Ginekol Pol. 2013, 84, 754-757

Estimated breast cancer risk and screening outcomes among premenopausal women with non-cyclic mastalgia

Szacowane ryzyko raka sutka oraz wyniki badań skriningowych u przedmenopauzalnych kobiet z niecykliczną mastalgią

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Abstract

Objectives: *Breast pain is a common but worrisome symptom, which can cause a significant psychological burden of cancer stress. It is not known whether breast cancer risk estimation models can be used as an adjunct to the clinical and radiological assessment in counseling women with mastalgia. The aim of our study was to compare the estimated breast cancer risk and screening outcomes between patients with mastalgia and women requesting prophylactic examinations.*

Material and methods: *112 premenopausal women with non-cyclic breast pain and 182 control women who presented for prophylactic examination were screened with mammography and ultrasound. Breast cancer risk estimated with the Gail and Tyrer-Cuzick models along with screening outcomes were compared between the groups.*

Results: *Premenopausal patients with mastalgia had lower estimated breast cancer risk than controls. The difference was observed with both the Gail and Tyrer-Cuzick models (Gail 5-year risk: 0.66 ± 0.4% vs. 0.77 ± 0.4%, p=0.0002; Tyrer-Cuzick 5-year risk: 0.85 ± 0.4% vs. 0.95 ± 0.3%, p=0.002; Gail lifetime risk: 8.98 ± 3.6% vs. 9.6 ± 3.9%, p=0.015; Tyrer-Cuzick lifetime risk: 8.3 ± 3.1 % vs. 8.9 ± 2.7 %, p=0.045). Radiological and clinical outcomes were comparable between the groups.*

Conclusions: *Breast pain was associated with lower estimated breast cancer risk but had no effect on screening outcomes in the study population.*

Keywords: **breast cancer** / **breast pain** / **risk assessment** / **statistical models** /

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Otrzymano: **05.11.2012**
Zaakceptowano do druku: **10.06.2013**

Streszczenie

Cel pracy: *Ból sutków jest częstym, lecz niepokojącym dla kobiety objawem, mogącym powodować lęk o jego potencjalnie nowotworowe przyczyny. Przy klinicznej i radiologicznej ocenie kobiet z mastalgią nie stosowano do tej pory analizy ryzyka raka sutka przy wykorzystaniu modeli statystycznych. Celem naszej pracy było porównanie szacowanego ryzyka raka sutka oraz wyników badań obrazowych pomiędzy pacjentkami z mastalgią a kobietami zgłaszającymi się w celu przeprowadzenia badań profilaktycznych sutków.*

Materiał i metody: *112 przedmenopauzalnych pacjentek z niecyklicznym bólem sutków oraz 182 kobiety zgłaszające się do badania profilaktycznego poddano mammografii oraz ultrasonografii sutków. Porównano pomiędzy grupami ryzyko zachorowania na raka sutka oszacowane przy użyciu modelu Gail'a oraz Tyrer-Cuzick'a jak również wyniki badań skriningowych.*

Wyniki: *Przedmenopauzalne pacjentki z mastalgią miały niższe szacowane ryzyko zachorowania na raka sutka w porównaniu z grupą kontrolną. Różnice obserwowano zarówno dla modelu Gail'a jak i Tyrer-Cuzick'a (5-letnie ryzyko wg Gail'a 0.66 ± 0.4% vs. 0.77 ± 0.4%, p=0.0002; 5-letnie ryzyko wg Tyrer-Cuzick'a: 0.85 ± 0.4% vs. 0.95 ± 0.3%, p=0.002; całkowite ryzyko wg Gail'a: 8.98 ± 3.6% vs. 9.6 ± 3.9%, p=0.015; całkowite ryzyko wg Tyrer-Cuzick'a: 8.3 ± 3.1 % vs. 8.9 ± 2.7 %, p=0.045). Wyniki kliniczne i radiologiczne nie różniły się istotnie.*

Wnioski: *Ból sutków był związany z niższym szacowanym ryzykiem raka sutka, lecz nie miał wpływu na wyniki badań skriningowych w badanej populacji.*

Słowa kluczowe: **rak sutka** / **ból sutka** / **ocena ryzyka** / **modele statystyczne** /

Introduction

Epidemiological models for breast cancer risk estimation are proven and reliable tools for identification of women who are more likely to develop breast cancer and may require additional screening measures or preventive interventions [1, 2]. However, they have not yet been used as an adjunct to the clinical and radiological assessment in counseling women with common breast symptoms such as mastalgia.

Objective

The aim of our study was to establish whether premenopausal women with breast pain have different estimated breast cancer risk and screening outcomes compared to asymptomatic women requesting prophylactic examination.

Materials and methods

Cross-sectional study. 112 premenopausal patients who presented to a breast diseases clinic with non-cyclic mastalgia between May 2009 and May 2011 were assessed clinically (including clinical breast examination) and screened with mammography and breast ultrasound (mastalgia group). 182 premenopausal women who presented in the same period for prophylactic examinations underwent identical procedure and were used as a control group.

Non-cyclic mastalgia was defined as a localized, unilateral or bilateral breast pain, unrelated to a menstrual cycle, of more than three months in duration. Additional inclusion criteria were: age between 35-50 years, premenopausal status with ruled out pregnancy. Patients with positive personal history for breast cancer or clinically palpable breast or axillary lesions were excluded from the study. The study was approved by the local bioethical committee and all women signed an informed consent form before participating.

Individual breast cancer risk was calculated from the modified Gail and Tyrer-Cuzick models [3, 4]. Ultrasound examinations were performed using Aloka ProSound SSD-4000 equipped with 10 MHz linear probe by a gynecologist trained in breast sonography. Mammographic examinations were performed using Siemens Novation digital mammography system and assessed by two independent radiologists. Further diagnostic and therapeutic steps were provided according to national oncological guidelines, regardless of the estimated breast cancer risk.

Personal - demographic and reproductive - data, estimated breast cancer risk, radiological studies results and relevant clinical outcomes were compared between the groups. Fisher's exact test and Mann-Whitney's U test were used to compare categorical and continuous variables, respectively. P-values less than 0.05 were considered statistically significant. Multivariate linear and logistic regression was used to ascertain that each variable is independently significant. Data were analyzed with STATISTICA 8.0 software (Statsoft, Inc.).

Results

Patients with mastalgia had lower mean estimated breast cancer risk than the prophylactic group. The difference was observed with both, Gail and Tyrer-Cuzick models. Patients with mastalgia gave first live births earlier and the time span between menarche and the first live birth was significantly shorter in that group. There were no significant differences in other personal characteristics, frequency of positive family history, radiological and clinical outcomes. Study results are summarized in **Table 1**. Ultrasound examination detected one cancer case missed by mammography in the prophylactic group. Three of the detected breast cancers were stage IA and one was stage IB.

Discussion

Breast pain is the most common breast symptom. Its pathophysiology is associated primarily with endocrine disorders, but the details remain poorly understood. Up to 70% of women experience regular premenstrual discomfort, while approximately

Table I. Study results.

	Mastalgia	Prophylactic	P
N	112	182	
Age (years)	43.8 ± 0.4	44.1 ± 0.3	NS
Height (m)	160 ± 6.4	161.7 ± 6.3	NS
BMI (kg/m2)	26.6 ± 5	26.7 ± 5.9	NS
Age at menarche (years)	13.3 ± 1.4	13.6 ± 1.2	NS
Age at first live birth (years)	22.6 ± 3.9	23.5 ± 3.8	0.03#
Nulliparity	12 (10.6%)	12 (6.6%)	NS
Time between menarche and first live birth (years)	8.4 ± 3.4	9.5 ± 3.8	0.013#
Previous breast biopsies	2 (1.8%)	5 (2.7%)	NS
Positive family history for:			
Breast cancer (total)	9 (8 %)	21 (11.5%)	NS
1 relative	8 (7.1%)	19 (10.4%)	NS
2+ relatives	1 (0.9%)	2 (1.1%)	NS
Ovarian cancer	0 (0%)	1 (0.5%)	NS
Estimated breast cancer risk:			
Gail 5-year risk:	0.66 ± 0.4%	0.77 ± 0.4%	0.0002#
Gail lifetime risk:	8.98 ± 3.6%	9.61 ± 3.9%	0.015#
Tyrer-Cuzick 5-year risk:	0.85 ± 0.4%	0.95 ± 0.3%	0.002#
Tyrer-Cuzick lifetime risk:	8.33 ± 3.1%	8.94 ± 2.7%	0.045#
Radiological and clinical outcomes:			
Mammographically dense breasts (American College of Radiology class 3 and 4)	66 (58.9%)	102 (56%)	NS
Fibrocystic changes	38 (33.9%)	49 (27%)	NS
Short term follow-up needed	5 (4.4%)	7 (3.8%)	NS
Biopsy needed	3 (2.7%)	6 (3.3%)	NS
Invasive cancer detected	1 (0.9%)	3 (1.6%)	NS

Continuous variables expressed as means ± standard deviation; proportions expressed as absolute values and percentages.
Mann-Whitney's U test; NS - not significant.

10% of women experience moderate to severe breast pain for more than 7 days in a month. About half of the women with severe breast pain look for medical help [5]. Studies using McGill pain questionnaire have shown that breast pain can be as intense as the symptoms of rheumatoid arthritis or metastatic cancer [6]. Women often interpret breast pain as a sign of breast cancer. Classically described breast cancer pain is one-sided, intense and of constant intensity. In terms of presentation it corresponds to non-cyclic mastalgia [7]. Although observational and retrospective studies conducted in 1980s assessed that the risk of detecting breast cancer in a patient with non-cyclic mastalgia is between 2 and 7%, newer studies yielded contradictory results [7, 8]. Dujim et al., have even shown that patients with breast pain have slightly lower risk of detecting cancer on screening mammography than asymptomatic women who present for prophylactic examinations (0.5% vs. 0.7%) [9].

The results of our study indicated that breast pain was not associated with an increased estimated breast cancer risk assessed with the Gail and Tyrer-Cuzick models or difference in screening outcomes. The risk estimates in patients with mastalgia were actually lower than in women requesting prophylactic examinations. This was attributable to a more favorable

reproductive history. The study was the first to assess breast cancer risk estimation models in the population of women with breast pain. Its results, however indirectly, stand in line with the cited more recent studies indicating that mastalgia is not associated with elevated breast cancer risk. It is also one of the first studies covering the application of breast cancer risk estimation models in a Polish population [10, 11].

Limitations apply when interpreting the results of our study. Its cross-sectional character does not allow any premise on absolute breast cancer risk in patients with mastalgia. Its conclusions rely on the assumption that breast pain is not an independent risk factor for breast cancer and represents a cross product of various reproductive factors influencing breast endocrine environment. Until such thesis is confirmed by prospective observations breast cancer risk estimation with epidemiological models should not deter a thorough clinical and radiological assessment of women presenting with breast pain.

Conclusions

Breast pain was associated with lower estimated breast cancer risk but had no effect on screening outcomes in the study population.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Ethical approval

The study was approved by the bioethical committee of the Polish Mother's Memorial Institute in Lodz, Poland in February, 2009.

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