RESEARCH ARTICLE

Prevalence of the Metabolic Syndrome and Associated Factors in Korean Cancer Survivors

Jung-Yun Lee[1], Noh Hyun Park[1], Yong-Sang Song[1], Sang Min Park[2]*, Hae-Won Lee[2], Kyae Hyung Kim[2], Kyung-Hyun Choi[3]

Abstract

Background: This study was designed to evaluate prevalence of the metabolic syndrome among cancer survivors compared to non-cancer controls from a population-based sample and to identify associated risk factors. Materials and Methods: Data from the fourth Korean National Health and Nutrition Examination Survey were analyzed to compare the prevalence of metabolic syndrome, as defined by 2009 consensus criteria. Associated factors with were identified using multiple logistic regression analysis among cancer survivors. Results: The prevalence of the metabolic syndrome in cancer survivors (n = 335) was similar to that in the non-cancer population (n = 10,671). However, gastric cancer survivors showed lower risk of metabolic syndrome than non-cancer controls (adjusted odds ratio [aOR] 0.42, 95% confidence interval [CI] 0.20-0.86). Age of more than 60 years (aOR 4.83, 95% CI 1.94–12.03), BMI between 23 and 25 (aOR 6.71, 95% CI 2.90–15.6), BMI more than 25 (aOR 12.23, 95% CI 5.20–28.77) were significantly associated with the metabolic syndrome in cancer survivors. Conclusions: Cancer survivors are unlikely to have a higher risk of the metabolic syndrome than non-cancer controls in Korea. This finding may be due to a relatively high proportion of gastric cancer survivors in Korea than in Western countries. The risk for metabolic syndrome among cancer survivors would appear to vary according to oncological and non-oncological factors.

Key words : Metabolic syndrome - cancer survivors - prevalence - risk factors - Korea

Asian Pacific J Cancer Prev, **14**, 1773-1780

Introduction

The number of cancer survivors has increased rapidly due to increased incidence of overall cancer and the improved survival of cancer patients (Boyle and Levin, 2008; Jung et al., 2011). The proportion of cancer survivors is up to 3.7% in the United States and 1% in Korea (National Cancer Information Center, 2011; National Cancer Institute, 2012). Cancer survivors have more comorbidities than the general population (Shin et al., 2008). Furthermore, cancer survivors had an increased risk of developing cardiovascular disease as results of late effects of several cancer therapies such as platinum compounds, angiogenesis inhibitors, and radiation treatment (Redig and Munshi, 2010). Thus, evaluation and management of accompanied comorbidities as well as survival itself have become important issues in cancer survivors. Cardiovascular disease is the most important cause of non-cancer death in cancer-survivors that affect life expectancy and quality of life (Brown et al., 1993; Shin et al., 2010a). It is now well recognized that metabolic syndrome is associated with increased risk of cardiovascular events and mortality (Gami et al., 2007). Therefore, risk for cardiovascular disease could be assessed by measuring metabolic syndrome components (Cabre et al., 2008).

Previous studies showed inconsistent results whether the risk of metabolic syndrome is more increased in cancer survivors than general populations. In long-term survivors of childhood cancer, the trends for increased risk of metabolic syndrome were observed in several studies (Talvensaari et al., 1996; Follin et al., 2006; Gurney et al., 2006; Oeffinger et al., 2006; Annaloro et al., 2008). As for survivors of adult-onset solid tumors, most studies were limited to some specific cancer types such as testicular cancer and prostate cancer (Nuver et al., 2005; Braga-Basaria et al., 2006; Haugnes et al., 2007). Several studies from adult-onset solid tumors have demonstrated that the results were inconsistent according to types of cancer and treatment modalities (Nuver et

*[1]Department of Obstetrics and Gynecology, [2]Department of Family Medicine, Seoul National University College of Medicine, Seoul, [3]Department of Family Medicine, Dongnam Institute of Radiological & Medical Science, Busan, Korea *For correspondence: sangmin.park.snuh@gmail.com*

al., 2005; Haugnes et al., 2007; Liavaag et al., 2009; Ulaganathan et al., 2012). A recent meta-analysis showed no significant association with metabolic syndrome for non-hematologic malignancies (Jung et al., 2012).

Few studies about the association between metabolic syndrome and cancer survivors have been performed in Asia, where the leading causes of cancer differ from Western countries. In Korea, the top five prevalent cancer types are the stomach, colorectum, liver, prostate, and lung among male cancer survivors, whereas thyroid, breast, stomach, colorectum, and cervix uteri are the top five among female (Jung et al., 2011). The risk of metabolic syndrome in Korean cancer survivors could be affected from the differences in race and in leading cancer types. Moreover, socio-demographic, behavioral, and cultural factors of Korean cancer survivors are different from western countries, and could affect the long-term consequences. The objectives are to evaluate the prevalence of metabolic syndrome and identify risk factors, including oncological and non-oncological factors, among Korean cancer survivors.

Materials and Methods

Overview of survey and study population

The fourth Korean National Health and Nutrition Examination Survey 2007-2009 (KNHANES IV) was a nationally representative survey conducted by the Division of Chronic Disease Surveillance under the Korea Centers for Disease Control and Prevention on an annual basis since 1998 to accurately determine national health and nutrition levels and for the purpose of gaining basic data (Korea Centers for Disease Control and Prevention, 2010). The survey is composed of 3 parts: (1) health interview survey, (2) health examination survey, and (3) nutritional survey. A face to face interview at participants' home by trained interviewers was applied to gather health interview survey. The standardized health examination survey was conducted in specially equipped mobile examination centers.

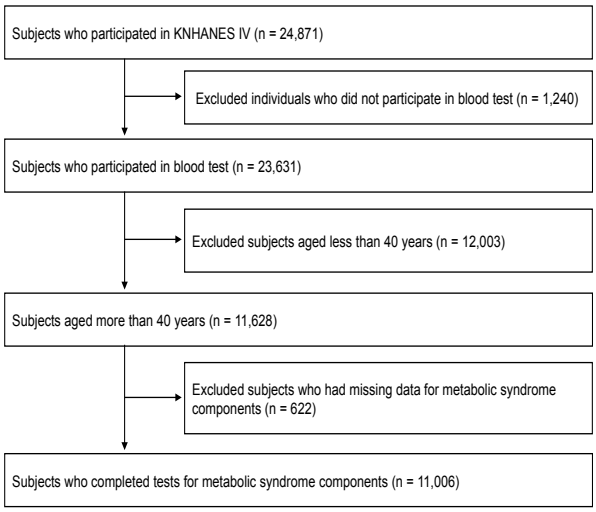

Figure 1. Flow Diagram Showing Selection of the Study Population

A stratified multistage clustered probability sampling was used to choose a representative sample of the non-institutional civilian population (see Figure 1). The sampling frame of participants was derived from the 2005 Population Census. Stratification was conducted based on the 13 areas of Korea (seven metropolitan cities and six provinces), administrative unit (dong or eup-myeon; Korean units), and the dwelling type (apartment house or others). From a total of 3,573 administrative units, 500 primary sampling units (PSUs) were randomly allocated as follows: 100 in 2007, 200 in 2008 and 200 in 2009, respectively. Twenty households per PSU were randomly derived from those primary sampling units with age and sex stratification. A total of 4594, 9744, and 10533 participated in the health interview survey or health examination surveys of 2007, 2008, and 2009, respectively, with response rates of 71.2, 77.8, and 82.8%. Out of 24,871 subjects, blood tests were performed on 23,631 (4246 in 2007, 9307 in 2008, and 10078 in 2009) individuals aged ≥10 years. After excluding 12,003 participants aged less than 40 years, 11,628 subjects were used for the current study. Subjects with any missing data for the metabolic syndrome component of the survey were excluded (n=622). The subjects included in our study were 11,006 persons who were aged ≥ 40 years and completed tests for metabolic syndrome component. Cancer survivors were classified if they reported having ever been told by a doctor that they had cancer or a malignancy of any kind. The cancer survivors were 335 persons as the final population. Institutional Review Board approval was waived due to using open data sets to public.

Associated factors and definition of metabolic syndrome

We collected information about various factors that could be associated with risk of metabolic syndrome. We assessed variables related to socio-demographic factors, behavioral factors, psychological factors, and oncological factors. The socio-demographic variables were sex, current age (<60 years and ≥60 years), education level (less than elementary school, middle/high school, and more than college), monthly household income (<573 $, 573-1,332$ and ≥1,332$) and residential area (urban or rural). Household monthly income was divided into tertiles, and income per adult equivalent was calculated using the formula household income/square root of the number of persons in the household.

Behavioral risk factors included body mass index (BMI), current smoking status (no or yes), heavy alcohol consumption (no or yes), and the level of physical activity (inadequate or adequate). BMI was obtained from each subjects and categorized as follows: <23, 23–25, and ≥25 (WHO, 2000). Heavy alcohol consumption was defined as consumption of 5 or more drinks on a single occasion, or drinking almost every day. Subjects were asked about their average frequency and amount of alcoholic beverage intake during the year before the interview. Heavy alcohol consumption was defined by self-reported

more than 5 drinks on a single occasion, or daily drinking of more than 1 drink per day (Amparo et al., 2011). We defined adequate physical activity as doing 30 minutes of moderate-intensity physical activity on 5 or more days of the week or 20 minutes of vigorous-intensity physical activity on 3 or more days of the week as recommended by the American College of Sports Medicine and the American Heart Association (Haskell et al., 2007).

Psychological factors were self-reported depression (no or yes) and suicidal ideation within 1 year (no or yes). Self-reported depression was determined if participants reported having ever been diagnosed as depression by a doctor. Oncological factors were cancer types (gastric, breast, cervix uteri, and other cancer type) and duration since diagnosis (<5, 5–10, ≥10 years). Cancer survivors were also asked about the site and the age of diagnosis. In our study, we classified cancer types as gastric, colon, breast, cervix uteri, and other cancer. The cancer type which included less than 20 subjects was classified as other cancer. Therefore, several common cancers such as liver, lung, prostate, thyroid, esophagus, pancreas, and ovary were classified as other cancer type due to small number in this survey.

Metabolic syndrome were defined as a combination of clinical disorders that includes the presence of three or more indicators: 1) abdominal obesity (waist circumference >90 cm in males or 80 cm in females), standard values modified by Asian standards; 2) high triglyceride level (≥150mg/dL); 3) low level of high density lipoprotein (<40 mg/dL); 4) high blood pressure (≥130/85 mmHg); 5) high fasting plasma glucose (≥100mg/dL); 6) current medication for treatment of any of the above conditions such as statins, anti-hypertensive drugs, anti-diabetic medications, according to the 2009 consensus criteria and the waist circumference criteria of the Regional Office for the Western Pacific Region of World Health Organization (Alberti et al., 2009).

Statistical Analysis

The calculated sampling weights were available from the KNHANES dataset to consider the sampling and response rates. This was particularly important for survey data because the sampling probabilities could be different among sampling clusters (Lehtonen and Pahkinen, 2004). Thus, we used the sampling weights that the KNHANES provided for all of the data analyses in this study. All estimates in the analysis were properly weighted to represent the general population. Descriptive statistical methods were used to demonstrate the basic characteristics of the study population; estimated proportion and standard errors were reported for each variable. The prevalence of each component of metabolic syndrome was measured according to cancer survivors and non-cancer controls. We evaluated the adjusted proportion of metabolic syndrome according to each cancer type (gastric, colon, breast, cervix uteri) and non-cancer controls. Multi-dimensional approach to identify factors associated with metabolic syndrome among cancer survivors was used. First, odds ratios (OR) for metabolic syndrome were calculated by univariate analysis. Then, multiple logistic regression analysis was performed by adjusting socio-demographic factors, psychological factors, behavioral factors, and

Table 1. Baseline Characteristics

Variables	Non–cancer controls (N=10671)	Cancer survivors (N=335)	P-value
Socio–demographic factors			
Sex			
Male	48.9(0.6)	34.9(3.4)	
Female	51.1(0.6)	65.1(3.4)	<0.001
Age			
40–59	68.6(0.5)	48.8(3.5)	
≥60	31.4(0.5)	51.2(3.5)	<0.001
Education level			
≤Elementary	34.2(0.6)	43.1(3.4)	
Middle/high	46.6(0.6)	42.1(3.6)	
≥College	19.2(0.6)	14.8(2.8)	0.037
Monthly income ($)			
<573	26.1(0.5)	28.5(2.9)	
573–1,332	36.2(0.6)	35.0(3.4)	
≥1,332	34.1(0.6)	31.3(3.4)	0.483
Residential area			
Urban	45.8(0.6)	51.8(3.5)	
Rural	54.2(0.6)	48.2(3.5)	0.092
Behavioral factors			
BMI			
<23	36.9(0.6)	45.7(3.5)	
≥23 & <25	26.5(0.5)	23.9(3.1)	
≥25	36.6(0.6)	30.5(3.4)	0.042
Smoking			
Non or past smoker	77.3(0.5)	90.3(2.5)	
Current smoker	22.7(0.5)	9.7(2.5)	<0.001
Alcohol			
Non	71.1(0.6)	91.9(2.4)	
Heavy drinking[a]	28.9(0.6)	8.1(2.4)	<0.001
Physical activity			
Inadequate	73.7(0.5)	70.3(3.3)	
Adequate[b]	26.3(0.5)	29.7(3.3)	0.283
Psychological factors			
Self–reported depression			
No	94.9(0.2)	94.2(1.4)	
Yes	5.1(0;2)	5.8(1.4)	0.614
Suicidal idea within 1 year			
No	81.4(0.5)	78.1(2.8)	
Yes	18.3(0.5)	21.7(2.8)	0.306
Oncological factors			
Type			
Gastric		21.5 (2.7)	
Colon		9.8(2.4)	
Breast		16.1(2.7)	
Cervix uteri		21.2(3.0)	
Other		31.4(3.2)	
Duration since diagnosis			
<5		50.0(3.5)	
≥5 & <10		21.2(2.8)	
≥10		28.9(3.3)	

SE, standard error; [a] Heavy drinking defined as self-reported more than 5 drinks on a single occasion, or daily drinking of more than 1 drink per day; [b]Adequate physical activity defined as doing 30 minutes of moderate-intensity physical activity on 5 or more days of the week or 20 minutes of vigorous–intensity physical activity on 3 or more days of the week

Table 2. Metabolic Syndrome Components among Cancer Survivors and Controls (N = 11,106)

Components	Non–cancer controls (N = 10,671)	Cancer Survivors (N = 335)	Gastric cancer survivors (N = 82)	Colon cancer survivors (N = 30)	Breast Cancer survivors (N = 48)	Uterine cervix Cancer Survivors (N = 65)	Other Cancer survivors (N = 110)
Abdominal Obesity							
Estimated proportion % (SE)	41.7 (0.6)	41.9 (3.5)	19.8 (6.2)	46.7 (13.1)	60.1 (8.7)	43.4 (7.8)	45.1 (6.0)
Crude OR (95% CI)	1	1.01 (0.76–1.34)	0.35 (0.16–0.75)	1.22 (0.43–3.45)	2.10 (1.03–4.30)	1.07 (0.57–2.00)	1.15 (0.72–1.85)
Adjusted OR[b] (95% CI)	1	1.00 (0.61–1.64)	0.44 (0.23–0.85)	3.39 (0.95–12.12)	1.06 (0.47–2.38)	0.60 (0.16–2.28)	1.26 (0.57–2.80)
High triglyceride							
Estimated proportion % (SE)	35.3 (0.6)	23.1 (3.1)	7.7 (2.6)	23.0 (9.1)	24.5 (9.7)	28.4 (7.6)	29.4 (5.3)
Crude OR (95% CI)	1	0.55 (0.39–0.78)	0.15 (0.07–0.32)	0.55 (0.20–1.49)	0.60 (0.21–1.66)	0.73 (0.35–1.52)	0.76 (0.46–1.27)
Adjusted OR[b] (95% CI)	1	0.67 (0.46–0.97)	0.18 (0.09–0.36)	0.43 (0.13–1.41)	0.77 (0.26–2.25)	1.13 (0.47–2.75)	0.89 (0.54–1.48)
Low HDL cholesterol							
Estimated proportion % (SE)	43.7 (0.6)	48.2 (3.5)	36.8 (6.7)	48.4 (13.0)	73.2 (7.1)	47.1 (8.0)	43.8 (6.0)
Crude OR (95% CI)	1	1.20 (0.90–1.59)	0.75 (0.42–1.32)	1.21 (0.44–3.36)	3.51 (1.72–7.18)	1.15 (0.61–2.16)	1.01 (0.62–1.62)
Adjusted OR[b] (95% CI)	1	1.05 (0.78–1.41)	0.84 (0.48–1.44)	1.39 (0.46–4.18)	2.28 (1.17–4.46)	0.82 (0.40–1.67)	0.91 (0.54–1.54)
High blood pressure							
Estimated proportion % (SE)	38.7	30.9 (3.2)	31.5 (5.6)	39.1 (13.6)	44.9 (9.1)	28.2 (6.6)	22.6 (4.8)
Crude OR (95% CI)	1	0.71 (0.53–0.95)	0.73 (0.44–1.22)	1.02 (0.33–3.14)	1.29 (0.62–2.67)	0.62 (0.33–1.18)	0.46 (0.27–0.79)
Adjusted OR[b] (95% CI)	1	0.68 (0.50–0.92)	0.62 (0.37–1.05)	0.70 (0.25–2.01)	1.61 (0.78–3.34)	0.86 (0.46–1.60)	0.38 (0.22–0.67)
Impaired glucose tolerance							
Estimated proportion % (SE)	34.4 (0.6)	31.1 (3.2)	24.9 (5.5)	25.7 (9.0)	30.9 (9.6)	28.1 (6.7)	39.1 (5.9)
Crude OR (95% CI)	1	0.86 (0.64–1.16)	0.63 (0.36–1.13)	0.67 (0.26–1.67)	0.85 (0.35–2.07)	0.75 (0.39–1.43)	1.23 (0.75–2.00)
Adjusted OR[b] (95% CI)	1	0.92 (0.66–1.27)	0.64 (0.37–1.11)	0.52 (0.18–1.51)	1.04 (0.40–2.74)	1.03 (0.53–1.98)	1.19 (0.69–2.06)
Metabolic Syndrome[a]							
Estimated proportion % (SE)	33.5 (0.6)	28.5 (3.3)	13.5 (4.5)	43.3 (13.4)	43.9 (9.5)	26.8 (6.4)	28.1 (4.9)
Crude OR (95% CI)	1	0.79 (0.58–1.09)	0.34 (0.16–0.72)	1.51 (0.52–4.41)	1.59 (0.74–3.40)	0.73 (0.38–1.38)	0.72 (0.45–1.16)
Adjusted OR[b] (95% CI)	1	0.80 (0.56–1.14)	0.42 (0.20–0.86)	1.60 (0.57–4.54)	1.40 (0.62–3.18)	0.75 (0.33–1.71)	0.67 (0.37–1.22)

SE, standard error; OR, odds ratio; CI, confidence interval; HDL, high density lipoprotein; [a]Clinical diagnosis of metabolic syndrome was made on the basis of meeting ≥3 of the following criteria: (1) abdominal obesity, waist circumference > 90 cm (males) or 80 cm (females); (2) triglycerides ≥ 150 mg/dL; (3) HDL cholesterol < 40 mg/dL (males) or 50 mg/dL (females); (4) systolic blood pressure ≥ 130 mm Hg, diastolic blood pressure ≥ 85 mm Hg; (5) fasting glucose ≥ 100 mg/dL; or current medication for treatment of any of the above conditions such as statins, anti–hypertensive drugs, and anti–diabetic medications; [b]Adjusted by gender, age, education, income, residential area, BMI, smoking, alcohol drinking, physical activity, depression, and suicidal idea

oncological factors. Adjusted odds ratio (aOR) and 95% confidence intervals (CI) were calculated to show the strength of each association. P-values less than 0.05 were considered significant, and all statistical tests were two-sided. All statistical tests were performed using STATA 11.0 (Stata Corp., College Station, Texas, USA).

Results

Baseline characteristics

A positive cancer history was reported by approximately 3% of the study population. The baseline characteristics of study participants are summarized in Table 1. Cancer survivors were older than non-cancer controls (≥ 60 years: 51.2% vs. 31.4%, respectively), and more likely to be female (65.1% vs. 51.1%, respectively). Cancer survivors were less likely to be obese than the general population (BMI ≥25: 30.5% vs. 36.6%, respectively). High risk behaviors such as smoking and heavy alcohol drinking were less likely to be observed in cancer survivors than in non-cancer controls (current smoking: 9.7% vs. 22.7% and heavy alcohol consumption 8.1% vs. 28.9%, respectively). Among cancer survivors, gastric cancer was the most common cancer (23%), followed by cervix uteri (21.2%), breast cancer (16.3%), and colon cancer (9.8%). Approximately 50% survived more than 5 years after diagnosis.

Metabolic syndrome components among cancer survivors and non-cancer controls

The crude proportions of metabolic syndrome were 28.5% in cancer survivors and 33.5% in the general population, respectively. Table 2 showed the prevalence of each metabolic syndrome component according to cancer status. The prevalence of elevated blood pressure, systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, was 30.9% in cancer survivors and 38.7% in non-cancer controls (P = 0.02). In addition, the crude proportion of elevated triglycerides was 23.1% in cancer survivors and 35.3% in the general populations (P < 0.001). The risk for metabolic syndrome among cancer survivors was lower than non-cancer controls, but this association was not statistically significant (aOR 0.80, 95% CI 0.56–1.14). Gastric cancer survivors showed decreased aOR for metabolic syndrome than non-cancer controls (aOR 0.42, 95% CI 0.20–0.86). When we evaluated cancer survivors by excluding gastric cancer survivors, a similar risk for metabolic syndrome was observed compared to non-cancer controls (aOR 0.96, 95% CI 0.64–1.45). Colon cancer and breast cancer survivors had higher risk for metabolic syndrome than non-cancer controls, but none of them were statistically significant.

We separated our sample into two subgroups according to age group (40–59 years and ≥60 years) and performed a subgroup analysis. We did not find a significant difference in the risk of metabolic syndrome between cancer survivors and non-cancer controls across different age groups. In participants who aged 40–59 years, cancer survivors were not at higher risk for metabolic syndrome compared to non-cancer controls (aOR 0.66, 95% CI 0.34–1.28). Similarly in the older age group (≥60 years), cancer survivors did not have significantly different risk for metabolic syndrome

Table 3. Factors in Univariate and Multivariate Analysis Models

Variables	Model 1		Model 2	
	Univariate OR	95% CI	Multivariate OR	95% CI
Socio–demographic factors				
Sex				
Male	1		1	
Female	1.55	(0.76–3.18)	1.42	(0.56–3.58)
Age				
40–59	1		1	
≥60	2.11	(1.08–4.15)	4.83	(1.94–12.03)
Education level				
≤Elementary	1		1	
Middle/high	0.57	(0.29–1.12)	0.69	(0.29–1.68)
≥College	0.29	(0.06–1.54)	0.4	(0.91–1.73)
Monthly income ($)				
< 573	1		1	
573–1,332	1.04	(0.52–2.10)	1.86	(0.77–4.45)
≥ 1,332	0.59	(0.26–1.33)	1.26	(0.45–3.45)
Residential area				
Urban	1		1	
Rural	0.8	(0.43–1.47)	0.82	(0.42–1.61)
Behavioral factors				
BMI				
<23	1		1	
≥23 & <25	6.08	(2.56–14.46)	6.71	(2.90–15.57)
≥25	9.34	(4.18–20.91)	12.2	(5.20–28.77)
Smoking				
Past smoker	1		1	
Current smoker	1.67	(0.50–5.80)	1.47	(0.42–5.15)
Alcohol				
Non	1		1	
Heavy drinking[a]	1.65	(0.39–6.94)	1.27	(0.29–5.61)
Physical activity				
Inadequate	1		1	
Adequate[b]	0.71	(0.36–1.38)	1.04	(0.49–2.19)
Psychological factors				
Self–reported depression				
No	1		1	
Yes	1.09	(0.38–3.84)	0.71	(0.16–3.42)
Suicidal idea within 1 year				
No	1		1	
Yes	1.56	(0.79–3.05)	0.89	(0.34–2.31)
Oncological factors				
Type				
Others	1		1	
Gastric cancer	0.34	(0.18–0.64)	0.56	(0.24–1.30)
Duration since diagnosis				
<5	1		1	
≥5 & <10	1.06	(0.49–2.29)	1.05	(0.45–2.46)
≥10	1.32	(0.62–2.78)	1.05	(0.45–2.48)

OR, odds ratio; CI, confidence interval; [a]Heavy drinking defined as self–reported more than 5 drinks on a single occasion, or daily drinking of more than 1 drink per day; [b] Adequate physical activity defined as doing 30 minutes of moderate–intensity physical activity on 5 or more days of the week or 20 minutes of vigorous–intensity physical activity on 3 or more days of the week

compared to non-cancer controls (aOR 0.89, 95% CI 0.59–1.34).

Factors associated with metabolic syndrome among cancer survivors

The factors shown to be associated with metabolic syndrome by univariate analysis (Model 1) were age group, BMI, and cancer type (Table 3). All variables used in the univariate analysis were included in the multivariate analysis (Model 2). Model 2 controlled for socio-demographic factors, psychological factors, behavioral factors, and oncological factors. The risk for metabolic syndrome among cancer survivors was related with age group, and BMI after adjusting co-variates. Cancer survivors aged ≥60 years had higher risk for metabolic syndrome (aOR 4.83, 95% CI 1.94–12.03) compared with those in the reference category (40–59 years). Cancer survivors with BMI level 23–25 had higher odds ratio for metabolic syndrome (aOR 6.71, 95% CI 2.90–15.57) than group with BMI <23. Highest odds ratio for metabolic syndrome was found in cancer survivors who had BMI ≥25 (aOR 12.23, 95% CI 5.20–28.77). Gastric cancer survivors were less likely to have metabolic syndrome than other cancer types excluding stomach cancer (aOR 0.56, 95% CI 0.24–1.30). However, this association was not statistically significant.

Discussion

In this study, cancer survivors had similar or even better metabolic syndrome component compared to the non-cancer controls. Among Korean cancer survivors aged ≥40years, 28.5% had metabolic syndrome. Previous studies from western countries have demonstrated that the results varied according to cancer types. Cancer survivors from hematologic malignancies showed higher odds ratios for metabolic syndrome (Kourti et al., 2005; Follin et al., 2006; Gurney et al., 2006; Trimis et al., 2007). However, inconsistent results were observed in cancer survivors with solid tumors (Nuver et al., 2005; Braga-Basaria et al., 2006; Haugnes et al., 2007). Based on the Third National Health and Nutrition Examination, U.S. population-based surveys, the prevalence of metabolic syndrome was higher among cancer survivors than non-cancer controls (Ness et al., 2005). In Korea, the distribution of prevalent cancer type is different from Western countries. Furthermore, there are few studies about the associations between the gastric cancer and metabolic syndrome, which is one of the most common cancers in Korea.

Gastric cancer patients had lower risk for metabolic syndrome compared to the general population. Gastrectomy is the gold standard for curative treatment modality performed on gastric cancer patients (Brennan and Karpeh, 1996). Previous studies have shown that poor nutritional status was observed in patients who had undergone gastrectomy (Bae et al., 1998; Carey et al., 2011). After the operation, severe fat malnutrition and vitamin deficiency were found (Bae et al., 1998). Major upper gastrointestinal surgery affects permanent alterations to the gastrointestinal tract, and therefore results in weight loss, body change, and malabsorption (Carey et al., 2011). Moreover, bariatric surgery can provide sustained weight loss and reduced obesity-related mortality by reducing gastric size (Ashrafian et al., 2011).

Although there are few studies about the association between gastric cancer and metabolic syndrome, we could explain the lower prevalence of metabolic syndrome among Korean cancer survivors through the relatively high proportions of gastric cancer patients in Korea. Despite failing to show statistical significance, breast cancer and colon cancer survivors had higher aOR for metabolic syndrome than non-cancer controls. There can be an increasing prevalence for metabolic syndrome in the near future due to the increasing trend of breast and colon cancer and the decreasing trend of gastric cancer in Korea (Jung et al., 2011).

General risk factors for metabolic syndrome are female, old age, high BMI, current smoking status, heavy alcohol consumption, inadequate physical activity and low socio-economic level (Park et al., 2004; Erem et al., 2008; Mohamud et al., 2011; Rodrigues et al., 2013). In our study, only 2 risk factors (age and BMI) among many variables showed a significant association with metabolic syndrome in cancer survivors. Age is well accepted to be one of the strongest predictor of metabolic syndrome in the general population (Riediger and Clara, 2011). This finding is consistent with those of other studies carried out in Korea as well as world-wide (Ford et al., 2002; Park et al., 2004; Erem et al., 2008; Mohamud et al., 2011; Rodrigues et al., 2013). This association is due to the inevitable physiological processes of aging, such as declining basal metabolic rate, changes in body composition, and unhealthy lifestyle (Bechtold et al., 2006). While muscle mass decreases up to 40% from 20 to 70 years of age (Villareal et al., 2005), fat mass increases with the predominance of abdominal fat accumulation (Visser et al., 1998), and these aging-related changes lead to increasing intra-abdominal fat, specifically central obesity, which is associated with cardiovascular disease risk factors (Grinker et al., 1995; Bo et al., 2009). Management of metabolic syndrome in the elderly is difficult because co-management of multiple co-morbid conditions is often required (Bechtold et al., 2006). Especially for cancer survivors, a higher proportion of non-cancer mortalities was observed in the elderly than the younger age-group (Shin et al., 2010a). Moreover, cancer survivors were less likely to have an appropriate medication adherence, and the proportion of adherence was lower in the old age group than in the young age group (Shin et al., 2010b). Considering the previously mentioned aspects, treatment of metabolic syndrome among elderly cancer survivors is one of the most challenging issues. Therefore, primary prevention and early intervention should be required to manage the metabolic syndrome among cancer survivors, especially for the elderly.

We observed that aOR increased with higher BMI when adjusting for other variables, and that BMI was the most sensitive marker for the metabolic syndrome. This finding is consistent with previous studies from general population in Korea and the United States (Park et al., 2003; Park et al., 2004). The pathophysiology of the metabolic syndrome is largely attributable to insulin resistance. Overweight, obesity, and especially a central pattern of fat accumulation are related to insulin resistance (Lechleitner, 2008). Obesity is associated with cancer recurrence and mortality in some cancer types such as breast, colon, and prostate cancer (Meyerhardt et al., 2003; Amling et al., 2004; Whiteman et al., 2005). Obese survivors in cancers with high long-term survival, such as breast, colon, and prostate cancers, may have greater chance to be exposed to the obesity-related co-morbidities and mortalities than patients with aggressive cancers (Park et al., 2006). Moreover, treatment-related weight gain is often observed in breast and prostate cancer patients due to hormonal therapy or reduced physical activity (Tayek et al., 1990; Chlebowski et al., 2002). Efforts to control weight may be a key strategy to reduce mortality from cancer as well as to prevent metabolic syndrome. In breast cancer survivors, significant reductions in fasting serum insulins and leptin as well as significant improvement in quality of life were observed with weight control intervention (Befort et al., 2012).

As the number of long-term cancer survivors is growing, the evaluation and management of their health-related problems have become an important issue. Cardiovascular disease is the most common cause of non-cancer mortality in cancer survivors, and metabolic syndrome represents the link to the increased cardiovascular disease (Brown et al., 1993; Shin et al., 2010a). Among cancer survivors, old age and high BMI are identified as risk factors for metabolic syndrome. It is important for the healthcare provider to assess and screen the metabolic syndrome of cancer survivors who are elderly and obese. While age and cancer type are non-modifiable factors, BMI can be modifiable with efforts to control weight. Thus, weight control intervention program should be suggested for long-term cancer survivors to prevent metabolic syndrome.

Several limitations should be considered in our studies. First, we could not document causal association between factors and metabolic syndrome because of the cross-sectional nature of our study design(Forootan et al., 2012). Because obesity is associated with increased risk for some cancer types such as breast and endometrial cancer, the causal relationship between obesity and cancer is obscure(Ronco et al., 2012). In addition, Preexisting metabolic syndrome before diagnosis and treatment among cancer survivors could not be identified due to lack of available data. Second, several important information could not be collected from survey. We could not know treatment modalities of each patient from survey. Changes in endocrine and metabolic functions varied according to treatment modality such as systemic cancer therapy (hormone therapy and chemotherapy), and local treatments (radiation and surgery). Because several common cancer types such as liver, lung, thyroid and prostate cancer were included in other cancer groups, we could not estimate the precise association with metabolic syndrome in those cancer survivors. Therefore, information about various cancer

types and treatment modalities should be included in future studies. Third, most of the information was from self-reported questionnaires, so reporting bias cannot be excluded. Moreover, we excluded incomplete data or non-participation in the survey.

In spite of these limitations, this study identified risk factors for metabolic syndrome among cancer survivors and suggested a strategy to prevent cardiovascular mortality. To the best of our knowledge, this is the first Asian study to evaluate the prevalence of metabolic syndrome between cancer survivors and non-cancer controls. Our study demonstrated that cancer survivors in Korea were not at an increased risk of metabolic syndrome. However, as cancer patterns are changing to a more Westernized style, there is an increasing trend in breast and colon cancer and a decreasing trend in gastric cancer. Therefore increasing metabolic syndrome in cancer survivors will be expected in the near future in Korea. Screening and treatment of the metabolic syndrome should be performed comprehensively considering disease status and risk factors of survivors, taking into account high risk groups identified here. Large scale cohort studies including information about various cancer types and treatment modalities are needed to investigate and evaluate the association between cancer survivors and metabolic syndrome.

Acknowledgement

We thank the members of the Korea Institute for Health and Social Affairs who conducted the national survey and everyone who contributed to this project.

References

Alberti KG, Eckel RH, Grundy SM, et al (2009). Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*, **120**, 1640-5.

Amling CL, Riffenburgh RH, Sun L, et al (2004). Pathologic variables and recurrence rates as related to obesity and race in men with prostate cancer undergoing radical prostatectomy. *J Clin Oncol*, **22**, 439-45.

Amparo P, Farr SL, Dietz PM (2011). Chronic disease risk factors among American Indian/Alaska Native women of reproductive age. *Prev Chronic Dis*, **8**, A118.

Annaloro C, Usardi P, Airaghi L, et al (2008). Prevalence of metabolic syndrome in long-term survivors of hematopoietic stem cell transplantation. *Bone Marrow Transplant*, **41**, 797-804.

Ashrafian H, Ahmed K, Rowland SP, et al (2011). Metabolic surgery and cancer: protective effects of bariatric procedures. *Cancer*, **117**, 1788-99.

Bae JM, Park JW, Yang HK, et al (1998). Nutritional status of gastric cancer patients after total gastrectomy. *World J Surg*, **22**, 254-60; discussion 60-1.

Bechtold M, Palmer J, Valtos J, et al (2006). Metabolic syndrome in the elderly. *Curr Diab Rep*, **6**, 64-71.

Befort CA, Klemp JR, Austin HL, et al (2012). Outcomes of a weight loss intervention among rural breast cancer survivors. *Breast Cancer Res Treat*, **132**, 631-9.

Bo M, Sona A, Astengo M, et al (2009). Metabolic syndrome in older subjects: coincidence or clustering? *Arch Gerontol Geriatr*, **48**, 146-50.

Boyle P, Levin B (2008). World cancer report 2008, Lyon, IARC Press.

Braga-Basaria M, Dobs AS, Muller DC, et al (2006). Metabolic syndrome in men with prostate cancer undergoing long-term androgen-deprivation therapy. *J Clin Oncol*, **24**, 3979-83.

Brennan MF, Karpeh MS, JR (1996). Surgery for gastric cancer: the American view. *Semin Oncol*, **23**, 352-9.

Brown BW, Brauner C, Minnotte MC (1993). Noncancer deaths in white adult cancer patients. *J Natl Cancer Inst*, **85**, 979-87.

Cabre JJ, Martin F, Costa B, et al (2008). Metabolic syndrome as a cardiovascular disease risk factor: patients evaluated in primary care. *BMC Public Health*, **8**, 251.

Carey S, Storey D, Biankin AV, et al (2011). Long term nutritional status and quality of life following major upper gastrointestinal surgery - a cross-sectional study. *Clin Nutr*, **30**, 774-9.

Chlebowski RT, Aiello E, Mctiernan A (2002). Weight loss in breast cancer patient management. *J Clin Oncol*, **20**, 1128-43.

Erem C, Hacihasanoglu A, Deger O, et al (2008). Prevalence of metabolic syndrome and associated risk factors among Turkish adults: Trabzon MetS study. *Endocrine*, **33**, 9-20.

Follin C, Thilen U, Ahren B, et al (2006). Improvement in cardiac systolic function and reduced prevalence of metabolic syndrome after two years of growth hormone (GH) treatment in GH-deficient adult survivors of childhood-onset acute lymphoblastic leukemia. *J Clin Endocrinol Metab*, **91**, 1872-5.

Ford ES, Giles WH, Dietz WH (2002). Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA*, **287**, 356-9.

Forootan M, Tabatabaeefar M, Yahyaei M, et al (2012). Metabolic syndrome and colorectal cancer:a cross-sectional survey. *Asian Pac J Cancer Prev*, **13**, 4999-5002.

Gami AS, Witt BJ, Howard DE, et al (2007). Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol*, **49**, 403-14.

Grinker JA, Tucker K, Vokonas PS, et al (1995). Body habitus changes among adult males from the normative aging study: relations to aging, smoking history and alcohol intake. *Obes Res*, **3**, 435-46.

Gurney JG, Ness KK, Sibley SD, et al (2006). Metabolic syndrome and growth hormone deficiency in adult survivors of childhood acute lymphoblastic leukemia. *Cancer*, **107**, 1303-12.

Haskell WL, Lee IM, Pate RR, et al (2007). Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Med Sci Sports Exerc*, **39**, 1423-34.

Haugnes HS, Aass N, Fossa SD, et al (2007). Components of the metabolic syndrome in long-term survivors of testicular cancer. *Ann Oncol*, **18**, 241-8.

Jung HS, Myung SK, Kim BS, et al (2012). Metabolic

syndrome in adult cancer survivors: a meta-analysis. *Diabetes Res Clin Pract*, **95**, 275-82.
Jung KW, Park S, Kong HJ, et al (2011). Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2008. *Cancer Res Treat*, **43**, 1-11.
Korea Centers for Disease Control and Prevention (2010). The fourth Korean National Health and Nutrition Examination Survey [Online], Available from: http://knhanes.cdc.go.kr. [2012, Sepember 1]. [Online].
Kourti M, Tragiannidis A, Makedou A, et al (2005). Metabolic syndrome in children and adolescents with acute lymphoblastic leukemia after the completion of chemotherapy. *J Pediatr Hematol Oncol*, **27**, 499-501.
Lechleitner M (2008). Obesity and the metabolic syndrome in the elderly--a mini-review. *Gerontology*, **54**, 253-9.
Lehtonen R, Pahkinen E (2004). Practical methods for design and analysis of complex surveys (2nd ed.). Chichester, England: John Wiley & Sons.
Liavaag AH, Tonstad S, Pripp AH, et al (2009). Prevalence and determinants of metabolic syndrome and elevated Framingham risk score in epithelial ovarian cancer survivors: a controlled observational study. *Int J Gynecol Cancer*, **19**, 634-40.
Meyerhardt JA, Catalano PJ, Haller DG, et al (2003). Influence of body mass index on outcomes and treatment-related toxicity in patients with colon carcinoma. *Cancer*, **98**, 484-95.
Mohamud WN, Ismail A, Khir AS, et al (2011). Prevalence of metabolic syndrome and its risk factors in adult Malaysians: results of a nationwide survey. *Diabetes Res Clin Pract*, **96**, 91-7.
National Cancer Information Center (2011). Cancer incidence [Online], Available from: http://www.cancer.go.kr/ncic/cics_f/01/011/index.html. [2012, September 14].
National Cancer Institute (2012). SEER Cancer Statistics Review, 1975-2009 [Online], Available from: http://seer.cancer.gov/csr/1975_2009_pops09/. [2012, April 1].
Ness KK, Oakes JM, Punyko JA, et al (2005). Prevalence of the metabolic syndrome in relation to self-reported cancer history. *Ann Epidemiol*, **15**, 202-6.
Nuver J, Smit AJ, Wolffenbuttel BH, et al (2005). The metabolic syndrome and disturbances in hormone levels in long-term survivors of disseminated testicular cancer. *J Clin Oncol*, **23**, 3718-25.
Oeffinger KC, Mertens AC, Sklar CA, et al (2006). Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med*, **355**, 1572-82.
Park HS, Oh SW, Cho SI, et al (2004). The metabolic syndrome and associated lifestyle factors among South Korean adults. *Int J Epidemiol*, **33**, 328-36.
Park SM, Lim MK, Shin SA, et al (2006). Impact of prediagnosis smoking, alcohol, obesity, and insulin resistance on survival in male cancer patients: National Health Insurance Corporation Study. *J Clin Oncol*, **24**, 5017-24.
Park YW, Zhu S, Palaniappan L, et al (2003). The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med*, **163**, 427-36.
Redig AJ, Munshi HG (2010). Care of the cancer survivor: metabolic syndrome after hormone-modifying therapy. *Am J Med*, **123**, 87 e1-6.
Riediger ND, Clara I (2011). Prevalence of metabolic syndrome in the Canadian adult population. *CMAJ*, **183**, E1127-34.
Rodrigues AD, Theodoro H, Mendes KG, et al (2013). Factors associated with metabolic syndrome in climacteric women of southern Brazil. *Climacteric*, **16**, 96-103.
Ronco, AL, De Stefani E. Deoneo-Pellegrini H, et al (2012). Diabetes, overweight and risk of postmenopausal breast cancer : a case-control study in Uruguay. *Asian Pac J Cancer Prev*, **13**, 139-46.
Shin DW, Ahn E, Kim H, et al (2010a). Non-cancer mortality among long-term survivors of adult cancer in Korea: national cancer registry study. *Cancer Causes Control*, **21**, 919-29.
Shin DW, Nam JH, Kwon YC, et al (2008). Comorbidity in disease-free survivors of cervical cancer compared with the general female population. *Oncology*, **74**, 207-15.
Shin DW, Park JH, Park EC, et al (2010b). Antihypertensive medication adherence in cancer survivors and its affecting factors: results of a Korean population-based study. *Support Care Cancer*, **19**, 211-20.
Talvensaari KK, Lanning M, Tapanainen P, et al (1996). Long-term survivors of childhood cancer have an increased risk of manifesting the metabolic syndrome. *J Clin Endocrinol Metab*, **81**, 3051-5.
Tayek JA, Heber D, Byerley LO, et al (1990). Nutritional and metabolic effects of gonadotropin-releasing hormone agonist treatment for prostate cancer. *Metabolism*, **39**, 1314-9.
Trimis G, Moschovi M, Papassotiriou I, et al (2007). Early indicators of dysmetabolic syndrome in young survivors of acute lymphoblastic leukemia in childhood as a target for preventing disease. *J Pediatr Hematol Oncol*, **29**, 309-14.
Ulaganathan V, Kandiah M, Zalilah MS, et al (2012). Colorectal cancer and its association with the metabolic syndrome:a Malaysian multi-centric case-control study. *Asian Pac J Cancer Prev*, **13**, 3873-7.
Villareal DT, Apovian CM, Kushner RF, et al (2005). Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, The Obesity Society. *Obes Res*, **13**, 1849-63.
Visser M, Langlois J, Guralnik JM, et al (1998). High body fatness, but not low fat-free mass, predicts disability in older men and women: the Cardiovascular Health Study. *Am J Clin Nutr*, **68**, 584-90.
Whiteman MK, Hillis SD, Curtis KM, et al (2005). Body mass and mortality after breast cancer diagnosis. *Cancer Epidemiol Biomarkers Prev*, **14**, 2009-14.
WHO/IASO/IOTF (2000). The Asia-Pacific Perspective: Redefining Obesity and its Treatment. Melbourne: Health Communication, Australia. Pty Ltd.