Evaluation of the applicability of Gail's method in patients undergoing breast biopsy at a brazilian hospital

Avaliação da aplicabilidade do método de Gail em pacientes submetidas a biópsia de mama em um hospital brasileiro

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ABSTRACT
OBJECTIVES: To verify the accuracy of the Gail Model (GM) in risk assessment in patients with suspected breast cancer and to determine the need to adapt the GM or develop a new model for accurate risk assessment of these patients. METHODS: This is a descriptive, cross-sectional and retrospective study, based on the analysis of data provided by the medical records of 200 patients treated between 2017 and 2021, from the Mastology Outpatient Clinic of the Hospital Universitário Evangélico Mackenzie (HUEM). RESULTS: 155 women were diagnosed with breast cancer and 45 were not. The mean age was 54.23 years and the mean age at menarche was 13 years. Also, only 13 medical records contained information on age at birth of the 1st child or absence of children, and the mean age obtained was 26.77 years. Ethnic prevalence was white and most patients had no first-degree relatives with breast cancer. Regarding previous breast biopsies, most had already performed at least one, but few received a result of atypical hyperplasia. Furthermore, most of the study patients diagnosed with breast cancer had no positive family history of the disease. CONCLUSION: The study shows that the GM isn't reliable in assuming the risk of the studied population to develop breast CA, since, when comparing the GM data between groups that had and didn't have the disease, there was no significant difference.

Keywords: breast neoplasms, breast, risk factors, primary prevention, early diagnosis.

RESUMO
OBJETIVOS: Verificar a acurácia do Modelo de Gail (MG) na avaliação de risco em pacientes com suspeita de câncer de mama e determinar a necessidade de adaptação do MG ou elaboração de um novo modelo para avaliação de risco precisa dessas pacientes. MÉTODOS: Trata-se de um estudo descritivo, transversal e retrospectivo, elaborado a partir da análise de dados fornecidos por prontuário de 200 pacientes atendidas entre 2017 e 2021, do Ambulatório de Mastologia do Hospital Universitário Evangélico Mackenzie (HUEM). RESULTADOS: Foram diagnosticadas 155 mulheres com câncer de mama e 45 não, com média da idade de 54,23 anos e a média de idade na menarca foi de 13 anos. Ainda, apenas 13 prontuários continham a informação de idade ao nascimento do 1º filho ou de ausência de filhos e a média de idade obtida foi de 26,77 anos. A prevalência étnica foi branca e a maioria das pacientes não tinha parentes de primeiro grau com câncer de mama. Em relação às biópsias anteriores de mama, a maioria já havia realizado pelo menos uma, mas poucas receberam um resultado de hiperplasia atípica. Ainda, a maioria das pacientes do estudo diagnosticadas com câncer de mama não tinham história familiar positiva para a doença. CONCLUSÃO: O estudo apresenta indícios de que o MG não presume de forma fidedigna o risco da população estudada de desenvolver CA de mama, uma vez que, ao compararmos os dados do MG entre grupos que tiveram e não tiveram a doença, não houve diferença significativa.

Palavras-chave: neoplasias, mama, fator de risco, prevenção primária, diagnóstico precoce.

1 INTRODUCTION

Breast cancer is a multifactorial disease caused by the uncontrolled multiplication of cells, leading to abnormalities that progress and form the tumor. The main factors related to an increased risk of developing the disease are age, endocrine factors, environmental and genetic factors, alcoholism, smoking, obesity, as well as reproductive history such as early menarche, late menopause, first pregnancy after age 30, nulliparity, and use of oral contraceptives and postmenopausal hormone therapies[1,2].

In 2020, the estimate from the National Cancer Institute José Alencar Gomes da Silva (INCA) for new cases was 66,280 and, according to the Cancer Mortality Atlas, approximately 18,000 women died from breast cancer in 2019[1]. Recent epidemiological data indicate that only 20-50% of patients in poorer countries are diagnosed in the early stages of the disease, while in richer countries this percentage reaches 70%[3]. Such discrepancies are evident in Brazil, where at least one-third of diagnosed cases are in advanced stages[4]. Even closer to our reality, a study conducted in Paraná between 2000 and 2017 indicated that there were 2,215 deaths from breast cancer, with an average of 17.30 deaths per year in the state[5].

The detection of breast cancer is based on a triad composed of histopathological analysis (percutaneous biopsies performed with a thick needle), clinical examination, and imaging. In Brazil, according to the Guidelines for Early Detection of Breast Cancer, mammography is the only examination whose application in screening strategies has proven efficacy in reducing mortality from the disease, and is recommended to be performed biennially by women aged 50 to 69[1,2,6,7].

The Unified Health System (SUS) in Brazil is known for its extensive campaigns in favor of breast cancer screening and early diagnosis. However, the mortality rates from the disease remain high in Brazil due to the diagnosis in advanced stages. In response to this growing global issue, several studies have proposed risk calculation models to estimate a woman's probability of developing breast cancer. The most commonly used models include the Claus Tables, the Ford Model, BRCAPRO, Myriad, BOADICEA, the Gail Model (GM), and the Tyrer-Cuzick model[8,9].

In Brazil, although there is no validated risk assessment model, the Food and Drug Administration (FDA) recommends the use of the Gail Model (1989). This risk calculation method aims to estimate the chance that a woman, with known age and risk factors, has of developing breast cancer within five years and throughout her life up to the age of 90, using variables that will be presented throughout the study[9,10].

Based on research conducted in the country and the proven indispensability of breast cancer screening in Brazilian women, it is evident that risk assessment is particularly important in primary care within the hospital network, as it has the potential to reduce morbidity and mortality and avoid unnecessary screenings [10,11]. However, there are few studies on the applicability and accuracy of the GM in Paraná women, and this study aims to evaluate the accuracy of the model in assessing these patients.

The objective of this study was to verify the accuracy of the Gail Model in risk assessment in patients with suspected breast cancer. It also aimed to determine the need for adaptation of the GM or the development of a new model for accurate risk assessment of these patients.

2 METHODS

This study is characterized by a cross-sectional observational design with descriptive and retrospective evaluation of medical records. The study was conducted at the mastology outpatient clinic of the Evangelical Mackenzie University Hospital (HUEM) between October 2021 and May 2022, and involved the analysis of medical records of patients who attended routine consultations between 2017 and 2021.

Women with suspected breast cancer who were treated at HUEM were studied. Patients with abnormal findings on imaging tests who underwent histological evaluation (by biopsy or surgical specimen), patients with imaging tests that did not show any suspicion, patients with incomplete medical records, and patients with recurrent breast cancer were excluded from the study.

The study was approved by the Ethics Committee for Research (CEP) of the Mackenzie Evangelical University of Paraná (FEMPAR) on May 26, 2021, and the approval was registered in the Brazil Platform under number 4.736.101 and registered with the CAAE 46933721.7.0000.0103. As it is an observational cross-sectional study, the Informed Consent Form (ICF) was waived.

The following data were obtained from the analyzed medical records:

a) Epidemiological data: age, age at menarche, age at birth of first child, presence of first-degree relatives with breast cancer, and race/ethnicity.

b) Presence or absence and number of breast biopsies, presence of biopsy with atypical hyperplasia.

c) Diagnosis of breast cancer or not.

For the quantitative response variables, normality distribution was checked using the Shapiro-Wilk test, and results were reported using the mean (± standard deviation). For the qualitative variables, the values for each group were expressed as absolute numbers (percentage of the total).

To verify the statistical significance of our conclusions, different tests were applied depending on the nature of the variable. To verify the statistical difference between a quantitative and a qualitative variable, the parametric T-test was applied if the distribution of the quantitative variable was normal, and the non-parametric Mann-Whitney test was applied if it was not. To verify a quantitative variable in two or more qualitative groups, we applied the parametric ANOVA test, and the Kruskal-Wallis test if the distribution was not normal. To verify the association between two qualitative variables in our study, the chi-square test methodology was applied. To test the correlation between two quantitative variables, the Pearson correlation test was applied for parametric variables, and the Spearman correlation test was applied for non-parametric variables. For all tests, p values < 0.05 were considered sufficient to reject the null hypothesis and consider the result statistically significant.

All statistical analyses, graph and table construction were performed using the JAMOVI statistical software version 1.6.7, which is based on the R language.

3 RESULTS

Of the 503 patients attended, 200 met the study criteria, with 155 diagnosed with breast cancer and 45 not. The mean age was 54.23 years (standard deviation of ±11) and the mean age at menarche was 13 years (±1.67), with 14 (6.89%) medical records not containing this information.

Only 13 (6.5%) medical records contained information on age at first childbirth or absence of children, and the mean age obtained was 26.77 years (±6.58). Regarding the race/ethnicity of the patients, there were 181 (90.5%) White; 10 (5%) Brown; 1 (0.50%) Black, and information was not available in the medical records of 8 (4.00%) patients, as shown in Table 2. In addition, 162 patients (81%) had no first-degree relatives with breast cancer, 26 (13%) had a positive family history, and in 12 (6%) this information was unknown.

Regarding previous breast biopsies, 143 (71.5%) did not undergo any; 47 (23.5%) underwent only one, 10 (5%) were biopsied at least twice. Among those who underwent biopsy, 17 (8.5%) were diagnosed at least once with atypical hyperplasia.

Table 1 - General Characteristics of the Sample in the Study

CHARACTERISTIC	N = 200
Age (diagnosis)	54.23 (±11)
Menarche	12.99 (±1.67)
Age at first childbirth	26.77(±6.58)
First-degree relatives with breast cancer (mother, sister, daughter)	
No	162 (81%)
Yes	26 (13%)
Unknown family history	12 (6%)
Previous breast biopsy (how many)	
None	143 (71,5%)
One biopsy	47 (23,5%)
Two or more	10 (5%)
Breast biopsy with atypical hyperplasia	
No	40 (20%)
Yes	17 (8.5%)
Race/Ethnicity	
White	181 (90,5%)
Brown	10 (5%)
Black	1 (0.5%)
Not specified	8 (4%)
5-year breast cancer risk (%)	1.32 (±1.34)
Lifetime breast cancer risk (%)	8.44 (±5.7)
Do you have Cancer?	
No	45 (22,5%)
Yes	155 (77.5%)

1Mean (±SD); n (%)

Source: The authors, 2022

Regarding the Gail Model (GM), the mean 5-year breast cancer risk was 1.58% (±1.20), while the mean lifetime breast cancer risk was 9.28% (±7.50). When crossing the data between GM and the presence or absence of breast cancer, it was found that the mean GM in 5 years in patients with cancer is higher, and the mean Gail lifetime is higher in patients without cancer, and there was no significant difference between the groups, as shown in Table 2.

Table 2 - Comparison Between Average Breast Density And Presence Of Breast Cancer

	Mean breast density over 5 years in patients without breast cancer	Mean breast density over 5 years in patients with breast cancer	Mean breast density throughout life in patients without breast cancer	Mean breast density throughout life in patients with breast cancer
Mean	1,31	1,58	10,22	9,28
Median	1,10	1,20	8,40	7,50
Standard deviation	1,18	1,63	6,23	6,47
n	45	155	45	155
p	0,4710		0,0086	

Source: The authors, 2022.

When relating the presence or absence of breast cancer with average age (Table 3) and average age at menarche, it was observed that older patients and those with earlier menarche have a higher incidence of cancer, with respective p-values of 0.0031 and 0.25.

Table 3 - Comparison Between Average Age And Presence Of Breast Cancer

	Mean age of patients without breast cancer	Mean age of patients with breast cancer
Mean	49,96	55,47
Median	49,00	56,00
Standard deviation	11,25	11,94
n	45	155
p	0,003134163	

Source: The authors, 2022.

Furthermore, it was found that most women with breast cancer had no family history of the disease (61%), with only 10.5% having a positive family history and a cancer diagnosis, as shown in Table 4.

Table 4 - Relationship Between Family History Of Breast Cancer And Presence Or Absence Of Breast Cancer

	n	%
No family history and absence of breast cancer	40	20,00%
No family history and presence of breast cancer	122	61,00%
Family history and absence of breast cancer	5	2,50%
Family history and presence of breast cancer	21	10,50%
Unknown family status and presence of breast cancer	12	6,00%
Total	200	100,00%

Source: The Authors, 2022.

Finally, Table 5 shows that the majority of patients with breast cancer had no previous biopsy (67.5%). The proportion of patients with previous biopsy, with and without hyperplasia, and with cancer were similar (5.00%).

Table 5 - Relationship Between Atypical Hyperplasia And Presence Or Absence Of Breast Cancer

	n	%
Patient without biopsy and with cancer	135	67,5%
Patient without hyperplasia and without cancer	30	15,00%
Patient without hyperplasia and with cancer	10	5,00%
Patient with hyperplasia and without cancer	7	3,50%

Patients with hyperplasia and with cancer	10	5,00%
Total	192	96,00%

Source: The Authors, 2022.

4 DISCUSSION

This study evaluated the epidemiology, risk factors listed by the Gail model, the presence or absence of breast biopsy – and in case of a positive result, the quantity performed -, the presence of atypical hyperplasia in the biopsy and the confirmation or not of a diagnosis of breast cancer. All the patients studied through medical records were female, as this is the target audience of the selected location for the study, and the Gail model does not have a variation to calculate the risk of breast cancer in males.

The literature shows that the Gail model plays an important role as a risk predictor, as it can identify women at high risk of the disease, promoting closer monitoring by healthcare professionals and earlier preventive measures[8]. However, from the study and in line with the work of Crusoé et al. (2015), it was found that despite the ease of applying the Gail calculation and its worldwide recognition, it still presents flaws when used for Latin American women.

In this research, the fact that 155 patients (77.50% of the total that met the study criteria) had a diagnosis of breast cancer reflects the difficulty of real applicability of the Gail model in a clinic linked to the Brazilian Unified Health System (SUS), as the patients, in their first consultations, already had some complaint, physical, laboratory or imaging examination suggestive of alteration that later confirmed a malignant tumor, when they underwent routine consultations. Such a scenario of late diagnosis regarding breast cancer became even more evident during the COVID-19 pandemic period when INCA recommended that health services should instruct the population not to perform screening exams, rescheduling consultations and exams for when restrictions were lower. Although necessary at the time of calamity, this conduct negatively affected the segment and vigilance of high-risk patients, delaying diagnoses[12,13].

The mean age at diagnosis (54.23 years) observed in the study group is consistent with the literature, which clarifies that most cases occur after 50 years[14]. As previously stated in the study, the Gail model does not assess the risk for women under 35 years old, but it is known that the aggressiveness of the tumor when diagnosed in this age range is higher, similar to cases of triple-negative breast cancers, responsible for 25% of breast cancer deaths. Although age is an important risk factor, it is crucial to emphasize that the correlation between age and disease development is not linear[9,15,16].

Regarding the race of the study group, it was found that more than 90.50% were identified as white in the medical records, and only one patient was considered black. Such data reflects a serious negligence in the way the document is filled out, as the data is not obtained through the patient's self-declaration, so it can be affirmed that the number of white people was lower than the percentage revealed. The literature points out that the incidence and mortality of breast cancer vary among ethnicities and races, with higher incidence among Caucasian and African-American women[17]. In the present study, it is evident that the Gail risk calculation fails to take into account the race/ethnicity factor since the possible options are: white, African-American, Hispanic, Asian, Native American, and unknown[18]. Such options cannot cover the racial heterogeneity of Brazil, and therefore the final calculated risk is not reliable and results in an underestimated or overestimated risk. Furthermore, as only one patient was black, it was not possible to establish a comparison with those identified as white.

Also, regarding the race factor, the discrepancy in accessible health conditions between white and black people persists in Brazil. According to data from INCA (2021), a lower proportion of mammograms were performed on women classified as brown[14]. In addition, race is still a factor of exposure to worse access to health, social services, and resources, and studies show that self-declared Black women receive the diagnosis at more advanced stages of the disease and the survival of these patients is up to 10% lower than that of white women[19,20]. In addition to age and ethnicity, family history also represents a risk factor for the disease. First-degree relatives (mother, sister, daughter) with breast cancer are an important risk factor for the diagnosis of the disease before the age of 50. Furthermore, women who have more than one case of the disease in the family, one or more cases of ovarian cancer in blood relatives, and a family history of male breast cancer also have a greater genetic predisposition to this type of malignancy[21]. In the present study, 162 patients (81%) did not have first-degree relatives with breast cancer, but 61% developed the disease, supporting current literature. Studies estimate that about 85% of women with a family history of the disease do not develop the pathology, and only 5 to 10% of cases are hereditary. In addition, 95% of women with breast cancer do not have a genetic factor involved, demonstrating that the data obtained in the study agrees with the literature[9,21].

The Gail Model also considers data on breast biopsies in predicting risk. In the present study, the majority (71.5%) had not undergone a biopsy before the consultation recorded in the medical record - a similar statistic to studies in North America, where a

large part of the women analyzed did not have previous biopsy results[8]. Of the percentage mentioned in the present study, only 8.5% received a pathological report of atypical hyperplasia. The fact that a woman has had a breast biopsy at some point in her life indicates that at least some abnormality was suspected, and further investigation was necessary[9]. Among benign breast changes, women with non-proliferative disease have a 1.3 to 1.9 times lower risk of developing breast cancer compared to those with proliferative disease without atypia. Patients with atypical hyperplasia, on the other hand, have a 4 to 6 times higher risk of having the disease compared to those with non-proliferative breast disease[9].

It is known that breast cancer is an estrogen-dependent pathology, with some reproductive factors related to it. One of these is menarche, associated with an increased risk of breast cancer, since the earlier the menarche, the more estrogen exposure a woman will have throughout her life[22]. Currently, the literature considers that menarche normally occurs between 12 and 13 years of age[23]. In the analyzed group, the average age at which menarche occurred was 13 years, so these women did not have the predictive risk factor of "early menarche". However, the information on the age at which the patient had her first menstruation was not available in 6.89% of the medical records analyzed, indicating that this is a relatively frequent failure in filling out the document by the responsible professional.

Another risk factor addressed by the Gail Model is the woman's age at the time of the birth of her first child, but only 13 medical records (6.5%) provided this data. Among these, the average age obtained was 26.77 years at the time of the birth of the first child. Some studies indicate late pregnancy (after 30 years of age) or nulliparity as a risk factor for the development of breast cancer, because the time of estrogen exposure is longer[9].

In addition, research indicates that having the first child after the age of 30 increases the risk of this type of cancer compared to a woman who has never had children.

The current study also showed that the average risk of developing breast cancer within 5 years was higher in those patients whose pathological analysis confirmed the diagnosis of cancer later on. On the other hand, when looking at the average risk over a lifetime, it was higher in women whose pathological report excluded the diagnosis of cancer. The data illustrated in the results show that there was no significant difference in the risks obtained by mammography between the groups with and without breast cancer diagnosis, although the limitation of this research lies in the inadequacy of record keeping, often incomplete.

5 CONCLUSION

The present study fails to demonstrate the accuracy of the model, indicating that it does not reliably predict the risk of the studied population to develop breast cancer. This is because when comparing the GM data between groups with and without the disease, there was no significant difference or even a tendency towards a higher risk for the patients.

Therefore, a national-level study of the Gail Model in Primary Health Care is necessary, as there are still few references in the literature that actually analyze its applicability in the Brazilian population, taking into account ethnic heterogeneity.

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