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Dietary Mushroom Intake and the Risk of Breast Cancer Based on Hormone Receptor Status

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Although many studies have documented the antitumor activities of mushrooms, the association between mushroom intake and breast cancer, defined by hormone receptor status, has received minimal empirical investigation. This study evaluated the association between mushroom intake and the risk of breast cancer according to hormone receptor status among Korean women. Mushroom intake and breast cancer risk were examined among 358 breast cancer patients and 360 cancer-free controls. Intake of mushrooms was assessed using a quantitative food frequency questionnaire. Greater mushroom intake was related to lower risk of breast cancers among premenopausal women (odds ratio [OR] = 0.35, 95% confidence interval [CI] = 0.13–0.91 for the highest vs. the lowest quartile intake). The association was stronger for premenopausal women with estrogen receptor (ER)+/progesterone receptor (PR) + tumors (OR = 0.30, 95% CI = 0.11–0.79 for the highest vs. the lowest quartile intake) than those with ER–/PR– tumors. Our results suggest that high consumption of mushrooms might be related to lower risks for breast cancers among premenopausal women; this association may be more robust among women with hormone receptor positive tumors.

INTRODUCTION

Hormone receptor status has been used to determine optimal treatment strategies for patients with breast tumors (1). Previous studies have shown that the characteristics of breast cancer tumors differ by race/ethnicity due to both biological and lifestyle factors (2). In the United States, the proportion of hormone receptor-positive tumors has increased from 1992 to 1998 as the proportion of hormone receptor-negative tumors has decreased (1,3). The overall rise in breast cancer incidence seems primarily attributable to the increase in the incidence of hormone receptor-positive tumors (3). Women with estrogen receptor-positive (ER+)/progesterone receptor-negative (PR–), ER–/PR+, or ER–/PR– tumors have a higher risk of mortality than women with ER+/PR+ tumors (4,5).

The results of previous studies have associated several risk factors with the development of breast cancer. Although some factors, such as age, sex, familial, menstrual and reproductive histories, lie beyond human control, dietary habits are subject to modification (6). The potentially antitumor effects of mushroom extracts and constituents include blocking the formation of carcinogens, suppressing DNA synthesis, enhancing cell differentiation, and competing with estrogen for estrogen receptors (7). Most research has entailed isolating pharmaceutically active mushroom compounds, and these compounds have been hypothesized as plausible biological links to the mechanisms by which mushrooms function on macrophages, natural killer cells, and subsets of T cells (8–13). Although antitumor activities have been reported, very few studies have investigated the association between mushrooms and breast cancer as defined by hormone receptor status. The antiaromatase activity of mushroom extract suggests a differential role of dietary mushroom intake on the risk of breast cancer defined by hormone receptor status (9). Asians consume a relatively high amount of mushrooms as a part of their usual diet (14); therefore, Koreans are an optimal study population for the association between dietary mushroom intake and disease risks. Hence, in this study, we sought to

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evaluate the association between dietary mushroom intake and the risk of breast cancer as defined jointly by ER and PR status. In addition, we investigated the differential effects of mushroom intake among premenopausal and postmenopausal women with breast cancer as defined by hormone receptor status.

MATERIALS AND METHODS

Subjects

Eligible breast cancer cases were enrolled at the Center for Breast Cancer in the National Cancer Center Hospital in Korea between July 2007 and September 2008. Participants with a previous history of cancer were excluded from the study population. Among 424 incident breast cancer patients aged 25 to 77 yr and admitted for surgery during this period, 398 agree to participate in the study. Out of 398, 14 were excluded due to previous histories of other cancers, and one was excluded due to an inability to cooperate in the interview. Eligible controls were recruited among women who visited for regular health checkups at the Center for Early Detection and Prevention at the same hospital during the same time period. Exclusion criteria included women with a history of malignant neoplasm or other benign breast disease and women with missing information in their dietary intake. Among 723 recruited participants, 617 met eligibility criteria and were available for analysis. Among the cases and controls recruited, those with daily energy intakes of $<$600 kcal or $>$3,500 kcal were excluded ($n = 4$ in the cases; $n = 2$ in the controls), and the controls were frequency matched to cases by a 5-yr age distribution. Finally, the data from 358 cases and 360 controls were used for analysis. Study protocols and consent forms were approved by the institutional review board of the National Cancer Center Hospital (IRB protocol number NCCNCS 07–083), and all subjects provided informed consent for study participation.

Data Collection

A trained dietitian used a structured questionnaire to collect information pertaining to demographics, lifestyle factors, smoking habits, and alcohol intake. Reproductive information was also obtained, including age at menarche, menopause status, age at menopause, type of menopause, postmenopausal hormone use, and parity. The food frequency questionnaire (FFQ) used in this study was developed and validated to determine regular dietary intake. The reliability and validity of the FFQ has been reported previously (15). Subjects were presented with a list of 103 food items and queried about the average frequency with which they ate specific foods and the typical portion sizes of their meals during the previous year. The average daily nutrient intake for each subject was measured by adding the intake amount and associated nutrient content per 100 g for each of the 103 foods. This value was converted to daily nutrient intake using the scales for consumption frequency (i.e., never or rarely, once a month, 2 or 3 times a month, once or twice a week, 3 or 4 times a week, 5 or 6 times a week, once a day, twice a day, and 3 times a day) and portion size (i.e., small, medium, and large) included in the FFQ.

Analysis of ER and PR

ER and PR contents were analyzed on tissue sections cut from formalin-fixed, paraffin-embedded breast tumors by immunohistochemistry (Ventana Medical Systems, Tucson, AZ). Detailed information for laboratory procedures can be found in Nam et al. (16).

Statistical Methods

Chi-square (χ^2) tests were used to evaluate the statistical differences for categorical variables between case and control groups. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated by unconditional logistic regression models, and the significance level was set at 0.05 for all statistical tests. The LOGISTIC procedure provided by SAS 9.1 (SAS Institute, Inc., Cary, NC) was utilized to perform the calculations. Potential effect modifiers included age, body mass index (BMI; weight, kg/height m^2), family history of breast cancer, current use of dietary supplements, marital status, education, occupation, smoking status, alcohol intake, age at menarche, physical activity, menopausal status, parity, energy, and fruit and vegetable intake. Smoking history was categorized as nonsmoker, ex-smoker, or current smoker. Alcohol consumption was divided into two categories according to whether subjects had ever consumed alcohol (never/ever). Physical activity was measured using the short form (version 2.0, April 2004) of the International Physical Activity Questionnaire (IPAQ) and summarized into metabolic equivalent (MET) units-minutes/week. Data were stratified by menopausal status. The postmenopausal group was further adjusted for age at menopause, type of menopause, and postmenopausal hormone use. Quartile distribution of all controls was used for categorization of mushroom intake for both case and control groups. Median intake of each quartile category of mushroom was used as a continuous variable to test for trends. Polytomous logistic regression was used to detect relationships between mushroom intake and breast cancer characterized by hormone positive/negative tumors.

RESULTS

The general characteristics of the participants are presented in Table 1. The mean ages of the case and control subjects were 48.3 and 47.9 yr, respectively, which represented no significant difference. BMI of the case group was lightly higher than that of control group. Other statistically significant differences between the cases and controls were observed with regard to dietary supplement use ($P = 0.001$), education ($P < 0.001$), occupation ($P = 0.012$), age at menarche ($P < 0.001$), and postmenopausal hormone use ($P < 0.001$).

Data on selected dietary intake habits of subjects are presented in Table 2. In general, the women in the case group consumed significantly higher amounts of energy ($P = 0.032$) but lower amounts of all vegetables ($P < 0.001$), and mushrooms

TABLE 1
General characteristics of study subjects[a]

Variable	Control, *n* (%)[b]	Case, *n* (%)[c]	*P*
Age, yr[d]	47.9 ± 8.7	48.3 ± 8.6	0.633
BMI (kg/m^2)			
<18.5	8(2.2)	16(4.5)	0.003
18.5–22.9	150(42.4)	153(42.7)	
23–24.9	121(34.2)	85(23.7)	
≥25	75(21.2)	104(29.1)	
Family history of breast cancer (yes)	12(3.6)	17(4.8)	0.429
Dietary supplement use (yes)	167(67.1)	194(54.3)	0.001
Marital status			
Married	288(83.0)	289(80.7)	0.588
Single	14(4.0)	20(5.6)	
Divorced, widowed, other	45(13.0)	49(13.7)	
Education			
≤Elementary school	21(6.1)	59(16.5)	<0.001
Middle school	17(4.9)	44(12.3)	
High school	176(51.2)	174(48.6)	
≥College	130(37.8)	81(22.6)	
Occupation			
Housewife	212(61.1)	217(60.6)	0.012
Profession, office worker	75(21.6)	54(15.1)	
Sales, service	43(12.4)	51(14.3)	
Agriculture, laborer, unemployed, other	17(4.9)	36(10.0)	
Smoking status			
Nonsmoker	305(93.3)	318(89.1)	0.066
Ex-smoker	12(3.7)	28(7.8)	
Current smoker	10(3.0)	11(3.1)	
Alcohol consumption habit			
Never	175(52.9)	189(53.1)	0.954
Ever	156(47.1)	167(46.9)	
Physical activity (MET min/week)[e]			
≤396	77(22.9)	59(16.6)	0.076
396–1,271	91(27.0)	114(32.0)	
1,272–2,771	81(24.0)	101(28.4)	
≥2,772	88(26.1)	82(23.0)	
Age at menarche (yr)			
≤13	97(28.9)	91(25.4)	<0.001
14	74(22.0)	97(27.1)	
15	86(25.6)	53(14.8)	
≥16	79(23.5)	117(32.7)	
Menopausal status			
Premenopause	196(54.4)	210(58.7)	0.254
Postmenopause	164(45.6)	148(41.3)	
Age at menopausef (yr)			
<46	37(26.6)	43(29.5)	0.697
46–48	35(25.2)	31(21.2)	
49–52	39(28.1)	47(32.2)	
≥52	28(20.1)	25(17.1)	

(Continued on next page)

TABLE 1
General characteristics of study subjects[a] *(Continued)*

Variable	Control, *n* (%)[b]	Case, *n* (%)[c]	*P*
Type of menopause[f]			
Natural	109(75.2)	98(66.7)	0.109
Surgery, other	36(21.8)	49(33.3)	
Postmenopausal hormone use[f]			
Never	88(62.0)	115(80.4)	<0.001
Ever	54(38.0)	28(19.6)	
Childbirth			
No	46(12.8)	31(8.7)	0.074
Yes	314(87.2)	327(91.3)	

[a]Abbreviations are as follows: BMI, body mass index; METs, metabolic equivalent units.
[b]$n = 360$.
[c]$n = 358$.
[d]Mean ± SD.
[e]METs are multiples of the resting metabolic rate and calculated using the short form (version 2.0, April 2004) of the International Physical Activity Questionnaire.
[f]In postmenopausal women.

($P < 0.001$). Among premenopausal women, cases reported lower intake of all vegetables ($P < 0.001$) and mushrooms ($P < 0.001$), whereas no significant difference in energy intake was observed between two groups. Among postmenopausal women, cases reported higher energy intake ($P = 0.039$) but lower total vegetable ($P < 0.001$) and mushroom ($P < 0.001$) intake.

Table 3 presents ORs and 95% CIs of breast cancer risk in relation to mushroom intake in both univariate and multivariate adjusted models. After adjusting for confounding variables in multivariate logistic regression models, the reduced risk for breast cancer was most significant in the highest quartile (OR = 0.43, 95% CI = 0.21–0.88, *P* for trend = 0.011) compared to the lowest quartile intakes of mushroom. The protective effect of mushroom intake among premenopausal women was most significant in the highest quartile intake (OR = 0.35, 95% CI = 0.13–0.91, *P* for trend = 0.026) compared to the lowest intake. However, no significant association between mushroom intake and breast cancer risk was found among postmenopausal women.

Table 4 shows the ORs and 95% CIs of breast cancer risk characterized by ER and PR status according to mushroom intake. For those with an ER+/PR+ tumor, the reduced risk for

TABLE 2
Selected dietary intake of study subjects

Dietary Intake	Control, Mean ± SD	Case, Mean ± SD	*P*
Total subjects (control/case $n = 360/358$)			
Energy intake (kcal/day)	1752.5 ± 548.5	1813.8 ± 492.9	0.032
Total vegetables (g/day)	151.3 ± 118.4	99.0 ± 63.1	< 0.001
Total fruits (g/day)	270.1 ± 246.7	244.4 ± 212.3	0.315
Mushrooms (g/day)	9.7 ± 13.5	5.1 ± 4.9	< 0.001
Premenopausal women (control/case $n = 196/210$)			
Energy intake (kcal/day)	1797.6 ± 574.9	1811.1 ± 460.8	0.353
Total vegetables (g/day)	149.6 ± 131.3	98.7 ± 65.2	< 0.001
Total fruits (g/day)	258.9 ± 240.6	241.9 ± 207.7	0.947
Mushrooms (g/day)	10.9 ± 14.5	5.7 ± 5.1	< 0.001
Postmenopausal women (control/case $n = 164/148$)			
Energy intake (kcal/day)	1698.5 ± 511.6	1817.8 ± 536.8	0.039
Total vegetables (g/day)	153.2 ± 101.3	99.5 ± 60.2	< 0.001
Total fruits (g/day)	283.5 ± 253.9	247.9 ± 219.2	0.165
Mushrooms (g/day)	8.2 ± 12.1	4.1 ± 4.6	< 0.001

TABLE 3
ORs and 95% CIs of breast cancer risk in association with mushroom intake[a]

Quartiles of Daily Mushroom Intake (g/Day)	No. of Case/Control	Crude OR (95% CI)	Multivariate Adjusted OR (95% CI)[b]
Total subjects	358/360		
Q1 (<2.61)	138/90	1.00 (referent)	1.00 (referent)
Q2 (2.62 < 5.36)	101/90	0.73(0.49–1.08)	0.96(0.57–1.61)
Q3 (5.36 < 11.37)	83/90	0.60(0.40–0.89)	0.84(0.48–1.48)
Q4 (≥11.37)	36/90	0.26(0.16–0.41)	0.43(0.21–0.88)
P for trend[c]		<0.001	0.011
Premenopausal women	210/196		
Q1 (<2.61)	63/42	1.00 (referent)	1.00 (referent)
Q2 (2.62 < 5.36)	65/47	0.92(0.53–1.58)	0.76(0.36–1.60)
Q3 (5.36 < 11.37)	57/52	0.73(0.42–1.25)	0.76(0.34–1.70)
Q4 (≥11.37)	25/55	0.30(0.16–0.56)	0.35(0.13–0.91)
P for trend[c]		<0.001	0.026
Postmenopausal women	148/164		
Q1 (<2.61)	75/48	1.00 (referent)	1.00 (referent)
Q2 (2.62 < 5.36)	36/43	0.53(0.30–0.94)	1.20(0.54–2.63)
Q3 (5.36 < 11.37)	26/38	0.43(0.23–0.81)	0.77(0.32–1.81)
Q4 (≥11.37)	11/35	0.20(0.09–0.43)	0.74(0.23–2.33)
P for trend[c]		<0.001	0.472

[a]Abbreviations are as follows: OR, odds ratio; 95% CI, 95% confidence interval; Q, quartile.

[b]Total adjusted for age (continuous), body mass index (calculated as weight/kg divided by height m2; <18.5, 18.5–23, 23–25, and ≥25), family history of breast cancer (yes/no), current use of dietary supplements (yes/no), education (≤elementary school, middle school, high school, and ≥college), job (housewife, profession/office worker, sales/service, agriculture/laborer/unemployed, and others), smoking (nonsmoker, ex-smoker, current smoker), alcohol intake (never, ever), physical activity (metabolic units min/wk; ≤396, 396–1,272, 1,272 < 2,772, and ≥2,772), menopausal status (pre menopausal/postmenopausal), age at menarche (≤13, 14, 15, and ≥16 yr), parity (yes/no), total energy intake (continuous), and vegetable intake (continuous). Premenopausal: adjusted for the same covariates as the model among total subjects with the exception of menopausal status. Postmenopausal: additionally adjusted for postmenopausal hormone use (never, ever).

[c]Test for trends calculated with the median intake for each category of mushroom intake as a continuous variable.

breast cancer in all subjects was most pronounced in the highest quartile (OR = 0.36, 95% CI = 0.17–0.77, *P* for trend = 0.006) compared to the lowest quartile intakes of mushroom. The inverse association was more pronounced in premenopausal women with an ER+/PR+ status. The OR was 0.30 (95% CI = 0.11–0.79) with significance in *P* for trend ($P = 0.009$) among premenopausal women who consumed the most mushrooms compared to those who consumed the least. However, no significant association was found between mushroom intake and ER+/PR+ breast cancer risk in postmenopausal women. In addition, no statistically significant difference was observed in women with an ER–/PR– status in any quartile category of mushroom intake compared to women with the lowest intake of mushrooms. In summary, dietary mushroom intake was inversely associated with the risk of breast cancer among premenopausal women with an ER+/PR+ status.

DISCUSSION

Higher mushroom intake was associated with lower risk of breast cancers among premenopausal women. The inverse association was more distinct among premenopausal women who were ER and PR positive.

To our knowledge, only one epidemiological study has investigated the impact of dietary mushroom intake on breast cancer risk (14). Their findings, which showed a potential decrease in breast cancer risk with higher consumption of dietary mushroom intake, were consistent with those of this study. However, they found significant association between mushroom intake and breast cancer risk in both premenopausal and postmenopausal women (14), whereas this study found breast cancer risk reduction only among premenopausal women. The average intakes of mushrooms in cases and controls in our study were 5.1 g/day in cases and 9.7 g/day in controls, which were lower than the previous study (7.8 g/day in cases and 11.4 g/day in controls) (14). Since the total energy intake of control groups of this study was 14% lower than that of Hong et al. (14), the mushroom intake level of this study is comparable with the intake level of that study. The most commonly consumed mushrooms in this study were *Pleurotaceae ostreatus* (oyster mushroom), followed by *Lentinus edodes* (oak mushroom), *Agaricus bisporus* (button mushroom), and *Flammulina velutipes* (winter fungus).

TABLE 4
Odds ratios (OR) and 95% confidence intervals (CI) of breast cancer risk characterized by estrogen receptor (ER) and progesterone receptor (PR) status according to mushroom intake

Quartiles of daily mushroom intake (g/day)	No. of control	ER+/PR+			ER–/PR–		
		No. of case	Crude OR (95% CI)	Multivariate OR‡ (95% CI)	No. of case	Crude OR (95% CI)	Multivariate OR‡ (95% CI)
Total							
Q1 (<2.61)	90	86	1.00 (referent)	1.00 (referent)	38	1.00 (referent)	1.00 (referent)
Q2 (2.62-<5.36)	90	62	0.72(0.46–1.11)	0.79(0.47–1.32)	27	0.71(0.40–1.26)	1.17(0.58–2.37)
Q3 (5.36-<11.37)	90	43	0.50(0.31–0.79)	0.55(0.30–0.98)	27	0.71(0.40–1.26)	1.37(0.64–2.92)
Q4 (≥11.37)	90	24	0.27(0.16–0.47)	0.36(0.17–0.77)	7	0.18(0.07–0.43)	0.45(0.14–1.40)
P for trend†			<0.001	0.006		<0.001	0.156
Premenopausal							
Q1 (<2.61)	42	51	1.00 (referent)	1.00 (referent)	9	1.00 (referent)	1.00 (referent)
Q2 (2.62–<5.36)	47	49	0.85(0.48–1.52)	0.80(0.40–1.59)	11	1.09(0.41–2.89)	1.71(0.49–5.88)
Q3 (5.36–<11.37)	52	35	0.55(0.30–1.00)	0.57(0.27–1.22)	14	1.25(0.49–3.18)	1.81(0.49–6.62)
Q4 (≥11.37)	55	18	0.27(0.13–0.52)	0.30(0.11–0.79)	3	0.25(0.06–0.99)	0.40(0.06–2.57)
P for trend†			<0.001	0.009		0.027	0.158
Postmenopausal							
Q1 (<2.61)	48	35	1.00 (referent)	1.00 (referent)	29	1.00 (referent)	1.00 (referent)
Q2 (2.62-<5.36)	43	13	0.41(0.19–0.88)	0.79(0.29–2.11)	16	0.61(0.29–1.28)	1.55(0.56–4.26)
Q3 (5.36-<11.37)	38	8	0.28(0.12–0.69)	0.34(0.11–1.08)	13	0.56(0.25–1.23)	1.09(0.36–3.30)
Q4 (≥11.37)	35	6	0.23(0.08–0.62)	0.56(0.14–2.26)	4	0.18(0.06–0.58)	0.57(0.11–2.90)
P for trend†			0.002	0.291		0.003	0.480

Abbreviations: ER+, estrogen receptor positive; ER–, estrogen receptor negative; PR+, progesterone receptor positive; PR–, progesterone receptor negative; OR, odds ratio; 95% CI, 95% confidence interval.

†Test for trend calculated with the median intake for each category of mushroom intake as a continuous variable.

‡Total: Adjusted for age (continuous), body mass index (calculated as weight in kilograms divided by the square of the height in meters; <18.5, 18.5–23, 23–25, and ≥25), family history of breast cancer (yes/no), current use of dietary supplements (yes/no), education (≤elementary school, middle school, high school, and ≥college), job (housewife, profession/office worker, sales/service, agriculture/laborer/unemployed and others), smoking (nonsmoker, ex-smoker, current smoker), alcohol intake (never, ever), physical activity (Met-min/week; ≤396, 396–1272, 1272–<2772, and ≥2772), menopausal status (pre/post), age at menarche (≤13, 14, 15, and ≥16), parity (yes/no), total energy intake (continuous), vegetable intake (continuous)

Premenopausal: adjusted for the same covariates as the model among total subjects with the exception of menopausal status; Postmenopausal: additionally adjusted for postmenopausal hormone use (never, ever).

The ER/PR status of breast tumors may explain the emergence of subtypes of breast cancer with different etiologies (17). In an ethnic comparison study among Danish women (18), the incidence of breast cancer among women with an ER+/PR+ status was found to continue to increase with age after menopause, whereas the incidence for women with other tumor subtypes declined after menopause. In contrast, the incidence of breast cancer among Japanese women declined after menopause, regardless of their ER/PR status. In addition, ER– breast cancers have a higher histologic grade and are less responsive to hormonal therapy as well as being associated with worse prognoses than ER+ breast cancers (19–22).

Epidemiological studies have supported the association between risk factors and subtypes of breast cancer by hormone receptor status (17,23–28). However, several studies have produced inconsistent results with regard to the intake of fruit, vegetable, and micronutrients based on ER status (27–34). In a cohort study of postmenopausal women, dietary intake of selected antioxidants was inversely associated with breast cancer characterized by both ER and PR, but not with those jointly defined by ER and PR status (21). In another recent study among postmenopausal women, red meat intake was strongly associated with elevated risk for ER+/PR+ breast cancers but not with those that were ER–/PR– (20). Similar results were found by Gaudet et al. (22) who reported an inverse association for fruit and vegetable intake among postmenopausal but not premenopausal patients with breast cancer, especially among those with ER+ tumors. The previous data can be construed as suggesting that breast cancer, defined according to hormone receptors, represents clinically distinct diseases and that ER and PR status are important in determining the clinical relevance.

The potentially beneficial effects of mushrooms, especially with regard to antitumor activities, have been investigated primarily in terms of their extracts and constituents. It has been hypothesized that mushrooms block the formation of carcinogens, alter membrane structure, suppress DNA synthesis, enhance cell differentiation, and compete with estrogen for estrogen receptors (10). Most research has entailed isolating pharmaceutically active mushroom compounds (e.g., α- and β-glucans from *Agaricus blazei,* lentinan from *Lentinus edodes,* schizophyllan from *Schizophyllum commune,* grifolan from *Grifola frondosa*) (7). Such polysaccharides have been hypothesized as plausible biological links to the mechanisms by which mushrooms function on macrophages, natural killer cells, and subsets of T cells. In vitro effects of selected mushroom species have been reported on proliferation, apoptosis, colony inhibition, and aromatase activity (8–13). Only two epidemiological studies, one on gastric cancer (35) and the other on breast cancer, have focused on the effect of dietary mushrooms (14). Several studies with patients diagnosed with advanced non-small-cell lung cancer (36) and prostate cancer (37) used orally administered mushroom in placebo-controlled, double-blind clinical trials.

This study showed significantly different effects for mushroom intake on breast cancer risk in premenopausal and postmenopausal women. The reasons underlying the stronger associations among premenopausal women remain unclear, but several hypotheses are possible in terms of the etiologies of premenopausal and postmenopausal breast cancer (38,39). Adiposity and reproductive factors could have opposite effects on the sensitivity of breast cancer tissue in these populations (39,40). In addition, diets may carry a stronger impact on breast cancer risk during early adult life compared to later (41).

To the best of our knowledge, this study is the first to explore the association between dietary mushroom intake and the risk of breast cancer according to hormone receptor status. The data were gathered in face-to-face interviews, enabling the collection of comprehensive information on related lifestyle factors and thus lessening the potential for misclassification and measurement errors. In spite of such strengths, this study also possesses some of the limitations that are inherent in case-control study designs (i.e., selection and recall biases). In particular, the hospital-based control group may have overrepresented those with healthier habits in comparison to their community-based counterparts. Cancer patients may differ from controls in their recall of dietary habits. For this reason, the interviewer tried to collect information as soon as possible after diagnosis, mostly right after surgery. In addition, a wide range of potentially confounding factors, including demographic and lifestyle characteristics, remain to be considered. We were also constrained by our inability to obtain information regarding other sources of mushrooms. The addition of supplements may have enabled us to identify the impact of total mushroom intake. Further studies should stratify by tumor characteristics and incorporate larger numbers of women.

In conclusion, our findings suggest that a high intake of mushrooms is inversely associated with breast cancer risks, especially among premenopausal women, and that dietary mushroom intake may play a role in preventing breast cancer in patients with ER+/PR+ tumors. Given the paucity of evidence in support of the association between diet, especially the intake of mushrooms, and breast cancers as defined by hormone receptor status, further studies are needed to underpin more detailed guidelines for breast cancer prevention.

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