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Is the Gail Model Suitable for Predicting Breast Cancer Risk in the Mexican Population? An Analysis of a Prospective Cohort of 1000 Patients

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ABSTRACT

Background: Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death in females in Mexico as in other Western countries. The most widely used model for breast cancer risk assessment is the Gail Model, which is currently the most validated tool. However, considering it was mainly made for Western populations, its validation in an international context is required. The validation of the Gail Model has never been done for a Latin American country. **Methods:** In 2002 a cohort of 1000 female patients were recruited at the National Institute of Medical Sciences and Nutrition "Salvador Zubirán", a tertiary referral center in Mexico City. An assessment of individual breast cancer risk was performed for these patients. At that time, the mean calculated absolute risk utilizing the Gail Model at five years was 1.18%. These patients were followed for 10 years and those who developed breast cancer were identified retrospectively from the medical charts at the institute. **Results:** Thirty-three patients were lost to follow up. Twenty-four out of 967 individuals developed invasive breast cancer (2.48%). The mean age of these individuals at the time of cancer diagnosis was 63. By the five-year mark, 12 of these patients had developed invasive breast cancer, exactly the same as the predicted Gail Model risk calculated in 2002.

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Conclusions: Despite the limitation of a small sample, our results suggest that the Gail Model is a well-suited model for breast cancer risk assessment for a Mexican population. (J CANCEROL. 2015;2:51-5)
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Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related death in females worldwide and in Mexico, with 460,000 deaths reported in 2008[1-4]. Fourteen percent of cancer-related deaths in women in Mexico are due to breast cancer and mortality has risen to 67 per 100,000 inhabitants, similar to other middle-income countries worldwide. In 2009, the national incidence of breast cancer in Mexico was 15 per 100,000 women[4]. The largest and fastest growing demographic group in the USA is Hispanic, accounting for 16.3% (50.5 million) of the US population. In Hispanic females in the USA, breast cancer is the leading cause of estimated new cancer cases and estimated deaths, accounting for 17,100 (29%) and 2,400 (15%), respectively[5]. Breast cancer incidence and mortality has been rising in Latin American countries and currently account for 10% of breast-cancer deaths worldwide[4].

The most widely used model for breast cancer risk assessment is the Gail Model (GM). There are numerous other tools for risk assessment and counseling like the Claus, BRCAPRO, and Jonker models, but these have more limitations because they mostly consider family history and/or are aimed at Caucasians only[6,7]. The GM predicts a woman's risk of developing invasive breast cancer over a period of time given her age and risk factor profile: age at menarche, age at first live birth or nulliparity, number of first-degree relatives with breast cancer, number of previous benign breast biopsies, atypical hyperplasia in a previous breast biopsy and, more recently, race[8]. The probability of developing breast cancer is calculated by combining relative risks estimated from the Breast Cancer Detection Demonstration Project (BCDDP) with the epidemiological breast cancer data from the Surveillance, Epidemiology, and End Results (SEER) program[9]. Combining genetic factors to the GM offers a minor improvement for the classification of breast cancer risk, but at an increased cost[10].

The GM is currently the most validated tool[11,12]. However, considering it was mainly made for Western populations, its validation in an international context is required. This is primarily due to the geographical difference in breast cancer incidence rates between races[13]. The National Comprehensive Cancer Network (NCCN) points out that the GM may not accurately assess breast cancer risk in non-Caucasian women[8]. This is due predominantly to the lack of evidence or validation study trials in non-Caucasian races. For example, the GM underestimates breast cancer risk in African American women[14]. The validation of GM has been done predominantly for Western populations and recently in Singapore but never for a Latin American country[15].

The identification of those women who are at high risk enables us to offer them more intensive surveillance and in some cases prophylactic measures such as chemoprevention or surgery[7]. However, Rockhill, et al. point out "the modest discriminatory accuracy in assessing breast cancer risk at the individual level and its possible implications for clinical use"[16]. The identification of those women who are at high risk, defined by a GM absolute risk ≥ 1.66%, benefit from chemoprevention[17]. Validation of GM in other races enables use of the guidelines outside a Caucasian-only population.

METHODS

Between January and June 2002 a cohort of female patients was recruited at the outpatient clinic of the National Institute of Medical Sciences and Nutrition "Salvador Zubirán", a tertiary referral center in Mexico City. The cohort included a population of 1000 female Mexican patients as previously reported[18]. An assessment of individual breast cancer risk was performed for these patients. Briefly, the results of this project revealed that: the mean patient age was 50 years (range 20-85), 56% (564) of patients were postmenopausal, 10.4% (104) had at least one first-degree relative with a history of breast cancer, and from 790 patients older than 40 years, only 48% reported yearly screening mammogram. The five-year and lifetime risk of developing invasive breast cancer was calculated using the GM, available on the website of the National Cancer Institute of the United States (http://www.cancer.gov/bcrisktool/). According to the GM, the mean calculated absolute risk utilizing the GM at five years was 1.18% (range 0-5.7%) and the mean lifetime calculated absolute risk was 9.29% (range 1.4-30.1%) of the female population evaluated in 2002.

This cohort was followed for up for 10 years; 33 patients discontinued medical consultations at the outpatient clinic of the Institute and therefore were considered lost to follow-up. Patients who developed breast cancer were identified retrospectively, and their medical history was reviewed obtaining the following: the estimated risk of developing breast cancer according to the GM, months since the GM's questionnaire was applied to histological diagnosis, the histology type of the cancer developed, and months of follow-up of each patient. Also, all women were classified at end point as alive with breast cancer, no evidence of disease, dead from breast cancer, or dead from other causes; this status and all previous variables were taken from the medical charts in the Institute. The study was International Review Board approved at our institution. Descriptive statistics were used as necessary.

RESULTS

Up to January 2012, we followed the remaining 967 patients from our original cohort. The mean calculated absolute risk utilizing the GM at five years was 1.18% (range 0-5.7%) and the mean lifetime calculated absolute risk was 9.29% (range 1.4-30.1%) of the female population evaluated in 2002. Twenty-four of 967 individuals developed invasive breast cancer (2.48%). The mean age of these individuals was 63 (range 38-89). Out of 24 patients, 22 (91.7%) developed invasive ductal carcinoma and two (8.3%) invasive lobular carcinoma. By the five-year mark, only 12 of these patients had developed invasive breast cancer, analogous to the predicted GM risk calculated in 2002 (1.18%). Of these 12 patients, at the time of last follow-up (December 2012), six had no evidence of disease (50%), two were alive with breast cancer (16.7%), four had passed away (33.3%), two had breast cancer-related death (16.7%), and two died from other medical causes. The various breast cancer risk factors had an important influence on the incidence of invasive breast cancer corresponding with the estimated impact on risks as calculated by the GM in the Mexican female population.

DISCUSSION

The GM has been widely used to predict a woman's risk of developing invasive breast cancer over a period of time and it is currently the most validated tool[11]. However, considering the geographical difference in breast cancer incidence rates between races and the fact that this tool has mainly been validated for a Caucasian population[6,7], its validation for a Latin American country is important. This is the only prospective trial that pretends to validate the GM in Mexico and for that matter for any Latin American country.

This is the first demonstration of an association between breast cancer incidence and the GM risk

factors in a Mexican population. In our previous study, the mean calculated absolute risk utilizing the GM at five years was 1.18% (range 0-5.7%) and the mean lifetime calculated absolute risk was 9.29% (range 1.4-30.1%) of the female population evaluated in 2002. In our cohort, according to Mexican national healthcare recommendations and hospital protocol, mammography was performed annually and 24 of 967 individuals developed invasive breast cancer (2.48%) after 10 years. Interestingly enough, by the five-year mark, only 12 of these patients had developed invasive breast cancer, analogous to the predicted GM risk calculated in 2002 (1.18%). In addition, patients who had a calculated risk at five years ≥ 1.66% were originally classified as high-risk. The 12 patients who developed invasive breast cancer were all considered high-risk because they had a mean calculated absolute risk at five years using the GM of 3.03% (range 1.74-5.7%). This clearly establishes that the various breast cancer risk factors had an important influence on the incidence of invasive breast cancer corresponding with the estimated impact on risks as calculated by the GM in the Mexican female population.

In the USA, breast cancer incidence in the Hispanic population is 92.3 per 100,000 per year[19]. In Mexico, the breast cancer incidence is 15 per 100,000 per year[4]; however, we have reason to believe that this rate has been grossly underestimated due to our country's limitations on epidemiological data. Each day 25 women are diagnosed with breast cancer and we have 10 breast cancer-related deaths[1,20]; the latest projection on breast cancer incidence estimates 16,500 new breast cancer cases per year[21].

Currently, there is no clear evidence on validation of the GM outside a Western population. The NCCN points out that the GM may not accurately assess breast cancer risk in non-Caucasian women[8]. There are several techniques to measure the calibration performance of a model; the E/O statistic and the C statistic are two of the most commonly used. The E/O statistic compares the expected (E) numbers to observed (O) numbers of events, so a well-fitting or calibrated model should have the number close to one[11]. Surprisingly, in our cohort the expected number of cases at the five-year interval was 12 and the observed was 12, giving us a ratio of 1:1. This indicates that the GM is a well-suited model for the Mexican population.

In conclusion, our results demonstrate an association between breast cancer incidence and the GM risk factors in a Mexican population. Using the E/O statistic method, the GM accurately estimates absolute risk of invasive breast cancer in our country. We believe the breast cancer incidence rate in Mexican patients may be comparable to Caucasian populations, and perhaps that may be the reason why the GM estimated calculated risk was not so farfetched for our limited female Mexican population. These results may indicate that those Mexican women classified as high-risk using the GM (defined as ≥ 1.66% at five years) may benefit from intensive surveillance and perhaps from a pharmacologic intervention like tamoxifen[9,17,22]. One of the main limitations of this study is our sample size; we believe more research is required to further validate the GM for a Mexican population. Currently, the National Health Public Institute (Instituto Nacional de Salud Pública, INSP) in Mexico is conducting a prospective study called ESMAESTRAS (Estudio de seguimiento de la salud de las maestras)[23] where they plan to follow Mexican teachers for up to 20 years. The epidemiological data obtained from this study could provide additional information for validation of the GM in the Mexican population.

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