Analysis of Breast Cancer Cases According to County-Level Poverty Status in 3.5 Million Rural Women Who Participated in a Breast Cancer Screening Program of Hunan Province, China from 2016–2018

Xiong Lili
hunan province maternal and children hospital
https://orcid.org/0000-0002-0608-5928

Liu Zhiyu
Hunan province maternal and children hospital

Wu Yinglan
hunan province maternal and children hospital

Wang Aihua
hunan province maternal and children hospital

Li Hongyun
hunan province maternal and children hospital

Liang Ting
hunan province maternal and children hospital

Wang Yingxia
hunan province maternal and children hospital

Yang Guanghui
hunan province maternal and children hospital

Chen Xianghua (✉ 1610194981@qq.com)
hunan province maternal and children hospital

Fang Junqun
hunan province maternal and children hospital

Xie Donghua
hunan province maternal and children hospital

Kong Fanjuan
hunan province maternal and children hospital

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Abstract

Purpose Thus far there has been no study on the breast cancer screening program in China, especially one exploring differences between poor and non-poor areas. Therefore, we aimed to assess the effectiveness of the population-based breast cancer screening programs, and clinical epidemiological characteristics of breast cancers in poor and non-poor counties in rural areas of Hunan province from 2016–2018.

Methods 3,151,679 rural women took part in the screening program and 1,169 breast cancer cases was identified. Chi-square and Fisher’s exact tests, and binary logistic regression analysis were used for analyzing the difference in risk factors, clinical examination results, and clinicopathological features of breast cancer patients in poor counties compared with those in non-poor counties in rural areas of Hunan province.

Results The breast cancer incidence was 37.09/10^5. Breast cancer incidence was lower in poor counties (29.68/10^5) than in non-poor counties (43.13/10^5). There were differences between breast cancers in poor counties and non-poor counties in cyst, margin, internal echo, and blood flow in solid masses in the right breast in ultrasonic examination, lump structure in mammography examination, and clinicopathological staging and grading in pathological examination. Breast cancer in poor counties was more likely to be diagnosed at later stages as determined from the classification in ultrasonic, mammography and pathological examination. Furthermore, indexes of the breast screening program including early detection, incidence, pathological examination, and mammography examination were reduced in poor compared with non-poor counties. Binary logistic regression analysis showed that education, ethnicity, reproductive history and the year 2017 were associated with an increased risk of breast cancer in poor counties (OR >1, P < 0.05).

Conclusions Women in poor areas were more likely to be diagnosed at a later breast cancer stage than those in non-poor areas, and therefore, women should have better access to diagnostic and clinical services in poor areas in Hunan province to help rectify this situation.

Introduction

Breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer-related deaths in women worldwide. It is estimated that over 508,000 women die from breast cancer each year globally and approximately 58% of those live in low- and middle-income countries. Breast cancer is now the most common cancer in Chinese women and the incidence has increased by 3–5% annually in China for the last 20 years, much faster than the world average annual increase of 0.5%. Noteworthy, breast cancer incidence and mortality rates among Chinese women in rural areas during the last 10 years have been increasing rapidly. The incidence and mortality rates of breast cancer in the eastern and middle areas were similar and higher than those in western areas of China. It was estimated that the age-standardized death rate of breast cancer among women in Hunan province in 2013 was 7.3/10^5, which was higher than the average of 6.7/10^5 in China.

China has undergone significant development and remarkable change in its social economy that has resulted in a shift from a predominately rural lifestyle to a more Western/urban style over the past decades. The risk factors of breast cancer are prevalent and include early menarche, late menopause, nulliparity, and absence of a history of breastfeeding. The incidence and mortality of breast cancer in China will continue to increase in the future, and in particular, the rate of disease and death will rise significantly faster in rural than in urban areas. Individuals living in poorer areas are less likely to seek cancer screening compared with individuals living in wealthier areas because of the lack of diagnostic and screening opportunities throughout rural areas. Furthermore, women in poor areas are more likely to be diagnosed at later breast cancer stages than those in more affluent areas. Breast cancer screening programs are mostly located in upper-middle and high income countries, while breast cancer screening programs are unlikely to be found in low-income and lower-middle income countries. Therefore, it is necessary to carry out population-based breast cancer screening in poor areas. To date, nationwide breast cancer population screening has never been implemented in China because of the difficulties associated with large-scale screening programs. As yet, there is no large-scale, geographically representative study of breast cancer screening among the general population. However, Hunan province has organized a population-based breast cancer screening program in rural areas from 2016–2018 with government support. This study explored the influence of economics on population-based breast cancer screening programs and clinical epidemiological characteristics of breast cancer in poor and non-poor counties in rural areas of Hunan province, China, from 2016–2018. We also provided policy suggestions for improving breast cancer screening programs, improving health, and alleviating poverty in rural areas in the future.

Patients And Methods

Study patients and study design

This study was based on breast screening programs in Hunan province, China, which were required to carry out breast screening for at least one million rural women each year from 2016–2018. Inclusion criteria were: 1) age between 35–64 years; 2) never been diagnosed with breast cancer; 3) rural registered women; 4) voluntarily amenable to undergo breast screening; and 5) not pregnant at the time of enrollment. Exclusion criteria were: 1) pregnant women; 2) refusal to participate; 3) a history of breast cancer; 4) difficulty in obtaining information from the woman; and 5) not locally registered rural women. All the subjects were familiar with the purpose and procedures of the breast screening program and signed informed consent forms to participate in the study. All study protocols were approved by the Ethics Committee of the Hunan Provincial Maternal and Children Health Care Hospital.

Screening protocols and procedures

Trained investigators registered subjects and obtained basic information such as age, education, ethnicity, menstrual history, family history, and fertility history. Subjects then had their clinical breast examination and breast ultrasonography (BUS). In the ultrasound, the physician scanned each quadrant of the breast using the radiating and crossing method at the center of the nipple and completed the ultrasound examination and diagnosis report for each subject.
Subjects with positive and suspected positive results of BUS received mammography (MAM). Those who were MAM-positive or suspected of being positive were subjected to further pathological examination. Upon pathological examination, subjects who were found to be positive were recalled for treatment and followed in the clinic. A schematic of the screening process is shown in Fig. 1.

Data collection
We collected breast cancer screening information from China's major public health service projects' direct reporting system. We obtained quarterly report data on the breast cancer screening program in the rural areas of Hunan province in China from 2016–2018. Data in the quarterly report included the yearly checkup information, the results of BUS, MAM, and pathological examination, as well as the tumor, node, and metastasis (TNM) stage. We obtained information on breast cancer cases in the system, including basic and clinical information, results of BUS, MAM, and pathological examination, and TNM stage and grade.

Hunan province is located in central China, covers 21.18 km², and has a population of 71.47 million people, with 90 counties in rural and 33 in urban areas¹⁶. There are 51 poor counties and 39 non-poor counties in rural areas. The list of poor and non-poor counties was also stipulated by the provincial government. The system was established in 2009 and has now expanded to cover all 90 counties in rural areas in the entire province from 2016.

Data quality control
In order to ensure data accuracy, the information system was subjected to four audit levels: county, prefectural, provincial, and national. The county level unit submitting the original data was responsible for the examination, verification, and modification of the data after it had received all suggestions made during the initial review. The health administration departments at the prefectural, provincial, and national levels were subsequently responsible for reviewing the reported data.

Statistical analyses
Statistical analyses were performed using SPSS 20.0 software. Differences in the basic information, results of BUS, MAM, and pathological examination, and differences in treatment between breast cancer patients in poor and non-poor counties were analyzed using chi-square and Fisher's exact tests. Binary logistic regression analyses were performed to assess the risk factors of breast cancer patients in poor counties. All statistical tests were considered significant when P < 0.05.

Results
Comparison of the breast cancer screening program
Comparison of the breast cancer screening programs in non-poor and poor counties is summarized in Table 1. There were 3,151,679 rural women who were screened for breast cancer. There were a total of 82,333 women who were found to be 0-grade and 3-grade in the BUS examination. The total number of women who underwent MMA was 62,577, which was 76% of all women who were found to be 0-grade or 3-grade in BUS examination. The proportion of women who underwent a histopathological examination in non-poor and poor counties was 79.60% and 63.60%, respectively. The total number of breast cancer cases was 1,169. The total number of women given an early diagnosis of breast cancer was 601. The incidence of breast cancer in non-poor and poor counties was 43.13/10⁵ and 29.68/10⁵, respectively.
Table 1
Comparison the evaluation indicators in the breast population screening population between poor and non-poor counties.

| Variables                                     | Non-poverty counties | Poverty counties | Total  |
|------------------------------------------------|----------------------|------------------|--------|
| The total checks                               | 1736684              | 1414995          | 3151679|
| **BUS**                                        |                      |                  |        |
| The checks                                     | 1725041              | 1414046          | 3139087|
| 0-grade                                        | 11453                | 3056             | 14509  |
| 1-grade                                        | 1184113              | 1065950          | 225063 |
| 2-grade                                        | 485113               | 313281           | 798394 |
| 3-grade                                        | 38826                | 28998            | 67824  |
| 4-grade                                        | 5376                 | 2669             | 8045   |
| 5-grade                                        | 160                  | 92               | 252    |
| **MAM**                                        |                      |                  |        |
| The checks                                     | 36277                | 26300            | 62577  |
| 0-grade                                        | 898                  | 983              | 1881   |
| 1-grade                                        | 7810                 | 5804             | 13614  |
| 2-grade                                        | 14209                | 10239            | 24448  |
| 3-grade                                        | 11885                | 8247             | 20132  |
| 4-grade                                        | 1397                 | 985              | 2382   |
| 5-grade                                        | 78                   | 42               | 120    |
| **Histopathological examination**              |                      |                  |        |
| The NO. to be verified                         | 6607                 | 3753             | 10360  |
| The checks                                     | 5259                 | 2387             | 7646   |
| Dysplasia                                      | 58                   | 30               | 88     |
| Lobular carcinoma in situ                      | 6                    | 17               | 23     |
| Ductal carcinoma in situ                       | 48                   | 44               | 92     |
| Invasive ductal carcinoma                      | 617                  | 322              | 939    |
| Invasive lobular carcinoma                     | 67                   | 42               | 109    |
| Other types                                    | 13                   | 11               | 24     |
| **TNM staging**                                |                      |                  |        |
| The NO. to be verified                         | 697                  | 372              | 1069   |
| The NO. to be obtained                         | 621                  | 296              | 917    |
| 0-staging                                      | 17                   | 11               | 28     |
| 1-staging                                      | 143                  | 75               | 218    |

**The classification of BUS and MAM is based on the Breast Imaging Reporting And Data System (BI-RADS). The criteria for grading the BUS and MAM results as follows:**

0-grade: Incomplete assessment. Further imaging evaluation and comparison with previous findings is required.

1-grade: Negative. The Positive Predictive Value (PPV) is almost zero.

2-grade: Benign. The PPV is almost zero.

3-grade: Benign is more likely. The PPV is between 0% and 2%.

4-grade: Maybe malignant. The PPV is between 2% and 95%.

5-grade: Almost malignant. The PPV is between 95% and 100%.

**The TNM grades refer to specific stages of pathological or clinical stages. Priority should be given to pathological staging, if no pathological stages obtained, the clinical stages were filled in.**

TNM staging of 0-staging, 1-staging and 2-staging represents the early diagnosis of breast cancer.
### Variables

| Variables                | Non-poverty counties | Poverty counties | Total |
|--------------------------|----------------------|------------------|-------|
| 0a-staging               | 251                  | 104              | 355   |
| 0b-staging               | 108                  | 43               | 151   |
| ≥0-staging               | 102                  | 63               | 165   |
| The NO. of follow-up     | 806                  | 464              | 1270  |
| The NO. of treatment     | 800                  | 453              | 1253  |

#### Statistical indicators

| Variables                                                                 | Non-poverty counties | Poverty counties | Total |
|---------------------------------------------------------------------------|----------------------|------------------|-------|
| The No. of precancerous lesions and breast cancer                         | 796                  | 455              | 1251  |
| The No. of breast cancer                                                  | 749                  | 420              | 1169  |
| The No. of early diagnosis of breast cancer                               | 411                  | 190              | 601   |
| Breast cancer incidence ($/10^5$)                                         | 43.13                | 29.68            | 37.09 |
| Early detection proportion of breast cancer (%)                           | 66.18                | 64.19            | 65.54 |

**The classification of BUS and MAM is based on the Breast Imaging Reporting And Data System (BI-RADS). The criteria for grading the BUS and MAM results as follows:

0-grade: Incomplete assessment. Further imaging evaluation and comparison with previous findings is required.

1-grade: Negative. The Positive Predictive Value (PPV) is almost zero.

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5-grade: Almost malignant. The PPV is between 95% and 100%.

** The TNM grades refer to specific stages of pathological or clinical stages. Priority should be given to pathological staging, if no pathological stages obtained, the clinical stages were filled in.

TNM staging of 0-staging, I-staging and ≥a-staging represents the early diagnosis of breast cancer.

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### Comparison of basic and clinical information

Basic and clinical information are shown in Table 2. Breast cancer cases in poor counties increased in 2017 (N = 181, 43.10% vs. N = 255, 34.05%, P = 0.003). Breast cancer patients in non-poor and poor counties mainly received middle high school (N = 336, 44.86%) and primary school educations (N = 205, 48.84%), respectively. The proportion of breast cancer patients of Han ethnicity was lower in poor than in non-poor counties (N = 310, 73.81% vs. N = 682, 91.05%, P < 0.001, respectively). Most of the breast cancer patients in the two groups experienced menarche at 13–14 years of age (N = 406, 54.21% vs. N = 231, 55.00%, P = 0.046). The proportion of breast cancer patients with a reproductive history was lower in poor than in non-poor counties (N = 414, 55.27% vs. N = 741, 98.93%, P = 0.04). However, there were no significant differences between breast cancer patients in the two groups with respect to age, age at menarche, breastfeeding history, surgical history, hormone replacement history, and family history.
| Variables                  | Non-poverty counties | Poverty counties | $\chi^2$ | p     |
|----------------------------|----------------------|------------------|---------|-------|
| Year                       |                      |                  |         |       |
| 2016                       | 186                  | 104              | 11.634  | 0.003 |
| 2017                       | 255                  | 181              |         |       |
| 2018                       | 308                  | 135              |         |       |
| Age                        |                      |                  |         |       |
| 35–40                      | 58                   | 37               | 3.977   | 0.553 |
| 41–45                      | 110                  | 68               |         |       |
| 46–50                      | 232                  | 108              |         |       |
| 51–55                      | 188                  | 113              |         |       |
| 56–60                      | 92                   | 51               |         |       |
| ≥61                        | 69                   | 43               |         |       |
| Education                  |                      |                  |         |       |
| ≥Junior College           | 11                   | 8                | 68.105  | <0.001|
| High school                | 172                  | 40               |         |       |
| Middle high school        | 336                  | 151              |         |       |
| Primary school            | 204                  | 205              |         |       |
| Missing data               | 26                   | 16               |         |       |
| Ethnicity                  |                      |                  |         |       |
| Han                       | 682                  | 310              | 129.49  | <0.001|
| Others                    | 12                   | 90               |         |       |
| Missing data               | 55                   | 20               |         |       |
| Age at menarche            |                      |                  |         |       |
| <13                       | 133                  | 61               | 7.988   | 0.046 |
| 13–14                     | 406                  | 231              |         |       |
| 15–16                     | 156                  | 104              |         |       |
| >16                       | 20                   | 22               |         |       |
| Missing data               | 34                   | 2                |         |       |
| Reproductive history       |                      |                  |         |       |
| Yes                       | 741                  | 414              | 4.211   | 0.04  |
| No                        | 1                    | 4                |         | 0.95  |
| Missing data               | 7                    | 2                |         | 0.48  |
| Age at fertility           |                      |                  |         |       |
| 18–21                     | 261                  | 162              | 3.578   | 0.311 |
| 22–25                     | 416                  | 224              |         |       |
| 26–29                     | 33                   | 28               |         |       |
| ≥30                       | 4                    | 3                |         | 0.40  |
| Missing data               | 35                   | 3                |         | 0.40  |
| Menopause                  |                      |                  |         |       |
| Yes                       | 384                  | 227              | 0.772   | 0.38  |
| No                        | 358                  | 190              |         |       |
| Missing data               | 7                    | 3                |         | 0.71  |
| Breastfeeding history      |                      |                  |         |       |
| Yes                       | 682                  | 369              | 3.848   | 0.05  |
| No                        | 61                   | 49               |         | 1.16  |
| Missing data               | 6                    | 2                |         | 0.48  |
| Surgery history            |                      |                  |         |       |
| No                        | 712                  | 401              | 0.008   | 0.931 |
| Yes                       | 31                   | 17               |         | 4.05  |
| Missing data               | 37                   | 2                |         | 0.48  |
| Hormone replacement history|                      |                  |         |       |
| No                        | 727                  | 413              | 1.38    | 0.24  |
| Yes                       | 16                   | 5                |         | 1.19  |
Comparison of BUS results

Table 3 shows significant differences in the aspect ratio and edge of the solid mass in the left breast and cyst, the edge of the solid mass and the internal echo and blood flow of the solid mass in the right breast. Breast cancers in poor counties were more likely to have an aspect ratio of a solid tumor of more than 1 (N = 94, 40.17% vs. N = 162, 37.85%, P = 0.039) and an unclear edge of the solid mass in the left breast (N = 141, 60.26% vs. N = 232, 54.21%, P = 0.028). Conversely, cancers in non-poor counties were less likely to have a complicated cyst (N = 18, 2.00% vs. N = 15, 4.29%, P = 0.016) in the right breast. Moreover, the proportion of cancers without blood flow in the solid mass (N = 156, 36.19% vs. N = 51, 21.61%, P < 0.001) and with a clear edge of the solid mass (N = 140, 32.48% vs. N = 53, 22.46%, P = 0.02) in the right breast was higher in non-poor counties. On the whole, women with breast cancer in non-poor counties were encouraged to undergo a pathological examination compared with those in poor counties (N = 444, 59.28% vs. N = 203, 48.33%, P < 0.001, respectively). In a word, BUS examination results showed that there were differences in the cyst, margin, internal echo, and blood flow in the solid mass in the right breast. Women with breast cancer in poor counties were examined and found to have complex cysts, unclear edges, high internal echoes, an aspect ratio of the solid mass of more than 1, and rich blood flow to the solid mass.
### Table 3
Comparison of BUS results among female breast cancer cases between and non-poor counties.

| Variables          | Left Non-poverty counties | Left Poverty counties | Right Non-poverty counties | Right Poverty counties | χ² | P  |
|--------------------|---------------------------|-----------------------|---------------------------|------------------------|----|----|
|                    | N  | %      | N  | %      | N  | %      | N  | %      | χ² | P  |
| Cyst               |    |        |    |        |    |        |    |        |    |     |
| None               | 615 | 82.11  | 332 | 79.05  | 594 | 79.31  | 311 | 74.05  | 1.52 | 0.468 |
| Simple cysts       | 58  | 7.74   | 31  | 7.38   | 61  | 8.14   | 22  | 5.24   | 1.47 | 0.016 |
| Complicated cysts  | 18  | 2.40   | 15  | 3.57   | 15  | 2.00   | 18  | 4.29   |     |     |
| Missing data       | 58  | 7.74   | 42  | 10.00  | 79  | 10.55  | 69  | 16.43  |     |     |
| Total              | 749 | 100.00 | 420 | 100.00 | 749 | 100.00 | 420 | 100.00 |     |     |
| Solid mass         |    |        |    |        |    |        |    |        |    |     |
| None               | 321 | 42.86  | 186 | 44.29  | 318 | 42.46  | 184 | 43.81  | 2.124 | 0.346 |
| Single             | 346 | 46.19  | 179 | 42.62  | 323 | 43.12  | 179 | 42.62  |     |     |
| Multiple           | 52  | 6.94   | 37  | 8.81   | 50  | 6.68   | 31  | 7.38   |     |     |
| Missing data       | 30  | 4.01   | 18  | 4.29   | 58  | 7.74   | 26  | 6.19   |     |     |
| Total              | 749 | 100.00 | 420 | 100.00 | 749 | 100.00 | 420 | 100.00 |     |     |
| Solid mass -morphology |    |        |    |        |    |        |    |        |    |     |
| Round              | 23  | 5.37   | 13  | 5.56   | 20  | 4.64   | 12  | 5.08   | 6.086 | 0.108 |
| Oval               | 126 | 29.44  | 49  | 20.94  | 103 | 23.90  | 45  | 19.07  |     |     |
| Irregular          | 209 | 48.83  | 128 | 54.70  | 208 | 48.26  | 111 | 47.03  |     |     |
| Lobulated          | 18  | 4.21   | 6   | 2.56   | 16  | 3.71   | 10  | 4.24   |     |     |
| Missing data       | 52  | 12.15  | 38  | 16.24  | 84  | 19.49  | 58  | 24.58  |     |     |
| Total              | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 234 | 100.00 |     |     |
| Solid mass-aspect ratio |    |        |    |        |    |        |    |        |    |     |
| <1                 | 179 | 41.82  | 70  | 29.91  | 164 | 38.05  | 76  | 32.20  | 4.264 | 0.039 |
| ≥ 1                | 162 | 37.85  | 94  | 40.17  | 166 | 38.52  | 78  | 33.05  |     |     |
| Missing data       | 87  | 20.33  | 70  | 29.91  | 101 | 23.43  | 82  | 34.75  |     |     |
| Total              | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 234 | 100.00 |     |     |
| Solid mass-border  |    |        |    |        |    |        |    |        |    |     |
| Echo halo ring     | 107 | 25.00  | 59  | 25.21  | 108 | 25.06  | 55  | 23.31  | 1.264 | 0.261 |
| Sharp              | 210 | 49.07  | 92  | 39.32  | 197 | 45.71  | 83  | 35.17  |     |     |
| Missing data       | 111 | 25.93  | 83  | 35.47  | 126 | 29.23  | 98  | 41.53  |     |     |
| Total              | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 234 | 100.00 |     |     |
| Solid mass-edge    |    |        |    |        |    |        |    |        |    |     |
| Clear              | 140 | 32.71  | 56  | 23.93  | 140 | 32.48  | 53  | 22.46  | 4.836 | 0.028 |
| Non-clear          | 232 | 54.21  | 141 | 60.26  | 207 | 48.03  | 124 | 52.54  |     |     |
| Missing data       | 56  | 13.08  | 37  | 15.81  | 84  | 19.49  | 59  | 25.00  |     |     |
| Total              | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 234 | 100.00 |     |     |
| Solid mass-internal echo |    |        |    |        |    |        |    |        |    |     |
| Uniform            | 19  | 4.44   | 11  | 4.70   | 14  | 3.25   | 15  | 6.36   | 1.99 | 0.738 |
| Uneven             | 166 | 38.79  | 95  | 40.60  | 139 | 32.25  | 81  | 34.32  |     |     |
| Low                | 174 | 40.65  | 78  | 33.33  | 185 | 42.92  | 69  | 29.24  |     |     |
| Deng               | 7   | 1.64   | 3   | 1.28   | 7   | 1.62   | 3   | 1.27   |     |     |

*The classification of BUS is based on the Breast Imaging Reporting And Data System (BI-RADS). The criteria for grading the BUS results as follows:

0-grade: Incomplete assessment. Further imaging evaluation and comparison with previous findings is required.

1-grade: Negative. The Positive Predictive Value (PPV) is almost zero.

2-grade: Benign. The PPV is almost zero.

3-grade: Benign is more likely. The PPV is between 0% and 2%.

4-grade: Maybe malignant. The PPV is between 2% and 95%.

5-grade: Almost malignant. The PPV is between 95% and 100%.
### High

|      | 17 | 3.97 | 10 | 4.27 | 10 | 2.32 | 12 | 5.08 |
|------|----|------|----|------|----|------|----|------|
| Missing data | 45 | 10.51 | 37 | 15.81 | 76 | 17.63 | 56 | 23.73 |
| Total | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 236 | 100.00 |

### Solid mass-rear echo

| No change | 143 | 33.41 | 85 | 36.32 | 76 | 35.17 | 56 | 23.73 |
|----------|-----|-------|----|-------|----|-------|----|-------|
| Attenuation | 98 | 22.90 | 51 | 21.79 | 14 | 3.25 | 15 | 6.36 |
| Enhancement | 54 | 12.62 | 27 | 11.54 | 87 | 20.19 | 44 | 18.64 |
| Lateral acoustic shadow | 8 | 1.87 | 14 | 5.98 | 40 | 9.28 | 16 | 6.78 |
| Missing data | 125 | 29.21 | 57 | 24.36 | 103 | 23.90 | 78 | 33.05 |
| Total | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 236 | 100.00 |

### Solid mass-calculations

| No | 186 | 43.46 | 86 | 36.75 | 3.927 | 0.14 |
| Tiny | 111 | 25.93 | 52 | 22.22 | 99 | 22.97 | 38 | 16.10 |
| Thick | 61 | 14.25 | 44 | 18.80 | 61 | 14.15 | 33 | 13.98 |
| Missing data | 70 | 16.36 | 52 | 22.22 | 94 | 21.81 | 70 | 29.66 |
| Total | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 236 | 100.00 |

### Solid mass-blood flow

| No | 153 | 35.75 | 74 | 31.62 | 1.313 | 0.14 |
| Little | 137 | 32.01 | 70 | 29.91 | 123 | 28.54 | 75 | 31.78 |
| Rich | 73 | 17.06 | 46 | 19.66 | 59 | 13.69 | 51 | 21.61 |
| Missing data | 65 | 15.19 | 44 | 18.80 | 93 | 21.58 | 59 | 25.00 |
| Total | 428 | 100.00 | 234 | 100.00 | 431 | 100.00 | 236 | 100.00 |

### Classication

| 0 | 16 | 2.14 | 7 | 1.67 | 6.956 | 0.224 |
| 1 | 199 | 26.57 | 109 | 25.95 | 214 | 28.57 | 104 | 24.76 |
| 2 | 59 | 7.88 | 46 | 10.95 | 57 | 7.61 | 38 | 9.05 |
| 3 | 109 | 14.55 | 73 | 17.38 | 104 | 13.89 | 70 | 16.67 |
| 4 | 235 | 31.38 | 112 | 26.67 | 243 | 32.44 | 114 | 27.14 |
| 5 | 50 | 6.68 | 24 | 5.71 | 28 | 3.74 | 24 | 5.71 |
| Missing data | 81 | 10.81 | 49 | 11.67 | 88 | 11.75 | 61 | 14.52 |
| Total | 749 | 100.00 | 420 | 100.00 | 749 | 100.00 | 420 | 100.00 |

### Comparison of MAM results

We found that breast cancers in poor counties were more likely to have a structural disorder in the solid mass in both the left (N = 54, 25.35% vs. N = 85, 23.61%, P = 0.006) and right breast (N = 48, 22.54% vs. N = 68, 18.89%, P = 0.045), and to follow-up with a pathological examination (N = 201, 47.86% vs. N = 323, 43.12%, P = 0.022) (Table 4). In a word, breast cancers of women in poor counties were larger as judged by the MAM results of the two breasts.

*The classification of BUS is based on the Breast Imaging Reporting And Data System (BI-RADS). The criteria for grading the BUS results as follows:

0-grade: Incomplete assessment. Further imaging evaluation and comparison with previous findings is required.

1-grade: Negative. The Positive Predictive Value (PPV) is almost zero.

2-grade: Benign. The PPV is almost zero.

3-grade: Benign is more likely. The PPV is between 0% and 2%.

4-grade: Maybe malignant. The PPV is between 2% and 95%.

5-grade: Almost malignant. The PPV is between 95% and 100%.
Table 4
Comparison of MAM results among female breast cancer cases between poor and non-poor counties.

| Variables                  | Non-poverty counties | Poverty counties | \( \chi^2 \) | p    | Non-poverty counties | Poverty counties | \( \chi^2 \) | p    |
|----------------------------|---------------------|-----------------|-------------|------|---------------------|-----------------|-------------|------|
| X-ray examination          |                     |                 |             |      |                     |                 |             |      |
| No                        | 389                 | 207             | 0.756       | 0.385|                     |                 |             |      |
| Yes                       | 360                 | 213             |             |      |                     |                 |             |      |
| Total                     | 749                 | 420             |             |      |                     |                 |             |      |
| Variables                  |                     |                 |             |      |                     |                 |             |      |
| Left                      |                     |                 |             |      |                     |                 |             |      |
| Classification            |                     |                 |             |      |                     |                 |             |      |
| 0                         | 4                   | 3               | 2.877       | 0.719| 8                   | 3              | 2.22       | 0.661|
| 1                         | 65                  | 38              |             |      | 72                  | 38             | 20.00      | 22.54|
| 2                         | 55                  | 36              |             |      | 62                  | 36             | 17.22      | 17.37|
| 3                         | 47                  | 22              |             |      | 55                  | 22             | 15.28      | 12.21|
| 4                         | 133                 | 78              |             |      | 136                 | 78             | 37.78      | 38.50|
| 5                         | 26                  | 9               |             |      | 19                  | 9              | 5.28       | 7.98 |
| Missing data              | 30                  | 27              |             |      | 8                   | 2              | 2.22       | 0.00 |
| Total                     | 360                 | 213             |             |      | 360                 | 213            | 100.00     | 100.00|
| Solid mass                |                     |                 |             |      |                     |                 |             |      |
| No                        | 130                 | 77              | 0.295       | 0.587| 140                 | 82             | 38.89      | 38.50|
| Yes                       | 178                 | 95              |             |      | 158                 | 96             | 43.89      | 45.07|
| Missing data              | 52                  | 41              |             |      | 62                  | 35             | 17.22      | 16.43|
| Total                     | 360                 | 213             |             |      | 360                 | 213            | 100.00     | 100.00|
| Solid mass -Suspected calcification | | | | | | | |
| No                        | 80                  | 36              | 0.004       | 0.951| 74                  | 40             | 20.56      | 18.78|
| Yes                       | 83                  | 38              |             |      | 72                  | 33             | 20.00      | 15.49|
| Missing data              | 197                 | 139             |             |      | 214                 | 140            | 59.44      | 65.73|
| Total                     | 360                 | 213             |             |      | 360                 | 213            | 100.00     | 100.00|
| Solid mass -structure disorder | | | | | | | |
| No                        | 78                  | 22              | 7.613       | 0.006| 71                  | 28             | 19.72      | 13.15|
| Yes                       | 85                  | 54              |             |      | 68                  | 48             | 18.89      | 22.54|
| Missing data              | 197                 | 137             |             |      | 221                 | 137            | 61.39      | 64.32|
| Total                     | 360                 | 213             |             |      | 360                 | 213            | 100.00     | 100.00|
| Solid mass site           |                     |                 |             |      |                     |                 |             |      |
| The central               | 13                  | 11              | 5.711       | 0.222| 7                   | 5              | 1.94       | 2.35 |
| Up inside                 | 7                   | 0               |             |      | 7                   | 1              | 1.94       | 0.47 |

*analyzed using Fisher's exact test.

The classification of MAM is based on the Breast Imaging Reporting And Data System (BI-RADS). The criteria for grading the MAM results as follows:

0-grade: Incomplete assessment. Further imaging evaluation and comparison with previous findings is required.

1-grade: Negative. The Positive Predictive Value (PPV) is almost zero.

2-grade: Benign. The PPV is almost zero.

3-grade: Benign is more likely. The PPV is between 0% and 2%.

4-grade: Maybe malignant. The PPV is between 2% and 95%.

5-grade: Almost malignant. The PPV is between 95% and 100%.
|                | 22 | 6.11 | 11 | 5.16 | 22 | 6.11 | 12 | 5.63 |
|----------------|----|------|----|------|----|------|----|------|
| Down inside    | 12 | 3.33 | 4  | 1.88 | 9  | 2.50 | 9  | 4.23 |
| Up outside     | 91 | 25.28| 45 | 21.13| 76 | 21.11| 43 | 20.19|
| Down outside   | 215| 59.72|142 | 66.67|239| 66.39|143 | 67.14|
| Missing data   |    |      |    |      |    |      |    |      |
| Total          | 360| 100.00|213|100.00|360|100.00|213|100.00|

*analyzed using Fisher's exact test.

The classification of MAM is based on the Breast Imaging Reporting And Data System (BI-RADS). The criteria for grading the MAM results as follows:

0-grade: Incomplete assessment. Further imaging evaluation and comparison with previous findings is required.

1-grade: Negative. The Positive Predictive Value (PPV) is almost zero.

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4-grade: Maybe malignant. The PPV is between 2% and 95%.

5-grade: Almost malignant. The PPV is between 95% and 100%.

Comparison of pathological examination results

Pathological characteristics are displayed in Table 5. Regarding clinical and pathological staging, breast cancers were staged to a lesser extent in poor counties than in non-poor counties (N = 203, 49.27% vs. N = 484, 65.58%, P < 0.001 and N = 187, 45.39% vs. N = 439, 59.49%, P < 0.001, respectively). Breast cancers in non-poor counties were more likely to be considered as c-TNM clinical staging grade two (N = 282, 59.75%, N = 82, 43.62%, P = 0.008) and p-TNM clinical staging grade two (N = 245, 57.92%, N = 72, 41.62%, P = 0.009). However, breast cancer patients in poor counties were less likely to be treated following a pathological diagnosis (N = 394, 93.81%, N = 713, 95.19%, P = 0.026). Breast cancer cases in poor counties had a lower proportion of clinical and pathological staging and higher breast cancer rates for those that obtained clinical and pathological staging in both breasts compared with women in non-poor counties.
Table 5
Comparison of pathological examination results among female breast cancer cases between poor and non-poor counties

| Variables                        | Non-poverty counties | Poverty counties | χ²  | p     | Variables                        | Non-poverty counties | Poverty counties | χ²  |
|----------------------------------|----------------------|-----------------|-----|-------|----------------------------------|----------------------|-----------------|-----|
| Pathological examination        |                      |                 |     |       | Classification                   |                      |                 |     |       |
| Yes                              | 738                  | 98.53           | 412 | 98.10 | Dysplasia                        | 1                    | 0.14            | 0   | 0.00 |
| No                               | 3                    | 0.40            | 2   | 0.48  | Invasive lobular carcinoma       | 70                   | 9.49            | 38  | 9.22 |
| Missing data                     | 8                    | 1.07            | 6   | 1.43  | Invasive ductal carcinoma        | 570                  | 77.24           | 309 | 75.00|
| Total                            | 749                  | 100.00          | 420 | 100.00| Invasive lobular carcinoma and Invasive ductal carcinoma | 1                    | 0.14            | 1   | 0.24 |
|                                  |                      |                 |     |       | fibrous adenoma                  | 6                    | 0.81            | 0   | 0.00 |
| Treatment                        |                      |                 |     |       | Lobular carcinoma in situ        | 2                    | 0.27            | 0   | 0.00 |
| Yes                              | 713                  | 95.19           | 394 | 93.81 | Other types                      | 25                   | 3.39            | 12  | 2.91 |
| No                               | 4                    | 0.53            | 9   | 2.14  | Missing data                     | 63                   | 8.54            | 52  | 12.62|
| Missing data                     | 32                   | 4.27            | 17  | 4.05  | Total                            | 749                  | 100.00          | 420 | 100.00|
| Total                            | 778                  | 100.00          | 420 | 100.00|                                  |                      |                 |     |       |
| Clinical staging                 |                      |                 |     |       |                                  |                      |                 |     |       |
| Obteimention                     | 484                  | 65.58           | 203 | 49.27 | Pathological staging             | 439                  | 59.49           | 187 | 45.39|
| Not-obtainment                   | 191                  | 25.88           | 163 | 39.56 |                                  | 216                  | 29.27           | 156 | 37.86|
| Missing data                     | 63                   | 8.54            | 46  | 11.17 |                                  | 83                   | 11.25           | 69  | 16.75|
| Total                            | 738                  | 100.00          | 420 | 100.00|                                  |                      |                 |     |       |
| p-TNM clinical staging           |                      |                 |     |       |                                  |                      |                 |     |       |
| Yes                              | 472                  | 97.52           | 188 | 92.61 | Dobcription                       | 423                  | 96.36           | 173 | 92.51|
| No                               | 8                    | 1.65            | 5   | 2.46  |                                  | 10                   | 2.28            | 6   | 3.21 |
| Missing data                     | 4                    | 0.83            | 10  | 4.93  |                                  | 6                    | 1.37            | 8   | 4.28 |
| Total                            | 484                  | 100.00          | 203 | 100.00|                                  |                      |                 |     |       |
| c-TNM clinical staging grade     |                      |                 |     |       | p-TNM clinical staging grade      |                      |                 |     |       |
| 0                                | 4                    | 0.85            | 1   | 0.53  | 0                                | 0                    | 0.95            | 2   | 1.16 |
| 1                                | 103                  | 21.82           | 48  | 25.53 | 1                                | 88                   | 20.80           | 51  | 29.48|
| 2                                | 282                  | 59.75           | 82  | 43.62 | 2                                | 245                  | 57.92           | 72  | 41.62|
| 3                                | 64                   | 13.56           | 41  | 21.81 | 3                                | 66                   | 15.60           | 37  | 21.39|
| 4                                | 7                    | 1.48            | 3   | 1.60  | 4                                | 8                    | 1.89            | 3   | 1.73 |
| Missing data                     | 12                   | 2.54            | 13  | 6.91  | Missing data                     | 12                   | 2.84            | 8   | 4.62 |
| Total                            | 472                  | 100.00          | 188 | 100.00| Total                            | 423                  | 100.00          | 173 | 100.00|

*analyzed using Fisher's exact test.

*c-TNM clinical staging grade was made before treatment and obtained by physical diagnosis, imageological diagnosis, pathological biopsy and other means.

*p-TNM clinical staging grade was made only for definitive surgical and postoperative pathologic inspections, which was based on a combination of clinical staging and surgical outcome. The meaning of c-TNM clinical staging grade and p-TNM clinical staging grade was based on the seventh edition of the cancer staging manual of the American Joint Committee on Cancer (AJCC).

Binary logistic regression analysis results of risk factors among breast cancer patients in poor counties
Binary logistic regression analysis was performed in 1015 cases after deleting the cases with missing values in the analysis variables. It indicated that the following risk factors were related to breast cancer in poor counties: year (2017 compared with 2016), education, ethnicity and reproductive history (OR > 1, P < 0.05). All results of the binary logistic regression analysis are listed in Table 6.

**Tables 6. Binary logistic regression analysis of female breast cancer related factors in poor counties.**

| Variables                        | B    | S.E. | Wals  | df | Sig. | aOR  | aOR 95% C.I. |
|----------------------------------|------|------|-------|----|------|------|--------------|
| Year (Ref. = 2016)               |      |      |       |    |      |      |              |
| 2017                             | 0.376| 0.185| 4.150 | 1  | 0.042| 1.456| 1.014 – 2.091|
| 2018                             | -0.217| 0.188| 1.337 | 1  | 0.248| 0.805| 0.556 – 1.163|
| Education (Ref. = junior college)| 55.901| 3     | 1     | 0  | 0.000|      |              |
| High school                      | -0.817| 0.588| 1.934 | 1  | 0.164| 0.442| 0.140 – 1.397|
| Middle high school               | -0.119| 0.565| 0.044 | 1  | 0.833| 0.888| 0.293 – 2.685|
| Primary school                   | 0.711 | 0.565| 1.584 | 1  | 0.208| 2.035| 0.673 – 6.155|
| Ethnicity of others (Ref. = Han) | 2.674 | 0.324| 67.958| 1  | 0.000| 14.494| 7.675 – 27.369|
| Reproductive history (Ref. = Yes)| 0.432 | 0.167| 5.573 | 1  | 0.016| 1.567| 1.086 – 2.262|
| constant                         | -0.907| 0.560| 2.620 | 1  | 0.106| 0.404|              |

*Forward Wald of Binary logistic regression analysis.*

* *aOR was adjusted by age, age at menarche, age at fertility, reproductive history, menopause, Breastfeeding history.*

**Discussion**

To the best of our knowledge, this is the first study analyzing data from the breast cancer screening program in China. In this study, we explored differences related to the effects of implementing the breast cancer screening program and to the clinical examination results between breast cancer patients in poor and non-poor counties in rural areas of Hunan province from 2016–2018. In this study, we found that indexes of the breast cancer screening program including the proportion of breast cancers detected early, the breast cancer incidence, the proportion of breast cancer cases that underwent pathological examination, and the MAM examination rate were lower in poor counties than in non-poor counties. This study indicated that the incidence of breast cancer was lower in poor areas, which was similar with other studies. The prevalence of breast cancer in rural areas in our study was 37.09/10^5 in Hunan province, which was higher than the 25.28/10^5 in rural areas of China in 2010, sourced from a total of 145 population-based cancer registries and the 21.0/10^5 in rural areas of Jiangsu province based on statistics from eligible cancer registries in Jiangsu in China from 2006–2010. Furthermore, it was lower than that reported in developed countries of 73.4/10^5, but higher than that in developing countries of 31.3/10^5, according to global cancer statistics from 2012. In poor rural areas, breast cancer patients were undereducated and menarche occurred at an older age. Worldwide, the incidence of breast cancer increases in parallel with socioeconomic development. There is no doubt that changes in breast cancer risk have taken place in parallel with socioeconomic development and urbanization over the past three decades in China. The allocation of and accessibility to health resources was reduced in poor counties compared with those in non-poor counties, resulting in lower pathological examination and MAM rates. When planning breast screening programs, regional differences in breast cancer incidence and allocation of and accessibility to health resources should be taken into account.

In this study, we first found that there were differences in various factors including year, level of education, ethnicity, age at menarche, and reproductive history between breast cancer patients in poor and non-poor counties. Second, binary logistic regression analysis showed that the year (2017 vs. 2016), non-Han ethnicity, education, and reproductive history were associated with an increased risk of breast cancer in poor counties. Since the program was launched in 2016, women with symptoms volunteered to participate in the program in 2017, resulting in an increase in the number of patients with breast cancer detected.

Racial disparity persists in breast screening, such as Hispanic and non-Hispanic white women. In this study, other ethnicities except Han have been found to have a lower education level and socioeconomic status, and reduced access to health care. Age at menarche was one of the breast cancer risk factors. Early age at menarche is associated with an increased risk of breast cancer.

Doctors more readily advised women with breast cancer in poor counties to receive pathological examination following BUS and MAM examinations. The proportion of women receiving treatment for breast cancer in poor counties was lower than that for those in non-poor counties. In other words, women with breast cancer in poor counties were found to have a higher rate of malignancy and reduced access to medical services despite the lower incidence of breast cancer in poor compared with non-poor counties. Other similar studies have come to the same conclusion. For example, Williams et al. found that the odds of a late diagnosis among women living in non-metropolitan or rural counties was over 11% higher compared with their metropolitan or urban counterparts, and...
that black women had a 1.5-fold increased odds of being diagnosed with late-stage breast cancer compared with their white counterparts, despite the fact that black women have a lower incidence of breast cancer than white women\textsuperscript{29}. Nguyen-Pham et al. found that rural breast cancer patients had 1.19 higher odds of being diagnosed with late-stage breast cancer compared with urban breast cancer patients\textsuperscript{30}. Anderson et al. concluded that a lack of breast cancer screening and living in poorer rural areas were associated with a 3.31 times greater rate of women diagnosed with later stage breast cancer in Appalachia compared with those living in less deprived regions\textsuperscript{31, 32}. Although socioeconomic status has been found to be a key determinant of cancer stage at diagnosis in Western countries\textsuperscript{33}, there was a systematic study on the relationship between socioeconomic status and breast cancer stage at diagnosis in China, which also concluded that women in low socioeconomic status areas were more likely to be diagnosed at a later breast cancer stage than those in higher socioeconomic status areas in China\textsuperscript{34, 35}. From our study, it appears that women with breast cancer in poor counties are in need of more diagnostic and clinical than screening services. This finding helps to emphasize the fact that just providing free screening services is not enough to make up for a lack of preventive care for low income and uninsured women\textsuperscript{36}.

Environmental factors play an important role in the development of cancer and suggest that region-tailored cancer prevention strategies are warranted\textsuperscript{37}. For improving breast cancer outcomes in rural areas of China, we suggest providing free screening services that are also supported with more diagnostic and clinical services as a long-term policy of benefiting women in rural areas and ensuring that they be made available in poor areas in Hunan province.

Our study had some limitations. First, we did not investigate some important risk factors such as economic income and body mass index because we obtained the data from the unified national table. Most importantly, we could not analyze and compare the age distribution between poor and non-poor counties to see whether the differences that the breast cancer incidence was lower in poor counties are due to the age distribution because of the data unavailability. Second, there was recall bias regarding the basic information that was obtained for the breast cancer cases. Third, though the whole province had carried out a unified training for all doctors involved in administering BUS, MAM, and pathological examinations, there were differences in the quality of the examinations and information filling. It was also the reason of information missing.

Conclusions

Population-based breast cancer screening programs in rural areas showed that there were differences in the evaluation indicators and clinicopathological characteristics of the breast cancer cases according to the county-level poverty status. Though the incidence of breast cancer was lower in poor than in non-poor counties, women in poor areas were more likely to be diagnosed at later breast cancer stages than those in non-poor areas, and additional diagnostic and clinical services should be provided in poor areas to address these concerns.

Abbreviations

BUS Breast ultrasonography
MAM Mammography
TNM Tumor, Node, and Metastasis
km\textsuperscript{2} Square kilometer,
OR Odds ratio
BI-RADS Breast Imaging Reporting And Data System
AJCC American Joint Committee on Cancer

Declarations

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Author contributions

Conceptualization: XLL and WYL. Data curation: XLL, WAH, LHY, LT, WYX, XDH, KFJ , LZY, CHX and FJQ. Formal analysis: XLL and YGH. Methodology: XLL, WYL, LZY, CXH and FJQ. Project administration: XLL, FJQ and CXH. Supervision: FJQ, WYL and LZY. Visualization: XLL and LZY. Writing original draft: XLL. Writing, review & editing: XLL, LZY, WYL, FJQ and CXH.

Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflicts of interest.

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**Ethical approval** This article does not contain any studies with animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study. The study was approved by the Ethics Committee of the Hunan Provincial Maternal and Children Health Care Hospital. (No. 2019-15).

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Figures
Figure 1

Schematic of the breast cancer screening process followed in Hunan province, China.

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