RESEARCH ARTICLE

Prevalence of and Factors Associated with Osteoporosis among Korean Cancer Survivors: A Cross-Sectional Analysis of the Fourth and Fifth Korea National Health and Nutrition Examination Surveys

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Abstract

Background: Identifying and managing osteoporosis among cancer survivors is an important issue, yet little is known about the bone health of cancer survivors in Korea. This study was designed to measure the prevalence of osteoporosis and to assess related factors among Korean cancer survivors. Materials and Methods: This study was designed as a cross-sectional analysis. Data were obtained from dual energy X-ray absorptiometry measurement of the lumbar vertebrae and femoral neck, and from standardized questionnaires among 556 cancer survivors and 17,623 non-cancer controls who participated in the Fourth and Fifth Korea National Health and Nutrition Examination Surveys (2008-2011). We calculated adjusted proportions of osteoporosis in non-cancer controls vs. cancer survivors, and we performed multivariate logistic regression analysis. Results: The prevalence of osteoporosis among cancer survivors was significant higher than that of the non-cancer controls after adjusting for related factors. Furthermore, osteoporosis among cancer survivors was higher in elderly subjects (60-69 years : adjusted odds ratio (aOR) 3.04, 95% CI : 1.16-8.00, ≥70 years : aOR 6.60, 95% CI 2.20-19.79), in female cancer survivors (aOR: 7.03, 95% CI: 1.88-26.28), and in a group with lower monthly income (aOR: 3.38, 95% CI: 1.31-8.71). In male cancer survivors, underweight and lower calcium intake were risk factors. Conclusions: These data suggest that the osteoporosis among cancer survivors varies according to non-oncologic and oncologic factors. Effective screening should be applied, and a sufficient and comprehensive management should be matched to individual cancer survivors early after cancer treatment.

Keywords: Osteoporosis - prevalence - risk factor - cancer survivors - Korea

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Introduction

Five-year relative cancer survival rates have been improving worldwide (Jung et al., 2011; Siegel et al., 2012) In Korea, the prevalence of cancer was 1925.9 per 100,000 people in 2010; in other words, approximately 1 in 52 persons is a cancer patient (National Cancer Information Center, 2011). As the number of cancer survivors has increased, evaluating and managing their other health-related problems have become important issues (Moon et al., 2013). One of the most common long-term health effects in cancer survivors is bone loss, including osteoporosis (Guise, 2006; Saad et al., 2008). Bone loss in cancer survivors is generally known to be more rapid and severe than that in non-cancer population with normal age-related osteoporosis (Stava et al., 2009).

Risk for osteoporosis is increased in cancer patients, and damage to bone health can be exacerbated by cancer itself as well as treatments such as chemotherapy, radiation, and hormone therapy (Brown and Guise, 2009; Stava et al., 2009; Ding et al., 2013). Such decline in bone density greatly increase the risk of bone fracture and can have other serious effects on the quality of life (Guise, 2006). Appropriate screening, lifestyle interventions, and osteoporosis therapy for cancer survivors can prevent the morbidity and mortality associated with bone loss. Therefore, assessing and managing the risk factors for the development of osteoporosis are critical issues for all cancer survivors and their healthcare providers (Gralow et al., 2009).

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Bone densitometry is a tool for assessing osteoporosis and is readily accessible for a reasonable price in Korea because of the wide coverage of the National Health Service. Therefore, many patients in Korea, including cancer survivors, undergo bone densitometry to screen and treat osteoporosis. However, to the best of our knowledge, few studies have addressed the bone health of cancer survivors in Korea. Therefore, this study assessed the prevalence of osteoporosis and many non-oncologic and oncologic factors associated with a risk of osteoporosis using data from the Fourth Korean National Health and Nutrition Examination Survey 2008-2009 (KNHANES IV) and KNHANES V 2010-2011.

Materials and Methods

Study population

We used the data of the KNHANES IV (2008–2009) and KNHANES V (2010-2011); these are nationwide surveys representing the general Korean population and include comprehensive information on health status, health behavior, and sociodemographics. A stratified multistage probability sampling design was used. Face-to-face interviews at participants' homes were conducted by trained interviewers to gather health information. Each participant gave informed consent prior to inclusion in the studies.

Initially, 36,043 candidates who completed both the health interview and health examination surveys participated in this study. We then selected 18,179 persons aged ≥20 years who had undergone dual-energy X-ray absorptiometry (DXA). Finally, 556 cancer patients were selected as the study population (Figure 1). Because the survey data analyzed are publicly available, this study did not require the ethical approval of our Institutional Review Board.

Associated factors and definition of osteoporosis

From the surveys, we collected information about various factors potentially associated with the risk of osteoporosis. The risk factors were divided into 3 groups: sociodemographic, behavioral, and clinical factors (Figure 2). The sociodemographic factors were current age (20-59, 60-69 or ≥70 years), sex, education level (more than college education, middle/high school, below elementary school), household monthly income (<1,000,000 won, 1,010,000-3,000,000 won, or ≥3,000,000 won), area of residence (urban or rural), and health insurance types (medical assistance or none, government health insurance without private health insurance, government health insurance with private health insurance). Socioeconomic status or educational level were included as a risk factor potentially associated with osteoporosis because these factors were known to be associated with a number of chronic diseases including osteoporosis in many previous studies (Allali et al., 2010).

The behavioral risk factors included body mass index (BMI; underweight, normal or obese), smoking status (nonsmoker or past smoker, current smoker), alcohol consumption (nondrinker or non-risky drinker, risky drinker), weekly physical activity (tertiles: <8, 8-34.5, and >34.5 metabolic equivalents/week), and dietary calcium intake. BMI was calculated in kilograms per meter squared, and the participants were divided into 2 categories :<18.5 and ≥18.5 kg/m^2 (Lim et al., 2007). Risky drinking was defined as alcohol consumption exceeding 3 standard drinks per day (Ganry et al., 2000). Dietary calcium intake was monitored by 24-h recall, analyzed by CAN-Pro software 3.0 (Korean Nutrition Society, Seoul, Korea), and divided into tertiles: <336, 336-563, and >563 mg/day.

The clinical factors include familial history of osteoporosis or fracture, all cancer types (gastric cancer, hepatic cancer, colon cancer, breast cancer, cervical cancer, lung cancer, thyroid cancer and other cancers), and time since cancer diagnosis(less than 5 years, more than 5 years). In analysis of female cancer survivors, menopause status was included.

The system logics for BMD judgement based on 2007 International Society for Clinical Densitometry (ISCD) Official positrons and guidelines for BMD test with quality control, and interpretation of BMD results was corrected and complemented (Lewiecki et al., 2008). Furthermore, educated and quality-controlled osteoporosis examination surveyors calculated accurate and reliable results from the gathered data. The BMD (g/cm^2) measurements of the lumbar spine and femoral neck were obtained using DXA (DISCOVERY-W fan-beam densitometer; Hologic Inc., USA) (Korea National Health and Nutrition Examniation Survey, 2012). Osteoporosis was defined according to the World Health Organization (WHO) T-score criteria (T-score ≤–2.5). We used the maximum BMD value for Japanese patients (Orimo et al., 2001) because of the lack of established Korean diagnostic criteria. If a participant had a low T-score(T-score ≤–2.5) in a BMD measurement of the lumbar spine or femoral neck or both, the participant was classified as having osteoporosis. In addition, we considered participants taking some medications for osteoporosis (e.g., bisphosphonate, raloxifene, and hormonal agents) as having osteoporosis because of the possibility that the medication had increased their BMD.

Data analysis

We used a weighted population sample to reflect the sampling method and response rate.

We calculated the estimated proportions and standard errors for factors associated with osteoporosis in non-cancer controls and cancer survivors. The statistical significance of difference in groups according to cancer status was assessed using logistic regression. We calculated the adjusted proportions of osteoporosis in all, female, and male non-cancer controls vs. cancer survivors, and adjusted proportions of osteoporosis according to all cancer types. Next, we performed multivariate logistic regression analysis by adjusting for all sociodemographic, behavioral, and clinical factors in all cancer survivors, female cancer survivors, and male cancer survivors. The level of significance was set at p value < 0.05. All estimates in the analysis were properly weighted to represent the general Korean population using a complex, multistage, probability sampling design. All statistical analyses were performed using STATA 10.0 (Stata Corp., College

Station, TX, USA)

Results

General characteristics and prevalence of osteoporosis

The characteristics of the study participants are summarized in Table 1. Difference between two groups of non-cancer controls and cancer survivors were according to age, sex, educational level, monthly income level, smoking status, drinking status, menopause status, and health insurance types. The most common cancer type among all patients was gastric cancer (18.33%). The most prevalent cancer types in men were gastric cancer (32.62%), colon cancer (14.46%), and liver cancer (10.66%), whereas those in women were cervical cancer (22.99%), breast cancer (22.17%), and gastric cancer (11.20%). This distribution is a little different from the data of the Korea Central Cancer Registry. According to national statistics, the most prevalent cancer among all individuals in Korea is thyroid cancer. The most common cancers among male patients are gastric and colon cancers, whereas the most prevalent cancers among female patients are thyroid and breast cancers (National Cancer Information Center, 2011). And group with less than 5 years since cancer diagnosis was 43.23%. The group with 20 - 59 years old, 60-69 years old, and above 70years old was 52.61, 24.52, and 22.87%, respectively. 33.30% were men and 66.70% were women among cancer survivors. Among the study participants, 5.45% had a BMI <18.5 kg/m^2. Based on the WHO criteria, the prevalence of osteoporosis among cancer survivors over the age of 20 was 22.50% (T-score of the lumbar vertebrae or femoral neck ≤–2.5 or taking anti-osteoporotic medications).

Adjusted proportions of osteoporosis in non-cancer controls and cancer survivors, and in cancer survivors according to cancer types

The adjusted proportions for patient characteristics

Table 1. Characteristics of Non-Cancer Controls(n=17,623) vs. Cancer Survivors (n=556)

Variables			Total population Estimated proportion % (SE)	Non-cancer controls Estimated proportion % (SE)	Cancer survivors Estimated proportion % (SE)	p value
Age	20-59		80.74(0.53)	81.44(0.52)	52.61(2.74)	
	60-69		10.61(0.32)	10.26(0.31)	24.52(2.03)	<0.05
	≥70		8.65(0.30)	8.30(0.30)	22.87(1.99)	<0.05
Sex	Male		50.08(0.37)	50.50(0.38)	33.30(2.70)	
	Female		49.92(0.37)	49.50(0.38)	66.70(2.67)	<0.05
BMI	≥18.5		95.30(0.21)	95.32(0.21)	94.55(1.30)	
	<18.5		4.70(0.21)	4.68(0.21)	5.45(1.30)	0.53
Education	≥college		31.41(0.76)	31.75(0.76)	18.36(2.28)	
	Middle/high school		48.97(0.65)	49.13(0.66)	42.81(2.61)	<0.05
	≤elementary school		19.62(0.60)	19.12(0.61)	38.83(2.40)	<0.05
Monthly income (thousand won)	≥3,010		40.67(0.96)	40.87(0.96)	32.99(3.04)	
	1,010-3,000		42.12(0.86)	42.25(0.87)	37.07(2.91)	0.58
	≤1,000		17.21(0.57)	16.88(0.57)	29.94(2.50)	<0.05
Area of residence	Urban		80.07(1.74)	80.16(1.73)	76.47(2.67)	
	Rural		19.93(1.74)	19.84(1.73)	23.53(2.67)	0.08
Smoking	Non/past smoker		61.85(0.47)	61.47(0.48)	76.63(2.29)	
	current smoker		38.15(0.47)	38.53(0.48)	23.37(2.29)	<0.05
Alcohol	non/non-risky drinking		46.29(0.58)	45.50(0.58)	77.03(2.32)	
	risky drinking**		53.71(0.58)	54.50(0.58)	22.97(2.32)	<0.05
Weekly physical activity†	3rd tertile		38.15(0.55)	38.15(0.55)	38.29(2.62)	
	2nd tertile		35.25(0.45)	35.32(0.46)	32.37(2.56)	0.49
	1st tertile		26.60(0.51)	26.53(0.52)	29.34(2.50)	0.46
Calcium intake‡	3rd tertile		32.84(0.53)	32.80(0.54)	34.35(2.77)	
	2nd tertile		33.69(0.48)	33.85(0.48)	27.82(2.56)	0.11
	1st tertile		33.47(0.53)	33.35(0.54)	37.84(2.61)	0.54
Health insurance type	Medical assistance or none		2.81(0.24)	2.73(0.24)	6.00(1.32)	
	Gov. HI without private HI		25.39(0.60)	24.98(0.60)	41.27(2.70)	0.24
	Gov. HI with private HI		71.80(0.63)	72.29(0.63)	52.73(2.74)	<0.05
Familial history of osteoporosis or fracture		No	85.59(0.36)	85.61(0.37)	83.60(1.86)	
		Yes	14.41(0.36)	14.39(0.37)	16.40(1.86)	0.26
Menopause		No	81.71(0.41)	82.28(0.41)	58.83(2.81)	
		Yes	18.29(0.41)	17.72(0.41)	41.17(2.81)	<0.05
Cancer type	Others				38.39(2.34)	
	Gastric				18.33(2.02)	
	Hepatic				4.17(1.03)	
	Colon				7.67(1.31)	
	Breast				14.79(2.02)	
	Cervical				15.34(1.90)	
	Lung				2.10(0.67)	
	Thyroid				7.22(1.42)	
Time since cancer diagnosis (years)	<5				43.23(2.84)	
	≥5				56.77(2.84)	
Osteoporosis§	No		90.55(0.29)	90.88(0.29)	77.50(2.32)	
	Yes		9.45(0.29)	9.12(0.29)	22.50(2.32)	<0.05

*Abbreviations: BMI, body mass index, HI, health insurance, Data are weighted to the residential population of Korea; **Risk drinking is defined as consuming more than 3 standard drinks per day on average; †<8, 8–34.5, and >34.5 metabolic equivalents/week; ‡<336 mg/day, 336–563 mg/day, and >563 mg/day, §Osteoporosis was defined using both WHO T-score of the lumbar spine and femoral neck (T-score≤-2.5), and included those taking anti-osteoporotic medications

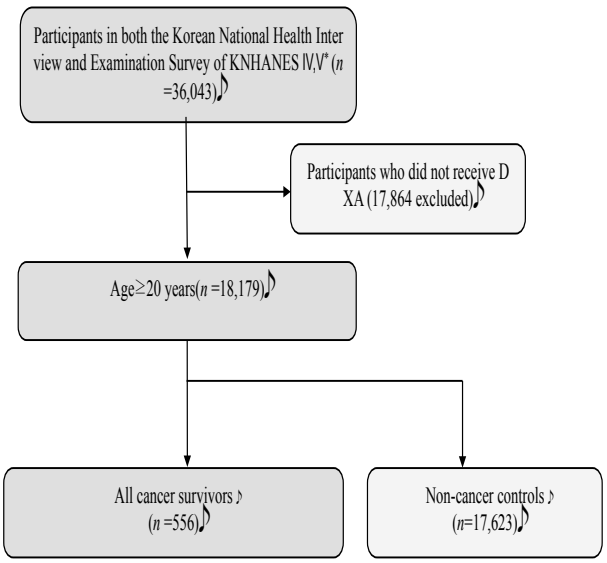

Figure 1. The Study Population Framework. *Fourth korean national health and nutrition examination survey 2008–2009 (KNHANES IV) and KNHANES V 2010-2011

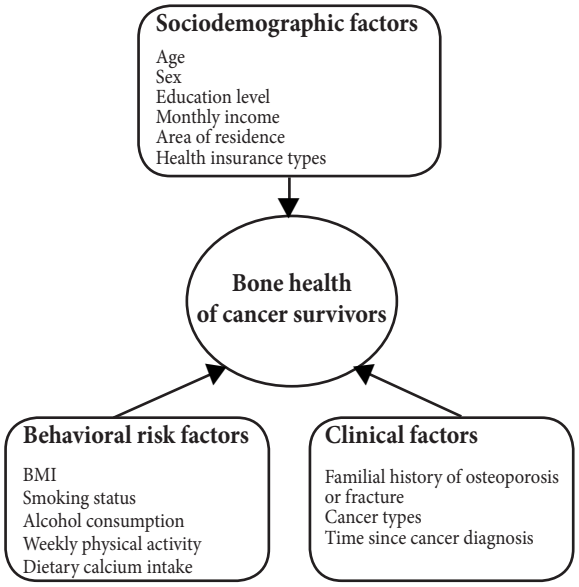

Figure 2. Factors Associated with Osteoporosis of Korean Cancer Survivors

Table 2. aors of Osteoporosis in Cancer Survivors Using Multivariate Logistic Regression Analysis Adjusted for all Sociodemographic, Behavior, and Clinical Factors

Variables		Cancer survivors (n=556) aOR(95% CI)	Female cancer survivors (n=363) aOR(95% CI)	Male cancer survivors (n=193) aOR(95% CI)
Age	20-59	1	1	1
	60-69	**3.04**(1.16-8.00)	**3.24**(1.19-8.81)	0.66(0.07-5.97)
	≥70	**6.60**(2.20-19.79)	**7.39**(2.57-21.30)	1.18(0.13-10.97)
Sex	Male	1		
	Female	**7.03**(1.88-26.28)		
BMI	≥18.5	1	1	1
	<18.5	1.75(0.63-4.86)	0.90(0.25-3.26)	**12.95**(2.11-79.44)
Education	≥college	1	1	1
	Middle/high school	1.00(0.32-3.16)	0.82(0.21-3.27)	2.32(0.28-18.85)
	≤Elementary school	1.90(0.61-5.90)	2.64(0.66-10.57)	1.06(0.12-9.73)
Monthly income	≥3,010	1	1	1
(thousand won)	1,010-3,000	1.69(0.72-3.97)	1.28(0.53-3.08)	2.91(0.28-30.36)
	≤1,000	**3.38**(1.31-8.71)	**3.14**(1.07-9.22)	3.21(0.38-27.26)
Area of residence	Urban	1	1	1
	Rural	0.81(0.42-1.56)	0.59(0.6-1.37)	2.12(0.66-6.83)
Smoking	Non/past smoker	1	1	1
	current smoker	1.18(0.44-3.16)	3.48(0.73-16.53)	0.77(0.22-2.72)
Alcohol	risky drinking	1.20(0.50-2.88)	1.40(0.38-5.15)	0.69(0.21-2.28)
Weekly physical activity	3rd tertile	1	1	1
	2nd tertile	0.81(0.36-1.79)	0.81(0.31-2.09)	1.11(0.34-3.60)
	1st tertile	0.87(0.38-1.96)	0.79(0.36-1.75)	1.38(0.20-9.98)
Calcium intake	3rd tertile	1	1	1
	2nd tertile	**2.67**(1.17-6.14)	2.41(0.78-7.41)	4.32(0.79-23.55)
	1st tertile	1.54(0.78-3.07)	1.28(0.54-3.00)	**5.07**(1.09-23.67)
Health insurance type	Medical assistance or none	1	1	1
	Gov. HI without private HI	0.95(0.32-2.85)	1.64(0.45-5.94)	0.39(0.02-7.64)
	Gov. HI with private HI	0.78(0.24-2.53)	1.39(0.36-5.43)	0.27(0.01-8.58)
Familial history of osteoporosis or fracture	No	1	1	1
	Yes	0.93(0.46-1.87)	0.87(0.38-2.04)	0.83(0.12-5.97)
Menopause	No		1	
	Yes		1.52(0.66-3.51)	
Cancer type	Others	1	1	1
	Gastric ca.	1.96(0.91-4.24)	2.12(0.71-6.30)	1.16(0.34-3.94)
	Hepatic ca.	7.68(0.65-90.78)	N/A	4.18(0.45-39.07)
	Colon ca.	1.51(0.34-6.73)	1.34(0.11-17.04)	1.88(0.43-8.19)
	Breast ca.	0.94(0.31-2.82)	0.86(0.26-2.88)	N/A
	Cervical ca.	1.02(0.46-2.27)	1.10(0.41-2.92)	N/A
	Lung ca	2.58(0.47-14.09)	1.63(0.30-8.93)	1.56(0.24-10.24)
	Thyroid ca.	0.78(0.05-1.50)	0.35(0.07-1.79)	N/A
Time since cancer diagnosis	< 5years	1	1	1
	≥5years	0.82(0.43-1.56)	0.92(0.43-1.97)	0.28(0.07-10.7)

*N/A : Not applicable

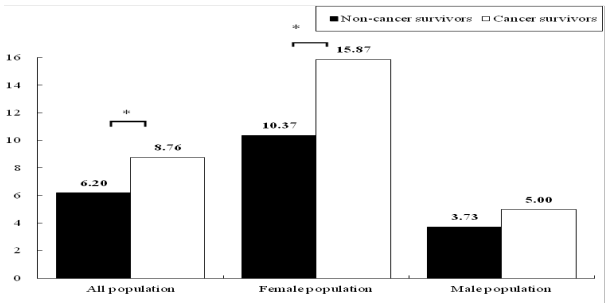

Figure 3. Adjusted Proportions of Osteoporosis among Korean Non Cancer Controls vs. Cancer Survivors. Adjusted for patient characteristics (age, sex, body mass index, educational level, monthly income, residential area, health insurance types) *p<0.05

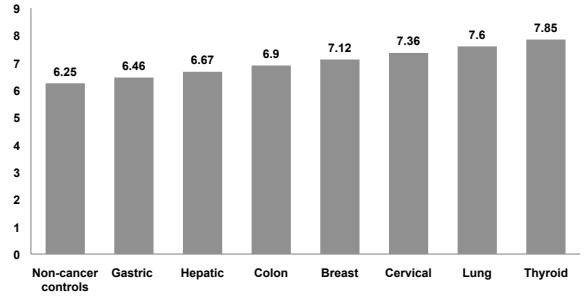

Figure 4. Adjusted Proportions of Osteoporosis among Korean Cancer Survivors according to Cancer Types. Adjusted for patient characteristics (age, sex, body mass index, educational level, monthly income, residential area, health insurance types)

(age, sex, body mass index, educational level, monthly income, residential area, health insurance types)of osteoporosis in non-cancer controls and cancer survivors were 6.20% and 8.76%, respectively (p value<0.05). In female population, the adjusted proportions of osteoporosis were 10.37%, and 15.87% in cancer survivors, and non-cancer controls, repectively (p value<0.05). In male population, the adjusted proportions of osteoporosis were 3.73%, and 5.00% in cancer survivors, and non-cancer controls, repectively (p value=0.34) (Figure 3). The adjusted proportions of osteoporosis among cancer survivors were 6.46% in gastric cancer, 6.67% in hepatic cancer, 6.90% in colon cancer, 7.12% in breast cancer, 7.36% in cervical cancer, 7.60% in lung cancer and 7.82% in thyroid cancer, respectively. The prevalence of cancer survivors according to cancer types was not significantly higher than non-cancer controls (Figure 4).

Factors associated with osteoporosis among cancer survivors

In multivariate logistic regression analysis by adjusting for all sociodemographic, behavioral, and clinical factors, the risk of osteoporosis among cancer survivors was related to age, sex, and monthly income. The elderly subjects had a high risk for osteoporosis(60-69 years : aOR 3.04, 95% CI :1.16-8.00, ≥70 years: aOR 6.60, 95%CI 2.20-19.79). The prevalence of osteoporosis was higher in female than in male cancer survivors (aOR: 7.03, 95%CI: 1.88-26.28). Low monthly income (≤1,000,000 won) was significantly associated with a risk of osteoporosis (aOR: 3.38, 95% CI: 1.31-8.71) (Table 2).

In female cancer survivors, the prevalence of osteoporosis were also higher in elderly population(60-69 years: aOR 3.24, 95% CI: 1.19-8.81, ≥70 years: aOR 7.39, 95% CI 2.57-21.30), and group with lower monthly income (≤1,000,000 won aOR: 3.14, 95%CI: 1.07-9.22). And in male cancer survivors, underweight group (BMI<18.5) (aOR 12.95, 95% CI: 2.11-79.44), and group with lower calcium intake (aOR 5.07, 95% CI : 1.09-23.67) had a higher risk of osteoporosis (Table 2).

Discussion

In the present study, we examined the prevalence of osteoporosis among cancer survivors in Korea and analyzed the factors related to osteoporosis. Among the Korean cancer population aged ≥20 years, an estimated 22.50% had osteoporosis. The prevalence of osteoporosis in cancer patients varies greatly (20%-70%) among studies because of different study samples and cancer types (Reuss-Borst et al., 2011; Lim and Lee, 2011; Chen et al., 2005). In the present study, the prevalence of osteoporosis among cancer survivors after adjusting related factors was higher than that among the non-cancer subjects. However, the prevalence of osteoporosis among male cancer survivors compared with non- cancer controls was not substantially higher after adjusting related factors. The higher prevalence of osteoporosis was mark predominant in female cancer survivors. The incidence of osteoporosis in cancer survivors are known to be associated with side effects of cancer treatment and health behaviors as well as general risk factor of osteoporosis. The oncologic treatment such as surgery, radiation therapy, chemotherapy, hormone suppressive therapy may have detrimental long-term effects on bone health including significant bone loss and increased risk of fracture(Miro and Orecchia, 2002; Smith, 2002; Fontanges et al., 2004; Olmos Martinez and Gonzalez Macias, 2007; Brown and Guise, 2009; Stava et al., 2009). And, various other causal factors such as low body mass index (BMI), lack of exercise, and an unhealthy lifestyle is also known be risk factors of osteoporosis among cancer survivors (Ryan et al., 2007; Grossmann et al., 2011). In this study, particularly higher prevalence of osteoporosis was in cancer survivors with special factors. The well-known general risk factors for osteoporosis for non-cancer survivors, such as old age, female sex, and low socioeconomic level, are significantly associated with the prevalence of osteoporosis among cancer survivors.

Elderly group has a higher risk for osteoporosis. Osteoporosis and cancer are considered to be primarily diseases of aging (VanderWalde and Hurria, 2011). The types of therapies used in the treatment of these cancers may compound the inherent risk of osteoporosis and accelerate osteoporosis (Khan and Khan, 2008). Osteoporosis is associated with age-related changes and hormonal change in bone microarchitecture, decreased bone mineral density (BMD), increased bone fragility, and a tendency to develop bone fractures (Camacho et al., 2008; Khan and Khan, 2008). Aging alone tends to be associated with a rate of bone loss of between 0.5% and 1% per year in both men and women starting from middle age (Nordin et al., 1998). And, many previous

studies of osteoporosis among cancer survivors in various cancer types indicated that increasing age, as well as cancer therapies, can lead to bone loss and increased risk for osteoporosis or fragility fractures (Goodwin et al., 1999; Malcolm et al., 2007; van Londen et al., 2008). For this reason, The National Comprehensive Cancer Network (NCCN) suggests some method of screening of osteoporosis for all cancer patients, regardless of cancer type, who are at an increased risk of fracture due to old age (VanderWalde and Hurria, 2011).

Female cancer patients have a higher risk of osteoporosis than male cancer patients. Osteoporosis in older women is prevalent due to the hormonal influence of estrogen on bone health dissipates especially after menopause (Christenson et al., 2012). In addition, physical inactivity and lower calcium intake are related to osteoporosis in female non-cancer controls (Shin et al., 2010). The prevalence of osteoporosis in our female cancer survivors is considerably higher than that expected in a healthy age-matched comparison group (Reuss-Borst et al., 2011). Female cancer survivors have higher additional risk to general risks because surgery and chemotherapy can induce ovarian failure (either medical or surgical), especially in patients with ovarian, cervical, or breast cancer (Goodwin et al., 1999; Shapiro et al., 2001). Ovarian ablation accelerates bone loss in premenopausal women (VanderWalde and Hurria, 2011). And, the osteoporotic fracture rate was increased comparing to the standardized incidence ratios of the population at large (Melton et al., 2003). Early diagnosis of osteoporosis and a sufficient treatment in female cancer survivors are extremely important to prevent skeletal sequelae due to osteoporosis.

In this study, cancer survivors with low-income levels had a high risk of osteoporosis. In general, annual household income is strongly related to the use of healthcare services. A high income is positively associated with higher BMD testing and prescription treatment after bone density screening (Meadows et al., 2012; Brennan et al., 2004). There was few study to investigate the effect of income on osteoporosis among cancer survivors. The results of this study may reflect the uniqueness of the situation in Korea. In Korea, not all people with osteoporosis receive treatment (Kim et al., 2012). This may be because the National Health Insurance in Korea provides relatively narrow or similar coverage for osteoporosis treatment compared to other countries (Choi HJ and YH SC, 2010) despite the reasonable prices and accessibility of anti-osteoporotic medication and DXA. Moreover, socioeconomic status (including the income level) along with distinct characteristics mediate the effects of healthcare utilization for screening, knowledge, and therapy for osteoporosis.

In analysis according to gender, elderly age and low income level of female cancer survivors also statistically significantly affected on osteoporosis as well as in analysis including all cancer survivors. However, in male cancer survivors, low body weight or low calcium intake were more associated with incidence of osteoporosis than age, income level. Male cancer survivors with underweight had an increased risk of osteoporosis like underweight non-cancer subjects (Felson et al., 1993). Previous studies indicate that weight loss is common among cancer patients with malnutrition status during and after treatments such as surgery and radiation (Ouattara et al., 2012; Ehrsson et al., 2012). Being underweight increases the risk of osteoporosis along with the general risk factors. Calcium malnutrition and calcium malabsorption are considered to be a risk of osteoporosis in both gender, apart from hormonal imbalances (Peterlik et al., 2013). Lower serum levels of vitamin D and calcium result in higher PTH levels, increasing the rate of bone loss(Filipponi et al., 1990). Previous studies indicated that a nutritional calcium deficit was popular in different population groups, however, level of calcium intake in male population was not so lower than female population (Peterlik et al., 2009). However, male cancer survivors can undergo difficulties of calcium intake because of loss of GI tract due to surgery or loss of appetite due to chemotherapy. Osteoporosis in male cancer survivors may be more affected by modifiable behaviors factors than physiological factors such as aging or hormonal changes. And, the behavior factors such as lower body weight or lower calcium intake can be more worsened by cancer itself or cancer treatment. Therefore, it is important for healthcare providers to assess the bone health of male cancer survivors with these modifiable risk factors, and it may be important to maintain optimal weight and calcium intake of cancer survivors to prevent osteoporosis.

In analysis according to cancer types, there was no significant difference prevalence of osteoporosis after adjusting for related factors according to cancer types.

Although we determined the prevalence of osteoporosis in cancer survivors and related factors, this study has several limitations that should be considered. First, given the cross-sectional nature of the surveys, we were unable to determine causal relationships between osteoporosis and other independent variables. Future studies should employ a prospective design to test the factors that predict the risk of osteoporosis among cancer survivors. Second, because much information was collected from the self-reported questionnaires, reporting bias cannot be excluded. Third, we unfortunately could not assess the kinds of osteoporosis medication that the study participants received. In particular, breast cancer patients are possible to take for medication affecting bone mineral density such as tamoxifen. Fourth, we could not assess the kind of cancer treatment. Some patients may not receive surgery or chemotherapy depending on cancer types or clinical situations. Therefore, this study could not provide the detail reasons why there was a high risk of osteoporosis in cancer survivors compared to non-cancer controls. Future study will be required more specific investigation for the mechanism of highly incidence osteoporosis in cancer survivors or accordance to cancer types.

The present study is one of the few to investigate the prevalence of osteoporosis among cancer survivors in Korea in detail. This study showed that osteoporosis is common in cancer survivors. Cancer survivors, likewise non-cancer patients, shared the risk factors of osteoporosis such as old age, female sex, the lower socioeconomic status, underweight and lower calcium intake. Despite

the evidence that cancer survivors have a increased risk of bone loss due to various reasons, the patients with cancer treatment have been shown to have a insufficient knowledge or understanding of osteoporosis and its risk factors (McKean et al., 2008).The need for cancer survivors education and special management also should be required. Consensus guidelines recommend the routine use of calcium, vitamin D, and taking weight-bearing physical activity in patient with high risk factors for the prevention of osteoporosis or osteoporotic fractures (Murray, 1996; Gralow et al., 2009). In addition, cancer survivors, regardless of cancer types, should undergo BMD screening and treatment based on the results (Gralow et al., 2009). In conclusion, the present results suggest that effective screening ,especially, in group with higher risk of osteoporotic fracture, should be applied to cancer survivors in accordance with current clinical guidelines, and comprehensive therapeutic options for management should be matched to patients' sociodemographic and clinical circumstances.

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