

## Preferring fried dishes increases risk of benign breast disease, but not breast cancer

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**Abstract:** **B a c k g r o u n d:** Unhealthy diet and cooking method used may influence the risk of breast cancer (BC), but there is only limited evidence with regard to benign breast disease (BBD). The aim of this study was to assess a relationship between cooking technique, especially fried to boiled meals ratio in the diet, and the risk of BC and BBD in a group of Polish women.

**M a t e r i a l a n d m e t h o d s:** A case-control study involving 34 BC cases, 81 BBD cases and 122 healthy controls was conducted between July 2007 and November 2011. All the women were asked about their nutritional habits, especially the way of preparing meat and fish dishes. Then the ratio of fried to boiled meals was calculated.

**R e s u l t s:** High fried to boiled ratio was associated with increasing risk of BBD, but not BC. Women consuming fried dishes more often than boiled dishes had elevated risk of BBD: OR = 3.04 and OR = 3.65 for the second and the third tertile, respectively. Adjustment for the other confounders only slightly altered this relationship.

**C o n c l u s i o n:** Women who preferred frying as a cooking technique had increased risk of benign breast disease, but not breast cancer. There is a need of more precise investigation to confirm this association.

**Key words:** benign breast disease; breast cancer; cooking method; nutritional habits; retrospective study.

Breast cancer (BC) is the most common cancer among women across the world and its incidence is continuously rising. It was estimated that in 2012 about 1.7 million women heard this diagnosis (crude incidence rate: 47.8 per 100,000), which constitute more than one quarter of all cancer incident cases among women and it is the second, after lung cancer, most common cancer in the world — among both sexes. Across the world, BC is also the most common cause of cancer deaths among women — more than half million in 2012, representing 15% of all cancer deaths in this group. Furthermore, BC is a frequent cause of disability: a 5-year prevalence in adult women population is estimated at 239.9 per 100,000, which means that more than 6 million women are currently living with consequences of diagnosis of BC [1]. Poland is a country with relatively high BC incidence. According to Polish National Cancer Registry, in 2014 breast cancer was diagnosed in 17,379 women, most often at the age of 50–69, and reached the crude incidence rate 87.5 per 100,000. In the same year, 5975 women died due to this cancer and BC mortality rate was 30.08 per 100,000 [2]. Despite a decreasing trend in BC mortality that has been observed in recent years, incidence is continuously rising.

Benign breast diseases (BBD), including a large number of physiopathological lesions of different components, are far more common than breast cancer, especially among younger women. Unfortunately, data concerning their prevalence are scarce and incomplete, mostly due to neglecting this problem as a non-life-threatening condition and the fact that most of BBD are asymptomatic. According to autopsy studies, more than 50% of women are dying with an undiagnosed BBD, whereas a cumulative incidence before the age of 65 of biopsy-proven fibroadenoma is estimated to be 2.2% and for fibrocystic breast disease to be 8.8% in epidemiological observational studies [3, 4]. Some of these lesions, particularly the proliferative ones, later increase the risk of developing BC [5].

Many studies have investigated an impact of diet or specific nutrients on BC, but the results are inconsistent. A substantial amount of research has explored the influence of dietary patterns on BC risk. It is considered that adherence to Mediterranean dietary pattern protects against cancer, whereas adherence to Western/unhealthy dietary patterns has detrimental effects [6, 7]. However, a protective effect of Mediterranean diet does not seem to be universal for all the populations; as far as in southern European countries protective effect of this diet is observed, but in more northern populations adherence to Mediterranean diet does not reduce BC risk [8, 9]. Likewise, a detrimental effect of Western/unhealthy diet reported in some studies seems to be caused mostly by high alcohol consumption, which is commonly included in this pattern [6]. Moreover, taking into account single nutritional factors, the strongest association was observed between high alcohol intake and risk of BC [10, 11]. Other studies suggest a harmful effect of high fat and meat consumption, and opposite — a protective effect of high fruit, vegetables and soy products

consumption, but results are less coherent [12–14]. Nutritional risk factors for BBD were studied much less intensively, but also in this case results are inconsistent and mostly did not confirm any relationship between nutrition and BBD [4, 15, 16].

Taking into account that some studies indicate the detrimental effect of high fat and red meat intake, and also the premises that substances formed during the preparation of meat and fish in high temperature have mutagenic properties, the aim of our study was to assess a relationship between the preferred cooking technique, especially fried to boiled meals ratio in the diet, and the risk of breast cancer and benign breast disease in a group of Polish women.

### **Material and methods**

The present study is a part of research project realized between July 2007 and November 2011. Outpatients awaiting for surgical removal of breast lesions in the Regional Outpatient Department for the Early Diagnostics and Treatment of Breast Diseases of First Chair of General, Oncological, and Gastrointestinal Surgery, Jagiellonian University Medical College, were enrolled. After the surgery, all the lesions were histopathologically examined and on the basis of diagnosis, two subgroups were created — breast cancer (BC) group and benign breast disease (BBD) group. A control group was recruited from acquaintances of cases being at similar age; only women without history of previous breast disease and without any symptoms or complaints for breast disease at the time of recruitment were enrolled. All the procedures performed during the study were in accordance with the ethical standards and were approved by the Jagiellonian University Bioethics Committee (122.6120.279.2016). Informed consent was obtained from all the individual participants included in the study.

All the women were asked to fill a self-administered questionnaire; from the distributed 335 questionnaires (190 for cases and 145 for controls), the overall response rate was 73.3% for BC and BBD group and 86.9% for controls. Questionnaires with missing nutritional data were excluded from the present study; finally, the analysis included 34 cases of BC, 81 cases of BBD and 122 controls.

Self-administered questionnaire contained questions about demographic and anthropometric characteristics, reproductive history and nutritional habits: age of respondents, place of residence, level of education, marital status and employment status, weight and body mass one year before recruiting to the study, number of children, age at the first pregnancy, breastfeeding duration, smoking and alcohol drinking habits. Questions about nutritional habits included a number of meals eaten daily, a number of portions of different food groups consumed per day or week, frequency of fruit and vegetables intake, cooking method used to prepare meat and fish dishes, snacking.

## Statistical analysis

To assess the relationship between the preferred cooking technique and breast lesions risk, the ratio of frequency of consumption of fried to boiled (fried/boiled ratio) meat and fish dishes was calculated, where women not eating frying dishes had 0 value and women consuming only fried dishes — arbitrary had 100 value. Then fried/boiled ratio was divided into tertiles of distribution in the whole study population, with cut-points for the first tertile  $\leq 1.0$ , the second  $\leq 2.5$  and the third  $> 2.5$  times often consumed fried than boiled meals.

Chi<sup>2</sup> test was used to compare qualitative variables distribution between BBD and BC groups and controls. Frequency of consumption of fruit, vegetables and boiled and fried meals as well as fried/boiled ratio between the study groups was compared using analysis of variance (ANOVA). Kolmogorov–Smirnov test was applied to evaluate the normality of the data distribution and Levene's test — for homogeneity of variances.

Multinomial logistic regression models were used to evaluate the association of fried/boiled ratio (in tertiles, with the first tertile as referent) with both breast disease types. Several different models were created — crude, adjusted for age, for age and nutritional variables, and finally, fully adjusted model including the following potential confounders: age, intake of fruit and vegetables (in tertiles), alcohol consumption (yes, no), educational level (vocational or lower, secondary, university), BMI (normal, overweight, obesity), age at the first live birth (nulliparous, below 30 and 30 or more) and breastfeeding duration (0, up to 6 months and longer than 6 months).

The analyses were performed using STATA ver. 13. All statistical tests were two-sided and  $p \leq 0.05$  was considered statistically significant.

## Results

The basic characteristics of the study population are shown in Table 1. The youngest women were in BBD group, the oldest in BC group, and, as controls for this study were selected for both cases groups irrespective of the type of disease, they tended to be older than BBD group and younger than BC group. The mean age within the groups was respectively 43.8, 57.1, and 49.4 years ( $p < 0.001$ ). In BC group there was the highest frequency of women with excess BMI, more than 73% of them were overweight or obese. They were also less educated compared to the others, 38.2% of women diagnosed with BC have had at most vocational education. There were not any statistically significant differences between the groups with regard to reproductive history and alcohol consumption.

The average frequency of fruit and vegetables intake, boiled and fried dishes consumed per week are presented in Table 2. The study groups did not differ with regard to consumption of fruit and vegetables, but there were clear preferences

**Table 1.** Characteristic of the study population.

		Breast cancer (n = 34)		Benign breast disease (n = 81)		Control group (n = 122)		P
		n	%	n	%	n	%	
Age group	<50	8	23.5	47	58.0	47	38.5	0.001
	50+	26	76.5	34	42.0	75	61.5	
Educational level	vocational and lower	13	38.2	17	21.0	18	14.8	0.050
	secondary	11	32.4	29	35.8	46	37.7	
	university	10	29.4	35	43.2	58	47.5	
BMI	<25	9	26.5	48	59.3	59	48.4	0.015
	25–29.99	15	44.1	25	30.9	39	32.0	
	30 and more	10	29.4	8	9.9	24	19.7	
Age (years) at first live birth	nulliparous	8	23.5	25	30.9	31	25.4	0.790
	below 30	22	64.7	45	55.6	78	63.9	
	30 and more	4	11.8	11	13.6	13	10.7	
Breastfeeding duration (months)	none	11	32.4	31	38.3	44	36.1	0.970
	up to 6 months	7	20.6	17	21.0	24	19.7	
	longer than 6 months	16	47.1	33	40.7	54	44.3	
Alcohol consumption	long life abstainers	14	41.2	25	30.9	37	30.3	0.468
	yes	20	58.8	56	69.1	85	69.7	

**Table 2.** Selected nutritional habits of the study population.

Consumption frequency per week	Breast cancer (n = 34)		Benign breast disease (n = 81)		Control group (n = 122)		P
	Mean	SD	Mean	SD	Mean	SD	
fruits	6.0	2.67	6.0	3.42	5.9	2.84	0.945
vegetables	6.3	3.31	6.8	3.57	7.1	3.56	0.543
boiled meals	2.0	1.93	1.4	1.23	1.8	1.25	0.014
fried meals	2.4	1.49	2.4	1.32	2.2	1.50	0.542

concerning the preferred cooking methods between the groups — women with BC most often declared eating boiled meat and fish dishes, while women with BBD, the least frequently ( $p = 0.014$ ).

Table 3 shows the relationship between the ratio of fried/boiled meals and breast lesions. The analysis did not confirm any harmful effects of high consumption of fried dishes on breast cancer, however, higher intake of fried food was positively associated with benign breast disease. Women consuming fried dishes more often than boiled dishes had more than 3-fold greater risk of developing benign breast disease. Adjustment for age and other nutritional confounders slightly weakened the relationship, but in fully adjusted model, the association between the dominance of fried meals over boiled meals in diet and BBD was even stronger — for the third tertile fried/boiled ratio OR = 3.76 (95% CI: 1.66–8.53).

**Table 3.** Relationship between ratio of fried/boiled meals and breast disease — crude and adjusted odds ratio and 95% confidence interval.

		Fried/boiled ratio					
		≤1		≤2.5		>2.5	
		OR		OR	95% CI	OR	95% CI
Breast cancer	model 1	1.00	ref.	0.90	0.34–2.36	1.47	0.61–3.57
	model 2	1.00	ref.	1.05	0.39–2.87	1.57	0.62–4.01
	model 3	1.00	ref.	1.02	0.37–2.88	1.35	0.51–3.55
Benign breast disease	model 1	1.00	ref.	3.04	1.46–6.36	3.65	1.75–7.63
	model 2	1.00	ref.	2.95	1.38–6.31	3.56	1.64–7.74
	model 3	1.00	ref.	2.97	1.36–6.47	3.76	1.66–8.53

Model 1 — crude.

Model 2 — adjusted for age, intake of fruits and vegetables (tertiles) and alcohol (yes, no).

Model 3 — adjusted for variables included in the model 3 + educational level, BMI, age at the first live birth and breastfeeding duration.

## Discussion

It is thought that BC and BBD have the same risk factors, especially related to reproductive history, and that the lifestyle factors play a secondary role in the development of these diseases. However, in the literature a strong association between the reproductive factors is confirmed only for BC risk, much weaker and inconsistent evidence concerns BBD [3, 4, 17]. From the lifestyle factors, diet has been investigated in numerous studies, mostly with a focus on BC risk and much less extensive — BBD.

However, results are inconsistent; the studies on dietary patterns and BC usually indicate a protective effect of “healthy” or Mediterranean dietary patterns (high consumption of fruit, vegetables, whole grains, soy products), whereas “unhealthy” or Western diet (high amount of meat, processed meat, saturated fats, refined grains, sweets and desserts) is associated with an increased risk of breast cancer, but some others studies show no association or even the opposite results [18, 19]. Nevertheless, most surveys taking into account also the cooking method indicate a harmful effect of dietary pattern involving frequent consumption of fried, grilled and processed meat on BC [20, 21], even though this relationship is not strong. Also the results of the EPIC cohort study revealed that in countries where high-temperature cooking is more common, there is a significant association between red meat consumption and breast cancer risk [13]. Surveys which evaluated specifically the associations between cooking method or well-done meat intake and BC risk indicated elevated risk among women consuming more often meat and fish dishes cooked in high temperature and also rising the risk with increasing doneness level of meat products [22–24].

In our study, we did not confirm this kind of relationship, what can be a result of both: a relatively weak association between BC and fried meat consumption and a small number of cancer cases in our survey. On the other hand, we found a clear association between cooking method and benign breast disease, as women preferring frying as a method of preparation of meat and fish dishes exhibited more than 3 times higher risk of developing benign breast disease. Unfortunately, there is only a small number of studies evaluating the influence of dietary factor on BBD risk. Recently more attention is paid to nutrition in adolescence and its role in etiology of benign breast disease in the later life, but results are equivocal. Some studies suggest that there is a positive association between high animal fat intake and negative with high vegetable fat and protein intake and BBD, but the others do not confirm the relationship [25, 26]. Previous case-control studies confirm positive associations between high fat and meat fat consumption and BBD risk. Hislop *et al.* reported an increased risk of severe atypia with highest intake of meat and dairy fat [15], in the other study women who consumed food containing more than 10% of fat had elevated risk of BBD and the risk for the highest quartile of fat intake was almost 3 times higher compared to the first [27], and in the survey comparing women with benign proliferative epithelial disorders with biopsy controls without epithelial proliferation, an increasing risk of this disease was observed with increasing fat intake [28]. However, other studies did not confirm this relationship. The later study by Rohan *et al.* conducted among women who had been enrolled in the Canadian National Breast Screening Study showed no association between benign proliferative epithelial disorder and total fat intake [29]. In the large prospective cohort — Nurses’ Health Study II, the authors reported only weak associations between the total and vegetable fat intake (RR = 1.06, p for trend = 0.03 and RR = 1.07, p for trend = 0.007,

respectively) as well as mono- and polyunsaturated fat intake and the risk of any type of BBD. However, these associations disappeared in the analysis restricted to the cases confirmed by tissue biopsy. Opposite, lower rates of proliferative breast diseases without atypia were observed with increasing vegetable fat intake [16]. Also recently published case-control study showed no association between “unhealthy” dietary pattern and BBD [30], but the authors did not take into account food preparation manner. Up to date there are no other studies assessing the relationship between cooking methods and BBD.

The possible association of frequent fried dish consumption and BBD can be explained by the fact that during the thermal processing of protein-rich food in high temperature, especially meat and fish, some harmful substances are created. Among them, the mutagenic activity of heterocyclic amines and polycyclic aromatic hydrocarbons has been studied the most extensively [31, 32]. Some surveys conducted in human population suggest a positive correlation between the intake of heterocyclic amines from food sources and with DNA adduct levels in breast tissue and elevated risk of BC [33] but another do not confirm this association [34]. A potential role of these substances in etiology of BBD has not been investigated to date.

A strong association between frequent consumption of fried food and BBD, which can be a precursor of BC, as shown in our study, and much less evident associations with BC indicated also in other studies, suggest that there is a possibility that substances formed in meat and fish dishes during cooking in high temperature can affect cellular proliferation in mammary gland, but there is another factor(s) initiating carcinogenesis.

The study has some constraints, such as a small number of BC cases, retrospective evaluation of dietary habits and no precisely evaluated dietary intake, but the main limitations of the presented survey are lack of information about age at menarche and menopausal status. But as far as both menarche and menopause age are related to BC risk, the existing evidence does not confirm the association of BBD with age at menarche, and age at menopause may possibly be related only with fibrocystic breast disease [3, 4].

## Conclusions

The presented study showed a harmful effect of frequent consumption of fried dishes; women preferring frying as a thermal method of preparing meals have had increased risk of benign breast disease, but not breast cancer. As diet is a modifiable risk factor, the identification of harmful dietary habits can be used to create effective prevention policies, and changing cooking techniques could be an easy way to reduce breast lesions occurrence. However, taking into account the limitations of the study, there is a need of more precise investigation in order to confirm this association.



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## Conflict of interest

No declared.

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