Evaluation on Risk Factors and Preventative Measures for Breast Cancer in China

Xiaolu Tang
University of Washington, Seattle, WA, 98105, U.S.A.

Keywords: Breast Cancer, Risk Factors, Screening, Prevention.

Abstract: Breast cancer is one of the leading causes of death among females worldwide. The number of people who have been diagnosed with breast cancer is increasing rapidly in China. To better understand the current situation of breast cancer and propose suggestions on reducing the risk of breast cancer, risk factors associated with breast cancer and measures that can effectively prevent the onset of breast cancer are introduced and discussed. The research is conducted in the form of a literature review by summarizing, comparing, and analyzing previous research and proposing constructive suggestions on how breast cancer can be prevented. The objective of this review is to analyze the risk factors and several preventative measures of breast cancer and to provide suggestions on future works.

1   INTRODUCTION

Breast cancer is the most commonly diagnosed cancer in women worldwide and ranks as second-highest cancer related death among cancers in women (Fahad Ullah 2019). Breast cancer is a type of metastatic cancer involving a series of mutations and can potentially affect other organs including the brain and liver (Collaborative Group on Hormonal Factors in Breast Cancer 2002). All women are at risk of developing breast cancer and a general trend is observed that the chances increase with age. The incidence and prevalence rates of breast cancer are relatively high in developed countries such as North America and Australia, and relatively low in Eastern Asia counties including China. However, the incidence rate and mortality rate of breast cancer of women in China are rising in recent years with an increase of about 20–30 % over the past three decades and an annual growth rate of 3-5% (Fan, Strasser-Weippl, St Louis, Finkelstein & Goss, etc. 2014). Breast cancer in China is not fully understood in terms of the causes of breast cancer and effective prevention and treatment measures lagged far behind developed countries. Although some risk factors, which are essential to understand the epidemiology of breast cancer, have been identified by previous research, no comprehensive analysis has been conducted to summarize risk factors associated with breast cancer. China has made a great effort focusing on the treatment of breast cancer, but preventative measures and diagnosis are largely neglected, and early diagnosis is essential to suppress the growth of primary tumors and lower the mortality rate significantly. This review mainly focuses on three parts. An overview of the current situation of breast cancer in Chinese women is presented by using statistics obtained on incidence rate and mortality rate in recent ten years. Several risk factors closely related to breast cancer are analyzed. Moreover, the efficacy of current preventative measures is evaluated, and new preventative measures are proposed.

2   CURRENT SITUATIONS OF BREAST CANCER IN CHINA

The incidence rate of breast cancer in China was low until the 1990s when the incidence rate rose more than twice as fast as have global rates. The China National Cancer Centre reported the incidence rate by using the age-specific rate from 2004 to 2009. The highest incidence rate occurred in age groups of 50–54 for females, with an age-specific rate of 92–108 per 100,000 Chinese women. The slope of the incidence-age group curve rose with increase in age, became flat for the age group of 60–69 years, and gradually decreased from the age of 70. The

incidence rate generally increased from 2004 to 2009 for almost all age groups and the differences in incidence rate became significant for people aged above 50 years old. (Figure 1) The incidence rate also varied significantly in different geographical locations in China. Previous studies have demonstrated that the average age-standardized rate was 31.3 in urban areas compared to 12.1 per 100,000^2 in rural areas. The difference in incidence rate can be attributed to factors such as variation in socioeconomic status, accessibility to health services, and difference in screening rate (Li, Mello-Thoms & Brennan 2016).
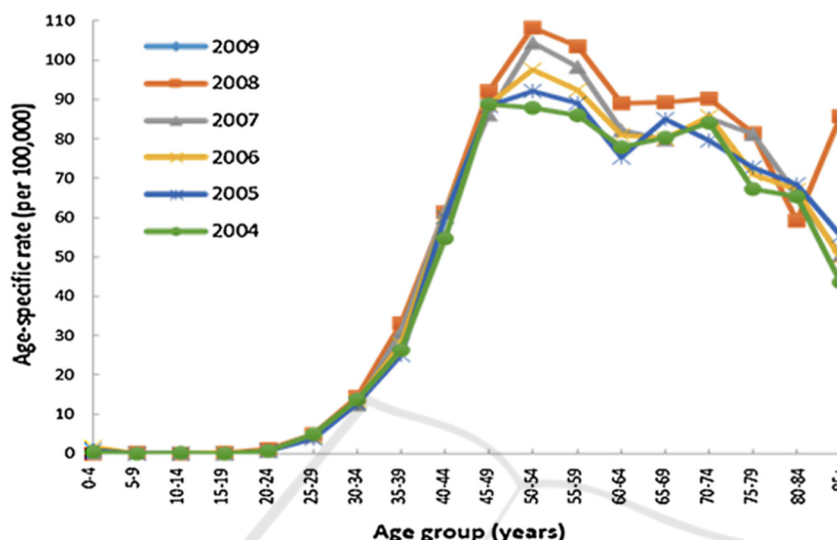
Figure 1: Age-specific incidence rates of breast cancer in female from 2004 to 2009.

The trend in the mortality rate of breast cancer, however, was inconsistent with the trend in incidence rate in China from 2004 to 2009. The incidence rate was lower for women aged above 60 years old compared to women aged between 45 and 49, but the mortality rate showed an increasing trend with age and rose exponentially for women aged 85 and over. (Fig. 2) Differences in mortality rates also existed across geographical regions. Data have suggested that the mortality rate tripled in urban areas compared to rural areas with an increase of only 16% from 2002 to 2008. The discrepancy can be explained by the availably of sample sizes and limited access to population-based statistics (Li, Mello-Thoms & Brennan 2016).
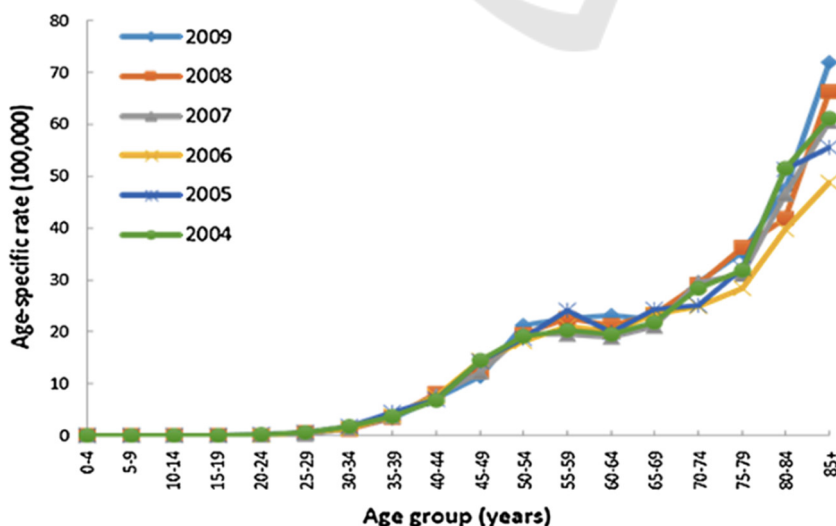
Figure 2: Age-specific mortality rates of breast cancer in female from 2004 to 2009.

Although some trends in the incidence rate and mortality rate have been analyzed by using data collected in recent one to two decades, only 13% of the population has been included in the national cancer registries in China. The dataset presented is very limited and hard to reflect the comprehensive situation of breast cancer through data interpretation in China. Thus, expansion of cancer registration data is essential, which would improve the accuracy in estimating the number and burden of breast cancer and better the current situation of breast cancer in China.

3 RISK FACTORS ASSOCIATED WITH BREAST CANCER

3.1 Genetic Factors

Breast cancer is largely caused by genetic factors and many genes are associated with the chance of getting breast cancer, including BRCA1/2, Epidermal Growth Factor Receptor (EGFR), and HER2. BRCA1/2 are tumor suppressor genes that suppress cell growth when tumor cells are been detected. They have the function of regulating the cell cycle checkpoint and repairing DNA breaks to make sure the normal function of cells. When deleterious mutations happened in BRCA1/2 genes, the genes lose functions and lead to the growth of tumor cells, thus greatly increasing the risk of breast cancer. However, developing cancer-related genes like BRCA1/2 genes does not necessarily mean little chance to survive through the disease. A meta-analysis study conducted by Yaning Zhu et. al examined the relationship between BRCA mutations and patients' survival rate, and the results are summarized here to infer the association between having BRCA 1/2 genes and breast cancer. The survival rate of patients with breast cancer was analyzed by using hazard ratios (HR) and breast cancer-specific survival (BCSS). By examining the results of 26 previous research reporting BRCA 1 mutation, BC patients with BRCA1mutation were associated with worse OS compared to non-breast cancer patients. The pooled HR was 1.69 (95% CI 1.35 to 2.12, p < 0.001; I2 = 59.1%) No association, however, was found between BRCA1 mutation and BCSS (HR = 1.14, 95% CI 0.81 to 1.61, p = 0.448; I2 = 68.1%) The results were similar when analyzing the BRCA2 mutations and patients had poor OS. Also, no association has been found between BRCA2 mutation and BCSS (HR 1.16, 95% CI 0.82 to 1.66,

p = 0.401; I2 = 50.9%). The results might be counterintuitive to many people but indicated positive promises. As BRCA1/2 mutation did not significantly influence the survival rate of patients, actively and promptly seeking screenings and treatments may increase the chance of survival for breast cancer patients (Zhu, Zhang, Liu & Zhang 2016).

3.2 Breastfeeding and Parity

Breastfeeding is another risk factor associated with breast cancer as breastfeeding and parity are related to reproductive and hormonal receptors like estrogen (ER). Parity is defined as the number of times that women had given birth to a fetus. Previous studies have confirmed that a 33% association was found between parity and the increased risk of ER disease (n = 1252; parous vs. nulliparous, RR = 1.33 [1.11–1.59]). Women with higher parity who did not breastfeed also had a higher risk of breast cancer (e.g., ≥ 4 vs. 1 birth, RR = 1.68 [1.15–2.44]) but not among women reporting ever breastfeeding (RR = 1.33 [0.91–1.95]). Consequently, breastfeeding and number of parity had been confirmed to significantly influence the chance of whether women would get breast cancer (Fortner, Sisti, Chai, Collins, Rosner & Eliassen 2019). The one-child policy was a policy unique in China implemented at the beginning of the 1980s, and it largely affected the breastfeeding pattern for pregnant Chinese women. The total fertility rate had decreased significantly from about 6.0 in 1950 to 1.6 in 2020 (Collaborative Group on Hormonal Factors in Breast Cancer 2002). Since women were only legally allowed to have one child, the number of parity and the time for breastfeeding declined dramatically. Thus, the risk of breast cancer would likely increase during those 30 years.

3.3 Dietary Pattern

As economics rapidly developed in China, the economic status of people have improved and they could choose more options in terms of eating and living. The diet of many Chinese people has changed from a healthy traditional diet based on vegetables, soybeans, and rice to a modern western diet that contains too much fat. The Women's Health Initiative Randomized Controlled confirmed the association between low-fat dietary patterns and risk of breast cancer by examining 48,835 postmenopausal women from 1993 to 1998 at 40 US clinical centers. The results demonstrated that during

the 8.5 years intervention, the number of deaths had reduced for breast cancer patients receiving the dietary intervention, compared to those in the control group (27 deaths [0.016% per year] v 61 deaths [0.024% per year]; HR, 0.67; 95% CI, 0.43 to 1.06; P = .08). A similar trend was found when dietary intervention lasted for 16.1 years with 3,030 incident breast cancers. Few deaths were observed in patients in dietary group in contrast to patients in control group (111 deaths [0.035% per year] v 185 deaths [0.039% per year]; HR, 0.91; 95% CI, 0.72 to 1.15) (Collaborative Group on Hormonal Factors in Breast Cancer, 2002). When changing to a low-fat dietary pattern, the risk of breast cancer and death was significantly decreased. Other than reducing the frequency of consuming food containing a lot of fat, eating fiber may help prevent the onset of breast cancer to some extent because fiber can reduce cholesterol levels in the blood and even destroy carcinogens.

4 PREVENTATIVE MEASURES OF BREAST CANCER

4.1 Screening

Early detection and screening are important for breast cancer prevention because many primary tumors can be removed by surgery. There are mainly two types of screening that are currently being used to screen for breast cancer. Mammography is an effective screening method that utilizes low-energy X-rays to obtain high-resolution images of the breast, but it can lead to problems like overdiagnosis. MRI is another screening tool that has been widely applied for breast cancer. The sensitivity of MRI is higher than mammography, but the specificity of MRI is much poorer than that of mammography with lower detection rates (Fan, Strasser-Weippl, St Louis, Finkelstein & Goss, etc. 2014).

Despite the development of screening technology that makes early detection of breast cancer possible, the screening rate is never optimistic in China. Statistics have shown that the screening rate for breast cancer was 25.7% for women aged between 35 and 64 years in 2015. Even though the screening rate increased by 3% from 2013 to 2015, the number was low compared to developed countries with a screening rate of above 50%. Moreover, women in rural areas and with low education levels had significantly lower screening rates. Some screening programs had been implemented since 2009 in China which specifically provide easy access to screening for rural female residents aged 35-59 years old, however, the screening rate only increased partially and there is no nationwide screening program for breast cancer in China at present (China CDC Weekly 2021). Therefore, continued efforts should be made by governments and organizations to give initiatives and financial support to implement more screening programs for breast cancer. Also, screening for breast cancer should be included in the regular health check-up for women especially those above 35 years old and screening expenditures can be included in health insurance to alleviate the burden of financial difficulties especially in rural areas.

4.2 Chemoprevention

Chemotherapy is a primary method used for the prevention and treatment of breast cancer worldwide. It is an aggressive form of chemical drug therapy that destroys the growing cells in the body. The estrogen receptor is often a major target for chemotherapy because over of 70% patients have ER-positive breast cancer. Currently, two major classes of anti-estrogen drugs are selective estrogen receptor modulators (SERMs) and aromatase inhibitors (AIs) (Zhu, Zhang, Liu & Zhang 2016). Although SERMs and AIs have certain efficacy in treating breast cancer, their side effects cannot be ignored including stroke, osteoporosis, and joint pain. Thus, researching on drugs that can be both effectively target the disease and with few side effects is of high priority. Neoadjuvant chemotherapy is a relatively advanced method in early-stage prevention and treatment for breast cancer. Neoadjuvant chemotherapy works by targeting the primary tumors fixed to the chest wall or skin, decreasing the size of tumor cells before conducting surgery. Studies conducted by MD Anderson have shown that the survival rate of breast cancer patients increased significantly if neoadjuvant chemotherapy was implemented, and the size of tumors was reduced by 50% in at least 67% of patients in the study (Redden & Fuhrman 2013).

In China, neoadjuvant chemotherapy is gradually being used in the prevention and treatment of breast cancer and in the stage of continuous development. With the emergence of various clinical trials and new treatment concepts, the treatment model has been transformed from single chemotherapy to current neoadjuvant chemotherapy based on different breast cancer molecular subtypes. As new evidence-based medicine data continue to be enriched, the differences between various therapeutic concepts

and clinical practice become more obvious. Thus, more emphasis should be placed on selecting and applying neoadjuvant chemotherapy in clinical practice, optimizing the treatment strategy for patients, and improving treatment outcomes.

4.3 Changes in Diet Pattern

Another effective preventative measure is to promote a healthy diet and lifestyle, which could be a risk factor leading to breast cancer. Evidence has demonstrated that a diet rich in saturated fat would increase the risk of breast cancer, so promoting a diet that includes rice, fresh vegetables, soy, pork would reduce the risk of breast cancer. Dietary fiber is also beneficial in preventing breast cancer as it promotes the growth of probiotics and inhibits the growth of pathogenic bacteria, which significantly reduces the risk of breast cancer, especially for postmenopausal women (Zhao, Zhang, Deng, etc. 2016). China has implemented some policies in an effort to increase the awareness of people in pursuing a healthy life. One of them is The Healthy China Initiative 2019-2030, which aims to improve national health policies and provide comprehensive health services for people. It addresses the urgent need to increase the awareness of having a healthy diet among people and to strengthen guidance on nutrition and health works in schools and institutions. The policies are essential to solve current health problems such as malnutrition and excessive intake of high-calorie food, thereby preventing breast cancer and other cancer diseases.

5 CONCLUSIONS

Breast cancer is becoming more common in China with a rising incidence rate and mortality rate. Identifying risk factors and implementing preventative measures are important to reduce the risk of breast cancer. The increase in the number of Chinese women getting breast cancer is due to the ignorant of risk factors that potentially lead to breast cancer, and low awareness and financial difficulties in conducting preventative measures timely. Concrete and comprehensive programs and policies, such as National Screening Program and Health China Initiative, are necessary to improve preventative measures and promote awareness of risk factors associated with breast cancer.

Chinese government and institutions should make continuous efforts in increasing the awareness and knowledge of the public, providing more convenient health services for early diagnosis

especially in rural areas, and improving biomedical techniques to increase the accuracy of the breast cancer diagnosis. The paper is subjected to some limitations. The data used for the incidence rate and mortality rate of breast cancer might not reflect the actual situations of breast cancer in China as many people are not included in the database. Moreover, only risk factors that have been shown to have a strong association with the risk of having breast cancer were included and risk factors such as stress and mood, which are hard to be analyzed quantitatively, did not add into consideration. For future works, more research and analysis can be conducted on testing whether improving the implementation of preventative measures of breast cancer mentioned would decrease the risk of breast cancer.

ACKNOWLEDGMENT

REFERENCES

Chlebowski, R. T. et al, (2017). Low-Fat Dietary Pattern and Breast Cancer Mortality in the Women's Health Initiative Randomized Controlled Trial. Journal of clinical oncology: official journal of the American Society of Clinical Oncology, 35(25), 2919–2926.

Collaborative Group on Hormonal Factors in Breast Cancer (2002). Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet (London, England), 360(9328), 187–195.

Fahad Ullah M. (2019). Breast Cancer: Current Perspectives on the Disease Status. Advances in experimental medicine and biology, 1152, 51–64.

Fan, L., Strasser-Weippl, K., Li, J. J., St Louis, J., Finkelstein, D. M., Yu, K. D., Chen, W. Q., Shao, Z. M., & Goss, P. E. (2014). Breast cancer in China. The Lancet. Oncology, 15(7), e279–e289.

Fortner, R. T., Sisti, J., Chai, B., Collins, L. C., Rosner, B., Hankinson, S. E., Tamimi, R. M., & Eliassen, A. H. (2019). Parity, breastfeeding, and breast cancer risk by hormone receptor status and molecular phenotype: results from the Nurses' Health Studies. Breast cancer research: BCR, 21(1), 40. https://doi.org/10.1186/s13058-019-1119-y

Li, T., Mello-Thoms, C., & Brennan, P. C. (2016). Descriptive epidemiology of breast cancer in China: incidence, mortality, survival and prevalence. Breast cancer research and treatment, 159(3), 395–406.

Redden, M. H., & Fuhrman, G. M. (2013). Neoadjuvant chemotherapy in the treatment of breast cancer. Surgical Clinics of North America, 93(2), 493-499.

Zhang, Mei; Zhong, Yijing; Bao, Heling; Zhao, Zhenping; Huang, Zhengjing; Zhang, Xiao; Li, Chun; Zhou, Maigeng; Wang, Limin; Wu, Jing; Zheng, Xiaoying; Wang, Linhong. China CDC Weekly. (2021). Vol.3 (13), p.267-273.

Zhao, P., Zhang, L., Liu, Y., Yu, Q., Deng, Q., & Zhang, K. (2016). Dietary fibre intake and risk of breast cancer: A systematic review and meta-analysis of epidemiological studies. Oncotarget, 7(49), 80980–80989.

Zhu, Y., Wu, J., Zhang, C., Sun, S., Zhang, J., Liu, W., Huang, J., & Zhang, Z. (2016). BRCA mutations and survival in breast cancer: an updated systematic review and meta-analysis. Oncotarget, 7(43), 70113–70127.