

Consumption of flaxseed, a rich source of lignans, is associated with reduced breast cancer risk

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Abstract

Purpose To investigate the association between intake of flaxseed—the richest source of dietary lignans (a class of phytoestrogens)—and breast cancer risk.

Methods A food frequency questionnaire was used to measure the consumption of flaxseed and flax bread by 2,999 women with breast cancer and 3,370 healthy control women who participated in the Ontario Women’s Diet and Health Study (2002–2003). Logistic regression was used to investigate associations between consumption of flaxseed and flax bread and breast cancer risk. Confounding by established and suspected breast cancer risk factors, as well as dietary factors, was assessed.

Results Flaxseed or flax bread was consumed at least weekly by 21 % of control women. None of the 19 variables assessed were identified as confounders of the associations between flaxseed or flax bread and breast cancer risk. Consumption of flaxseed was associated with a significant reduction in breast cancer risk (odds ratio (OR) = 0.82, 95 % confidence interval (CI) 0.69–0.97), as was consumption of flax bread (OR = 0.77, 95 % CI 0.67–0.89).

Conclusions This Canadian study is, to our knowledge, the first to report on the association between flaxseed alone and breast cancer risk and has found that flaxseed intake is associated with a reduction in breast cancer risk. As dietary intake of flaxseed is modifiable, this finding may be of public health importance with respect to breast cancer prevention.

Keywords Breast neoplasms · Flax · Lignans · Phytoestrogens

Introduction

Two recent meta-analyses concluded that high dietary intake of lignans, the class of phytoestrogens most commonly consumed in Western diets, is associated with a modest reduction in postmenopausal breast cancer risk [1, 2]. Lignans are found in many plant foods, but flaxseed is the richest source, containing more than 300 mg per 100 g serving [3, 4]. Despite its contribution to dietary lignan intake, flaxseed has not been measured in most studies assessing lignans and breast cancer risk [e.g., 5–10]. This omission has prevented the evaluation of associations between breast cancer risk and flaxseed consumption and has likely resulted in the underestimation and misclassification of lignan exposure in previous studies.

The Ontario Women’s Diet and Health Study is a population-based case–control study conducted to investigate associations between dietary phytoestrogens and breast cancer risk. Intakes of phytoestrogen-containing foods, including flaxseed and flax bread, were measured, and in 2008, we reported that total lignan intake may be associated with reduced risk of breast cancer [11]. Among controls, flaxseed was the major lignan contributor [11];

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similarly, a Swedish study reported that flaxseed contributed substantially to total lignan intake [12]. It was therefore of interest to examine the association between flaxseed consumption specifically and breast cancer risk.

Materials and methods

Data were collected in 2002–2003 from participants of the Ontario Women's Diet and Health Study [11, 13, 14]. Cases of first pathologically confirmed breast cancer diagnosed in women aged 25–74 years were identified through the Ontario Cancer Registry in Canada. Controls were women identified through random digit dialing of approximately 25,250 households in the province of Ontario. Of the households dialed, 4,352 were deemed to be eligible (~17,000 households were ineligible, for example, they did not have a woman aged 25–74 years with no history of breast cancer; the phone was not answered by ~2,000 households; ~2,000 households refused participation). Controls were 1:1 frequency matched to cases on 5-year age groups. The University of Toronto Research Ethics Board approved this study.

Approximately 75 % of cases (3,101/4,109) and 80 % of eligible controls (3,471/4,352) completed a mailed personal history questionnaire and a modified Block food frequency questionnaire [15]. Women who reported extreme energy intake (<600 kcal or >4,500 kcal) were excluded from the analyses (102 cases, 101 controls), resulting in a sample of 2,999 cases and 3,370 controls. The food frequency questionnaire collected information regarding consumption (2 years ago) of 178 food items including flaxseed (alone, in baked goods, snacks or other dishes) and flax or linseed breads (including bagels or buns). Intake was reported using nine frequency responses (ranging from never to daily) and four serving size options (minimum serving size was assigned when serving size responses were missing, ~3 % of flaxseed consumers). Intake of flaxseed oil was not assessed because it did not contain lignans. Flaxseed and flax bread exposures were categorized according to frequency of intake (never, monthly or less, daily/weekly) of the minimum serving size (¼ cup flaxseed, one slice flax bread); when a serving size greater than the minimum was reported, intake frequency was adjusted to reflect the minimum serving (e.g., intake of a ½ cup serving of flaxseed at a frequency of 2–3 times per month was categorized as daily/weekly consumption of a ¼ cup serving).

Logistic regression was used to estimate age group-adjusted odds ratios (OR) and 95 % confidence intervals (CI). Confounding was assessed by adding potential confounders, one at a time, to the regression model and evaluating the impact on the age group-adjusted OR. Potential

confounders assessed were established breast cancer risk factors (breast cancer in a first degree relative; ages at menarche, last menstrual period and first live birth; parity; oral contraceptives; hormone replacement therapy; benign breast disease; body mass index; alcohol intake), dietary factors (total energy intake; total dietary fat; as well as dietary fiber and omega-3 fatty acids since flaxseed contains substantial amounts of these compounds [16]) and behavioral and socioeconomic factors that may be associated with a health-conscious decision to consume flaxseed (smoking history; mammograms; income; education; immigrant status). A variable was considered to be a confounder if the age group-adjusted OR changed by >10 % [17]; none of the variables assessed met this definition. Analyses were stratified by menopausal status and hormone receptor status of cancers, and the statistical significance of interactions was assessed using the likelihood ratio test.

Results

Consumption of flaxseed, and of flax bread, was associated with statistically significant 20–30 % reductions in breast cancer risk (Table 1). Reductions in risk were consistently observed among all women consuming flaxseed, when compared to never consumers, regardless of intake category. After stratification by menopausal status, the association with flaxseed intake was observed among postmenopausal (daily/weekly, OR = 0.73, 95 % CI 0.60–0.89), but not premenopausal, women (Table 1); however, there was no statistically significant interaction. Significant associations between flax bread intake and breast cancer risk were observed for both pre- and postmenopausal women (e.g., daily/weekly, OR = 0.74, 95 % CI 0.62–0.88) (Table 1). Associations between flaxseed intake and breast cancer estrogen receptor (ER)/progesterone receptor (PR) subgroups did not differ substantially (e.g., daily/weekly consumption: ER+ PR+, OR = 0.81, 95 % CI 0.66–1.01; ER– PR–, OR = 0.75, 95 % CI 0.53–1.06), nor did associations with flax bread intake (e.g., daily/weekly consumption: ER+ PR+, OR = 0.81, 95 % CI 0.68–0.97; ER– PR–, OR = 0.77, 95 % CI 0.58–1.01) (data not shown).

Discussion

These flaxseed findings are consistent with recent meta-analyses suggesting that dietary lignan intake may be associated with a modest reduction in breast cancer risk, particularly in postmenopausal women [1, 2] and emphasize the need to capture flaxseed in dietary assessments of

Table 1 Distribution of flaxseed and flax bread consumption and odds ratios for breast cancer for all women, and pre- and postmenopausal women, in the Ontario Women's Diet and Health Study

| | All women | | | Premenopausal women | | | Postmenopausal women | | |
|-------------------------------|------------------------|---------------------------|------------------|----------------------|---------------------------|------------------|------------------------|---------------------------|------------------|
| | Cases (2,999) n (%) | Controls (3,370) n (%) | OR (95 % CI) | Cases (930) n (%) | Controls (1,211) n (%) | OR (95 % CI) | Cases (2,066) n (%) | Controls (2,154) n (%) | OR (95 % CI) |
| Flaxseed^a | | | | | | | | | |
| Never | 2,200 (74.2) | 2,329 (69.8) | 1.00 | 681 (74.0) | 877 (73.0) | 1.00 | 1,518 (74.4) | 1,447 (68.0) | 1.00 |
| Monthly or less | 482 (16.3) | 653 (19.6) | 0.76 (0.67–0.87) | 155 (16.9) | 225 (18.7) | 0.85 (0.68–1.07) | 326 (16.0) | 428 (20.1) | 0.72 (0.61–0.85) |
| Daily/weekly | 282 (9.5) | 354 (10.6) | 0.82 (0.69–0.97) | 84 (9.1) | 100 (8.3) | 1.03 (0.76–1.41) | 197 (9.7) | 254 (11.9) | 0.73 (0.60–0.89) |
| Flax bread^b | | | | | | | | | |
| Never | 1,981 (67.2) | 2,052 (61.6) | 1.00 | 629 (68.4) | 766 (63.8) | 1.00 | 1,351 (66.6) | 1,282 (60.4) | 1.00 |
| Monthly or less | 554 (18.8) | 738 (22.2) | 0.76 (0.67–0.86) | 164 (17.8) | 257 (21.4) | 0.74 (0.59–0.92) | 390 (19.2) | 480 (22.6) | 0.76 (0.65–0.89) |
| Daily/weekly | 415 (14.1) | 540 (16.2) | 0.77 (0.67–0.89) | 127 (13.8) | 178 (14.8) | 0.84 (0.66–1.09) | 287 (14.2) | 362 (17.0) | 0.74 (0.62–0.88) |

OR odds ratio, adjusted for 5-year age group (none of the 19 variables assessed as confounders met the definition), CI confidence interval

^a ¼ Cup of flaxseed was the minimum serving size option on food frequency questionnaire and contains 163 mg of total lignans (matairesinol, lariciresinol, pinoresinol, secoisolariciresinol) [3]

^b 1 Piece of flax bread was the minimum serving size option on food frequency questionnaire and contains 3.6 mg of total lignans (matairesinol, lariciresinol, pinoresinol, secoisolariciresinol) [3]

lignan consumption. The only other study to specifically assess lignan-rich foods reported reductions in breast cancer risk for certain seeds, such as sunflower and pumpkin, among German women [18].

In this study, 21 % of controls reported consuming flaxseed or flax bread at least weekly. There is a paucity of published literature on the prevalence of flaxseed consumption among the general population; however, an Australian study reported that 34 % of women consumed flaxseeds in the previous month [19]. As one teaspoon contains more than 13 mg of lignans [3], only a small daily serving of flaxseed is required to attain the level of lignan intake previously shown to be associated with a reduction in breast cancer risk (e.g., >5.4 mg/day [11]). As it appears that most women do not consume flaxseed and that small amounts may be associated with reduced breast cancer risk, interventions to increase the prevalence of flaxseed consumption might be considered. Intervention studies have been conducted to investigate the impact of flaxseed on markers of cardiovascular disease and diabetes management, with favorable results [20–22].

Strengths of the present study include its large sample size, population-based selection of cases and controls, and specific measurements of flaxseed and flax bread consumption in pre- and postmenopausal women. A limitation of the measure of flaxseed intake used is that the serving size options provided in the food frequency questionnaire were large (minimum response option was ¼ cup), as they also applied to more sizeable nut and seed items. It is likely that persons who supplement foods (such as breakfast cereals or blended drinks) with ground flaxseed use less than ¼ cup per serving. The vast majority (90 %) of flaxseed consumers reported the minimum serving, but it is unknown whether those whose usual serving size was smaller accurately reported their intake frequency or whether they accommodated for serving size by reporting a lower intake frequency (e.g., one tablespoon of flaxseed consumed per week was reported as ¼ cup per month). Reporting an altered frequency in such a manner could explain why a dose response by frequency was not observed, if one exists. However, as it has been suggested that intake variation between individuals is determined more by frequency than serving size [23], the food questionnaire may have reasonably captured variation in flaxseed exposure despite the limitations of the serving size options provided. Although we evaluated potential confounders, there is also the possibility that the associations observed are due to residual confounding by unknown factors associated with both flaxseed consumption and breast cancer risk.

In summary, flaxseed and flax bread consumption was associated with reduced breast cancer risk, particularly among postmenopausal women. This finding is not

surprising given that previous studies suggest high lignan intake may reduce breast cancer risk [1, 2, 11]. To our knowledge, this is the first epidemiologic study to assess the association between flaxseed alone and breast cancer risk. Flaxseed is the most concentrated source of dietary lignans, but it is not consumed by most women. Flaxseed intervention studies for breast cancer prevention may warrant future consideration.

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Conflict of interest The authors declare that they have no conflict of interest.

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