

Breast cancer risk after diagnosis by screening mammography of nonproliferative or proliferative benign breast disease: a study from a population-based screening program

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Received: 10 November 2014 / Accepted: 10 November 2014 / Published online: 13 December 2014
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Abstract Benign breast disease increases the risk of breast cancer. This association has scarcely been evaluated in the context of breast cancer screening programs although it is a prevalent finding in mammography screening. We assessed the association of distinct categories of benign breast disease and subsequent risk of breast cancer, as well as the influence of a family history of breast cancer. A retrospective cohort study was conducted in 545,171 women aged 50–69 years biennially screened for breast cancer in Spain. The median of follow-up was 6.1 years. The age-adjusted rate ratio (RR) of breast cancer for women with benign breast disease, histologically classified into nonproliferative and proliferative disease with

and without atypia, compared with women without benign breast disease was estimated by Poisson regression analysis. A stratified analysis by family history of breast cancer was performed in a subsample. All tests were two-sided. The age-adjusted RR of breast cancer after diagnosis of benign breast disease was 2.51 (95 % CI: 2.14–2.93) compared with women without benign breast disease. The risk was higher in women with proliferative disease with atypia (RR = 4.56, 95 % CI: 2.06–10.07) followed by those with proliferative disease without atypia (RR = 3.58; 95 % CI = 2.61–4.91). Women with nonproliferative disease and without a family history of breast cancer remained also at increased risk of cancer (OR = 2.23, 95 % CI: 1.86–2.68). An increased risk of breast cancer was observed among screening participants with proliferative or nonproliferative benign breast disease, regardless of a family history of breast cancer. This information may be useful to explore risk-based screening strategies.

María Sala on behalf of the BELE Study Group.

Xavier Castells and Laia Domingo have contributed equally to this work. This study was conducted on behalf of the BELE Study Group. The members of the BELE Study Group are listed in the Acknowledgments.

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Keywords Breast cancer · Benign breast disease · Screening · Early detection · Family history · Risk factors

Introduction

One of the most important risk factors for breast cancer is a previous diagnosis of benign breast disease [1–3]. Benign breast diseases are commonly classified as nonproliferative disease, proliferative disease without atypia, and proliferative disease with atypia [4–6]. A high risk of cancer has been observed for all three histological categories, but is particularly high for proliferative lesions, especially those with atypia [2, 7–9]. Although the risk is lower for non-proliferative lesions, they account for most diagnoses of benign breast disease [2, 8, 10].

To our knowledge, there are few studies on nonproliferative lesions [2, 9], and none have studied the relationship between benign breast disease and breast cancer within a cohort of screened women from the general population. The study by Hartmann et al. [2] was based on a cohort of women with benign breast disease from the Mayo Clinic and compared breast cancer rates with those in the general population. Wang et al. [9] used data from a breast cancer prevention trial that included women at high risk of the disease.

Although the widespread use of mammography screening has increased diagnoses of benign breast disease, no specific recommendations have been made for surveillance, except for women with atypias, who are usually recommended to undergo surgical excision [11]. In most screening programs, women with nonproliferative disease or with proliferative disease without atypia are recommended to follow the same screening strategy as women with negative mammograms (which is to continue screening). Studies performed in the screening context may be of interest to assess whether the use of different screening

strategies according to the histological classification of benign breast disease could improve the effectiveness of screening.

The role of a family history of breast cancer among women with different categories of benign breast disease remains controversial. Some authors have reported that a family history of breast cancer increased the risk of cancer for all histological categories [12], but others have refuted an increased risk for atypias [13]. In fact, Hartman et al. [2] observed an increased risk of cancer in women with non-proliferative disease only when there was family history of breast cancer.

We aimed to explore the association of benign breast disease and subsequent risk of breast cancer according to the histological classification, as well as the influence of a family history of breast cancer on this risk. This is the first study performed in the context of population-based mammography screening that compares the risk of cancer in women with and without benign breast disease from the same cohort.

Methods

Setting and study population

The study was conducted in a cohort of women screened in Spain between 1994 and 2011 and followed up until December 2012. The government-funded Breast Cancer Screening Program in Spain provides free breast cancer screening to all women aged from 50 to 69 years every 2 years. The program started in 1990 and was gradually implemented in different regions, becoming nationwide in 2000. Information from 549,422 women with at least one screening mammogram was obtained for this study. The study protocol was approved by the institutional review boards at all participating institutions. Informed consent was not required since our analysis was based on anonymous retrospective data.

Population-based breast cancer screening in Spain follows the recommendations of the European Guidelines for quality assurance in breast cancer screening and diagnosis [11], and its results meet the required standards [14]. The standard procedure for radiological performance in Spain is double projection (mediolateral-oblique and craniocaudal views) and double reading with consensus or arbitration, using the Breast Imaging Reporting and Data System (BIRADS) scale to rate the probability of cancer.

Screening procedures and cancer identification

Women with screening mammograms scored with BIRADS 3, 4, 5, or 0 are recalled for further assessments within a maximum of 2 months after the screening test to confirm

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or to rule out malignancy. Further assessments may include imaging procedures (additional mammography, ultrasonography, and magnetic resonance imaging) and/or invasive procedures (fine-needle aspiration, core-needle biopsy, and open biopsy) (hereafter referred as “biopsies”). If the further assessments rule out malignancy, women are invited to regular screening in 2 years.

Cancers detected at regular screening and interval cancers were included in the analyses. Interval cancers (primary breast cancers diagnosed after a negative screening test and before the next screening invitation) were identified by merging data from screening participants with population-based cancer registries, the regional Minimum Basic Data Set, and hospital-based cancer registries. Both invasive and in situ carcinomas were considered in this study.

Benign breast disease

All biopsies were examined and classified by hospital pathologists in each screening setting. Following the criteria of Page et al. and Dupond et al. [4, 6], and subsequent consensus in a conference of the College of American Pathologists [5], each diagnosis was classified into one of three risk categories: (1) nonproliferative disease; (2) proliferative disease without atypia; and (3) proliferative disease with atypia. The histological entities and the number of lesions corresponding to each group are shown in Table 1. Fibroadenoma, cysts, fibrosis, and microcalcifications were classified as nonproliferative disease. Biopsy specimens with ductal or lobular hyperplasia and benign breast tumors were classified as proliferative disease without atypia. Atypias and phyllodes tumors were classified as proliferative disease with atypia. If there was more than one diagnosis per biopsy or bilateral disease, we selected the biopsy with the highest grade.

Biopsies with indeterminate histological classification, for example, ‘negative for malignant cells’ or ‘benign’ ($n = 4,251$), were excluded from the analysis because they could not be classified in any of the abovementioned categories. Most of these biopsies with indeterminate classification came from fine-needle aspiration cytology.

The location of both benign breast disease and breast cancer was also collected. Two possible situations were considered: ipsilateral (when the benign breast disease and breast cancer were in the same breast), or contralateral (if they were in different breasts).

Family history of breast cancer

Information on the first-degree familial history of breast cancer was obtained from a face-to-face interview at each screening mammogram. This information was available in 6 out of 8 screening settings included in the study (in

Table 1 Distribution of the histological categories of benign breast disease

Histological category	N (%)
Nonproliferative disease	4,748 (79.0)
Fibroadenoma	2,199 (36.6)
Cyst	1,087 (18.1)
Microcalcifications	484 (8.1)
Fibrosis	420 (7.0)
Metaplasia, apocrine	85 (1.4)
Adipose tissue necrosis	67 (1.1)
Atrophy	64 (1.1)
Inflammation	39 (0.7)
Ectasia	35 (0.6)
Scar	14 (0.2)
Other nonproliferative diseases*	254 (4.2)
Proliferative disease without atypia	1,104 (18.4)
Benign mesenchymal tumors**	293 (4.9)
Hyperplasia	283 (4.7)
Sclerosing adenosis	176 (2.9)
Papilloma	118 (2.0)
Adenosis	107 (1.8)
Intraductal hyperplasia	101 (1.7)
Lobular hyperplasia	15 (0.3)
Hamartoma	4 (0.1)
Epithelial benign tumors***	7 (0.1)
Proliferative disease with atypia	159 (2.7)
Atypical ductal hyperplasia	68 (1.1)
Atypical lobular hyperplasia	29 (0.5)
Phyllodes tumor, benign/uncertain benign	28 (0.5)
Atypia	18 (0.3)
Other	16 (0.3)
Total	6,011 (100.0)

* Other nonproliferative diseases include abscess, osseous metaplasia, foreign body reaction, degeneration, hemorrhage, squamous metaplasia, bone formation, and others

** Benign mesenchymal tumors include lipoma, hemangioma, osteochondroma, neurofibroma, and granular cell tumor

*** Epithelial benign tumors include adenoma of the nipple, tubular adenoma, epithelial benign tumors, and others

413,873 women), representing 75.9 % of the women included in the analyses.

Statistical analyses

We compared screened women with a diagnosis of benign breast disease with screened women without this diagnosis. Breast cancer rates were calculated based on person-years at risk in both groups. Women contributed person-years at risk to the negative group (designated as women without benign breast disease) from their first screen until

censoring, end of follow-up, or until a diagnosis of benign breast disease. Women contributed person-years at risk to the benign breast disease group from the first benign breast disease diagnosis until censoring or end of follow-up. Women were censored at breast cancer diagnosis, at 30 months after the last mammogram, or at the end of follow-up on December 31, 2012, whichever occurred first. We extended the follow-up to 30 months after the last screening mammogram because we actively monitored the occurrence of interval cancers.

We fitted crude and age-adjusted Poisson regression models using a robust error variance [15], which assumed the log link and included log time as an offset variable. We estimated the rate ratio (RR) and the 95 % confidence intervals (95 % CI) of breast cancer for women with nonproliferative disease, proliferative disease without atypia, and proliferative disease with atypia compared with women without benign breast disease. We performed a stratified analysis by family history of breast cancer for the subset of women with available information on this variable. To guarantee sufficient statistical power, we considered proliferative disease (including lesions with and without atypia) and nonproliferative disease as histological categories. The interaction between benign breast disease and a family history of breast cancer was tested by using the likelihood ratio two-sided test.

For women with benign breast disease who subsequently developed breast cancer, we examined the occurrence of

ipsilateral and contralateral breast cancer. Finally, we plotted the time, in years, from the first screening mammogram (for women without benign breast disease) or from the diagnosis of benign breast disease to the breast cancer diagnosis.

The analyses were performed using SPSS (v.12) and STATA (v.11). $P < 0.05$ were considered statistically significant.

Results

Overall, 545,171 women were included in the analysis, after exclusion of 4,251 biopsies with indeterminate histological classification. From their first screen, the women accumulated 3,583,413 person-years at risk, with a median follow-up of 6.07 years. Of 6,671 breast cancers, 158 were diagnosed in women with previous benign breast disease. Distribution by age groups revealed a higher proportion of women aged 50–55 years without benign breast disease, whereas the proportion of women aged 65–70 years was higher for those with any kind of benign breast disease ($P < 0.001$). The highest percentage of women with a family history of breast cancer was found among women with proliferative disease with atypia (13.6 %; $P < 0.001$). From women with available information on family history of breast cancer, 71 % were women with nonproliferative disease and without family history of breast cancer, Table 2.

Table 2 Baseline characteristics of women without benign breast disease and women with distinct histological categories of benign breast disease

	Women without benign breast disease	Women with benign breast disease			<i>P</i> value***
		Nonproliferative disease	Proliferative disease without atypia	Proliferative disease with atypia	
Screened women	539,160	4,748	1,104	159	
Screening mammograms	1,740,150	13,576	2,771	346	
Person-years at risk	3,549,268	27,703	5,731	711	
Breast cancers	6,513	114	38	6	
Women's age* (%), year					
50–54	298,244 (55.3)	2,273 (47.9)	515 (46.6)	79 (49.7)	
55–59	115,671 (21.5)	1,042 (21.9)	265 (24.0)	38 (23.9)	
60–64	95,858 (17.8)	905 (19.1)	208 (18.8)	27 (17.0)	
65–69	29,387 (5.5)	528 (11.1)	116 (10.5)	15 (9.4)	<0.001
Family history of breast cancer (%)					
Yes	27,625 (6.8)	286 (7.6)	53 (5.4)	17 (13.6)	
No	381,391 (93.2)	3,466 (92.4)	927 (94.6)	108 (86.4)	<0.001
Unknown**	130,144	996	124	34	

* For women without benign breast disease, age corresponded to women's age at the first screen. For women with benign breast disease, age corresponded to women's age at diagnosis of benign breast disease

** Missing information on family history of breast cancer was excluded for the calculation of percentages

*** Chi-square test

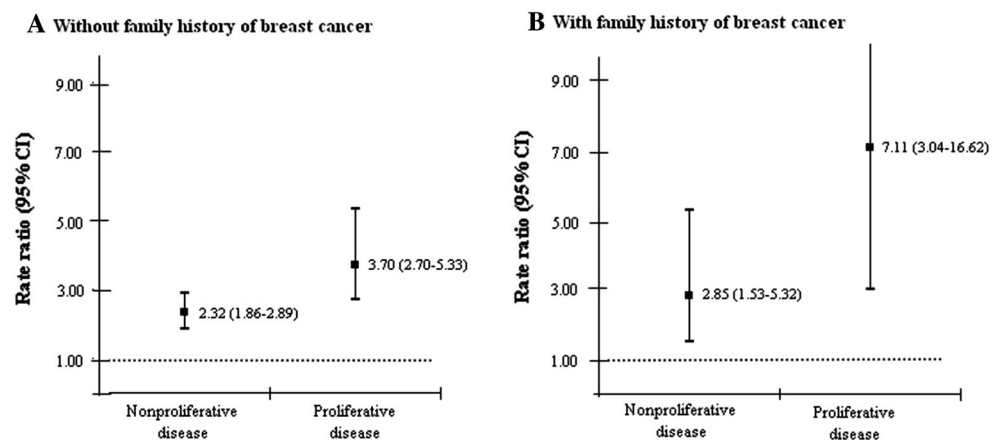
Table 3 Risk of breast cancer after a diagnosis of benign breast disease

	Person-years at risk	No. of breast cancers	Rate/1,000 person-years	Unadjusted RR (95 % CI)	Age-adjusted* RR (95 % CI)
No benign breast disease	3,549,268	6,513	1.84	1.00 (Referent)	1.00 (Referent)
Nonproliferative disease	27,703	114	4.12	2.24 (1.86–2.70)	2.23 (1.86–2.68)
Proliferative disease without atypia	5,731	38	6.63	3.61 (2.63–4.96)	3.58 (2.61–4.91)
Proliferative disease with atypia	711	6	8.44	4.60 (2.08–10.15)	4.56 (2.06–10.07)
Total benign breast disease	34,145	158	4.63	2.52 (2.16–2.95)	2.51 (2.14–2.93)

RR rate ratio, 95 % CI 95 % confidence interval

* Adjusted by continuous age

Fig. 1 Age-adjusted risk of breast cancer after a diagnosis of a nonproliferative and a proliferative lesion (with and without atypia) by family history of breast cancer*
*Information on family history of breast cancer was available in 413,873 out of 545,171 women



The age-adjusted RR of breast cancer after diagnosis of benign breast disease was 2.51 (95 % CI: 2.14–2.93) (Table 3) compared with women without benign breast disease. Nonproliferative disease showed a RR of 2.23 (95 % CI: 1.86–2.68), whereas proliferative disease with and without atypia showed a RR of 4.56 (95 % CI: 2.06–10.07) 3.58 (95 % CI: 2.61–4.91), respectively. We replicated the analysis by including all biopsies negative for malignancy, even those with indeterminate histological classification. This replication revealed that the risk of breast cancer remained significantly increased (data not shown).

The increased risk of breast cancer was statistically significant for both proliferative and nonproliferative disease, regardless of a family history of breast cancer (Fig. 1). Notably, the risk of breast cancer remained increased for women with nonproliferative disease without a family history of breast cancer (OR = 2.32, 95 % CI: 1.86–2.89). A family history of breast cancer increased the risk of subsequent breast cancer in proliferative disease (RR = 7.11, 95 % CI: 3.04–16.62 and RR = 3.70, 95 % CI: 2.70–5.33, for women with and without a family history of breast cancer, respectively) but the *P* value for interaction was not statistically significant (*P* = 0.448).

Table 4 Occurrence of ipsilateral and contralateral breast cancers, according to the histological category of benign breast disease

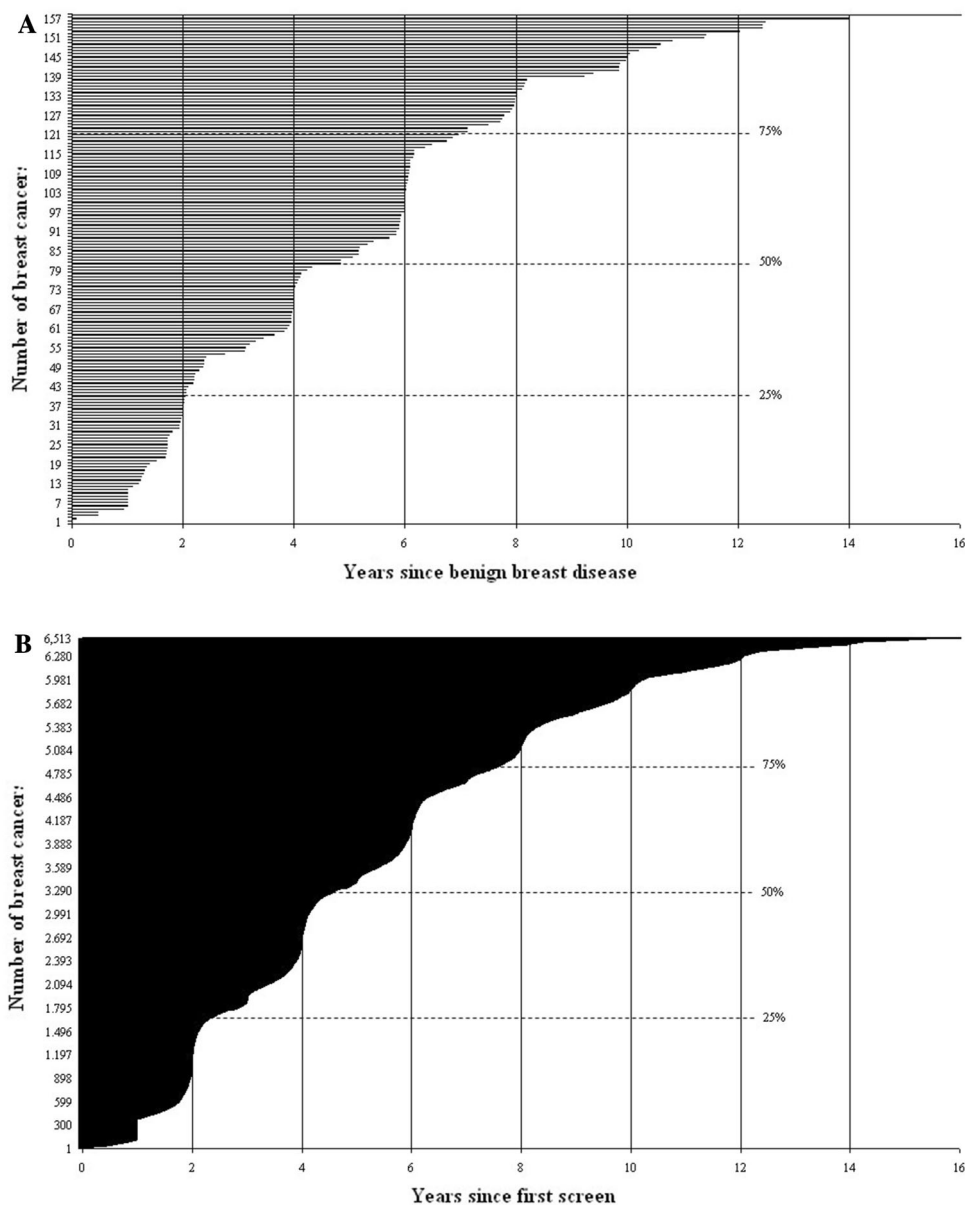
	Ipsilateral <i>n</i> (%)	Contralateral <i>n</i> (%)
Benign breast disease		
Nonproliferative disease	52 (59.1)	36 (40.9)
Proliferative disease without atypia	19 (57.6)	14 (42.4)
Proliferative disease with atypia	4 (80.0)	1 (20.0)
Total	75 (59.5)	51 (40.5)

Results are shown for 126 cancers. The histological category in the remaining 32 cases was unknown

Almost 60 % of tumors that arose after benign breast disease were ipsilateral to the prior benign breast disease (Table 4). This percentage increased for proliferative disease with atypia, although the number of cases was small.

We observed a linear trend in cancer diagnosis after benign breast disease, with 25 % of cancers appearing within 2 years after the benign breast disease, 50 % within 5 years, and 75 % within the next 7 years (Fig. 2). For women without benign breast disease, the interval between

Fig. 2 **A** Time distribution (years) of progression from benign breast disease to breast cancer. **B** Time distribution (years) from first screen to breast cancer in women without benign breast disease



the first screening test and cancer diagnosis followed a similar pattern.

Discussion

In this study, we analyzed data from 545,171 women screened biennially from 1994 to 2011 in the population-based screening program in Spain. For the first time, the relationship between benign breast diseases detected within the framework of mammography screening and the subsequent risk of breast cancer was explored, taking as a reference group all screened women without benign breast disease. We found that women with screen-detected benign breast disease had a more than two-fold risk of

breast cancer compared with women without. The histological appearance of benign disease was strongly associated with the risk of breast cancer, and both nonproliferative and proliferative lesions without atypia were also associated with this risk. Notably, the risk of breast cancer remained increased in women with nonproliferative lesions even through there was no family history of breast cancer.

Women with proliferative disease with atypia had a RR for breast cancer of 4.56. The risk was lower for women with proliferative lesions without atypia (RR = 3.58) and nonproliferative lesions (RR = 2.23). In line with the results in other contexts [2, 8, 10], the current findings provide further evidence of the importance of nonproliferative disease and proliferative lesions without atypia,

since these two categories accounted for more than 95 % of diagnoses of benign breast disease in our setting.

The relationship between benign breast disease and the risk of cancer is well documented in the clinical context [2–4, 6–9]. Adding to previous studies, we analyzed this relationship in the framework of population-based screening and therefore in the asymptomatic population. In comparison with our results, Hartmann et al. [2] reported a similar risk for atypias, but a somewhat lower risk for proliferative disease without atypia and nonproliferative disease. This difference could be explained by the inclusion of younger women in Hartman's study, while the current study included the target population for breast cancer screening, i.e., women aged 50–69 years, which could be expected to include a large percentage of menopausal women. This idea is supported by a previous study observing that the risk of breast cancer for women with nonproliferative disease was greater among postmenopausal women [9]. Comparison with other studies is difficult because women with nonproliferative diseases are often used as a referent group [7, 8].

In the current work, a family history of breast cancer increased the risk of cancer in women with proliferative disease, in agreement with previous studies [2, 3, 6, 9, 12], but this increase was not statistically significant. Contrasting with others studies [2], however, we found that the risk of cancer in women with nonproliferative disease remained significantly increased even for those without a family history of breast cancer. This finding is important because this subset encompasses most women with benign breast disease. In the new paradigm of breast cancer screening strategies based on individual risk of breast cancer, the current results suggest that women with proliferative disease and a family history of breast cancer would be candidates to receive more intensive screening.

We observed that 60 % of cancers were ipsilateral. This finding supports the idea of progression from benign breast disease to breast cancer, especially for atypias. Atypias are the best-characterized premalignant lesions [16–18], and excision is recommended by breast cancer management guidelines for most these lesions [11]. Nevertheless, the findings on progression should be interpreted with caution because of the small number of cases and the lack of information on the specific location within the breast. Importantly, 40 % of cancers were contralateral to the prior benign breast disease, suggesting that a large percentage of benign lesions may be risk markers rather than precursors of subsequent cancer.

The time from benign breast disease to diagnosis of breast cancer was almost constant during the follow-up, and was very similar to the time from first screen to cancer diagnosis in women without benign breast disease from the same cohort. As expected, most cancers were diagnosed at

regular screenings (i.e., every 2 years). In agreement with prior studies [19, 20], these results suggest a small misclassification of biopsies falsely deemed benign instead of malignant, and consequently with little impact on cancer risk estimation. Moreover, these results support the need for women to attend regular screening over time.

The strengths of the current study include its cohort perspective, its performance within the framework of a nationwide and established population-based screening program, and the use of women from the same cohort without a diagnosis of benign breast disease as a reference group. Reliable risk estimates for histological categories of benign breast disease within the framework of population-based screening are crucial to evaluate the risks and benefits of different decision-making strategies aiming to improve the effectiveness of screening. In view of our results, more intensive screening surveillance in women with proliferative disease and a family history of breast cancer would maximize early cancer detection in women at high risk. Nevertheless, risks and benefits should be estimated at the population level that may suppose a change in the screening protocols. Irrespective of this consideration, all women with benign breast disease, with or without a family history of breast cancer, should be informed that they have an increased risk of breast cancer and should be encouraged to return to screening.

Our study has some limitations. First, although data were drawn from a database including more than 500,000 screened women, the occurrence of cancer after benign breast disease is fairly infrequent, and therefore, the sample size was not enough to allow stratified analyses to be performed by family history and the three categories of benign breast disease. Second, our analyses were restricted to those cases with histological information, because our aim was to assess the risk associated with each category. This restriction reduced the sample size but ensured the quality of the histological classification in included cases. Third, we did not include tumor-related information and the specific location of lesions within the breast. This information would enrich our findings and would be required to obtain a complete picture of the relationship between benign breast disease and cancer. Finally, the association between proliferative disease with atypia and cancer may have been somewhat underestimated, as excision of benign breast disease is recommended in cases of atypical ductal hyperplasia and lobular intraepithelial neoplasia [11].

In conclusion, our results show a strong association between benign breast disease and subsequent risk of cancer during screening participations. Histological appearance was markedly associated with this risk. The risk of cancer remained significantly higher in women with

nonproliferative disease without a family history of breast cancer. This information emphasizes the different risk profiles among screening participants and supports the need to explore more personalized screening approaches.

Acknowledgments The authors acknowledge the dedication and support of the entire Benign Lesion (BELE) Study Group (alphabetical order): IMIM (Hospital del Mar Medical Research Institute), Barcelona: Andrea Burón, Xavier Castells, Josep Maria Corominas, Laia Domingo, Ana Rodríguez-Arana, Marta Roman, Sònia Servitja, Maria Sala, Isabel Torá-Rocamora, and Mar Vernet; Corporació Sanitària Parc Taulí, Sabadell: Marisa Baré and Xavier Andreu; Catalan Institute of Oncology, Barcelona: Núria Milà and Carmen Vidal; Hospital de la Santa Creu i Sant Pau, Barcelona: Maria Jesús Quintana; General Directorate of Public Health, Department of Health, Government of Cantabria: Mar Sánchez; Principality of Asturias Health Service: Carmen Natal; CIBERESP University of Oviedo: Ana Fernández-Somoano. Fundació Lliga per a la Investigació i Prevenció del Càncer, Reus, Universitat Rovira i Virgili: Jaume Galceran and Francina Saladié; Hospital Santa Caterina, Girona: Joana Ferrer; and Catalan Cancer Plan, Catalan Health Government, Barcelona: Josep Alfons Espinàs.

Conflict of interest The authors have declared no conflicts of interest.

Funding This work was supported by Grants from *Instituto de Salud Carlos III* FEDER, (PI11/01296). The funding sources had no role in the performance of the study or in the preparation of the manuscript.

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References

- Carter CL, Corle DK, Micozzi MS et al (1988) A prospective study of the development of breast cancer in 16,692 women with benign breast disease. *Am J Epidemiol* 128:467–477
- Hartmann LC, Sellers TA, Frost MH et al (2005) Benign breast disease and the risk of breast cancer. *N Engl J Med* 353:229–237
- London SJ, Connolly JL, Schnitt SJ et al (1992) A prospective study of benign breast disease and the risk of breast cancer. *JAMA* 267:941–944
- Dupont WD, Page DL (1985) Risk factors for breast cancer in women with proliferative breast disease. *N Engl J Med* 312:146–151
- Fitzgibbons PL, Henson DE, Hutter RV (1998) Benign breast changes and the risk for subsequent breast cancer: an update of the 1985 consensus statement. Cancer Committee of the College of American Pathologists. *Arch Pathol Lab Med* 122:1053–1055
- Page DL, Dupont WD, Rogers LW et al (1985) Atypical hyperplastic lesions of the female breast. A long-term follow-up study. *Cancer* 55:2698–2708
- Kabat GC, Jones JG, Olson N et al (2010) A multi-center prospective cohort study of benign breast disease and risk of subsequent breast cancer. *Cancer Causes Control* 21:821–828
- Tice JA, O'Meara ES, Weaver DL et al (2013) Benign breast disease, mammographic breast density, and the risk of breast cancer. *J Natl Cancer Inst* 105:1043–1049
- Wang J, Costantino JP, Tan-Chiu E et al (2004) Lower-category benign breast disease and the risk of invasive breast cancer. *J Natl Cancer Inst* 96:616–620
- Cote ML, Ruterbusch JJ, Alesh B et al (2012) Benign breast disease and the risk of subsequent breast cancer in African American women. *Cancer Prev Res (Phila)* 5:1375–1380
- Perry N (2006) European guidelines for quality assurance in breast cancer screening and diagnosis. In: Broeders M, de Wolf C, Törnberg S, Holland R, von Karsa L (eds) 4th edn. Office for Official Publications of the European Communities, Luxembourg
- Zhou WB, Xue DQ, Liu XA et al (2011) The influence of family history and histological stratification on breast cancer risk in women with benign breast disease: a meta-analysis. *J Cancer Res Clin Oncol* 137:1053–1060
- Degnim AC, Visscher DW, Berman HK et al (2007) Stratification of breast cancer risk in women with atypia: a Mayo cohort study. *J Clin Oncol* 25:2671–2677
- Ascunce N, Salas D, Zubizarreta R et al (2010) Cancer screening in Spain. *Ann Oncol* 21(Suppl 3):iii43–iii51
- Carter RE, Lipsitz SR, Tilley BC (2005) Quasi-likelihood estimation for relative risk regression models. *Biostatistics* 6:39–44
- Allred DC, Mohsin SK, Fuqua SA (2001) Histological and biological evolution of human premalignant breast disease. *Endocr Relat Cancer* 8:47–61
- Lopez-Garcia MA, Geyer FC, Lacroix-Triki M et al (2010) Breast cancer precursors revisited: molecular features and progression pathways. *Histopathology* 57:171–192
- Page DL, Schuyler PA, Dupont WD et al (2003) Atypical lobular hyperplasia as a unilateral predictor of breast cancer risk: a retrospective cohort study. *Lancet* 361:125–129
- Euler-Chelpin M, Kuchiki M, Vejborg I (2014) Increased risk of breast cancer in women with false-positive test: the role of misclassification. *Cancer Epidemiol* 38(5):619–622
- Shrestha DB, Ravichandran D, Baber Y et al (2009) Follow-up of benign screen-detected breast lesions with suspicious preoperative needle biopsies. *Eur J Surg Oncol* 35:156–158