Higher cancer detection risk in women with a False Positive result in breast cancer screening in Spain

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Introduction

Breast cancer screening reduces mortality from this disease through early detection. Despite its benefits, breast cancer screening presents some adverse effects, as false positive (FP) results. The association between FP results and breast cancer detection in the subsequent screening rounds could provide new insights to a better understanding of the natural history of breast cancer. Our aim was to evaluate the impact of previous false-positive results on the cancer detection risk over a sequence of breast cancer screening invitations.

Methods

We performed a retrospective cohort study of 702,785 women aged 45-69 years, who underwent 2,666,010 screening test in any of eight population-based screening programs in Spain between 1990 and 2006. Multilevel discrete time hazard models were used to estimate the effect of FP results and women's characteristics on the cancer detection risk.

Results

Women with a FP result had and increased risk of cancer detection in subsequent screening tests (OR= 1.89; 95%CI: 1.77-2.01). The strongest association with the cancer detection risk was observed among women with FP results after an invasive procedure ***(Table 1)***. A higher cancer detection risk was also observed in women with a first-degree family history of breast cancer, having previous invasive procedures, non-participating in the previous screening invitation, and in the oldest women ***(Table 1)***. The association between experiencing a FP result and the cancer detection risk was greater when the FP (invasive or non-invasive) was experienced in the previous screening participation compared to FP experienced two or more screenings in advance. However, a statistically significant increased risk was observed for FP experienced two or more screenings in advance ***(Figure 1)***. A stratified analysis showed that women with a previous FP result involving invasive procedures, and a first-degree familial history of breast cancer had an increased cancer detection risk ***(Table 2)***.

Table 1. Unadjusted and adjusted cancer detection risk (OR), from the regression models.

Risk Factor	Total (N)	OR (95% CI) Non adjusted	OR (95% CI) Adjusted†
False-Positive‡			
Never	1,663,403	Ref	Ref
Non-Invasive	278,013	1.73 (1.62-1.85)	1.81 (1.70-1.94)
Invasive	21,809	2.89 (2.48-3.37)	2.69 (2.28-3.16)
Attended previous screening invitation			
Yes	1,896,407	Ref	Ref
No	66,818	1.42 (1.25-1.61)	1.26 (1.11-1.43)
Age			
45-49	177,671	0.83 (0.73-0.94)	0.83 (0.73-0.95)
50-54	467,619	Ref	Ref
55-59	558,354	1.27 (1.18-1.38)	1.30 (1.20-1.42)
60-64	514,556	1.55 (1.43-1.68)	1.62 (1.49-1.77)
65-70	245,025	1.78 (1.63-1.95)	1.84 (1.67-2.03)
HRT			
No	1,743,323	Ref	Ref
Yes	219,902	0.93 (0.86-1.02)	0.96 (0.88-1.04)
Menopausal status			
Menopausal	1,656,585	Ref	Ref
Premenopausal	306,64	0.71 (0.65-0.77)	0.92 (0.83-1.02)
First-degree family history of breast cancer			
No	1,817,823	Ref	Ref
Yes	145,402	1.69 (1.56-1.84)	1.65 (1.52-1.79)
Previous invasive procedures			
No	1,826,679	Ref	Ref
Yes	136,546	1.38 (1.26-1.51)	1.24 (1.13-1.35)

95% CI= 95% confidence interval.
†Multivariate analysis adjusted by the women's screening number, screening period, and radiology unit (random effect).
‡At least one false-positive result in any previous screening round;
- Never: women who have never experienced a false-positive result
- Non-invasive: the first false-positive is consequence of a non-invasive procedure
- Invasive: the first false-positive is consequence of an invasive procedure
HRT: Hormone replacement therapy use at the time of the mammography or in the previous 6 months.

Table 2. Analysis to evaluate the association between experiencing a previous FP (non-invasive or invasive) and the cancer detection risk stratified by presence of first-degree familial history of breast cancer.

False positive †	Women with first-degree family history of breast cancer			Women without first-degree family history of breast cancer		
	Total (N)	Cancer (N)	OR (95% CI) Adjusted §	Total (N)	Cancer (N)	OR (95% CI) Adjusted §
Never	119,782	478	Ref	1,543,621	3,778	Ref
Non-invasive	23,859	170	1.82 (1.51-2.18)	254,154	1,091	1.81 (1.69-1.95)
Invasive	17,961	33	4.64 (3.23-6.66)	20,048	120	2.41 (2.00-2.89)

†At least one false-positive result in some of the previous screening rounds;
- Never: women who have never experienced a false-positive result
- Non-invasive: the first false-positive is consequence of a non-invasive procedure
- Invasive: the first false-positive is consequence of an invasive procedure
§Multivariate regression model adjusted by women's screening number, screening period, radiology unit (random effect), attended previous invitation, age group, HRT use, menopausal status, previous invasive procedures

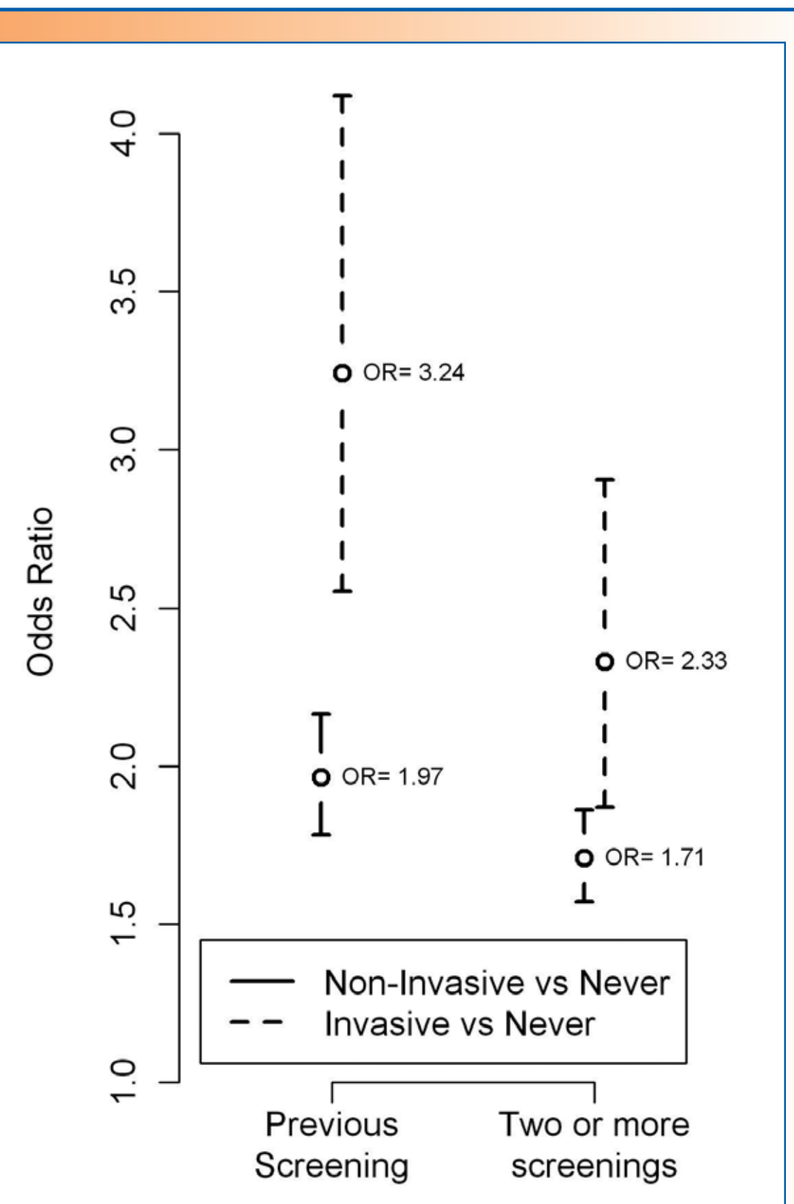

Figure 1. Odds ratios (OR) for the adjusted cancer detection risk depending on the elapse in the number of screening participations between the experience of a FP and the cancer detection.

Conclusion

Women with previous false-positive results are at higher risk of cancer detection in subsequent screening participations. Understanding the factors behind this association would allow a better tailoring of the breast cancer screening programs, improving its effectiveness and providing valuable information to outline more personalized cancer detection strategies.

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