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Original article

Metabolic syndrome in breast cancer survivors with high carbohydrate consumption: The first report in community setting

Boyoung Park [a, b, 1], Sun-Young Kong [a, c, d, 1], Eun Kyung Lee [c, d], Moo Hyun Lee [d, e], Eun Sook Lee [a, c, d, *]

[a] Graduate School of Cancer Science and Policy, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, 410-769, South Korea
[b] National Cancer Control Institute, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, 410-769, South Korea
[c] National Cancer Center Research Institute, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, 410-769, South Korea
[d] National Cancer Center Hospital, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, 410-769, South Korea
[e] Department of Surgery, Keimyung University School of Medicine, Daegu, South Korea

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SUMMARY

Background & aims: This study was conducted to examine the prevalence of and lifestyle factors associated with the metabolic syndrome in breast cancer survivors and to compare those factors with controls without cancer in a community setting.

Methods: This study included 584 female breast cancer survivors ≥3 years after the initial diagnosis and 2336 age-matched cancer-free female controls from 39 community health examination centers located in 14 urban areas in Korea. The prevalence of the metabolic syndrome is shown. Factors associated with the metabolic syndrome were analyzed as odds ratios (ORs) in cancer survivors and controls; differences between the two groups in the ORs of associated factors were evaluated by calculating p-heterogeneity values.

Results: The prevalence of metabolic syndrome in breast cancer survivors and age-matched controls were 26.8% and 26.9%, respectively. Higher percentage of caloric intake from carbohydrates was associated with increased metabolic syndrome only in the breast cancer survivors (OR for the highest vs. lowest quartile for survivors = 2.48 [95% CI = 1.20–5.14]; OR for controls = 1.11 [95% CI = 0.81–1.51]; P-heterogeneity = 0.046). Sweat-inducing exercise for ≥150 min/week was associated with a lower risk of metabolic syndrome only in controls (controls: OR = 0.72 [95% CI = 0.58–0.89]; survivors: OR = 0.88 [95% CI = 0.57–1.36]). Older age, higher body mass index, and a lower education level (≤12 years) was associated with an increased prevalence of metabolic syndrome in both groups.

Conclusions: Our results suggest that, in regions with excess carbohydrate intake, the association of the metabolic syndrome with percentage of caloric intake from carbohydrate might be more prominent than exercise in breast cancer survivors, compared with general population.

1. Introduction

Breast cancer is the most common cancer among women, with an incidence of 1,677,000 in 2012; it is also the most common cause of cancer deaths, with 522,000 [1]. This is the highest prevalence of any type of cancer worldwide [2]. As the prevalence of breast cancer has increased, the importance of the long-term care of breast cancer patients has become increasingly important [2]. Even after treatment completion, survivors of breast cancer are at risk not only of recurrence and secondary cancer but also of non-cancerous health effects, such as cardiovascular diseases, endocrine diseases, poor quality of life, and functional decline related to cancer treatment [3].

Metabolic syndrome is defined as a cluster of conditions including abdominal obesity, hypertension, dyslipidemia, and high fasting blood glucose, and it is a major risk factor for major chronic diseases, such as cardiovascular disease and diabetes

* Corresponding author. Center for Breast Cancer, National Cancer Center Hospital, National Cancer Center, 323 Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, 410-769, South Korea. Fax: +82 31 920 1511.
E-mail addresses: hayejine@ncc.re.kr (B. Park), ksy@ncc.re.kr (S.-Y. Kong), waterfol@ncc.re.kr (E.K. Lee), mhlee@ncc.re.kr (M.H. Lee), eslee@ncc.re.kr (E.S. Lee).
[1] Equally contributed as the 1st authors.

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[4,5]. Metabolic syndrome is common and increasing rapidly in frequency worldwide, which is largely related to increases in obesity and a sedentary lifestyle [5]. In addition, metabolic syndrome increases the risk of breast cancer by >50%, particularly in postmenopausal women [6], and increases the risk of breast cancer recurrence or distant metastasis [7,8]. Previous studies have confirmed that lifestyle interventions, including diet control, weight loss, exercise intervention, and their combinations, improve components of metabolic syndrome in general population [9].

Breast cancer survivors are at high risk of developing metabolic syndrome, because the negative effects related to components of metabolic syndrome, including weight gain, central obesity, and increased adiposity, may increase due to adjuvant chemotherapy, postmenopausal status post-diagnosis, and physical inactivity [10,11]. Lifestyle modifications, such as exercise, dietary changes, smoking cessation, and reducing alcohol intake, may play an important role in reducing metabolic syndrome morbidity but also in improving the cancer prognosis and quality of life for breast cancer survivors [12].

Thus, it is necessary to understand whether the beneficial effects of lifestyle modifications can be generalized to breast cancer survivors, who experience treatment- and chemotherapy-related changes, such as earlier menopause. This study was conducted to examine the prevalence of metabolic syndrome and assess the association of lifestyle factors on the risk of metabolic syndrome in female breast cancer survivors compared with a group of age-matched cancer-free control women.

2. Materials & methods

2.1. Data source and study population

Baseline examination data from the Health Examinee (HEXA) cohort, a sub-project of the Korea Genome Epidemiology Study (KoGES) was used in this study. The KoGES is an ongoing population-based cohort study conducted since 2001 to investigate environmental and genetic risk factors and their interactions with major diseases in the Korean population. The baseline examination of the HEXA cohort was performed at 38 community health examination centers located in 14 large urban areas in Korea; it included health examinees aged 40–70 years during 2004–2013. The participating centers had the capacity to recruit 2000 or more health examinees each year who represent the community and who have experience in multicenter network research. More information on the community characteristics, study design, and baseline characteristics is provided elsewhere [13]. Informed consent was obtained from all participants, and the participants completed an interviewer-administered questionnaire, which included socio-demographic and behavioral characteristics, and a validated food-frequency questionnaire, which asked about food items generally consumed by Koreans [14]. All participants received a physical examination, including anthropometric measurements and biochemical measurements performed in fasting venous blood samples [13].

The questionnaire identified 859 participants who reported a diagnosis of breast cancer by a physician, and their mean time since diagnosis was 6.0 ± 5.5 years (range, 0–41 years). Breast cancer survivors were defined as those who reported a diagnosis of breast cancer and who were ≥3 years from the initial diagnosis. We excluded subjects who were <20-years of age at first diagnosis and males with breast cancer. Via random selection, the subjects were frequency matched at a 1:4 ratio with female participants without a history of any type of cancer and by 5-year age groups. Ultimately, 584 breast cancer survivors and 2336 age-matched controls were selected for analysis. The Institutional Review Board of the National Cancer Center approved this study protocol, which was in compliance with the Declaration of Helsinki (IRB No: NCC2014-0098).

2.2. Metabolic syndrome criteria

Based on the recent consensus definition incorporating criteria of the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute, metabolic syndrome was defined as having three or more of the following: 1) large waist circumference (≥80 cm in women, as modified by the Western Pacific Regional Office of the World Health Organization); 2) high triglyceride (TG) level (≥150 mg/dL); 3) low HDL-cholesterol level (<50 mg/dL); 4) elevated blood pressure (systolic ≥ 130 mmHg and/or diastolic ≥85 mmHg); and 5) elevated fasting glucose (≥100 mg/dL) [4]. Individuals with a previous physician diagnosis of hypertension or diabetes mellitus and who were under treatment at the time of the survey according to the questionnaire were considered to have elevated blood pressure or elevated fasting glucose.

2.3. Definition of variables

Age was treated as a continuous variable. Education level was divided into ≤12 years (high school or less) or >12 years (college or more), and income level was divided into mean monthly household income <$2000 or ≥$2000 based on the tertile and median values of income. Post-menopausal women were defined as those who had not experienced menstruation for the past 12 months. Drinking and smoking were categorized as current or past/never. Exercise was measured as the number of sweat-inducing exercise days/week and the mean duration then multiplying number of exercising days/week by mean duration. We followed the American Cancer Society (ACS) Physical Activity Guidelines for Cancer Survivors for the exercise cut-off point, which recommend at least 150 min of exercise/week [15]. Body mass index (BMI) was categorized as <23, 23–24.9, or ≥25 kg/m^2 per the Asian guidelines [15]. Percentage of total caloric intake from carbohydrates was used as a relevant measure of dietary composition, as reported by Park et al. [5]. It was categories as lower (0–25%), middle (25–75%), or higher (75–100%).

2.4. Statistical analysis

The characteristics of the female breast cancer survivors and the age-matched randomly selected controls were compared using the chi-square test for categorical variables or the *t*-test for continuous variables. The proportions of breast cancer survivors and age-matched controls with metabolic syndrome and each of its component were compared using the chi-square test. Multivariate logistic regression analysis was applied to estimate the odds ratios (ORs) of metabolic syndrome by age, education and income levels, menopausal status, drinking status, exercise, BMI, and percentage of total caloric intake from carbohydrates. Smoking status was not included in the multivariate model due to the very small number of current smokers among the breast cancer survivors (n = 3, 0.5%). P-heterogeneity was calculated to investigate whether the OR of each variable for metabolic syndrome was significantly different between breast cancer survivors and age-matched controls. All statistical analyses were performed using SAS software ver. 9.1 (SAS Institute, Cary, NC, USA).

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