

Breast Cancer Risk Assessment and Gail Model among Chinese Women

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Abstract

Purpose: The Gail Model has been used to quantify an individual woman's risk of developing breast cancer with clinical parameters; however, limited information has been available for application of this model among Chinese women. The aim of the present study was to estimate the five-year and lifetime breast cancer risk among women in Shanghai, China.

Materials and Methods: In this cross-sectional study, a total of 2,340 women residing in Shanghai, China participated using the Gail Model to estimate their relative risk for breast cancer. Participants were ≥ 35 years of age without a history of breast cancer.

Results: The mean age of the study subjects was 52.5 ± 10.8 years. Eighty-one women (3.5%) were classified as high-risk because their estimated five-year risk was over 1.66%. The estimated mean values for the five-year risk and lifetime risk for breast cancer were $0.73 \pm 0.009\%$ and $5.25 \pm 0.005\%$ respectively among study participants. For the lifetime risk, 17.6% of the women participants had a higher risk than the average woman. The risk increased with age and the history of breast cancer in the family among the study sample.

Conclusion: Overall, Chinese women in this study population were found to have comparable five-year risk of breast cancer but a lower lifetime risk based on the risk assessment of the Gail Model. Considering the rapid increase in breast cancer incidence in recent decades in China, the development of breast cancer models targeting the Chinese female population is needed.

Keywords: Breast Cancer; Chinese; Risk Estimation

Introduction

Breast cancer is a major public health issue and the most commonly diagnosed cancer for women worldwide [1-3]. In China, breast cancer is the most common cancer and the leading cause of death from all cancers among women. Despite the lower incidence rate compared to those living in Western countries, data from the Second and Third National Retrospective Sampling Survey of Death Causes in China estimated that breast cancer-related mortality increased between 1990-1992 and 2004-2005 from 3.84 per 100,000 to 5.09 per 100,000 populations [4]. In 2008, breast cancer-related mortality was 5.7 per 100,000 populations, resulting in approximately 44,900 deaths [5]. In Shanghai, China, the incidence rate has been increasing rapidly to a rate of 30.1 per 100,000 person-years in 1993-97 [6,7] and the overall age-adjusted incidence increased by 134% between 1975 and 2004 [8-9].

A number of statistical models have emerged to calculate the risk of developing breast cancer. These models allow determination of a woman's composite relative risk for breast cancer as well as her cumulative lifetime risk including all the specified risk factors. Such models can provide a tool in identifying individuals at high

risk, and the results from risk assessment can be used to develop an individualized plan to assist patients in decision-making regarding the implementation of frequent surveillance, chemoprevention, or prophylactic surgery. Screening mammography had been proved effective in reducing the mortality rates [10,11]; nevertheless, a population-based screening program has not been implemented in China as in the U.S. and other Western societies. In addition, the mean age for breast cancer diagnosis in China is 10 to 15 years earlier than in western countries [12]. Prioritizing breast cancer screening and diagnostic work-up for abnormalities can be particularly important, especially in low- and middle-income countries such as China, in the formation, implementation and coordination of breast cancer prevention, education, screening, and treatment program.

Despite its limitations, the Gail Model has been widely used to calculate a woman's risk of developing breast carcinoma. Based on the information from 284,780 Caucasian women participating in the Breast Cancer Detection Demonstration Project from 1973-1980, Gail et al. [13] developed a mathematical model that provides individualized risk estimates of developing breast carcinoma with varying risk factors, including age, age at menarche, number of prior breast biopsies, age at first live birth, and number of first-degree relatives affected with breast cancer. Relative risk was calculated for each of these risk factors; these relative risks (i.e., the probability of developing breast cancer in a given population) then were used to calculate the absolute risk at five years from the time of assessment and a lifetime risk up to the age of 90 [14]. A relative risk shows how much higher, lower, or whether there is no difference in risk in people with a certain risk factor compared to the risk in people without the factor. The value for the relative risk greater than one indicates an increased risk among people with the risk factor compared to people without the factor while the value below one indicates a decreased risk among people with the factor [15]. The Gail Model has been widely used to assess women's risk of getting breast cancer; nevertheless, data using this model on women outside of Europe and North America are limited. The modified Gail score that was tailored to women of Asian descent as well as risk predictions scores were developed for Singapore and Korean women [16-19] while the application of Gail model in China is relatively scarce.

It is important to monitor the risk of developing breast cancer among a population with increasing incidence and mortality with this disease and implement appropriate public health interventions. The purpose of this study is to utilize quantitative assessment to estimate the relative and cumulative risk during the lifetime for Chinese women in Shanghai.

Materials and Methods

This study used a descriptive cross-sectional study; the data was collected from the city of Shanghai, one of the largest cities in China. Previous literature showed the rapid increase of incidence in this city. The study protocol was reviewed and approved by the Institutional Review Board of Eastern Michigan University and Hung Kuang University. The study team collaborated with Shanghai Municipal CDC for data collection. Based on the administrative database of Shanghai Municipal CDC, women living in street districts of urban areas or townships of rural areas received notifications about the study from their residential officials and were invited to participate. Data collection was conducted using face-to-face interview using standardized questionnaires by trained nurses or community physicians at local public health offices and stations. Similar data collection procedures were reported in other larger epidemiologic studies in China [20,21]. Every woman who agreed to participate was interviewed using structured interviews to obtain demographic and risk factor data, including information on age, family history of breast cancer among first-degree relatives (i.e., mother, sister, and daughter), personal history of biopsies, age at first live birth, and age at first menstrual period.

Risk Factors	Number	Percent (%)
Age (years)		
≤ 44	396	16.9
45-54	915	39.1
55-64	881	37.7
≥ 65	148	6.3
Age at menarche (years)		
7-11	47	2.0
12-13	307	13.1
≥ 14	1986	84.9
Age at first live birth (years)		
No children	37	1.6
< 20	14	0.6
20-24	823	35.2
25-29	1246	53.3
≥ 30	220	9.4
Number of first-degree relatives with breast cancer		
Zero relatives	2268	96.9
One relative	62	2.7
More than one	10	0.4
Biopsy		
No	2214	94.6
Yes	126	5.4
One time	108	4.6
More than one	18	0.8
Atypical hyperplasia (with prior biopsy)		
Yes	27	1.2
No	99	4.2

Table 1: Distribution of Risk Factors among Participants Using the Gail Model.

Risk	Mean (%), SD	Minimum Risk	Maximum Risk
Mean five-year risk of participants	0.73, 0.009	0.2	5.7
Mean five-year risk for women of the same age without risk factors	0.78, 0.003	0.2	1.0
Mean risk of participants up to age 90 years	5.25, 0.050	0.6	42.7
Mean risk up to age 90 years for women of the same age without risk factors	5.73, 0.022	0.9	7.5

Table 2: Descriptive Statistics of Breast Cancer Five-Year Risk and Life Time Risk Based on the Gail Model.

The study sample consisted of 2,340 Chinese women aged 40 years and older. Women were eligible for this study and were included in analyses if they were: ≥ 35 years of age (same as in the Gail Model), had no personal history of pre-invasive or invasive breast cancer or documented genetic predisposition to breast cancer (genetic testing or familial cancer syndrome based on pedigree and geneticist evaluation), breast surgery reduction or augmentation, or use of exogenous hormones. The nature and purpose of the study was explained to eligible women who were assured that their participations were voluntary and confidential. After consents were obtained, the participants completed the interview, which took approximately 15–25 minutes.

Statistical Analyses

In this study, the 5-year risk was calculated and compared with the criteria in Seyednoori et al. [22] in which 1.66% and above was considered as high risk. We used a SAS macro for the Gail Model provided from the NCI website [23] to calculate each woman's 5-year and lifetime risk. For the 137 women who reported no prior biopsy, their status of atypical hyperplasia was re-categorized as unknown even though they self-reported positive for the diagnosis. We excluded two women above 85 years old since the program only accepts the calculation of the five year risk up to age of 90. Descriptive statistics included mean, standard deviation, minimum, maximum, and percent for factors and the predicted risks. All the analyses were conducted in SAS version 9.3.

Results

The mean age of the participants was 52.8 ±10.8 years with the range from 35 to 85 years. Overall, approximately 3.5% (n=81) of the Chinese women in this sample had a five-year breast cancer risk of at least 1.67% when calculated using the Gail model. The mean five-year breast cancer risk was 0.73% (Range: 0.20–5.70%).

The distribution of the risk assessment variables are presented in Table 1. The majority of women were between age group of 45 to 64 years, whereas 39% of them were 45–54, and 38% were 55–64. The majority of participants (84.9%, n=1986) reported having menarche at age 14 or later. More than half of the participants (53.3%, n=1246) gave their first birth between age 25 to 29, while one-third of the participants (35.2%, 823) had their first birth in the 20 to 24 age group. Only a fraction of participants (3.1%, 72) had a family history of breast cancer among the first-degree relatives. Ten participants had more than two first-degree relatives with breast cancer (0.43%). Similarly, a small portion of participants, 5.4% (126) reported prior breast biopsies, while 0.8% (18) participants had more than one biopsy. In addition, twenty-seven (1.2%) participants reported having atypical hyperplasia (Table 1).

The mean 5-year risk for all participants was 0.7%, and the mean lifetime risk (up to age 90) was 5.3% (Table 2). Most of the participants (82.7%, n=1934) had a 5-year risk lower than the average woman of the same age without risk factors, and 17.3% (n=406) had a higher 5-year risk. For the lifetime risk, 82.4% (n=1929) had a lower risk than the average woman of the same age without risk factors, and 17.6% had a higher risk. In terms of age,

Group	Age (years)	N	Mean	Std Error	Minimum	Maximum	F	p-value
1	≤ 44 ¹	396	0.389	0.012	0.154	4.046	159.24	< 0.0001
2	45-54 ²	915	0.705	0.012	0.350	5.269		
3	55-64 ³	881	0.883	0.015	0.424	5.654		
4	≥ 65 ⁴	148	0.814	0.030	0.458	2.620		

Table 3: Five-year Risk within Four Age Groups (Note: Group 1-2, 1-3, 1-4, 2-3, 2-4 are significantly different from each other; Std=Standard).

Family History	N	Mean	Std Error	Minimum	Maximum	t	p-value
Without	2268	0.691	0.007	0.154	4.660	-11.35	<0.0001
With	72	1.806	0.098	0.629	5.654		

Table 4: Five-year Risk Based on Family History (Note: Std = Standard).

the 5-year risks for the two younger groups (mean=0.389 for < 44 years; mean=0.705 for 45-64 years) are significantly lower than the two older groups (mean=0.883 for 65-74 years; mean=0.841 for > 75 years (Table 3). Based on the family history of breast cancer, the 5-year risk for women without a family history (mean=0.691) is significantly lower than those with a family history (mean=1.806) (Table 4).

Discussion

In the past ten years, the incidence of breast cancer has increased rapidly in China. Emphases have been focused on early detection and identification of risk factors associated with breast cancer in highly prevalent geographic regions. The Gail Model has been widely implemented in western countries; nevertheless, this study is one of only limited applications of this model in Asian countries, particularly in China.

The mean estimated five-year risk of 0.7% is half of that reported among the primary care U.S. population [24] but similar to the lower range of 0.77% to 1.18% found at U.S. gynecology clinics [25] and similar to the mean of 0.68% reported in another U.S. gynecology clinic [26]. Compared to studies outside of the United States, the results of the present study are comparable to the study in Iran [27] and lower than studies in Korea [28], Turkey [29] and the United Kingdom [30]. In terms of lifetime risk, the result of 5.3% in present study is consistently lower than all other studies in the U.S. (12.3%) [31], Iran (9.0%) [27], Korea (7.9%) [28], Turkey (15%) [29] and the United Kingdom (9.0%) [30]. In addition, the proportion of Chinese women who had a five-year risk > 1.66% were also lower than the other studies [28,30]. Overall, the Chinese women in this study population were found to have generally lower risk of breast cancer based on the risk assessment of the Gail Model. The lower estimated risk for breast cancer in the study sample of Chinese women may be related to having fewer gynecologic abnormalities and younger age at first childbirth. A recent study reported that Chinese women had much less knowledge about breast cancer and risk factors [10]. Using the Gail Model can assist health providers to communicate with their clients about breast cancer risk factors and strategies/options to lower their risks including medications that reduce the risk of developing breast cancer and lifestyle changes.

For clinicians and practitioners, incorporating risk assessment as part of routine clinical visits can supply women with accurate information and inform those who may know little about breast cancer risks and those who may mistakenly consider themselves to be at higher or lower than average risk. As a result, the appropriate prevention strategies and screening modalities can be tailored to each individual woman's risk profile. When women are more knowledgeable about their personal risk, they can make informed decisions about prevention methods and screening options to detect cancer early. Ultimately, planning and implementing early

detection and screening programs of breast cancer can be more successful.

However in China, neither an organized screening program operates nor national breast cancer screening guidelines exist at present [31]. It is imperative for policy makers to understand how the general public is aware of their own breast cancer risk and health professionals estimate their clients' risks in order to promote evidence-based cancer control policies.

The current study had several limitations. First, the sample was not randomly selected and women in urban setting were oversampled which may result in a potential sample bias contributed to the rural-urban difference. In addition, the present study was conducted with a convenience sample and the representativeness of general population is unknown therefore, limits the generalization of study findings to other groups. Since all data were self-reported, there may be recall errors, which can reduce the accuracy of risk assessment results. Previous study using the Gail model has been shown to overestimate the risk of breast cancer for Asian women [17]. A recent Korean study showed a 50% underestimation of breast cancer risk among Korean women based on the modified Korean risk model developed using risk factors from a Korean case-control study and the incidence and mortality in Korea. For a more accurate prediction model, clinical information may not be adequate; biochemical data, such as estrogen level, mammographic density and molecular markers may need to be included to assure great discriminatory power [19].

To our knowledge, this is one of the few studies that applies the Gail Model and determines the breast cancer risk in Chinese women residing in Shanghai. Moreover, all the assessment data were obtained by trained nurses or physicians to ensure the accuracy and consistency in data collection. Considering the rapid increase in breast cancer incidence in recent decades in China, the development of breast cancer models targeting the Chinese female population is needed. In Shanghai China, breast cancer incidence rates have been increasing rapidly during a period of changing dietary and lifestyle patterns [32]. Appropriately tailored breast cancer risk reduction recommendations and referrals for risk modifications and screening modalities can potentially reduce the risks of breast cancer among Chinese women.

Key Messages

Using the Gail Model can empower women becoming familiar with breast cancer risk factors and communication strategies to distribution information about breast cancer. For clinicians or practitioners, incorporating risk assessment as part of routine clinical visits can supply women with comparatively accurate information. Appropriately tailoring breast cancer risk reduction recommendations and referring for risk modifications and

screening modalities can potentially reduce risks of breast cancer in Chinese women.

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