic syndrome, by regulating insulin sensitivity, blood lipid indicators, and blood pressure. Conversely, saturated fatty acids are positively associated with concentrations of inflammation markers in plasma and the risk of metabolic syndrome. However, in Korean population, investigation of associations between the intake of these dietary components and metabolic syndrome is limited due to the lack of a complete nutrient database, including fatty acids and antioxidants for Korean foods. Therefore, a Korean food composition database, including more specific nutrients, is necessary for future studies.

There is considerable debate over the concept of metabolic syndrome and its usefulness in clinical settings (Simmons, RK *et al.* 2010). The syndrome involves clustering of metabolic abnormalities, and insulin resistance is the underlying common trait. However, several dominant underlying risk factors that vary among different populations may exist. We found distinct clustering patterns in metabolic syndrome abnormalities, and each pattern was associated differently with dietary factors, with no clear explanation for the underlying mechanism. However, this study implied that high carbohydrate intake characterized by a rice-based diet in the Asian population was associated more with dyslipidemia rather than elevated blood glucose or blood pressure abnormalities. This result can be due to dietary practices of the Korean population that differ from the Western population, causing differences in the susceptibility and mechanism of metabolic diseases between Western and Korean populations. In this

study, mechanistic explanations for each clustering pattern of metabolic syndrome abnormalities were not determined; however, this work can be useful in future studies to explore potential mechanisms.

This study has several limitations. First, our subjects were recruited from a single hospital, which may not be applicable to other study populations. However, our study participants were enrolled mainly through the Family Medicine Division or the Health Examination Center, and we excluded people who were taking medication or had a serious illness. Second, the calculation of DGI and DGL in this study was based on values from the International Tables (Atkinson, FS *et al.* 2008, Foster-Powell, K *et al.* 2002), which were mainly developed for Western countries. It was also limited to an examination of the effects of carbohydrates on metabolic syndrome abnormalities. Finally, the cross-sectional nature of this study does not allow a causal inference. However, this study used multiple dietary recalls and closely estimated the usual dietary intake of this population. To our knowledge, this is the first observational study examining associations between different aspects of metabolic syndrome abnormalities and dietary factors in the Korean population.

In conclusion, metabolic syndrome abnormalities have three distinct clustering patterns independently associated with dietary factors in Korean adults. In particular, carbohydrate intake was differentially associated with clustering patterns of metabolic syndrome abnormalities. The results from this study may provide specific nutritional strategies addressing multiple traits of metabolic syndrome. Additionally, investigation of dietary factors associated with metabolic syndrome abnormalities is an important aspect of public health for prevention and management of chronic diseases during the early stages. To better understand the role of diet in the etiology of metabolic

syndrome, further investigation into the potential mechanisms of multiple underlying risk factors in the Korean population is warranted.

STUDY 8. Dyslipidemia patterns are associated with dietary factors in Korean adults

1. Introduction

Dyslipidemia is abnormal lipid metabolism characterized by elevated levels of total cholesterol, triglycerides, and LDL-cholesterol and by reduced level of HDL-cholesterol. Dyslipidemia is also a component of metabolic syndrome (Grundy, SM *et al.* 2005) and a strong predictor of cardiovascular diseases (Kostis, JB 2007, Ridker, PM *et al.* 2002). The prevalence of dyslipidemia in Korean adults in 2012 was 59 % (Roh, E *et al.* 2013), higher than that in Chinese adults (Cai, L *et al.* 2012). Among the lipid abnormalities, elevated triglycerides and low HDL-cholesterol were the most prevalent abnormalities in Korean adults, more prevalent than in US adults (Cohen, JD *et al.* 2010).

The underlying risk factors suggested for dyslipidemia include age, genetics, diet, smoking, physical activity, and stress (Haskell, WL 2003). Among these factors, diet has been targeted in the prevention and improvement of dyslipidemia because it is modifiable (NCEP 2002). Although the effects of diet on dyslipidemia are not fully understood, investigation of the dietary factors associated with dyslipidemia is important to prevent chronic diseases, such as cardiovascular diseases and type 2 diabetes.

Earlier studies in Western countries focused on the association between intakes of dietary fat and cholesterol and blood lipids (Brown, L *et al.* 1999, Clarke, R *et al.* 1997, Grundy, SM and Denke, MA 1990, Hopkins, PN 1992). Recent epidemiologic studies in Western countries reported that high consumption of fruits and vegetables was associated with a reduced LDL-cholesterol (Djousse, L *et al.* 2004, Fornes, NS *et al.* 2000), and increased consumption of milk and dairy products showed protective effects on concentrations of triglycerides and HDL-cholesterol (Merino, J *et al.* 2013, Pereira, MA *et al.* 2002). Several intervention studies also support the favorable effects on blood lipids of diets high in fruits, vegetables, dietary fiber, calcium, and potassium, but low in saturated fats and cholesterol (Appel, LJ *et al.* 2005, Obarzanek, E *et al.* 2001).

In contrast to Western diets, Asian diets are rice-based with plenty of plant foods. They are high in carbohydrates and low in fat. Several studies in Asian populations reported that low HDL-cholesterol concentrations were consistently associated with high carbohydrate intake (Choi, H *et al.* 2012, Kim, K *et al.* 2008, Song, Y and Joung, H 2012), whereas elevated triglycerides concentrations were related to lower consumption of milk and dairy products (Kim, J 2013, Lee, CJ and Joung, H 2012). In addition, high intake of polyunsaturated fatty acids was inversely associated with total cholesterol and LDL-cholesterol (Guo, Z *et al.* 2010), but positively associated with HDL-cholesterol (Okuda, N *et al.* 2005). However, only limited data are available on the associations between dietary factors and overall lipid profiles.

As blood lipid variables are highly correlated with each other, factor analysis has been used to identify inter-correlations among biochemical variables and to provide clustering patterns for these variables (Meigs, JB 2000). The aim of this study was to

identify dyslipidemia patterns using factor analysis based on four lipid indicators, triglycerides, total cholesterol, LDL-cholesterol, and HDL-cholesterol, and to examine dietary factors associated with the dyslipidemia patterns in urban Korean adults using repeated measurements of biochemical and dietary variables.

2. Methods

Study design and subjects

Study subjects were recruited by the Health Examination Center or the Family Medicine Division of Seoul National University Hospital in the Seoul metropolitan area in South Korea. Individuals were considered eligible if they were 20 years of age or older and were disease free at the time of study enrollment. A total of 277 subjects enrolled in the study between September 2010 and December 2012, of whom 160 subjects revisited the hospital two more times at intervals of 3 to 4 months during the study period. For each subject, anthropometric, biochemical, and dietary assessments were conducted three times at each visit, and a questionnaire for sociodemographic and lifestyle information was administered once at study enrollment (Figure V - 1). Among the 160 eligible subjects, subjects who had incomplete data regarding anthropometric or biochemical variables ($n = 11$) or who had taken hypolipidemic medications ($n = 11$) were excluded. A total of 138 subjects (45 men and 93 women) were included in the present cross-sectional analyses. The study protocol was approved by the

Institutional Review Board at Seoul National University Hospital, and written informed consent was obtained from each subject.

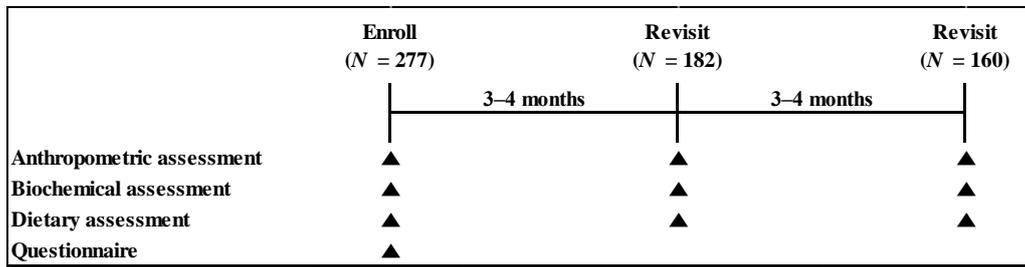


Figure V - 1. Study design

Assessment of dietary factors

Dietary intake data were obtained by 24-hour recall. Three days of dietary intake data were obtained through on-site interviews from all subjects in this study. Following a multiple three-step procedure (Kang, H *et al.* 2009), trained dietitians interviewed the subjects when they visited the hospital regarding their dietary intake over the previous 24-hour period. Briefly, in the first step, the subject quickly reported food items eaten the previous day. The subject was then questioned in detail about the food reported in the first step. Lastly, the subject was asked about any forgotten food items.

The mean daily intakes of energy and nutrients for each subject were calculated from the 3-day dietary intake data using the Diet Evaluation System (Human Nutrition Lab, Seoul National University, Seoul, South Korea), a web-based computer program for dietary assessment (Jung, HJ *et al.* 2013). Mean daily alcohol intake was estimated in grams per day for each subject based on their dietary intake data. We evaluated the specific alcohol content of each type of alcoholic beverage according to the Seventh Korean food composition table (RDA 2006).

Average DGI and DGL based on a glucose standard were calculated for each subject using a table of GI values for common Korean foods established in a previous study (Song, S *et al.* 2012). The GI values in this table were obtained from international tables of GI and GL values (Atkinson, FS *et al.* 2008, Foster-Powell, K *et al.* 2002) and from additional studies conducted in Asian populations (Chen, YJ *et al.* 2010, Kim, EK *et al.* 2009, Kim, HY *et al.* 2007, Murakami, K *et al.* 2008, Murakami, K *et al.* 2006). For foods without a specific published GI value, they were matched with a food with similar energy and carbohydrate contents and assigned that value. The GI values of foods with low carbohydrate contents were assigned a value of zero. The

DGI was calculated by multiplying the percentage contribution of each food to the amount of carbohydrates consumed by the food's GI value, and the values for all food items were then summed. The DGL was calculated by multiplying the amount of carbohydrates consumed from each food by the food's GI value, and the values for all food items were then summed (dividing by 100) (Foster-Powell, K *et al.* 2002).

Mean daily intakes of six food groups (grains; meat, fish, eggs, and beans; vegetables; fruits; milk and dairy products; and fats, oils, and sugars) were evaluated in servings per day for each subject based on their dietary intake data. The total amount of foods (in grams) that each subject consumed, as indicated by their dietary intake data, was converted to number of servings using a food group database for 4,370 common Korean foods (Song, S *et al.* 2014), which provided numbers of servings per 100 grams for each food item for the six food groups.

Assessment of anthropometric and biochemical variables

Anthropometric and biochemical variables were measured three times when the subject visited the hospital, and average values of these variables were included in the data analyses. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively, in subjects while wearing light clothing and no shoes using an automatic height and weight scale (BSM330, Biospace, Seoul, South Korea). BMI was calculated as weight (kg) divided by height squared (m²). Waist circumference was measured at the narrowest part of the waist over light clothing using a tape measure (Lim, S *et al.* 2011). Systolic and diastolic blood pressure was measured using an automatic sphygmomanometer (EASY X 800 R/L, Jawon Medical, Kungsan, South Korea) after subjects had rested for 10 minutes in the sitting position.

Blood samples were collected from each subject after fasting for at least 8 hours and were analyzed using an automatic analyzer (Toshiba 200 FR, Toshiba, Tokyo, Japan) in the clinical laboratory of Seoul National University Hospital. Blood glucose was measured using the oxidase method; triglycerides, total cholesterol, and LDL-cholesterol were measured using enzymatic methods; and HDL-cholesterol was measured using the elimination method.

Assessment of sociodemographic and lifestyle variables

Information on sociodemographic (e.g., sex, age, and education) and lifestyle variables (e.g., history of disease, medication use, smoking status, drinking status and physical activity) was collected through a combination of self-administered and interviewer-administered questionnaires. Education was categorized as elementary school, secondary school, and college or more. Smoking status and drinking status were classified into three categories: current, ex, or non. Physical activity was assessed based on how many days per week subjects had exercised for 30 minutes or more over the previous 6 months.

Statistical analyses

All statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, NC, USA). Factor analysis with varimax rotation (PROC FACTOR and VARIMAX options in SAS) was used to identify dyslipidemia patterns based on total cholesterol, LDL-cholesterol, triglyceride, and HDL-cholesterol. Because triglycerides and HDL-cholesterol showed skewed distributions, these variables were included in factor analysis after log transformation. The eigenvalue, scree test, and interpretability

were used to determine the patterns to retain (Newby, PK and Tucker, KL 2004). The derived patterns were interpreted and named according to the lipid indicators with high factor loadings ($\geq |0.3|$). Each subject had a pattern score for each identified pattern, and subjects were categorized by tertiles of pattern scores for each pattern.

Characteristics (e.g., sociodemographic, lifestyle, and biochemical variables) across tertiles of pattern scores were presented as adjusted means and SEM for continuous variables and as percentages for categorical variables. Dietary factors (e.g., mean daily intake of nutrients and food groups) across tertiles of pattern scores were presented as means and SD. Characteristics and dietary factors across tertiles of pattern scores were compared using the GLM (for continuous variables) and the Mantel-Haenszel chi-square test (for categorical variables). Sex (men or women), age (continuous), BMI (continuous), smoking status (current-, ex-, or non-smoker), drinking status (current-, ex-, or non-drinker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and total energy intake (continuous) were considered to be potential confounding variables and were adjusted for in all models. All statistical tests were two-sided and $P < 0.05$ represented statistical significance.

3. Results

Two dyslipidemia pattern

In the subjects of this study, the prevalence of dyslipidemia was relatively high. The prevalences of high total cholesterol and high LDL-cholesterol were significantly higher in women than in men (Table V - 9). Table V - 10 shows the factor loading matrix for two dyslipidemia pattern identified by factor analysis using the four lipid indicators. The first pattern was characterized by high positive loadings for total cholesterol and LDL-cholesterol, referred to as the TC & LDLC pattern. The second pattern was positively associated with triglycerides and inversely associated with HDL-cholesterol, referred to as the TG & HDLC pattern. The TC & LDLC pattern accounted for 47.7 % of the total variance in the dataset and the TG & HDLC pattern for 38.2 %.

Table V - 9. Prevalence of dyslipidemia of the study subjects by sex

	Total		Men		Women		<i>P</i> -value ^a
	<i>(n</i> = 138)		<i>(n</i> = 45)		<i>(n</i> = 93)		
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Triglycerides							
Borderline high (\geq 150 mg/dL)	48	34.8	20	44.4	28	30.1	0.1271
High (\geq 200 mg/dL)	20	14.5	10	22.2	10	10.8	0.1193
Total cholesterol							
Borderline high (\geq 200 mg/dL)	108	78.3	26	57.8	82	88.2	0.0001
High (\geq 240 mg/dL)	38	27.5	7	15.6	31	33.3	0.0411
LDL-cholesterol							
Borderline high (\geq 130 mg/dL)	98	71.0	25	55.6	73	78.5	0.0087
High (\geq 160 mg/dL)	38	27.5	9	20.0	29	31.2	0.2230
HDL-cholesterol							
Low (< 40 mg/dL in men, < 50 mg/dL in women)	27	19.6	8	17.8	19	20.4	0.8209

^a *P*-value was obtained using the chi-square test to test a difference in prevalences of dyslipidemia between men and women.

Table V - 10. Factor loading matrix for lipid indicators^a

	Pattern 1: The TC & LDLC	Pattern 2: The TG & HDLC
Triglycerides (TG)	0.12	0.89
HDL-cholesterol (HDLC)	0.28	-0.85
Total-cholesterol (TC)	0.97	-0.11
LDL-cholesterol (LDLC)	0.93	-0.02
Variance explained (%)	47.7	38.2

^a The patterns were identified by factor analysis with the four lipid indicators. Because triglycerides and HDL-cholesterol showed skewed distributions, factor analysis included these variables after log transformed.

Characteristics of the study subjects by tertiles of dyslipidemia pattern scores

Characteristics (e.g., sociodemographic, lifestyle, and biochemical variables) for the study subjects across tertiles of dyslipidemia pattern scores are presented in Table V - 11. Subjects in the highest tertile of the TC & LDLC pattern score tended to be women and to have higher concentrations of triglycerides, total cholesterol, and LDL-cholesterol than those in the lowest tertile. Subjects in the highest tertile of the TG & HDLC pattern score were more likely to be men and to have lower levels of physical activity than those in the lowest tertile. The TG & HDLC pattern scores were positively associated with BMI, waist circumference, fasting blood glucose, and triglycerides and inversely associated with HDL-cholesterol.

Table V - 11. Characteristics of the study subjects across tertiles of the pattern scores

	The TC & LDLC pattern				The TG & HDLC pattern			
	T1 (n = 46)	T2 (n = 46)	T3 (n = 46)	P for trend ^a	T1 (n = 46)	T2 (n = 46)	T3 (n = 46)	P for trend ^a
	%	%	%		%	%	%	
Sex								
Men	50.0	23.9	23.9	0.0078	21.7	30.4	45.7	0.0148
Women	50.0	76.1	76.1		78.3	69.6	54.4	
Education								
Elementary	8.7	2.2	4.4	0.2121	2.2	6.5	6.5	0.4759
Secondary	54.4	50.0	47.8		45.7	60.9	45.7	
College or more	37.0	47.8	47.8		52.2	32.6	47.8	
Smoking status								
Non-smoker	63.0	80.4	80.4	0.2060	80.4	76.1	67.4	0.0821
Ex-smokers	23.9	15.2	6.5		15.2	13.0	17.4	
Current-smokers	13.0	4.4	13.0		4.4	10.9	15.2	
Drinking status								
Non-drinker	47.8	52.2	65.2	0.0508	60.9	47.8	56.5	0.5150
Ex-drinker	2.2	8.7	6.5		8.7	4.4	4.4	
Current-drinker	50.0	39.1	28.3		30.4	47.8	39.1	
Physical activity								
Never or rarely	26.1	23.9	17.4	0.1318	8.7	30.4	28.3	0.0480
1–2 days/week	26.1	10.9	17.4		21.7	19.6	13.0	
3–4 days/week	28.3	32.6	37.0		32.6	28.3	37.0	
≥ 5 days/week	19.6	32.6	28.3		37.0	21.7	21.7	

Table V - 11. Characteristics of the study subjects across tertiles of the pattern scores (continued)

	The TC & LDLC pattern							The TG & HDLC pattern						
	T1 (n = 46)		T2 (n = 46)		T3 (n = 46)		P for trend ^a	T1 (n = 46)		T2 (n = 46)		T3 (n = 46)		P for trend ^a
	Mean ^b	SE ^b	Mean	SE	Mean	SE		Mean	SE	Mean	SE	Mean	SE	
Age (years)	57.1	8.7	56.7	9.2	57.9	10.2	0.7804	58.3	7.7	56.9	10.1	56.6	10.2	0.7799
BMI ^c (kg/m ²)	25.0	0.4	24.7	0.4	24.8	0.4	0.9105	23.9	0.4	24.8	0.4	25.6	0.4	0.0071
Waist circumference ^c (cm)	84.5	0.9	85.2	1.0	84.3	1.0	0.9364	81.6	0.9	84.7	0.9	87.1	0.9	0.0003
Systolic blood pressure ^d (mmHg)	124.9	1.7	126.1	1.8	126.1	1.8	0.4433	123.2	1.8	126.4	1.7	127.0	1.7	0.6880
Diastolic blood pressure ^d (mmHg)	74.5	1.2	75.6	1.2	76.0	1.2	0.2390	73.8	1.2	75.8	1.2	76.1	1.2	0.5839
Fasting blood glucose ^d (mg/dL)	99.8	1.5	93.2	1.6	95.7	1.6	0.2593	93.4	1.6	95.2	1.6	100.2	1.5	0.0154
TG ^d (mg/dL)	133.0	8.7	137.1	9.3	165.4	9.2	0.0066	91.3	5.9	124.6	5.7	206.0	5.6	< 0.0001
TC ^d (mg/dL)	190.4	2.0	220.4	2.2	248.1	2.1	< 0.0001	221.2	4.2	212.1	4.1	219.4	4.0	0.9756
HDLC ^d (mg/dL)	53.2	1.8	57.4	1.9	55.2	1.8	0.7545	67.6	1.3	53.4	1.2	46.3	1.2	< 0.0001
LDLC ^d (mg/dL)	115.4	2.1	140.9	2.3	167.0	2.2	< 0.0001	137.7	4.0	141.3	3.9	138.8	3.8	0.8089

HDLC, high-density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

^a P for trend was obtained from the Mantel-Haenszel chi-square test for categorical variables and the general linear model (GLM) for continuous variables.

^b Adjusted mean and standard error (SE) (all such values) were obtained from the GLM after adjustment for sex (men or women) and age (continuous).

^c P for trend was obtained from the GLM after adjustment for sex (men or women), age (continuous), education (elementary, secondary, or college or more), smoking status (current-, ex-, or non-smoker), drinking status (current-, ex-, or non-drinker), and physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week).

^d P for trend was obtained from the GLM after adjustment for sex (men or women), age (continuous), education (elementary, secondary, or college or more), smoking status (current-, ex-, or non-smoker), drinking status (current-, ex-, or non-drinker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), and BMI (continuous).

Associations between dyslipidemia patterns and dietary factors

Mean daily intakes of nutrients and food groups across pattern score tertiles are shown in Table V - 12 and Table V - 13, respectively. After adjustment for potential confounding variables, the TC & LDLC pattern score was positively associated with intakes of dietary fat and cholesterol but inversely associated with intakes of total carbohydrate, dietary fiber, iron, and vegetables (T1 vs. T3: 8.1 vs. 6.2 servings, *P* for trend = 0.0013 for vegetables). The TG & HDLC pattern score was inversely associated with intakes of calcium, potassium, milk and dairy products (T1 vs. T3: 1.1 vs. 0.7 servings, *P* for trend = 0.0140 for milk and dairy products) but positively associated with phosphorus intake.

Table V - 12. Mean daily intake of nutrients and food groups across tertiles of the high total- and LDL-cholesterol pattern scores

	The TC & LDLC pattern						<i>P</i> for trend ^a
	T1 (<i>n</i> = 46)		T2 (<i>n</i> = 46)		T3 (<i>n</i> = 46)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1747	334.9	1676	494.0	1598	349.5	0.5842
% Energy from carbohydrate	59.7	9.0	59.2	9.6	59.1	7.5	0.1372
% Energy from fat	20.1	4.9	21.7	6.0	22.6	5.3	0.0152
% Energy from protein	16.1	2.5	15.8	2.4	16.5	2.0	0.2946
% Energy from alcohol	4.1	7.5	3.4	7.0	1.7	4.4	0.4797
Nutrients							
Carbohydrate (g)	271.9	45.1	253.8	52.9	243.3	40.8	0.0418
Fat (g)	42.0	15.6	44.2	23.1	42.8	15.7	0.0158
Protein (g)	74.7	20.1	70.1	28.2	69.3	18.4	0.4305
Dietary fiber (g)	23.7	5.7	22.4	6.1	19.2	4.4	< 0.0001
Vitamin A (µg RE)	783.8	350.8	738.4	342.6	689.6	302.2	0.1079
Vitamin E (mg)	11.4	2.7	11.1	3.0	10.1	2.8	0.0282
Thiamin (mg)	1.1	0.3	1.0	0.3	1.0	0.3	0.2567
Riboflavin (mg)	1.2	0.5	1.1	0.5	1.1	0.3	0.9912
Niacin (mg)	15.8	5.3	14.6	6.3	14.3	4.7	0.8665
Vitamin C (mg)	103.4	47.1	94.8	35.6	98.5	46.4	0.4032
Calcium (mg)	561.3	161.0	516.5	190.0	526.4	191.4	0.3038
Phosphorus (mg)	1088	236.5	1017	346.2	995	241.9	0.4185
Sodium (mg)	4188	1007	3923	1334	3571	1108	0.1014
Potassium (mg)	2782	578.6	2717	852.6	2573	609.4	0.1676
Iron (mg)	16.4	3.8	14.9	5.3	13.7	3.6	0.0038
Cholesterol (mg)	248.9	134.8	272.5	169.0	265.8	119.6	0.0107
Alcohol (g)	12.9	24.3	10.5	21.3	5.2	15.8	0.5712
Dietary glycemic index ^b	55.0	3.4	54.6	3.8	55.1	3.9	0.6751
Dietary glycemic load ^b	150.2	27.4	139.1	30.4	134.7	25.1	0.1054
Food groups (servings)							
Grains	2.6	0.6	2.4	0.6	2.3	0.6	0.2132
Meat, fish, eggs, and beans	4.5	1.9	4.5	2.3	4.2	1.6	0.5973
Vegetables	8.1	2.5	7.6	3.3	6.2	2.0	0.0013
Fruits	1.9	1.5	1.9	1.2	2.0	1.4	0.5161
Milk and dairy products	0.8	0.7	0.9	0.7	1.1	0.9	0.4201
Fats, oils and sugars	5.3	2.6	5.5	3.3	4.9	2.4	0.4614

LDLC, low-density lipoprotein cholesterol; TC, total cholesterol.

^a *P* for trend was obtained from the general linear model after adjustment for sex (men or women), age (continuous), education (elementary, secondary, or college or more), smoking status (current-, ex-, or non-smoker), drinking status (current-, ex-, or non-drinker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), BMI (continuous), and total energy intake (continuous).

^b Average dietary glycemic index and dietary glycemic load based on a glucose standard were calculated for each subject using a table of glycemic index values for common Korean foods.

Table V - 13. Mean daily intake of nutrients and food groups across tertiles of the high triglycerides with low HDL-cholesterol pattern scores

	The TG & HDLC pattern						<i>P</i> for trend ^a
	T1 (<i>n</i> = 46)		T2 (<i>n</i> = 46)		T3 (<i>n</i> = 46)		
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>	
Total energy (kcal)	1579	280.9	1669	399.6	1773	481.4	0.1810
% Energy from carbohydrate	60.1	7.8	59.9	9.9	57.9	8.2	0.8357
% Energy from fat	21.2	5.4	21.1	5.9	22.0	5.1	0.9303
% Energy from protein	16.3	2.3	15.6	2.1	16.5	2.5	0.7866
% Energy from alcohol	2.3	5.4	3.3	7.5	3.6	6.4	0.8080
Nutrient							
Carbohydrate (g)	247.8	43.8	257.9	51.5	263.3	47.1	0.9557
Fat (g)	39.6	14.0	42.3	18.8	47.0	21.2	0.8063
Protein (g)	67.9	15.5	68.5	17.5	77.8	30.8	0.7397
Dietary fiber (g)	21.5	5.3	22.3	5.6	21.5	6.3	0.3058
Vitamin A (µg RE)	801.3	351.9	723.9	341.8	686.6	297.8	0.1455
Vitamin E (mg)	11.1	2.8	10.5	2.7	10.9	3.0	0.0626
Thiamin (mg)	1.0	0.3	1.0	0.3	1.1	0.4	0.7309
Riboflavin (mg)	1.1	0.2	1.2	0.4	1.2	0.6	0.2221
Niacin (mg)	14.3	3.6	14.0	4.2	16.4	7.6	0.6036
Vitamin C (mg)	98.2	43.4	101.4	41.5	97.1	45.3	0.9684
Calcium (mg)	559.2	199.5	551.2	187.5	493.9	149.0	0.0052
Phosphorus (mg)	1028	233.3	1022	234.5	1050	359.5	0.0111
Sodium (mg)	3535	912	3840	1060	4306	1398	0.0916
Potassium (mg)	2750	488.3	2684	701.9	2638	847.8	0.0208
Iron (mg)	14.3	3.2	15.1	4.0	15.6	5.7	0.7019
Cholesterol (mg)	241.5	120.4	246.4	131.4	299.3	165.8	0.4703
Alcohol (g)	6.5	15.9	10.7	25.6	11.3	20.1	0.7230
Dietary glycemic index ^b	54.1	3.7	55.2	3.8	55.4	3.5	0.0971
Dietary glycemic load ^b	134.7	26.5	143.6	31.2	145.7	26.2	0.5165
Food group (servings)							
Grains	2.3	0.6	2.5	0.7	2.5	0.5	0.6551
Meat, fish, eggs, and beans	4.0	1.5	4.1	1.5	5.0	2.5	0.4522
Vegetables	6.9	1.9	7.1	2.3	7.9	3.7	0.8960
Fruits	2.2	1.3	1.9	1.5	1.8	1.1	0.5516
Milk and dairy products	1.1	0.8	0.9	0.7	0.7	0.7	0.0140
Fats, oils, and sugars	5.0	2.2	4.9	2.8	5.8	3.3	0.7303

HDLC, high-density lipoprotein cholesterol; TG, triglycerides.

^a *P* for trend was obtained from the general linear model after adjustment for sex (men or women), age (continuous), education (elementary, secondary, or college or more), smoking status (current-, ex-, or non-smoker), drinking status (current-, ex-, or non-drinker), physical activity (never or rarely, 1–2 days/week, 3–4 days/week, or ≥ 5 days/week), BMI (continuous), and total energy intake (continuous).

^b Average dietary glycemic index and dietary glycemic load based on a glucose standard were calculated for each subject using a table of glycemic index values for common Korean foods.

4. Discussion and conclusions

Using repeated measures of biochemical and dietary variables, two dyslipidemia patterns were obtained by factor analysis: 1) the TC & LDLC pattern and 2) the TG & HDLC pattern. The dyslipidemia patterns were differentially associated with dietary factors. The TC & LDLC pattern was positively associated with intakes of dietary fat and cholesterol but inversely associated with intakes of dietary fiber, iron, and vegetables. The TG & HDLC pattern was not associated with dietary fat but was inversely related to intakes of calcium, potassium, milk and dairy products.

In this study, dietary fat and cholesterol intakes were positively associated with the TC & LDLC pattern, although Asian populations have a lower fat intake (< 25 % of energy) compared with Western populations. Early studies in Western populations reported that saturated and trans-fat intakes were positively associated and unsaturated fat intake negatively associated with high total cholesterol and LDL-cholesterol concentrations (Brown, L *et al.* 1999, Clarke, R *et al.* 1997, Grundy, SM and Denke, MA 1990). In addition, reducing total dietary fat intake without reducing saturated fatty acid intake did not significantly lower total cholesterol and LDL-cholesterol concentrations (Barr, SL *et al.* 1992). Many studies tried to determine the optimal intake amount of dietary fats and the proportion of various fatty acid types in the diet to lower plasma cholesterol concentrations, but there is limited evidence in Asian populations. Our study could not examine the effects of types of fatty acids because the database was incomplete. However, previous study conducted in a Japanese population

reported favorable effects of polyunsaturated fatty acids on blood lipids (Guo, Z *et al.* 2010, Okuda, N *et al.* 2005).

On the other hand, replacing total dietary fat with carbohydrate is associated with increased triglycerides and reduced HDL-cholesterol. Korean adults traditionally consume a high carbohydrate diet, which is suggested to have positive associations with elevated triglycerides and low HDL-cholesterol in Korean adults (Choi, H *et al.* 2012, Kim, K *et al.* 2008). Although this study did not report a significant association between high carbohydrate intake and the TG & HDLC pattern, the TC & LDLC pattern was associated with low intakes of vegetables and dietary fiber. It was interesting to find that our subjects showed two distinct patterns of blood lipid profiles and their associations with different dietary factors.

We also found that the TG & HDLC pattern was inversely associated with intake of milk and dairy products. This is consistent with previous findings in Western and Korean populations that high consumption of milk and dairy products, which are rich in calcium and potassium, was inversely associated with increased triglycerides and reduced HDL-cholesterol. In Spanish patients with hypertriglyceridemia, high intake of low-fat dairy products was associated with reduced triglycerides concentrations (Merino, J *et al.* 2013). Among obese US adults in the CARDIA study (Pereira, MA *et al.* 2002), individuals with more frequent consumption of dairy products had a lower risk of dyslipidemia (high triglycerides or low HDL-cholesterol) than those with less frequent consumption. In other studies conducted in Korean adults, intake of milk and dairy products was associated with a decreased prevalence of elevated triglycerides (Kim, J 2013, Lee, CJ and Joung, H 2012) and poor adherence to the recommended intake of milk and dairy products was associated with an increased prevalence of

hypertriglyceridemia (Jung, HJ *et al.* 2011). Calcium and potassium might mediate the inverse association between milk and dairy products consumption and the risk of dyslipidemia through their protective effects on insulin resistance and obesity (Pfeuffer, M and Schrezenmeir, J 2007). Consumption of milk and dairy products in Korean adults is much lower than the recommended level, according to the findings based on data from the KNHANES (Song, S *et al.* 2014). High consumption of milk and dairy products in Korean adults might play an important role in the prevention and management of elevated triglycerides and low HDL-cholesterol.

Our study has several strengths and limitations. The subjects in this study were recruited from a single hospital, making it difficult to apply our findings to the general Korean adult population. However, to our knowledge, this study was the first to examine the associations between dyslipidemia patterns and dietary factors using repeated measurements of biochemical and dietary variables. The cross-sectional design of this study did not allow us to determine a causal relationship between diet and disease. We excluded subjects who had taken medications intended to lower blood lipids because disease treatment might have caused dietary changes. When we examined the associations between dyslipidemia patterns and food group intakes, food group subtypes were not considered.

In conclusion, two dyslipidemia patterns were associated with dietary factors in urban Korean adults. Individuals with high total cholesterol and LDL-cholesterol might benefit from diets characterized by low intakes of fat and cholesterol and high intakes of vegetables and dietary fiber, while people with high triglycerides and low HDL-cholesterol might benefit from diets characterized by high consumption of milk and dairy products. Further large-scale studies using a prospective design should be

conducted to investigate specific dietary recommendations according to lipid profiles in the prevention and management of dyslipidemia in Korean adults.

CHAPTER VI. DISCUSSION AND CONCLUSIONS

Main findings of the study

In these multiple cross-sectional studies, various dietary determinants of metabolic syndrome and its components, such as carbohydrates, alcohol, food groups, and dietary patterns were examined in Korean adults based on three different datasets from the Fourth KNHANES and outpatient clinics in and near Seoul (Table VI - 1). Adults from the KNHANES data were large nationally representative samples although they had a single 24-hour recall. Adults from outpatient clinics had multiple days of dietary intake data, which closely estimated the usual intake in this population. Based on data from the KNHANES, high carbohydrate intake was a key determinant of metabolic syndrome and its components, such as insulin resistance and dyslipidemia. Among adults of outpatient clinics, intakes of nutrients and food groups differed by the presence of metabolic syndrome and individual components of metabolic syndrome were differentially associated with dietary determinants.

Table VI - 1. Main findings of multiple cross-sectional studies based on three different datasets

Data and subjects	Study	Age	Sex (n)	Dietary assessment	Dietary determinants	Outcomes	Association
Nationally representative adults who had no diabetes, dyslipidemia, and hypertension from the 4 th KNHANES data (2007–2009)	1	30–65y	M (2,631)	1d 24HR	% energy from CHO	MetS	(+)
			W (4,214)		Refined grains, white rice	MetS	(+)
	2	30–65y	M (2,618)	1d 24HR	Oils, fats, sugars	IR	(+)
			W (4,326)		CHO (g, % energy), DGI, DGL	IR	(+)
	3	30–65y	T (3,871)	FFQ with simple frequency	Whole grains and beans dietary pattern	IR	(-)
	4	≥20y	M (3,795)	1d 24HR	Rice-oriented dietary pattern	Elevated TG	(+)
			W (5,930)		Rice-oriented dietary pattern	Low HDL-chol.	(+)
	Adults who were recruited in four outpatient clinics in and near Seoul (2006–2012) and at high risk of MetS	5	≥30y	M (413)	3d 24HRs & DRs within 2 weeks	Fruits	MetS
W (255)				Milk and dairy products		MetS	(-)
6		≥30y	M (413)	3d 24HRs & DRs within 2 weeks	Heavy alcohol drinking (>30g/d)	Elevated BP	(+)
						Low HDL-chol.	(-)
						MetS in current-smokers	(+)
Adults who attended the SNUH (2010–2012) and disease-free at the time of study enrollment		7	≥20y	T (141)	2–4d 24HRs over 4 months (interval of 3–4 months)	Alcohol (g)	Elevated BP
	CHO (g, % energy), DGL					Elevated BP	(-)
	DGI, DGL					High TG, low HDL-chol. & AO	(+)
	Alcohol (% energy)					Elevated FBG	(+)
	8	≥20y	T (138)	3d 24HRs over 8 months (intervals of 3–4 months)	Fat, cholesterol	High TG & low HDL-chol.	(+)
				Dietary fiber, iron, vegetables	High TG & low HDL-chol.	(-)	
				Calcium, potassium, milk and dairy products	High total- & LDL-chol.	(-)	

24HR, 24-hour recall; AO, Abdominal obesity; BP, Blood pressure; CHO, Carbohydrate; Chol., Cholesterol; DR, Dietary record; FBG, Fasting blood glucose; IR, Insulin resistance; M, Men; MetS, Metabolic syndrome; 24HR, 24-hour recall; SNUH, Seoul National University Hospital; T, Total; TG, Triglycerides; W, Women.

High carbohydrate intake and metabolic syndrome

The current study examined the association between dietary carbohydrate intake and the risk for metabolic syndrome at multiple levels: DGI, DGL, the amounts and sources of dietary carbohydrates, and dietary patterns. The percentage of energy from carbohydrates in men and intakes of refined grains and white rice in women were positively associated with the prevalence of metabolic syndrome. In addition, DGI and DGL were higher in healthy women with insulin resistance than in those without insulin resistance. Of dietary patterns identified, the dietary pattern high in low GI foods, including whole grains and beans, was inversely associated with the prevalence of insulin resistance, but the white rice-oriented dietary pattern characterized by a high intake of white rice but low intakes of other food groups was positively associated with the prevalence of elevated triglycerides in men and low HDL-cholesterol in men and women.

In Korean adults, dietary carbohydrates account for a considerable part of daily energy intake and the entire dietary pattern. Koreans traditionally consume large amounts of white rice as a staple food. In addition, more refined grains such as white bread and noodles are currently available due to the development of food processing technology and the modern milling process. The percentage of energy from carbohydrates in the Korean population is higher (66 %) than those in the US population (51 %) and main sources of dietary carbohydrates are white rice (46 %), noodles and bread (8 %) according to the Fourth KNHANES report. The level of DGL in Korean adults (Kim, EK *et al.* 2009, Song, S *et al.* 2012) was higher than those in Western adults (Du, H *et al.* 2008, Liese, AD *et al.* 2005) but similar to those in Japanese adults (Nakashima, M *et al.* 2010).

The effect of a high carbohydrate diet on the development of metabolic syndrome is not fully understood. Hu, FB (2011) and Cheung, BM (2005) insisted that excessive carbohydrate intake based on refined grains and white rice caused the risk of metabolic diseases by abdominal obesity, insulin resistance, and dyslipidemia. A high carbohydrate diet results in an increase of insulin demand and hyperglycemia depending on the amounts and sources of carbohydrates. DGI and DGL represent the physiologic function of dietary carbohydrates, an ability to raise blood glucose. Diet high in carbohydrates, especially GI and GL might cause insulin resistance and abnormalities in blood glucose and lipids metabolism (Ludwig, DDS 2002). Previous epidemiologic studies have consistently shown that diets high in carbohydrates, DGI, and DGL were associated with elevated blood glucose, insulin, and triglycerides and reduced HDL-cholesterol in Western adult populations (Finley, CE *et al.* 2010, Levitan, EB *et al.* 2008, McKeown, NM *et al.* 2004, O'Sullivan, TA *et al.* 2010) and Asian adult populations (Choi, H *et al.* 2012, Kim, K *et al.* 2008, Murakami, K *et al.* 2006, Nakashima, M *et al.* 2010, Park, SH *et al.* 2010).

The association between carbohydrate intake and metabolic syndrome might differ according to the sources of dietary carbohydrates. Higher intakes of refined grains and white rice increased DGI and DGL, which results in an alteration of glucose and lipids metabolism and the development of metabolic diseases (Hu, EA *et al.* 2012, Nanri, A *et al.* 2010, Radhika, G *et al.* 2009, Sun, Q *et al.* 2010, Zuñiga, YL *et al.* 2014). On the other hand, whole grains intake have shown a protective effect on the development of metabolic syndrome and its components (Esmailzadeh, A *et al.* 2005, McKeown, NM *et al.* 2002, Sahyoun, NR *et al.* 2006) because whole grains contain higher amounts of dietary fiber, flavonoids, vitamin E, magnesium, folate, and zinc

than those in refined grains (Slavin, JL *et al.* 2000). These results are in agreement with those of the present study demonstrating that high consumption of refined grains and white rice was associated with increased risks for metabolic syndrome and its components, such as elevated triglycerides and low HDL-cholesterol, whereas a high intake of the whole grains and beans dietary pattern was associated with a low prevalence of insulin resistance.

Carbohydrate intake and white rice consumption are related to meal composition. In this study, adults in the highest group of carbohydrates intake (e.g., % energy or white rice) tended to consume less meat, fish, vegetables, fruits, and milk and dairy products compared with those in the lowest group. In addition, the rice-oriented dietary pattern identified in this study was characterized by a high intake of white rice but low intakes of other food groups. Therefore, the amounts and sources of carbohydrate intake should be evaluated in the overall dietary pattern. Of dietary patterns identified in the present study, the dietary pattern including low GI foods (e.g., whole grains and beans) and fruits reduced the risk of insulin resistance, but the rice-oriented dietary pattern was high in GI and GL but low in healthy food groups and increased risks for elevated triglycerides and low HDL-cholesterol. The protective effects of dietary patterns characterized by high intakes of healthy foods and low GI foods on metabolic syndrome and its components were also observed in previous studies of Western populations (Panagiotakos, DB *et al.* 2007, Rumawas, ME *et al.* 2009, Tortosa, A *et al.* 2007) and Asian populations (Esmailzadeh, A *et al.* 2007).

Dietary patterns associated with metabolic syndrome

In Western studies on the association between dietary patterns and metabolic diseases, the Western pattern and the healthy/prudent pattern have been commonly identified. The Western pattern was associated with increased risks for metabolic diseases, but the healthy/prudent pattern was associated with reduced risks for metabolic diseases (Denova-Gutierrez, E *et al.* 2010a, Fung, TT *et al.* 2004, Fung, TT *et al.* 2001b, Kerver, JM *et al.* 2003, van Dam, RM *et al.* 2002). Dietary patterns identified in Korean adults are unique and have shown different associations with metabolic diseases from those in Western populations. Previous studies in Korean adults showed that dietary patterns including healthy foods were inversely associated with risks for metabolic syndrome and its components (Baik, I *et al.* 2013, Cho, YA *et al.* 2011, Hong, S *et al.* 2012, Kim, J and Jo, I 2011), whereas the Korean traditional pattern high in white rice and kimchi was positively associated with risks for metabolic syndrome (Hong, S *et al.* 2012) and low HDL-cholesterol (Cho, YA *et al.* 2011, Song, Y and Joung, H 2012).

Dietary pattern analyses measure the effect of the overall diet rather than single nutrients or foods and provide comprehensive approaches to disease prevention and treatment. Therefore, nutritional epidemiologic studies on the association between diet and metabolic diseases have frequently used the dietary pattern analyses, such as factor analysis and cluster analysis (Hu, FB 2002, Newby, PK and Tucker, KL 2004). Recently, RRR has received a considerable attention because of its usefulness and strengths. RRR identifies dietary patterns that explain as much of the variation in disease related biomarkers or nutrients as possible and combines dietary information with prior knowledge about the pathway from diet to disease (Hoffmann, K *et al.*

2004). Therefore, RRR is useful to identify dietary patterns related to the risk of metabolic syndrome. To our knowledge, this study is the first to apply the RRR method to derive dietary patterns that explain dietary carbohydrate intake in Korean adults. Two white rice based dietary patterns which differed in carbohydrate quantity and quality were identified. These dietary patterns have not been identified in Western populations, and they reflect a unique dietary practice of Korean adults.

Unique dietary patterns in Korean adults might lead to different metabolic pathways in the development of metabolic syndrome from those of Western populations. A previous study (Lim, S *et al.* 2011) reported that the most prevalent components of metabolic syndrome differed between the US and Korean adults. The prevalences of elevated triglycerides and low HDL-cholesterol were higher in Korean adults than those in the US adults, whereas the prevalences of abdominal obesity, hypertension, and elevated blood glucose were higher in the US adults than those in Korean adults. Although Korean adults have lower total energy and fat intakes than those in Western adults, excessive energy from carbohydrates and refined carbohydrate foods might induce high DGI and DGL but lower proportion of healthy foods (e.g., protein source foods, fruits, vegetables, milk and dairy products) in the meal composition.

Food groups associated with metabolic syndrome

In Korean adults from outpatient clinics, low intakes of fruits and milk and dairy products were associated with the prevalence of metabolic syndrome. Although our study has a cross-sectional design, these findings imply that intakes of healthy food groups are important determinants of metabolic syndrome in Korean adults who have

very low intakes of fruits and milk and dairy products compared to the daily recommended amounts (Song, S *et al.* 2014). High intakes of fruits, vegetables, milk and dairy products have been associated with a reduced risk of metabolic syndrome because they are major sources of vitamins, minerals, and other beneficial nutritional components (Azadbakht, L *et al.* 2005, Elwood, PC *et al.* 2007, Esmailzadeh, A *et al.* 2006, Jung, HJ *et al.* 2011, Kwon, HT *et al.* 2010, Ruidavets, JB *et al.* 2007, Yoo, S *et al.* 2004). In addition, the protective effects of healthy food group consumption on metabolic syndrome might be attributed to other healthy lifestyle behaviors because people who frequently consume these healthy food groups are more likely to have an overall healthy lifestyle.

Alcohol intake and metabolic syndrome

In middle-aged Korean men, a high prevalence of heavy alcohol consumption is an important issue in public health because heavy alcohol drinking increases risks for several chronic diseases (Reynolds, K *et al.* 2003, Sun, K *et al.* 2013, Taylor, B *et al.* 2009). The positive association between heavy alcohol consumption and risks for metabolic syndrome and elevated blood pressure identified in this study are consistent with findings from previous studies in Western populations (Zhu, SK *et al.* 2004) and Asian populations (Baik, I and Shin, C 2008, Kim, BJ *et al.* 2012, Lee, MY *et al.* 2010, Park, SH 2012, Urashima, M *et al.* 2005, Wakabayashi, I 2010). The positive association between heavy alcohol drinking and metabolic syndrome might be attributed to elevated triglycerides (Baik, I and Shin, C 2008, Jin, L *et al.* 2011, Wakabayashi, I 2010), high blood glucose (Baik, I and Shin, C 2008, Stoutenberg, M *et al.* 2013), and elevated blood pressure (Jin, L *et al.* 2011, Sesso, HD *et al.* 2008, Xin,

X *et al.* 2001) although no association between alcohol consumption and the prevalences of elevated triglycerides and elevated blood glucose was observed in this study. Previous studies also reported an inverse association between light to moderate alcohol drinking and the risk of metabolic syndrome (Alkerwi, A *et al.* 2009, Freiberg, MS *et al.* 2004, Stoutenberg, M *et al.* 2013, Yoon, YS *et al.* 2004) due to increased insulin sensitivity and HDL-cholesterol by light to moderate alcohol drinking. In this study, heavy alcohol drinking was inversely associated with the risk of low HDL-cholesterol, but no association between moderate drinking (0 to 30 g/day) and metabolic syndrome was observed.

The accuracy of assessment of alcohol consumption should be considered to examine the association between alcohol intake and risks for metabolic syndrome and its components. In future studies, the recommended amount of alcohol consumption to prevent metabolic syndrome should be suggested based on previous findings and the association between alcohol intake and metabolic syndrome in women should be explored.

Clustering patterns of metabolic syndrome components

Metabolic syndrome is a useful concept to identify individuals who are at high risks for chronic diseases during the early stages. Several expert groups attempted to develop the unified definition of metabolic syndrome (Grundy, SM *et al.* 2005). However, there are several limitations to make a diagnosis of metabolic syndrome in clinical settings because metabolic syndrome is an ongoing symptom as a pre-morbid condition. The criteria for diagnosis of metabolic syndrome seem arbitrary due to having different components with different dichotomous cutoff points, measuring components using

different methods, and having difficulty in evaluation of the severity of symptoms (Simmons, RK *et al.* 2010). Recently, a new concept to define metabolic syndrome, examining clustering patterns of metabolic syndrome components, has been suggested (Carnethon, MR *et al.* 2004, Ferguson, TF *et al.* 2010). This approach explains that metabolic syndrome is developed by multiple pathophysiologic pathways and thus consists of multilayered symptoms, such as insulin resistance, obesity, dyslipidemia, and hypertension (Meigs, JB 2000, Shen, BJ *et al.* 2003). Therefore, metabolic syndrome should be addressed by specific strategies to reduce risks for individual components.

In this study, distinct clustering patterns of metabolic syndrome components were identified using six metabolic syndrome components (waist circumference, triglycerides, HDL-cholesterol, blood glucose, systolic and diastolic blood pressure): 1) high blood pressure, 2) dyslipidemia with abdominal obesity, and 3) high blood glucose. Especially, two different dyslipidemia patterns were found based on four lipid indicators, including total-, HDL-, LDL-cholesterol, and triglycerides. Three to four clustering patterns were consistently identified in Western populations (Gray, RS *et al.* 1998, Hanley, AJG *et al.* 2002a, Maison, P *et al.* 2001, Meigs, JB *et al.* 1997) and Korean populations (Choi, KM *et al.* 2003, Oh, JY *et al.* 2004, Park, YM *et al.* 2006), such as insulin resistance, dyslipidemia, hypertension, and glucose intolerance. Obesity related components were loaded into those patterns together. These findings are useful to explain potential mechanisms of the development of metabolic syndrome.

Dietary determinants of individual components of metabolic syndrome

Based on repeated dietary intake data of outpatient adults, individual components of metabolic syndrome were differentially associated with dietary determinants. Elevated blood pressure was associated with high alcohol intake; elevated triglycerides with low HDL-cholesterol was associated with high DGI and DGL but low intake of milk and dairy products; and elevated total- and LDL-cholesterol was associated with low vegetable consumption.

Consistent with previous findings in Western populations (Merino, J *et al.* 2013, Pereira, MA *et al.* 2002) and Korean populations (Kim, J 2013, Lee, CJ and Joung, H 2012), high consumption of milk and dairy products was inversely associated with increased triglycerides and low HDL-cholesterol. Milk and dairy products are major sources of calcium and potassium, which might reduce the risk of dyslipidemia through their protective effects on insulin resistance and obesity (Pfeuffer, M and Schrezenmeir, J 2007).

Earlier studies in Western populations confirmed that high intakes of saturated fat and cholesterol were positively associated with total cholesterol and LDL-cholesterol (Brown, L *et al.* 1999, Clarke, R *et al.* 1997, Grundy, SM and Denke, MA 1990, Hopkins, PN 1992). On the other hand, high intakes of fruits, vegetables, and dietary fiber were associated with decreased total cholesterol and LDL-cholesterol (Brown, L *et al.* 1999, Fornes, NS *et al.* 2000).

Although we did not examine the effects of subtypes of fats, previous studies reported the associations between consumption of subtypes of fatty acids and metabolic syndrome (Ebbesson, SO *et al.* 2005, Melanson, EL *et al.* 2009, Noel, SE *et al.* 2010). Intake of saturated fatty acid was positively associated with concentrations

of inflammation markers in plasma and the risk of metabolic syndrome. Conversely, low intakes of total fats, saturated fats, and cholesterol reduced the risk of metabolic syndrome by regulating insulin sensitivity, blood lipid indicators, and blood pressure (Appel, LJ *et al.* 2005, Obarzanek, E *et al.* 2001).

Conclusions

In conclusion, diets low in DGI and DGL based on higher intakes of whole grains rather than refined grains and white rice and high in beans, fruits, milk and dairy products might have a protective effect on the development of metabolic syndrome and its components, such as insulin resistance and dyslipidemia in Korean adults. Advice against heavy alcohol drinking should be suggested to attenuate the risks for metabolic syndrome and its components among men. In addition, individual components of metabolic syndrome are differentially associated with dietary determinants. Therefore, specific dietary guidelines should be suggested for the prevention and management of metabolic syndrome according to the combinations of its components. Findings from this study can be used to build nutrition intervention programs and dietary recommendations for individuals and populations at high risk of metabolic syndrome in Asian and Korean adult populations.

CHAPTER VII. SUMMARY AND SUGGESTIONS

1. Summary of study findings

In chapter III, high carbohydrate intake was a key determinants of metabolic syndrome and its components, such as insulin resistance and dyslipidemia in adults from the Fourth KNHANES data in 2007-2009.

Study 1.

- The percentage of energy from carbohydrates was positively associated with the prevalence of metabolic syndrome in men.
- Intakes of refined grains and white rice were positively associated with the prevalence of metabolic syndrome in women.

Study 2.

- Among women who had no symptom of metabolic syndrome, subjects with insulin resistance had higher intakes of carbohydrates (g, %), DGI, and DGL than those without insulin resistance.
- Among men who had no symptom of metabolic syndrome, subjects with insulin resistance had higher intakes of fats, oils, and sugars than those without insulin resistance.

Study 3.

- The dietary pattern characterized by high intakes of whole grain and beans pattern (low GI foods) was associated with a low prevalence of insulin resistance in adults.

Study 4.

- Using the RRR method, two dietary patterns were obtained in adults: 1) the balanced pattern characterized by high intakes of white rice, bread, noodle, vegetables, fruits, meat, eggs, and oils and 2) the rice-oriented pattern characterized by a high intake of white rice but low intakes of vegetables, fruits, meat, milk and dairy products.
- The rice-oriented pattern was positively associated with hypertriglyceridemia in men and low HDL-cholesterol in both men and women.

In chapter IV, differences in food group intake by the presence of metabolic syndrome were observed in adults from outpatient clinics. In addition, in men, alcohol consumption was positively associated with the prevalences of metabolic syndrome and elevated blood pressure

Study 5.

- Men with metabolic syndrome had a higher intake of alcohol but a lower intake of fruits than those without metabolic syndrome.
- Women with metabolic syndrome had a lower intake of milk and dairy products than those without metabolic syndrome.

Study 6.

- Heavy alcohol drinking was positively associated with a prevalence of elevated blood pressure but inversely associated with a prevalence of low HDL-cholesterol in men.
- Heavy alcohol drinking was a determinant of metabolic syndrome in current-smokers.

In chapter V, clustering patterns of metabolic syndrome components were differentially associated with dietary determinants based on multiple days of dietary data among adults recruited in Seoul National University Hospital.

Study 7.

- Metabolic syndrome components had three distinctive clustering patterns: 1) the high blood pressure, 2) the dyslipidemia (high triglycerides and low HDL-cholesterol) with abdominal obesity, and 3) the high blood glucose.
- The high blood pressure pattern was positively associated with alcohol intake and the dyslipidemia pattern was positively associated with DGI and DGL.

Study 8.

- Using repeated measures of lipid indicators, two dyslipidemia patterns were obtained: 1) the high total- and LDL-cholesterol and 2) the high triglycerides and low HDL-cholesterol.
- The high triglycerides and low HDL-cholesterol pattern was inversely associated with intakes of milk and dairy products, calcium, and potassium.

- The high total- and LDL-cholesterol pattern was positively associated with intakes of dietary fat and cholesterol but inversely associated with intakes of vegetables and dietary fiber.

2. Strengths and limitations

Strengths

To our knowledge, this study is the first to examine various dietary determinants, such as nutrients, food groups, and dietary patterns of metabolic syndrome and its components in Korean adults. Findings from this study were confirmed in different dietary intake datasets. Although dietary intake data were obtained from a single 24-hour recall in adults from the KNHANES, it captured an entire spectrum of dietary intake from large nationally representative samples. In addition, among adults of outpatient clinics, dietary determinants of metabolic syndrome were identified using repeated dietary intake data, which closely estimated the usual intake of this population. Especially, the amounts and the sources of carbohydrates, including DGI and DGL, were considered to examine the association between a high carbohydrate diet and the risk of metabolic syndrome. To identify dietary determinants of metabolic syndrome, the most recent methods used in nutritional epidemiologic area, such as the RRR and factor analysis for clustering patterns of metabolic syndrome components were applied to this study.

Limitations

The cross-sectional nature of this study does not allow us to find causal relationship between dietary determinants and metabolic syndrome. Potential measurement error should be considered to correctly interpret the results. For example, most GI values in the database for common Korean foods were from values of Western foods. Using an incomplete GI database for Asian and Korean foods might have altered the results and compromised the precision of data. Although we examined dietary determinants of metabolic syndrome after adjustment for potential confounding variables, we cannot rule out residual confounding. In addition, other risk factors of metabolic syndrome which are not included in the criteria for diagnosis of metabolic syndrome should be considered together. The data of this study did not include the information on the subjects' awareness of metabolic syndrome, which might affect their diet. Because metabolic syndrome is an ongoing symptom as a pre-morbid condition, it is difficult to diagnose metabolic syndrome based on the unified definition. The awareness of metabolic syndrome should be considered to correctly examine the association between diet and metabolic syndrome. It is necessary to be aware of metabolic syndrome in order to recognize and treat it effectively.

3. Implications

Findings from this study can be used to guide dietary practices in Korean adults for the prevention and management of metabolic syndrome and provide specific dietary

strategies aimed to control individual components of metabolic syndrome. In addition, researchers may extend the knowledge on the mechanism of dietary factors related to the development of metabolic syndrome and its components and policy makers can build nutrition programs and health policies based on the results of this study. From an international perspective, finding from this study can be applied to suggest dietary recommendations for the prevention and management of metabolic syndrome in Asian population who consume high carbohydrate diets based on refined grains and white rice as staple foods.

4. Suggestions for future studies

The development of a method of accurately evaluating an individual's overall diet is a prerequisite for further research regarding the relationship between diets and metabolic syndrome. In addition, dietary determinants of metabolic syndrome might differ by sex and individual components. Therefore, specific dietary determinants of metabolic syndrome should be examined according to sex and individual components.

Practical recommendations regarding dietary guidelines for the prevention and management of metabolic syndrome should be suggested. Nutritional intervention programs and policies should be developed by researchers and policy makers to guide and improve individual's dietary practice associated with the risk of metabolic syndrome. More prospective studies are required to ascertain dietary determinants which are linked to development of metabolic syndrome and its components.

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국 문 초 록

한국 성인에서 대사증후군 관련 식사 요인 연구

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대사증후군은 복부 비만, 이상지혈증, 혈당의 증가, 고혈압 등 대사 이상의 요소들이 동시에 나타나는 증상으로 제 2 형 당뇨 및 심혈관질환의 발병 위험을 증가시킨다고 알려져 있다. 한국 성인에서 대사증후군의 유병률은 증가하고 있는 추세로, 그 예방 및 관리에 대한 중요성이 강조되고 있다. 대사증후군과 관련한 식사 요인을 규명하기 위한 연구에 대한 관심이 고조되고 있으며, 특히 서구 지역의 성인을 대상으로 대사증후군과 관련한 영양소 및 식품 섭취와 식사 패턴에 대한 연구가 활발히 이루어지고 있다. 한국 성인은 서구 지역의 성인과는 다른 식사 패턴을 갖고 있으며, 쌀밥을 주식으로 하는 고탄수화물 식사를 주로 한다. 이에 따라 식사 요인에 의한 대사증후군의 발병 기전도 서구 지역의 성인과는 차이가 있을 것으로 예상되나 한국 성인에서 대사증후군과 관련한

식사 요인을 영양소, 식품, 식사 패턴의 수준에서 종합적으로 파악하고자 한 연구가 드문 실정이다. 대사증후군과 관련한 식사 요인을 밝히는 것은 만성 질환의 발병을 미리 예방하고, 그 위험을 줄일 수 있다는데 의의가 있다. 따라서 본 연구에서는 한국 성인에서 대사증후군 및 그 요소들과 관련한 식사 요인을 파악하고자 한다. 세부 연구 목적에 따라 식사 요인을 탄수화물, 알코올, 식품군 섭취 및 식사 패턴의 다양한 수준에서 살펴보고자 한다.

본 연구는 서로 다른 세 개의 데이터를 활용한 여러 개의 세부 연구로 구성되어 있다. 첫 번째 데이터의 대상자는 제 4 기 국민건강영양조사 (2007-2009)에 참여한 성인으로 한국 성인을 대표하는 대규모의 대상자이며, 특별한 만성 질환을 갖고 있지 않고, 주기적으로 약물을 복용하지 않는 사람들이다. 이들은 1 일의 24 시간 회상 조사와 식품섭취빈도조사를 통해 얻은 식사 자료를 갖고 있다. 두 번째 데이터의 대상자는 2006 년부터 2012 년까지 서울 시내 및 그 근교의 대형 병원 네 곳에서 모집한 외래환자로 이들은 대체로 대사증후군의 위험이 높은 편이고, 혈당, 혈압, 혈중 지질의 관리를 위해 주기적으로 약물을 복용하는 사람도 포함되어 있다. 이들은 24 시간 회상법과 식사기록법을 통해 얻은 3 일의 식사 자료를 갖고 있다. 세 번째 데이터의 대상자는 2010 년부터 2012 년 사이 서울대학교 병원 건강검진센터 또는 가정의학과에 주기적으로 내원한 환자 중 연구 참여 시기에 심각한 질병을 갖고 있지 않고, 주기적으로 약물을 복용하지 않는 성인이다. 이들은 24 시간 회상법으로부터 얻은 2-4 일의 식사 자료를

갖고 있다. 대상자들의 식사 자료를 바탕으로 개인별 영양소, 알코올, 식사혈당지수 및 식사혈당부하지수, 식품군 섭취를 평가하였으며, 요인분석 및 reduced rank regression 을 통해 식사 패턴을 얻었다. 대사증후군 및 그 요소들의 진단은 미국 국립 콜레스테롤 교육 프로그램의 기준을 따랐으며, 복부 비만 진단을 위해 아시아 및 한국 성인을 대상으로 설정된 허리둘레 기준을 적용하였다.

국민건강영양조사에 참여한 성인에서 탄수화물 섭취 증가가 대사증후군 및 그 요소들, 예를 들면 인슐린 저항성과 이상지혈증의 위험을 높이는 것으로 밝혀졌다. 특히 남자에서는 탄수화물로부터 얻는 에너지 비율의 증가 (Q5 vs. Q1: OR = 1.46, 95% CI = 1.07–2.01), 여자에서는 흰쌀을 포함한 정제 곡류의 섭취 증가 (정제 곡류 Q5 vs. Q1: OR = 1.72, 95% CI = 1.24–2.40; 흰쌀 Q5 vs. Q1: OR = 1.74, 95% CI = 1.23–2.48)가 대사증후군 유병률 증가와 관계가 있었다. 특히 대사증후군 요소를 하나도 갖지 않는 건강한 여자에서 인슐린 저항성을 갖고 있는 경우가 갖고 있지 않은 경우보다 식사혈당지수 (58.8 vs. 57.9) 및 식사혈당부하지수 (171.4 vs. 164.5) 수준이 높게 나타났다. 또한 통곡류나 두류와 같이 혈당지수가 낮은 식품을 많이 섭취하는 식사 패턴을 가진 성인에서 인슐린 저항성의 유병 위험이 낮은 반면 (Q5 vs. Q1: OR = 0.80, 95% CI = 0.61–1.03, *P* for trend = 0.0134), 쌀밥의 섭취가 높으면서 채소 및 과일류, 육류, 유제품류의 섭취가 낮아 식사혈당지수와 식사혈당부하지수가 높은 식사 패턴은 남자에서 혈중 중성지방의 증가와 관련이 있었고 (패턴 점수 Q5 vs. Q1: OR = 1.58, 95% CI = 1.20–2.09), 남녀

모두에서 HDL-콜레스테롤 감소와 관련이 있었다 (남자 Q5 vs. Q1: OR = 1.43, 95% CI = 1.12–1.82; 여자 Q5 vs. Q1: OR = 1.29, 95% CI = 1.08–1.55). 대형 병원의 외래환자에서는 대사증후군을 가진 남자의 경우 갖지 않은 경우보다 알코올 섭취가 높고 (22.9 vs. 14.4 g), 과일류의 섭취가 낮았다 (1.1 vs. 1.6 servings). 특히 현재 흡연을 하고 있는 남자에서 알코올 섭취가 증가함에 따라 대사증후군의 유병 위험이 크게 높았다. 대사증후군을 가진 여자에서는 갖지 않은 경우보다 우유 및 유제품의 섭취가 낮았다 (0.5 vs. 0.8 servings). 서울대학교 병원에서 모집한 환자들에서는 대사증후군 요소들의 군집들이 서로 다른 식사 요인과 관련이 있었다. 중성지방이 높으면서 HDL-콜레스테롤은 낮은 군집의 특성이 뚜렷한 성인에서는 식사혈당지수 (군집 점수 T3 vs. T1 = 56.5 vs. 54.1) 및 식사혈당부하지수 (T3 vs. T1 = 147.9 vs. 128.7) 수준이 높고, 칼슘, 칼륨, 우유 및 유제품류의 섭취 (T3 vs. T1 = 0.7 vs. 1.1 servings)가 낮았다. 고혈압 군집의 점수가 높은 성인에서는 알코올 섭취가 높았고 (T3 vs. T1 = 19.5 vs. 5.6 g), 총 콜레스테롤과 LDL-콜레스테롤이 높은 군집 특성을 가진 성인에서는 지방 및 콜레스테롤 섭취는 높고, 채소류 (T3 vs. T1 = 6.2 vs. 8.1 servings)와 식사 섬유소의 섭취는 낮았다.

한국 성인에서 대사증후군의 발병 위험을 줄이기 위해서는 식사혈당지수 및 식사혈당부하지수가 낮으면서 정제된 곡류 대신 통곡류의 섭취가 높은 식사를 바탕으로 두류, 과일류, 우유 및 유제품류의 섭취를 늘리고, 적절한 수준의 알코올의 섭취가 강조되어야 한다. 본 연구 결과를 활용하여 고탄수화물 식사를 주로 하는 아시아 지역의 성인에게 적용

가능한 대사증후군 예방 및 관리를 위한 식사 지침의 제시 및 영양 중재의
마련이 가능할 것이다.

주요어: 대사증후군, 탄수화물, 알코올, 식품군, 식사 패턴, 한국 성인

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