Original article

Can the Gail model increase the predictive value of a positive mammogram in a European population screening setting? Results from a Spanish cohort

A. Buron [a,b], M. Vernet [c,*], M. Roman [a,b], M.A. Checa [c], J.M. Pérez [d], M. Sala [a,b], M. Comas [a,b], C. Murta-Nascimiento [a,b], X. Castells [a,b], F. Macià [a,b]

[a] Department of Epidemiology and Evaluation, IMIM-Hospital del Mar, Barcelona, Spain
[b] CIBER de Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
[c] Obstetrics and Gynaecology Department, Hospital del Mar, Barcelona, Spain
[d] TedCas: Innovation and Technology for Health, Spain

ARTICLE INFO

ABSTRACT

Aims of the study: The Gail Model (GM) is the most well-known model to assess the individual risk of breast cancer (BC). Although its discriminatory accuracy is low in the clinical context, its usefulness in the screening setting is not well known. The aim of this study is to assess the utility of the GM in a European screening program.
Methods: Retrospective cohort study of 2200 reassessed women with information on the GM available in a BC screening program in Barcelona, Spain. The 5 year-risk of BC applying the GM right after the screening mammogram was compared first with the actual woman's risk of BC in the same screening round and second with the BC risk during the next 5 years.
Results: The curves of BC Gail risk overlapped for women with and without BC, both in the same screening episode as well as 5 years afterward. Overall sensitivity and specificity in the same screening episode were 22.3 and 86.5%, respectively, and 46.2 and 72.1% 5 years afterward. ROC curves were barely over the diagonal and the concordance statistics were 0.59 and 0.61, respectively.
Conclusion: The GM has very low accuracy among women with a positive mammogram result, predicting BC both in the concomitant episode and 5 years later. Our results do not encourage the use of the GM in the screening context to aid the referral decision or the type of procedures after a positive mammogram or to identify women at high risk among those with a false-positive outcome.

Introduction

Several models have been developed to assess the individual breast cancer (BC) risk[1,2] but the Gail model (GM) is undoubtedly the most frequently used and well known. The GM is a multivariable model that uses age, race, age at menarche, age at first live birth, number of first-degree relatives with breast cancer, number of breast biopsies and presence of atypical hyperplasia to estimate BC risk.[3] It has shown to accurately estimate the proportion of women who will develop invasive BC when used in large groups in the USA, although its discriminatory accuracy for individuals is considered to be moderate to low in the general population.[4–7]

Although not intended to be transplanted as-is to other countries, the GM has proven to be flexible enough to travel through time and across geographical boundaries and is currently being used in many European countries, most often in its unmodified form.[8–12] The widespread use of the GM is due to its inclusion as an eligibility criterion in several trials and because it is one of the parameters used to recommend chemoprevention.[7,13,14] In addition, the GM has been reported to have high accessibility and ease of use by the Breast Cancer Risk Assessment Tool, an interactive website provided by the National Cancer Institute (http://www.cancer.gov/bcrisktool/).

Although rare, risk prediction models have also been suggested to be useful in the general screening population as a tool to determine different risk profiles and to offer personalized screening strategies depending on the estimated risk.[15–17] Some authors have attempted to provide a revised prediction of the likelihood of breast cancer after the result of the mammogram is known,[16–19] but only two studies[16,19] formally tested the GM with this purpose. If proven valid, systematic calculation of the Gail score (GS) after a mammogram result could aid in the decision of

* Corresponding author. Tel.: +34 932483129.
E-mail address: mvernet@hospitaldelmar.cat (M. Vernet).

reassessment and the need for invasive procedures, thus increasing the positive predictive value of the mammogram and partially reducing the psychological distress related to recall.

Furthermore, women with a positive mammographic reading in which malignancy is ruled out after referral (false positives) have shown to present a higher risk of BC in some studies[17,20–22]; however, following the screening recommendations, these women are again invited to the screening program after 2 years.[23] Therefore, if applied after a false-positive outcome, the GM could enable tailored screening strategies and offer the reassessed women with more accurate information about risks.

This study has two aims: First, to evaluate the association between a woman's GS and the likelihood of being diagnosed with BC after a positive screening mammogram and second, to evaluate the association between the GS and BC risk over the following 5 years in women with previous false-positive results.

Patients and methods

Study population and setting

The breast cancer screening program of Parc de Salut Mar started in 1996. The target population of 80,000 women between 50 and 69 years in age living in four districts of Barcelona (Spain) was invited biennially for a routine-mammogram following the European Guidelines.[23]

The GS is not calculated systematically within the screening population in our screening program. However, information to calculate the GS is available for most reassessed women who are visited by a clinician, who are those women recalled for further evaluation to rule out malignancy. Because standard GS is calculated for a 5-year span but the screening program runs biennially, a minimum follow-up time was set at 6 years.

A total of 20,160 women were screened during from 1996 to 2010. The study population comprised the 5227 women who were reassessed and had at least one visit during this period (585 of these had no invasive procedure). We excluded all of the women without a known diagnosis of cancer or follow-up time less than 6 years (1911). Women who visited after 2003 (819) and those older than 64 years at the time of the first visit (183) were also excluded, as they could not be followed for the 6-year period. Furthermore, as the GM estimates the risk of invasive BC, 114 women with *in situ* BC were also excluded. Finally, the study population comprised 2200 women (Fig. 1).

Information on *age*, *age at menarche* and *number of first degree relatives with BC* were regularly gathered during the first visit; *age of first pregnancy* was assigned as the *age of first live birth* because the former was not specifically collected. Women's *race* was not addressed in the program and was derived from women's nationality. Hispanic race was applied only to 10 women, all other immigrant women were categorized as white because they came from countries in which white was the most common race. *Number of biopsies* and prior outcome of *atypical hyperplasia* were obtained from the hospital's pathology database, which included the results of all cytologies and biopsies performed in our catchment area. The variable *biopsy* included all fine-needle aspiration cytologies, needle-core biopsies and open biopsies performed prior to the date of the visit. The invasive procedure undergone in the concomitant screening episode was not taken into account. BC status was obtained from the screening program database and through linkage with the hospital-based cancer registry.

The study was approved by the Ethical Committee for Clinical and Epidemiological research of our institution.
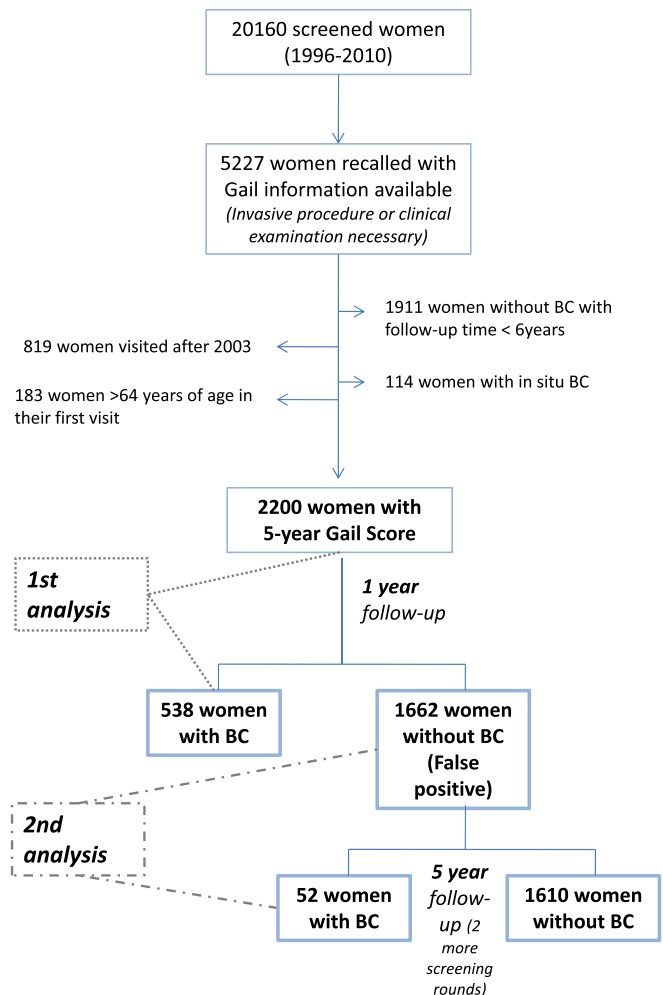

Fig. 1. Algorithm of the study population and the two approaches used.

Statistical analysis

Following the aims of the study, two approaches are presented (Fig. 1). The first approach evaluates the relationship between the woman's 5-year GS and the outcome of BC during the first 12 months after the concomitant screening visit (period of time in which the case of cancer is considered to be related to the screening episode). The second approach takes into account only those women in which malignancy is ruled out after their first visit and during the first 12 months after the concomitant screening visit (false positives), examining the correlation of their 5-year GS by the time of her first visit, with an outcome of BC during the following 5 years (years 1–6 after the date of the first visit).

Data for all risk factors were categorized according to the methods used for the GM[3] and specified in the source code (available at: http://www.cancer.gov/bcrisktool/download-source-code.aspx). GS represents the likelihood that a woman will develop invasive BC in the next 5 years. This risk was assessed through an *adhoc* implemented C-code to automatically provide the risk of any database with the specified variables. The C-code uses the original Breast Cancer Risk Assessment Tool free source code, also including an input/output interface to communicate with the database.

Comparison of the frequency of the study variables among women with and without BC was performed using chi-squared tests. Odds ratios (OR) and their 95% confidence interval (95%CI)