RESEARCH ARTICLE

Association between Vegetable, Fruit and Carbohydrate Intake and Breast Cancer Risk in Relation to Physical Activity

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Abstract

Background: Although the nutritional may exert effect on the breast cancer risk, it is not clear whether the role diet is the same in sedentary and physically active women. The aim of this study was to evaluate the association between fruit, vegetable and carbohydrate intake and the risk of breast cancer among Polish women considering their physical activity level. Materials and Methods: A case-control study was conducted that included 858 women with histological confirmed breast cancer and 1,085 controls, free of any cancer diagnosis, aged 28-78 years. The study was based on a self-administered questionnaire to ascertain physical activity, dietary intake, sociodemographic characteristics, reproductive factors, family history of breast cancer, current weight and high, and other lifestyle factors. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated in unconditional logistic regression analyses including a broad range of potential confounders. Results: With comparison of the highest vs lowest quartile of intake, strong significant associations were observed for total vegetables (OR=0.37, 95%CI=0.20-0.69 P for trend <0.01 and OR=0.53, 95%CI=0.29-0.96, P for trend <0.02), and total fruits (OR=0.47, 95%CI=0.25-0.87, P for trend <0.05 and OR=0.47, 95%CI=0.24-0.90, P for trend <0.02) among women characterized by the lowest and the highest quartile of physical activity. No associations were observed for total carbohydrate intake. Additional analysis showed a positive association for sweets and desert intake among women in the lowest quartile of physical activity (OR=3.49, 95%CI=1.67-7.30, P for trend <0.009) for extreme quartiles of intake comparing to the referent group. Conclusions: The results suggest that a higher consumption of vegetable and fruit may be associated with a decreased risk of breast cancer, especially among women who were low or most physically active throughout their lifetimes. These findings do not support an association between diet high in carbohydrate and breast cancer. However, a higher intake of sweets and deserts may by associated with an increased risk of breast cancer among women who were less physically active.

Keywords: Breast cancer - diet - physical activity - case-control study

Introduction

Among dietary components that have been suggested as agents for reduction of breast cancer risk a greater consumption of vegetables and/or fruits has attracted much attention. In a few meta-analysis, majority of studies reported an inverse association of a higher consumption of fresh vegetables/fruits and the risk of breast cancer (Gandini et al., 2000; Smith-Warner et al., 2001; Michels et al., 2007; Brennan et al., 2010; Albuquerque et al., 2013; Hui et al., 2013). However, the protective effect remains uncertain, due to the methodological limitations, such as a small sample size, risk adjustment for no full confounders or a limited number of food items in the questionnaires employed. In turn, fat, red meat, carbohydrates have been reported as a factor for increased breast cancer risk in some case-control studies (Holmes and Willett, 2004; Romieu and Lajous, 2009; Yun et al., 2010; Sulaiman et al., 2011; Kruk and Marchlewicz, 2013; Oxford University Press, 2014). However, the results remained uncertain as no

overall significant association between carbohydrates and breast cancer risk had been found in prospective studies of adult diet (Cho et al., 2003; Nielsen et al 2005; Silvera et al., 2005; Giles et al., 2006). Previous work from our group has shown that a high consumption of animal fat significantly increased risk of breast cancer independent of physical activity level (Kruk and Marchlewicz, 2013). The aim of this case-control study was to evaluate the association between fruit/vegetable and carbohydrate consumption and the risk of breast cancer among Polish women considering their physical activity level.

Materials and Methods

Study subjects

The design of this case-control study has previously been described in details (Kruk, 2007; Kruk, 2009). Briefly, this study was conducted between January 2003 and May 2007 in the Region of Western Pomerania. Cases were identified from the Szczecin Regional

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Cancer Registry that covered the mentioned geographic region. Cases were women aged 28-79 years old, were diagnosed with histologically confirmed invasive breast cancer. The overall response rate for the cases was 50.6% (881 questionnaires completed out of 1740 eligible and available cases). Female controls were frequency matched by age (5-year interval) and residence (urban, rural) to cases. They were free of any cancer diagnosis and randomly recruited among the outpatients of clinics, the largest hospital in Szczecin, and four hospitals located in the Region of West Pomerania. Most of the controls participating in the study (78.6%) was selected among patients visiting ambulatories for health controlling or when they caught a cold. Remaining controls were selected from hospital patients treated for fractures or sprains (5.4%), cardiovascular diseases (3.1%), back pain (2.8%), and other diseases (10.1%), such as skin, eye, laryngological. The overall response rate for controls was 69.4% (1121/1615). Finally, data from 858 cases and 1085 controls were included in analyses, since information collected from 23 cases and 36 controls contained too many missing data. A signed informed consent was obtained from each study subject before sending the questionnaire. This study was approved by The Ethics Committee of the Pomeranian Medical Academy in accordance with the Polish Department of Health and Human Services.

Data collection

Study subjects completed a 8-page self-administered questionnaire that includes questions about sociodemographic characteristics (age, residence, marital status, occupation, education, house-hold income), current weight, high, lifestyle habits (physical activity, dietary habits, sleeping, tobacco smoking, alcohol consumption, experience of psychological stress, use of hormones, multivitamin supplement, medical and screening history). Information on dietary intake and alcohol consumption during adult life (a separate section of the questionnaire) was gathered from case and control subject modeling on the Block et al. (1990), and Franceschi et al. (1993) food frequency questionnaires. This section included 18 main Polish-specific food group, for example red meat (boiled, fried, canned) and alternatives, milk and its products, grain products, vegetables and fruits, sweets, deserts, unsaturated and saturated fats. Each women was asked to report types of foods and beverages, including fruit and vegetable juices and milk. They reported their usual frequency of consumption as the number of times per week (≤ 2, 3-4, 5-6, ≥ 7) and portion size for food (small, medium, large) and at least one glass (250 ml) for milk and juices. In addition, the questionnaire contained a question for each type of food "Did you intake such type of nutrient"?, to check an answer. Drinking status was estimated by indicating frequency of alcohol intake per at least one drink what means a small bottle or tin of beer, 125 ml of wine or 30 g of high-grade alcohols. Tobacco use was estimated in terms of usual number of cigarettes smoked per day regularly at present or in past by a woman or her life partner. To assess total physical activity the respondents were asked to complete separate sections

of the questionnaire that included a comprehensive assessment lifetime household, occupational and leisure time activities. Details about physical activity were recorded in a table format using modified version of Kriska et al. (1990) and Friedenreich et al. (1998) questionnaires. The average weekly number of hours per year were estimated using the formulas given by Friedenreich et al. (1998) for lifetime record of recreational, household and occupational physical activities. Physical activity was quantified in terms of metabolic equivalent (MET) using the Ainsworth et al. (2000) compendium. The MET equivalent determines the number of kilocalories per hour each kilogram of body weight expended in physical activity. The lifetime averages for total activity were calculated by summing the average MET-hours/week/year for each type of activity.

Statistical analysis

Unconditional logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs). The relationships between dietary components and breast cancer risk in subgroups of physical activity levels quartiles were examined after adjusting for age (data not shown) and further examined after adjusting for various potential confounding factors selected a priori. Vegetables considered as confounders in multivariate models were: age, family history of breast cancer in mother, sisters or daughters (yes, no), education (elementary school, middle school, high school, academy, and above), place of residence (urban/rural), family income average over past 10 years (low, middle, high), marital status (never married, married, widowed/divorced), body mass index (BMI, continuous), age at menarche (continuous), age at first childbirth (<22, 22-29, ≥ 30 years), number of pregnancies (0, 1, 2, ≥ 3), months of breast feeding (0, <6, ≥ 6), use of oral contraceptives (never, ever), age at menopause (<50, 50-54, ≥ 55 years), postmenopausal hormone replacement therapy (HRT) use (never, ever), smoking status (yes, no), passive smoking from husband (yes, no), alcohol consumption (never, ≤ 1 drink/week, 2-4 drinks/week, ≥ 5 drinks/week). Additionally, models of vegetable, fruit, carbohydrate intake were adjusted for remaining groups, e.g. red meat, grain products, saturated fats. Final models included only variables that were statistically significant in the multivariate analyses and were found to influence the quality of the model fit; they were reported in legends of tables. The linear trend tests were performed by entering the categorical variables as continuous variables in the models by using the Walds χ^2 values. Physical activity was divided into 4 levels according to distribution of the controls. All P-values are two sided, and a P-value less than 0.05 is considered statistically significant. All analyses were conducted using statistical package STATISTICA 98 (stat Soft Polsca, Kraków, Poland).

Results

The socio-demographic, anthropometric, reproductive, and lifestyle characteristics of case and control subjects have been previously reported (Kruk, 2009). The mean age for cases was 55.3±9.7 years and 54.8±9.5 years for

controls. There was no significant difference between case and control subjects regarding their age (p=0.24). Cases and controls were similar with respect marital status, age at menarche, parity, age at first birth, age at menopause, red meat consumption, alcohol drinking, and usage of oral contraceptives. Compared to case subjects, controls we more likely to have a high education level, had lower BMI, reported longer duration of breast-feeding, were less likely to have had a family history of breast cancer in mother or a sister, and to be ever active or passive smokers. Cases also had lower lifetime total averages for lifetime total physical activity, were less likely to intake vegetables and fruits frequently, and were more likely than controls to experience of psychological stress. There

Table 1. Odds Ratios and 95% Intervals of Breast Cancer Associated with Dietary Components

Variable (frequency per week)	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)
Vegetables consumption by quartiles and total lifetime physical activity levels						
		<105 MET-h/week			105-<138 MET-h/week	
≤2	83	31	1.00[a]	51	29	1.00[b]
3-4	87	73	0.48(0.26-0.88)	65	75	0.78(0.39-1.56)
5-6	65	63	0.45(0.24-0.86)	49	76	0.59(0.27-1.29)
≥7	63	68	0.37(0.20-0.69)	48	59	0.74(0.36-1.51)
P trend			<0.01			<0.62
		138-<170 MET-h/week			≥170 MET-h/week	
≤2	23	22	1.00[c]	35	44	1.00[d]
3-4	37	87	0.50(0.21-1.22)	52	83	0.85(0.45-1.59)
5-6	35	65	0.57(0.25-1.31)	64	115	0.65(0.35-1.00)
≥7	43	72	0.63(0.28-1.42)	58	151	0.53(0.29-0.96)
P trend			<0.16			<0.02
Fruits consumption by quartiles and total lifetime physical activity levels						
		<105 MET-h/week			105-<138 MET-h/week	
≤2	69	28	1.00[a]	51	25	1.00[b]
3-4	57	43	0.60(0.30-1.19)	29	42	0.40(0.17-0.95)
5-6	56	58	0.48(0.24-0.99)	44	63	0.49(0.23-1.02)
≥7	116	106	0.47(0.25-0.87)	89	109	0.62(0.32-1.22)
P trend			<0.05			<0.61
		138-<170 MET-h/week			≥170 MET-h/week	
≤2	19	20	1.00[c]	29	29	1.00[d]
3-4	23	27	0.84(0.29-2.47)	40	57	0.60(0.27-1.33)
5-6	30	62	0.34(0.13-0.86)	41	96	0.36(0.17-0.76)
≥7	66	109	0.52(0.23-1.19)	99	211	0.47(0.24-0.90)
P trend			<0.16			<0.02
Carbohydrate consumption by quartiles and total lifetime physical activity levels						
		<105 MET-h/week			105-<138 MET-h/week	
≤2	34	29	1.00[a]	23	27	1.00[b]
3-4	20	28	0.54(0.21-1.39)	16	26	1.17(0.34-4.03)
5-6	51	40	1.01(0.48-2.14)	36	39	1.84(0.70-4.83)
≥7	193	138	1.20(0.65-2.24)	138	147	1.44(0.68-3.05)
P trend			<0.28			<0.38
		138-<170 MET-h/week			≥170 MET-h/week	
≤2	12	22	1.00[c]	20	35	1.00[d]
3-4	12	19	1.44(0.39-5.34)	12	31	0.65(0.22-1.93)
5-6	27	31	2.20(0.74-6.57)	33	46	1.17(0.52-2.65)
≥7	87	146	1.36(0.57-3.25)	144	281	0.74(0.39-1.42)
P trend			<0.63			<0.43
Sweets and deserts consumption by quartiles and total lifetime physical activity levels						
		<105 MET-h/week			105-<138 MET-h/week	
≤2	163	158	1.00[a]	148	150	1.00[b]
3-4	60	44	1.08(0.66-1.78)	23	43	0.39(0.18-0.79)
5-6	34	18	1.68(0.81-3.51)	15	25	0.84(0.38-1.85)
≥7	41	15	3.49(1.67-7.30)	27	21	1.33(0.64-2.77)
P trend			<0.009			<0.88
		138-<170 MET-h/week			≥170 MET-h/week	
≤2	89	131	1.00[c]	128	226	1.00[d]
3-4	20	48	0.71(0.35-1.43)	49	91	0.95(0.60-1.50)
5-6	17	26	1.17(0.55-2.52)	10	35	0.33(0.14-1.78)
≥7	12	13	1.76(0.68-4.51)	25	41	0.99(0.55-1.81)
P trend			<0.47			<0.30

*OR-odds ratio; CI-95% confidence interval. a Adjusted for age, BMI, education level, breast-feeding, psychological stress, multivitamins supplementation, family history of breast cancer, passive smoking. b Adjusted for age, BMI, education level, breast-feeding, psychological stress, family history of breast cancer, passive smoking. c Adjusted for age, BMI, education, breast-feeding, psychological stress, passive smoking. d Adjusted for age, education, breast-feeding, psychological stress, passive smoking

was a strong protective effect associated with higher consumption of raw vegetables among women in the lowest and highest quartile of physical activity (Table 1). The multivariate-adjusted OR in the upper quartile of vegetable intake (intake of seven or more servings per week) was decreased by 63% that for the referent group (intake of two or less servings per week) (OR=0.37, 95%CI=0.20-0.69, p<0.01) among women of the lowest level of physical activity (<105 MET-h/week). There was a weaker reduction in the risk associated with the fourth quartile of vegetable intake among women of the highest level of physical activity (OR=0.53, 95%CI=0.29-0.96, p<0.02). Among subjects in the second and third quartiles of physical activity, the risks were suggestively decreased, although were not statistically significant. ORs associated with total fruits (fruits plus fruit juice) consumption were not substantially different from those obtained when total vegetable consumption was considered. High intake of fruits was significantly associated with about 50% decrease in breast cancer risk among women categorized in the first and fourth quartiles of physical activity (OR=0.47, 95%CI=0.25-0.87, p<0.05, and OR=0.47, 95%CI=0.24-0.90, p<0.02, respectively), for subjects in the highest quartile of fruit consumption compared with subjects in the lowest quartile.

Carbohydrate intake was not associated with breast cancer, independently on physical activity level. The multivariate-adjusted ORs that compared the first and fourth quartiles of intake were: 1.20 (95%CI=0.65-2.24), p<0.28; 1.44 (95%CI=0.68-3.05), p<0.38; 1.36 (95%CI=0.57-3.25), p<0.63, and 0.74 (95%CI=0.39-1.42), p<0.43, for the first, second, third, and fourth quartile of physical activity, respectively.

We conducted further analysis to determinate whether dietary sweets and deserts were associated with breast cancer risk. We observed statistically important positive association between the risk of breast cancer for sweets and deserts intake only among women in the lowest quartile of physical activity. The OR for extreme quartile of sweets and deserts consumption was 3.49 (95%CI=1.67-7.30), p<0.009 comparing to the referent group (intake ≤2 serving per week).

Discussion

This case-control study with 858 cases and 1085 controls showed a statistically significant protective effect of vegetables and fruits intake on the development breast cancer among women in the lowest and in the highest level of lifetime total physical activity. Our findings are consistent with several previous studies and support the hypothesis that a greater intake of raw vegetables and fresh fruits is associated with a lower breast cancer (La Vecchia et al., 1987; Iscovich et al., 1989; Pawlega 1992; Freudenheim et al., 1996; Hirose et al., 2007; Lisowska et al., 2008; Cottet et al., 2009; Wu et al., 2009; Butler et al., 2010; Sangrajrang et al., 2013). For example, Freudenheim et al. (1996) presented a strong significant reduction of the risk for vegetable intake (OR=0.46, 95%CI=0.28-0.74, p<0.001) and non-significant reduction (OR=0.67, 95%CI=0.42-1.09) for fruits intake, for the

highest quartile of intake versus the lowest quartile. The inverse association between the vegetable-fruit-soy dietary pattern and breast cancer risk, particularly among postmenopausal women, with a dose-dependent trend for decreasing risk (RR=0.70, 95%CI=0.51-0.95) was observed among Singapore Chinese women (Butler et al., 2010). In turn, Lisowska et al. (2008) observed reduced risk of breast cancer with increasing levels of total fruit intake among Polish women from Warsaw and Lodz (OR=0.76, 95%CI=0.63-0.91) for the highest versus lowest quartile. Similarly, the study of Zhang et al. (2009) found that women in the highest quartile of total vegetable and fruit intake had a 72% and a 47% decreased risk of breast cancer (OR=0.28, 95%CI=0.18-0.43 and OR=0.53, 95%CI=0.34-0.82), respectively. Also, a recently published study by Zhang et al. (2011) indicated a 74% decreased the risk of breast cancer among women in the highest quartile of vegetable-fruit-soy-milk-poultry-fish intake relative to the lowest quartile. Similarly, a high consumption of soy food was reported to be inversely associated with the risk of breast cancer (Zhu et al., 2011; Liu et al., 2014).

It is also worth noting a 45% reduced risk of breast cancer associated with high intake of vegetables and a 43% reduction the risk consuming fruits frequently in Tay women (Sangrajrang et al., 2013). In addition, Bao et al. (2012) reported decrease in breast cancer risk among Chinese women for high intake of vegetables and citrus fruits.

A meta-analysis of 16 selected epidemiological studies by Brennan et al. (2010) reported a negative association between the prudent dietary/healthy pattern, defined by high consumption of vegetables and fruits (OR=0.89, 95%CI=0.82-0.99, p=0.02). Also, a meta-analysis of all published studies from 1982 to 1997 (17 studies for vegetables and 12 for fruits included) confirmed the protective effect of vegetables against breast cancer, although a lack of association between fruits intake and breast cancer (RR=0.75, 95%CI=0.66-0.85 and RR=0.94, 95%CI=0.79-1.11, respectively) (Gandini et al., 2000). In turn, a systematic review and meta-analysis by Gao et al. (2013) focused on the association between regular tea consumption and breast cancer risk reported that tea drinkers had decreased risk by a 21%.

While a few studies (Shibata et al., 1992; Verhoeven et al., 1997; Terry et al., 2001; Mannisto et al., 2005; Nkondjock and Ghadirian, 2005; Cui et al., 2007; Buck et al., 2011) have failed to find a relation between fruits and vegetables consumption and breast cancer. Consumption of vegetable pattern was characterized by high consumption of potatoes and carrots among examined subjects. Tomatoes contain lycopene, beta carotene, vitamin E, and other carotenoids. A previously published review of 72 epidemiological studies confirmed the protective effect of tomatoes and tomato products in reducing the risk of a variety cancers (Giovannucci, 1999). Findings indicated that these compounds decrease the proliferation of human cancer cells (London, 2006). Because of antioxidant properties dietary tomatoes and carotenoids as scavengers of oxygen free radicals (Zhang et al., 1999; Bartosz, 2003) and singlet oxygen (Krinsky

and Deneke, 1982) may reduce DNA damage, genetic mutations (Frei, 1994) and enhance immunologic system functioning (Kelley and Bendich, 1996). In addition, numerous other substances present in vegetables and fruits (flavonoids, indoles, sterols) may act as antioxidants and some of them are able affect estrogen metabolism (Gao et al., 2013). Growing evidence indicates that too intense or sporadic exercise training can promote the formation of cytotoxic reactive oxygen species (ROS) in muscle that induce disturbance cellular redox balance in muscle (Davies et al., 1982; Powers et al., 2004; Sarma et al., 2010). The role of oxidative stress in breast cancer development was addressed in several studies (Thomson, 1994; Brown and Bicknell, 2001; Klaunig et al., 2010; Clague and Bernstein, 2012). In contrast, nonexhaustive exercise reduces sex hormone levels (Alegre et al., 2013), the production of ROS, improves antioxidant defense system and enhances the resistance of tissues against these species (reviewed by Kruk, 2011). As vegetables/ fruits contain a wide range of antioxidants they consist an important component of antioxidant defense system that prevents damage of lipids, protein and DNA and suppresses cancer development in preclinical models (Reuter et al., 2010). Therefore, it is not surprising that we observed the preventive effect of vegetables and fruits among subgroup of women characterized by vigorous exercise training. All these actions are considered as hypothesized mechanisms involved in protection against breast cancer (Wettasinghe et al., 2002; Nyberg et al., 2003; Xiao et al., 2006). It is worth to add that there is growing awareness of the protective effect of vegetables and fruits consumption on breast cancer development. For example, the study conducted in Asian population among women after diagnosis of breast cancer reported that the breast cancer survivors had changed their dietary habits to improve their health by increased intake of fruits and vegetables by a 62.8% (Yaw et al., 2014). A study by George et al. (2011) found that women consuming better quality diet (rich in vegetables and fruits, poor in fat, processed foods and complex sugar) and engaging in regular recreational physical activity had a 88% reduced risk of death from breast cancer compared with physically inactive consuming poor quality diet.

In this study we did not observed a direct association between total carbohydrate intake and breast cancer risk. However, additional analysis showed that women with the lowest physical activity level and the highest category of sweets intake had about 3.5 times significantly higher risk for breast cancer, compared to those in the lowest category.

The literature data on the relation between carbohydrate intake and breast cancer are scant. Findings of two prospective studies suggested decrease in breast cancer associated with the highest quintile of carbohydrate intake compared with the lowest quintile (Knekt et al., 1990; Sieri et al., 2002). In contrast, a study by Barrett-Connor and Friedlander (1993) found a 93% increase in breast cancer risk when comparing extreme quintiles of carbohydrate intake with the lowest quintile. However, several large prospective studies (Kushi et al., 1992; Horn-Ross et al., 2002; Holmes et al., 2004; Silvera et al., 2005; Lajous et al., 2008) did not found the relationship

between carbohydrate intake and breast cancer risk, although results from a few studies suggested that this relation may be dependent on lifestyle and menopausal status (Holmes et al., 2004; Giles et al., 2006). No overall association was also seen between carbohydrate intake and breast cancer risk in a hospital-based case-control study of women in South Korea (Yun et al., 2010). Moreover, the recently published meta-analysis by Dong and Qin (2011) on the role of dietary glycemic index (GI) and glucemic load (GL) in relationship to breast cancer risk, based on 10 prospective cohort studies involving 15,839 cases and 577,538 participants, reported a 8% increased summary RR of breast cancer risk (RR=1.08, 95%CI=1.02-1.14) for the highest GI intake compared with the lowest, and no significant relationship between dietary GL and the risk of breast cancer. The GI ranks the carbohydrate content of particular foods, due to their glycemic effects. Consumption of diets of high GI is linked with high blood glucose and insulin levels (Dong and Qin, 2011). Both substances have been positively associated with breast cancer (Larsson et al., 2007; Tworoger et al., 2007; Gunter et al., 2009; Minatoya et al., 2013). There was evidence that plasma C-peptide is increased at high insulin concentrations, and the marker is directly linked with GL (Wu et al., 2004). In turn, elevated insulin levels may increase circulating insulin-growth factor 1 (IGF-1) - a protein showing strong proliferative and antiapoptic effects on human mammary cells (Haluska et al., 2006; Chlebowski, 2013).

The present study has some limitations that should be addressed. The case-control design of the study concerns the likelihood of selection and recall bias, that are common to this type of studies. This study was designed with ascertainment of total lifetime physical activity, diet and potentially risk factors. The overall response rate was lower among breast cancer cases than among controls. Although, the associations between risk factors and breast cancer found in this group of women examined previously (Kruk 2007) are generally consistent with those in the subject literature, thus probability of selection bias should be reduced in our findings. In addition, the study subjects were very similar in several medical, lifestyle, socioeconomic and diet characteristics with a women sample surveyed by Chief Central Statistical Office (GUS) as the Polish Population Health Survey (GUS 2004). Recall bias is the next major concern, because assessment of dietary habits in past meets several methodological problems. Additionally, cases may recall their diet after cancer diagnosis more clearly than controls. Our median time from the disease diagnosis to interview was about two years. However, Maruti et al. (2009) did not find any evidence for greater "differential recall bias" when they compared results for time intervals ≤2 years and >2 years. In addition, recall bias would be minimized as our women were assessed on diet and physical activity together with reproductive, anthropometric, socioeconomic, and other lifestyle factors (e.g. habits, possibility, Gorner et al., 2013) thus they were not influenced by knowledge of diet-breast cancer estimation as a breast cancer risk. Moreover, there is still limited awareness of the effect of diet and physical activity on breast cancer risk among

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Polish women. The study of Waśkiewicz et al. (2008), that evaluated the association between the health knowledge and the dietary behaviours among the Polish population with diagnosed cardiovascular diseases (7257 persons aged 24-74) found that the subjects had low level of knowledge of the preventive role of nutrition against heart diseases. Only 23% women had knowledge of the preventive role of regular fruit and vegetable intake against cardiovascular diseases. Misclassification of dietary intakes could also occur due to the questionnaire used, although this would tend to attenuate the estimate of the risk towards null. Like most studies on this subject, we did not have data for the changes of lifetime usual dietary habits, and total energy intake. However, Macdonald et al. (2005) and Chen et al. (2006) found that adults in general maintain a relatively stable nutrient intake for a long time. Random measurement error in examine of usual consumption would also tend to decrease the true risk. We used food-frequency questionnaire that is less accurate than that allowing to assess intake quantitatively. Although, we gathered information on portion size (large, medium, small), use of smoked or fried food, and fresh vegetables. Another noteworthy limitation is misclassification of the exposure variables, due to inaccurate self-reported data, although information was collected from case and control subjects using the same method.

This study has also several strengths. First, the study involved a large number of cases and controls, and therefore, we were able to perform dose-response analysis in subgroups regarding physical activity level. Second, all cases had histological confirmation of breast cancer. Third, detailed information about a broad range of potential confounding variables was collected and considered in the standard multivariate model. Effects of confounders were minimized by utilizing a range of covariates. Fourth, to our knowledge this was first case-control study that examined the association between total vegetable and fruit consumption and breast cancer among subgroup of Polish women that considered physical activity level. Another major strength of the present study is that our results agree with the recommendations of the WCRF/AICR Second Expert Report (2007) about diet and physical activity for cancer prevention.

In conclusion, the present findings indicate that greater intake of vegetables and fruits is associated with a lower risk of breast cancer in sedentary and high active women. The evidence was more consistent for vegetables than fruits. Furthermore, for vegetables and fruits a strong reduction in risk was also seen for the third compared with the lowest quartile. In turn, total carbohydrate consumption was not significantly linked to breast cancer except sweets and deserts intake among sedentary women. These results suggest that dietary sweets and deserts consumption may be relevance to the risk among women with low level of physical activity. These findings should be confirmed in other population studies with a more precise characterization of intake. If further studies confirm, the results can have great public implication as diet rich in vegetables and fruits and increased level of physical activity are inexpensive means targeting breast cancer risk.

References

Ainsworth BE, Haskell WL, Whitt WC, et al (2000). Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc*, **32**, 498-516.

Albuquerque RC, Baltar VT, Marchioni DM (2013). Breast cancer and dietary patterns: a systematic review. *Nutr Rev*, **72**, 1-17.

Alegre MM, Knowles MH, Robison RA, O'Neill KL (2013). Mechanics behind breast cancer prevention - focus on obesity, exercise and dietary fat. *Asian Pac J Cancer Prev*, **14**, 2207-12.

Bao PP, Shu XO, Zheng Y, et al (2012). Fruit, vegetable, and animal food intake and breast cancer risk by hormone receptor status. *Nutr Cancer*, **64**, 806-19.

Barrett-Connor E, Friedlander NJ (1993). Dietary fat, calories, and the risk of breast cancer in postmenopausal women: a prospective population-based study. *J Am Coll Nutr*, **12**, 390-9.

Bartosz G (2003). Druga twarz tlenu. Wolne rodniki w przyrodzie. Wyd. Naukowe PWN, Warszawa 2003.

Block G, Hatman AM, Naughton D (1990). A reduced dietary questionnaire: development and validation. *Epidemiology*, **1**, 58-64.

Brennan SF, Cantwell MM, Cardwell CR, et al (2010). Dietary patterns and breast cancer risk: a systematic review and meta-analysis. *Am J Clin Nutr*, **91**, 1294-302.

Brown NS, Bicknell R (2001). Hypoxia and oxidative stress in breast cancer. Oxidative stress: its effect on the growth, metastatic potential and response to therapy of breast cancer. *Breast Cancer Res*, **3**, 323-7.

Buck K, Vrieling A, Flesch-Janys D, Chang-Claude J (2011). Dietary patterns and the risk of postmenopausal breast cancer in a German case-control study. *Cancer Causes Control*, **22**, 273-82.

Butler LM, Wu AH, Wang R, et al (2010). A vegetable-fruit-soy dietary pattern protects against breast cancer among postmenopausal Singapore Chinese women. *Am J Clin Nutr*, **91**, 1013-9.

Chlebowski RT (2013). Nutrition and physical activity influence on breast cancer incidence and outcome. *The Breast*, **22**, 30-7.

Chen YM, Ho SC, Woo JL (2006). Greater fruit and vegetable intake is associated with increased bone mass among postmenopausal Chinese women. *Br J Nutr*, **96**, 745-51.

Cho E, Spiegelman D, Hunter DJ, Chen WY, Colditz GA, Willett WC et al (2003). Premenopausal dietary carbohydrate, glycemic index, glycemic load, and fiber in relation to risk of breast cancer. *Cancer Epidemiol Biomarkers Prev*, **12**, 1153-8.

Clague J, Bernstein L (2012). Physical activity and cancer. *Curr Oncol Rep*, **14**, 550-8.

Cottet V, Touvier M, Fournier A, et al (2009). Postmenopausal breast cancer risk and dietary patterns in the E3 N-EPIC prospective cohort study. *Am J Epidemiol*, **170**, 1257-67.

Cui X, Dai Q, Tseng M, et al (2007). Dietary patterns and breast cancer in the Shanghai breast cancer study. *Cancer Epidemiol Biomarkers Prev*, **16**, 1443-8.

Davies KJ, Quintanilha AT, Brooks GA, Parker L (1982). Free radicals and tissue damage produced by exercise. *Biochem Biophys Res Commun*, **107**, 1198-205.

Dong JY, Qin LQ (2011). Dietary glycemic index, glycemic load, and risk of breast cancer: meta-analysis of prospective cohort studies. *Breast Cancer Res Treat*, **126**, 287-94.

Franceschi S, Negri E, Salvini S, et al (1993). Reproducibility of an Italian food frequency questionnaire for cancer studies:

results for specific food items. *Eur J Cancer*, **29**, 2298-305.

Frei B (1994). Reactive oxygen species and antioxidant vitamins: mechanisms of action. *Am J Med*, **97**, 5-13.

Freudenheim JL, Marshall JR, Vena JE, et al (1996). Premenopausal breast cancer risk and intake of vegetables, fruits, and related nutrients. *J Natl Cancer Inst*, **88**, 340-8.

Friedenreich CM, Courneya KS, Bryant HE (1998). The lifetime total physical activity questionnaire: development and reliability. *Med Sci Sports Exerc*, **30**, 266-74.

Gandini S, Merzenich H, Robertson C, Boyle P (2000). Meta-analysis of studies on breast cancer risk and diet: the role o fruit and vegetable consumption and the intake of associated micronutrients. *Eur J Cancer*, **36**, 636-46.

Gao Y, Huang Y-B, Liu X-O, et al (2013). Tea consumption, alcohol drinking and physical activity associations with breast cancer risk among Chinese females: a systematic review and meta-analysis. *Asian Pac J Cancer Prev*, **14**, 7543-50.

George SM, Irwin ML, Smith AW, et al (2011). Postdiagnosis diet quality, the combination of diet quality and recreational physical activity, and prognosis after early-stage breast cancer. *Cancer Causes Control*, **22**, 589-98.

Giles GG, Simpson JA, English DR, et al (2006). Dietary carbohydrate, fiber, glycaemic index, glycaemic load and the risk of postmenopausal breast cancer. *Int J Cancer*, **118**, 1843-7.

Giovannucci E (1999). Tomatoes, tomato-based products, lycopene, and cancer. Review of epidemiologic literature. *J Natl Cancer Inst*, **91**, 317-31.

Glowny Urząd Statystyczny (GUS) (2004). Stan zdrowia ludnosci Polski w 2004 r. (In Polish) GUS, Warszawa 2006.

Gorner K, Jurczak A, Spieszny M, Mucha D, Makuch R (2013). Chosen individual factors of adolescents' physical development in their leisure time. *Centr Eur J Sport Sci Med*, **1**, 31-7.

Gunter MJ, Hoover DR, Yu H, et al (2009). Insulin, insulin-like growth factor-1, and risk of breast cancer in postmenopausal women. *J Natl Cancer Inst*, **101**, 48-60.

Haluska P, Carboni JM, Loegering DA, et al (2006). In vitro and in vivo antitumor effects of the dual insulin-like growth factor-I/insulin receptor inhibitor, BMS-554417. *Cancer Res*, **66**, 362-71.

Hirose K, Matsuo K, Iwata H, Tajima K (2007). Dietary patterns and the risk of breast cancer in Japanese women. *Cancer Sci*, **98**, 1431-8.

Holmes MD, Liu S, Hankinson SE, et al (2004). Dietary carbohydrates, fiber, and breast cancer risk. *Am J Epidemiol*, **159**, 732-9.

Holmes MD, Willett WC (2004). Does diet affect breast cancer risk? *Breast Cancer Res*, **6**, 170-8.

Horn-Ross PL, Hoggatt KJ, West DW, et al (2002). Recent diet and breast cancer risk: the California Teachers Study (USA). *Cancer Causes Control*, **13**, 407-15.

Hui C, Qi X, Qianyong Z, et al (2013). Flavonoids, flavonoid subclasses and breast cancer risk: a meta-analysis of epidemiologic studies. *PLoS One*, **8**, e54318.

Iscovich JM, Iscovich RB, Howe G, Shiboski S, Kaldor JM (1989). A case-control study of diet and breast cancer in Argentina. *Int J Cancer*, **44**, 770-6.

Kelley DS, Bendich A (1996). Essential nutrients and immunologic functions. *Am J Clin Nutr*, **63**, 994-6.

Klaunig JE, Kamendulis LM, Hocevar BA (2010). Oxidative stress and oxidative damage in carcinogenesis. *Toxicologic Pathology*, **38**, 96-109.

Knekt P, Albanes D, Seppanen R, et al (1990). Dietary fat and risk of breast cancer. *Am J Clin Nutr*, **52**, 903-8.

Krinsky NI, Deneke SM (1982). Interaction of oxygen and oxy-

radicals with carotenoids. *J Natl Cancer Inst*, **69**, 205-10.

Kriska AM, Knowler WC, LaPorte RE, et al (1990). Development of questionnaire to examine relationship of physical activity and diabetes in Pima Indians. *Diabetes Care*, **13**, 401-11.

Kruk J (2007). Association of lifestyle and other risk factors with breast cancer according to menopausal status: a case-control study in the region of Western Pomerania (Poland). *Asian Pac J Cancer Prev*, **8**, 513-24.

Kruk J (2009). Intensity of lifetime physical activity and breast cancer risk among Polish women. *J Sports Sciences*, **27**, 437-45.

Kruk J (2011). Physical exercise and oxidative stress. *Medicina Sportiva*, **15**, 30-40.

Kruk J, Marchlewicz M (2013). Dietary fat and physical activity in relation to breast cancer among Polish women. *Asian Pac J Cancer Prev*, **14**, 2495-502.

Kushi LH, Sellers TA, Potter JD, et al (1992). Dietary fat and postmenopausal breast cancer. *J Natl Cancer Inst*, **84**, 1092-9.

La Vecchia C, Decarli A, Franceschi S, et al (1987). Dietary factors and the risk of breast cancer. *Nutr Cancer*, **10**, 205-14.

Lajous M, Boutron-Ruault MC, Fabre A, Clavel-Chapelon F, Romieu I (2008). Carbohydrate intake, glycemic index, glycemic load, and risk of postmenopausal breast cancer in a prospective study of French women. *Am J Clin Nutr*, **87**, 1384-91.

Larsson SC, Mantzoros CS, Wolk A (2007). Diabetes mellitus and risk of a breast cancer: a meta-analysis. *Int J Cancer*, **121**, 856-62.

Lisowska J, Gaudet MM, Brinton LA, et al (2008). Intake of fruits and vegetables in relation to breast cancer by hormone receptor status. *Breast Cancer Res Treat*, **107**, 113-7.

Liu X-O, Huang Y-B, Gao Y, et al (2014). Association between dietary factors and breast cancer risk among Chinese females: systematic review and meta-analysis. *Asian Pac J Cancer Prev*, **15**, 1291-8.

London C (2006). Tomatoes and natural tomato complex may be the ultimate women's health food. *Total Health*, **28**, 20-1.

Macdonald HM, New SA, Reid DM (2005). Longitudinal changes in dietary intake in Scottish women around the menopause: changes in dietary pattern result in minor changes in nutrient intake. *Public Health Nutr*, **8**, 409-16.

Mannisto S, Dixon LB, Balder HF, et al (2005). Dietary patterns and breast cancer risk: results from three cohort studies in the DIETSCAN project. *Cancer Causes Control*, **16**, 725-33.

Maruti SS, Willett WC, Feskanich D, et al. (2009). Physical activity and premenopausal cancer: An examination of recall and selection bias. *Cancer Cause Control*, **20**, 549-58.

Michels KB, Mohllajee AP, Roset-Bahmanyar E, Beehler GP, Moysich KB (2007). Diet and breast cancer: a review of the prospective observational studies. *Cancer*, **109**, 2712-49.

Minatoya M, Kutomi G, Asakura S, et al (2013). Equol, adiponectin, insulin levels and risk of breast cancer. *Asian Pac J Cancer Prev*, **14**, 2191-9.

Nielsen TG, Olsen A, Christensen J, Overvad K, Tionneland A (2005). Dietary carbohydrate intake is not associated with the breast cancer incidence the ratio in postmenopausal Danish women. *J Nutr*, **135**, 124-8.

Nkondjock A, Ghadirian P (2005). Associated nutritional risk of breast and colon cancers: a population-based case-control study in Montreal, Canada. *Cancer Lett*, **223**, 85-91.

Nyberg F, Hou SM, Pershagen G, Lambert B (2003). Dietary fruits and vegetables protect against somatic mutation in vivo, but low or high intake of carotenoids does not. *Carcinogenesis*, **24**, 689-96.

Oxford University Press USA (2014). Consuming a high-fat diet is associated with increased risk of certain types of breast

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cancer. ScienceDaily. ScienceDaily, 9 April 2014. www.sciencedaily.com/releases/2014/04/140409204417.htm

Pawlega J (1992). Breast cancer and smoking, vodka drinking and dietary habits. A case-control study. *Acta Oncol*, **31**, 387-92.

Powers SK, De Ruisseau KC, Quindry J, Hamilton KL (2004). Dietary antioxidants and exercise. *J Sports Sci*, **22**, 81-94.

Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB (2010). Oxidative stress, inflammation, and cancer: How are they linked? *Free Radic Biol Med*, **49**, 1603-16.

Romieu I, Lajous M (2009). The role of obesity, physical activity and dietary factors on the risk for breast cancer: Mexican experience. *Salud Publica Mex*, **51**, 172-80.

Sangrajrang S, Chaiwerawattana A, Ploysawang P, et al (2013). Obesity, diet and physical inactivity and risk of breast cancer in Thai women. *Asian Pac J Cancer Prev*, **14**, 7023-7.

Sarma AD, Mallick AR, Ghosh (2010). Free radicals and their role in different clinical conditions: an overview. *Int J Pharma Sci Res*, **1**, 185-92.

Shibata A, Paganini-Hill A, Ross RK, Henderson BE (1992). Intake of vegetables, fruits, beta-carotene, vitamin C and vitamin supplements and cancer incidence among the elderly: a prospective study. *Br J Cancer*, **66**, 673-9.

Sieri S, Krogh V, Muti P, et al (2002). Fat and protein intake and subsequent breast cancer risk in postmenopausal women. *Nutr Cancer*, **42**, 10-7.

Silvera SA, Jain M, Howe GR, Miller AB, Rohan TE (2005). Dietary carbohydrates and breast cancer risk: a prospective study of the roles of overall glycemic index and glycemic load. *Int J Cancer*, **114**, 653-8.

Smith-Warner SA, Spiegelman D, Yaun SS, et al (2001). Intake of fruits and vegetables and risk of breast cancer: a pooled analysis of cohort studies. JAMA, Feb 14, **285**, 769-76.

Sulaiman S, Shahril MR, Shaharudin SH, et al (2011). Fat intake and its relationship with pre- and postmenopausal breast cancer risk: a case-control study in Malaysia. *Asian Pacific J Cancer Prev*, **12**, 2167-78.

Terry P, Suzuki R, Hu FB, Wolk A (2001). A prospective study of major dietary patterns and the risk of breast cancer. *Cancer Epidemiol Biomarkers Prev*, **10**, 1281-5.

Thomson HJ (1994). Effect of exercise intensity and duration on the induction of mammary carcinogenesis. *Cancer Res*, **54**, 1960-3.

Tworoger SS, Missmer SA, Eliassen AH, et al (2007). Physical activity and inactivity in relation to sex hormone, prolactin and insulin-like growth factor concentrations in premenopausal women – exercise and premenopausal hormones. *Cancer Causes Control*, **18**, 743-52.

Verhoeven DT, Assen N, Goldbohm RA, et al (1997). Vitamins C and E, retinol, beta-carotene and dietary fibre in relation to breast cancer risk: a prospective cohort study. *Br J Cancer*, **75**, 149-55.

Waśkiewicz A, Piotrowski W, Sygnowska E, et al (2008). Quality of nutrition and health knowledge in subjects with diagnosed cardio-vascular diseases in the Polish population – National Multicentre Health Survey (WOBASZ). *Kardiologia Polska*, **66**, 507-13.

Wettasinghe M, Bolling B, Plhak H, Parkin K (2002). Screening for phase II enzyme-inducing and antioxidant activities of common vegetables. *J Fod Sci*, **67**, 2583-8.

World Cancer Research Fund/American Institute for Cancer Research, Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective, The Panel's judgements Washington, DC: AICR 2007.

Wu AH, Yu MC, Tseng CC, Stanczyk FZ, Pike MC (2009). Dietary patterns and breast cancer risk in Asian American women. *Am J Clin Nutr*, **89**, 1145-54.

Wu T, Giovannucci E, Pischon T, et al (2004). Fructose, glycemic load, and quantity and quality of carbohydrate in relation to plasma C-peptide concentrations in US women. *Am J Clin Nutr*, **80**, 1043-9.

Xiao D, Vogel V, Singh SV (2006). Benzyl isothiocyanate-induced apoptosis in human breast cancer cells is initiated by reactive oxygen species and regulated by Bax and Bak. *Mol Cancer Ther*, **5**, 2931-45.

Yaw YH, Shariff ZM, Kandiah M, et al (2014). Diet and physical activity in relation to weight change among breast cancer patients. *Asian Pac J Cancer Prev*, **15**, 39-44.

Yun SH, Kim K, Nam SJ, Kong G, Kim MK (2010). The association of carbohydrate intake, glycemic load, glycemic index, and selected rice food with breast cancer risk: a case-control study in South Korea. *Asia Pac J Clin Nutr*, **19**, 383-92.

Zhang CX, Ho SC, Chen YM, et al (2009). Greater vegetable and fruit intake is associated with a lower risk of breast cancer among Chinese women. *Int J Cancer*, **125**, 181-8.

Zhang C-X, Ho SC, Fu J-H, et al (2011). Dietary patterns and breast cancer risk among Chinese women. *Cancer Causes Control*, **22**, 115-24.

Zhang S, Hunter DJ, Forman MR, et al (1999). Dietary carotenoids and vitamins A, C, and E and risk of breast cancer. *J Natl Cancer Inst*, **91**, 547-56.

Zhu Y-Y, Zhou L, Jiao S-C, Xu L-Z (2011). Relationship between soy food intake and breast cancer in China. *Asian Pac J Cancer Prev*, **12**, 2837-40.