ORIGINAL ARTICLE

Retrospective Study

Clinical and pathological features and risk factors for primary breast cancer patients

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Abstract

BACKGROUND

Breast cancer is the most common malignancy in women all around the world. According to the latest statistics in 2018, there were more than 2.08 million new breast cancer cases all around the world and more than 620000 deaths; the proportion of breast cancer deaths in women with cancer is 15%. By studying age, clinicopathological characteristics and molecular classification, age at menarche, age at birth, number of births, number of miscarriages, lactation time, surgical history of benign breast lesions, history of gynecological diseases, and other factors, we retrospectively summarized and compared the disease history of patients with primary breast cancer and patients with benign thyroid tumors admitted to our hospital in the past 10 years to explore the clinicopathological characteristics and risk factors for primary breast cancer.

AIM

To investigate the clinical and pathological features and risk factors for primary breast cancer treated at our center in order to provide a reference for the prevention and treatment of breast cancer in the Zhuhai-Macao region.

METHODS

Through a retrospective case-control study, 149 patients with primary breast cancer diagnosed and treated at Zhuhai Hospital of Guangdong Provincial Hospital of Traditional Chinese Medicine from January 2013 to March 2020 were included as a case group, and 165 patients with benign breast tumors diagnosed and treated from January 2019 to March 2020 were included as a control group. The data collected included age, age at menarche, age at first birth, number of births, number of miscarriages, lactation time, history of surgery for benign breast lesions, history of familial malignant tumors, history of gynecological diseases, history of thyroid diseases, and the tumor characteristics of the patients in the case

group including pathological diagnosis, pathological type, tumor size, lymph node metastasis, distant metastasis, stage, and molecular classification, among others. In the case group, the chi-square test was used to analyze the clinical and pathological features of patients in three age groups (< 40, 40-59, and ≥ 60 years). A multifactor logistic regression analysis was used to analyze correlations between the two groups.

RESULTS

Among 149 patients with primary breast cancer, the average age was 48.20 ± 12.06 years, and the proportion of patients at 40-59 years old was the highest, accounting for 61.8% of cases. The molecular type was mainly luminal B type, accounting for 69.2% of cases, and at the time of diagnosis, the tumor stage was mainly stage I/II, accounting for 62.4% of cases. There were no statistically significant differences in the distributions of tumor location, pathological type, tumor size, lymph node metastasis, stage, or molecular classification among the three age groups (< 40, 40-59, and ≥ 60 years) ($P ≥ 0.05$). The differences in the distribution of distant metastasis among the three age groups (< 40, 40-59, and ≥ 60 years) were statistically significant ($P < 0.01$). The differences in lactation time, history of familial malignant tumors, history of gynecological diseases, and history of thyroid diseases between the two groups were not statistically significant ($P ≥ 0.05$). The differences in age at disease diagnosis, age at menarche, and history of surgery for benign breast lesions were statistically significant ($P < 0.01$). The difference in age at first birth was also statistically significant ($P < 0.05$).

CONCLUSION

The highest incidence of breast cancer in the Zhuhai-Macao region is present among women aged 40-59 years. There is a larger proportion of stage I/II patients, and the luminal B type is the most common molecular subtype. Distant metastasis occurs mainly in the ≥ 60-year-old group at the first diagnosis; increased age, late age at menarche, and late age at first birth may be risk factors for primary breast cancer, and a history of surgery for benign breast lesions may be a protective factor for primary breast cancer.

Key Words: Primary breast cancer; Clinical pathological features; Risk factors; Retrospective study

Core Tip: This study found that distant metastasis is more common among elderly women aged ≥ 60 years; advanced age, late menarche, and late childbearing age are risk factors for the onset of primary breast cancer; and a surgical history of benign breast lesions is the primary protective factor against breast cancer.

INTRODUCTION

Breast cancer is the most common malignancy in women all around the world. According to the latest statistics in 2018, there were more than 2.08 million new breast cancer cases all around the world and more than 620000 deaths; the proportion of breast cancer deaths in women with cancer is 15%[1,2].

In this retrospective case-control study, the age, clinical pathological features and molecular classification, age of menarche, age of first birth, number of births, number of miscarriages, lactation time, history of operation of benign breast lesions, history of gynecological diseases, history of thyroid diseases, and so on of primary breast cancer

patients and patients with benign breast tumors admitted to our hospital in the past 10 years were retrospectively summarized and compared, in order to understand the clinical pathological characteristics and risk factors of primary breast cancer in Zhuhai area, and to provide reference for the prevention and screening of this malignancy.

MATERIALS AND METHODS

Through a retrospective case-control study, 149 patients with primary breast cancer diagnosed at the Department of Breast Medicine of Zhuhai Hospital of Guangdong Provincial Hospital of Traditional Chinese Medicine from January 2013 to March 2020 were included as a case group; they ranged in age from 26-95 years, with an average age of (48.20 ± 12.06) years. One hundred and sixty-five patients with benign breast tumors admitted to Zhuhai Hospital of Guangdong Traditional Chinese Medicine Hospital from January 2019 to March 2020 were included as a control group; they ranged in age from 28-69 years, with an average age of (42.36 ± 7.7) years.

Data including sex, age of disease, age of menarche, lactation time, family history of malignant tumor, history of gynecological disease, history of thyroid disease, history of benign breast surgery, contact telephone number, and so on[2,3] were collected in both groups. We also collected tumor location, tumor size, pathological diagnosis, lymph node metastasis, distant metastasis, stage, molecular type, and so on.

SPSS 22.0 statistical software was used for statistical analyses. The measurement data are expressed by the mean ± SD; the *t* test was used in the comparison between groups. The composition ratio was compared between groups using the chi-square test. Multi-factor Logistic regression analysis was used in the correlation analysis at α = 0.05.

RESULTS

Clinical and pathological features of patients with primary breast cancer

Among 149 patients with primary breast cancer, the proportion of patients at 40-59 years old was the highest, accounting for 61.8%; the proportion of patients ≥ 60 years old was the lowest, accounting for 15.4% (Table 1). The stage of tumor was mainly stage I/II, accounting for 69.2%; stage IV was rare, just accounting for 2.0%. Molecular type was mainly luminal B type, accounting for 62.4%, among which the human epidermal growth factor receptor 2 (HER2) negative type was higher than that of the HER2 positive type, and the proportion of HER2 overexpression type was the least, accounting for 7.4%.

Clinical and pathological features of primary breast cancer patients in different age groups

As shown in Table 2, there were no significant differences in the distributions of tumor location, pathological type, tumor size, lymph node metastasis, stage, or molecular classification in the three age groups. The proportion of patients with distant metastasis at the first diagnosis was different in the three age groups (*P* < 0.05). The patients at ≥ 60 years old most often developed distant metastasis, accounting for 8.7%, followed by patients at 40-59 years (1.09%) and patients at < 40 years old (0%).

Logistic regression analysis of risk factors for patients with primary breast cancer

As shown in Table 3, the number of births, number of miscarriages, lactation time, history of family malignant tumors, history of gynecological diseases, and history of thyroid diseases were not statistically significant between the two groups (*P* ≥ 0.05), but age, age at menarche, age at first birth, and history of benign breast surgery were statistically different in the two groups (*P* < 0.05); and odds ratio values showed that the risk of breast cancer increased with patient age. The risk of breast cancer in subjects between 40 and 59 years old was 1.828 times higher than that of subjects < 40 years old, and the risk of breast cancer in subjects ≥ 60 years old was 7.842 times higher than that of subjects < 40 years old. The risk of breast cancer increased with the age at menarche. The risk in subjects with the age at menarche > 14 was 2.2626 times higher than that of subjects with the age at menarche ≤ 14. The risk of breast cancer in subjects with late childbearing was higher than that of subjects with early childbearing (1.086 times). The history of benign breast surgery was a protective factor for breast cancer risk (0.286 times).

Table 1 Clinical and pathological features of patients with primary breast cancer

Clinical or pathological feature	*n* (%)
< 40 yr	34 (22.8)
40-59 yr	92 (61.8)
≥ 60 yr	23 (15.4)
Stage 0	16 (10.7)
Stage I	46 (30.9)
Stage II	57 (38.3)
Stage III	27 (18.1)
Stage IV	3 (2.0)
Luminal A	31 (20.8)
Luminal B (HER2 negative)	54 (36.2)
Luminal B (HER2 positive)	39 (26.2)
HER2 over expression type	11 (7.4)
Three negative type	14 (9.4)

HER2: Human epidermal growth factor receptor 2.

DISCUSSION

Breast cancer is the most common cancer among women in both developed and developing countries[1,3,4]. Luminal B (HER2 negative) breast cancer patients account for the majority of breast cancer patients in China, and luminal B cancer is common among Chinese breast cancer patients who are under 40 years old[5-7].

This study showed that the proportion of breast cancer patients aged 40-59 years was 61.8%. Invasive carcinoma occurred in 89.3% of the patients, and invasive ductal cancer was the main type of invasive carcinoma. Breast cancer patients with stage I/II disease accounted for 69.2% of cases. Luminal B was the most common molecular type, accounting for 62.4% of cases, of which 36.2% were HER2 negative and 26.2% were positive. This study is consistent with the large-sample data previously reported for age at disease, tumor type, stage, and molecular classification, among other variables[8-10].

Distant metastasis was more common in the older age group (≥ 60 years old), which is related to the lack of attention to physical examination of the breast among the elderly population. Community doctors should incorporate physical examination items into daily physical examinations to achieve early detection, early diagnosis, and early treatment.

The results of this study showed that increased age, late age at menarche, and late birth were risk factors for breast cancer. Gu *et al*[11] suggested that transcriptome alterations during aging may contribute to breast tumorigenesis and that dynein light chain Tctex-type 3, procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide III, and aristaless-like homeobox4 play significant roles in breast cancer progression. A randomized controlled trial[12,13] in the United Kingdom also suggested that reducing the lower age limit for screening could potentially reduce breast cancer mortality. On the other hand, recent research has proven that breast cancer is more strongly associated with exposure to female hormones[13-15], which is why late menarche age is a risk factor for breast cancer. Zhang *et al*[16] suggested that reproductive factors associated with breast cancer risk might also affect prognosis. Some studies have indicated an adverse effect of late age at first pregnancy[17-19], and gestational age at delivery may influence the risk of maternal breast cancer[20,21]. At the same time, our research results showed that the number of births, abortion times, lactation time, gynecological diseases, thyroid diseases, and family history of breast or other malignant tumors were not correlated with the risk of breast cancer.

There are some shortcomings in this study: (1) The data of hospitalized breast cancer patients in Zhuhai Hospital of Guangdong Traditional Chinese Medicine Hospital were collected for only 10 years, and this is a single-center study of clinical

Table 2 Clinical and pathological features of patients with primary breast cancer in different age groups, *n* (%)

	< 40 yr	40-59 yr	≥ 60 yr	χ^2	*P* value
Left	14 (41.2)	50 (54.3)	9 (39.1)	4.246	0.374
Right	20 (58.8)	40 (43.5)	13 (56.5)		
Bilateral	0 (0.0)	2(2.2)	1 (4.3)		
Carcinoma *in situ*	4 (11.8)	16 (17.4)	1 (4.3)	2.783	0.249
Invasive carcinoma	30 (88.2)	76 (82.6)	22 (95.7)		
Tis	2 (5.9)	14 (15.2)	0 (0.0)	15.469	0.051
T1	16 (47.1)	31 (33.7)	10 (43.5)		
T2	12 (35.3)	38 (41.3)	9 (39.1)		
T3	4 (11.8)	7 (7.6)	1 (4.3)		
T4	0 (0.0)	2 (2.2)	3 (13.0)		
N0	17 (50.0)	57 (62.0)	10 (43.5)	6.486	0.371
N1	11 (32.4)	19 (20.7)	8 (34.8)		
N2	5 (14.7)	8 (8.7)	2 (8.7)		
N3	1 (2.9)	8 (8.7)	3 (13.0)		
M0	34 (100)	9 1(98.9)	21 (91.3)	6.304	0.043
M1	0 (0.0)	1 (1.1)	2 (8.7)		
Luminal A	7 (20.6)	16 (17.4)	8 (34.8)	6.154	0.63
Luminal B(HER2 negative)	13 (38.2)	32 (34.8)	9 (39.1)		
Luminal B (HER2 positive)	8 (23.5)	28 (30.4)	3 (13.0)		
HER2 over expression type	3 (8.8)	6 (6.5)	2 (8.7)		
Three negative type	3 (8.8)	10 (10.9)	1 (4.3)		

HER2: Human epidermal growth factor receptor 2.

pathological data from a small sample, making parts of the analysis unrepresentative; and (2) There were no registered or classified household registrations or local residence times of patients; therefore, there may be selective bias in the analysis of the clinical pathological features of primary breast cancer in the Zhuhai-Macao region. Further studies with large multicenter samples are needed.

CONCLUSION

This study found that distant metastasis at first diagnosis is more common among elderly women aged ≥ 60 years, that aging, late menarche, and late childbearing age are risk factors for the onset of primary breast cancer, and that a surgical history of benign breast lesions is the primary protective factor against breast cancer.

Table 3 Correlation analysis of risk factors for patients with primary breast cancer

Variable	B	Standard error	Waldorf	*P* value	Exp (B)	95%CI of Exp (B)	
						Lower limit	Upper limit
< 40 yr			14.059	0.001			
40-59 yr	0.603	0.277	4.741	0.029	1.828	1.062	3.148
≥ 60 yr	2.059	0.568	13.128	< 0.001	7.842	2.574	23.892
Age at menarche (≤ 14 yr, > 14 yr)	0.965	0.261	13.633	< 0.001	2.626	1.573	4.384
Age at first birth	0.083	0.038	4.84	0.028	1.086	1.009	1.17
Number of births	0.266	0.176	2.291	0.13	1.305	0.924	1.843
Number of miscarriages	-0.207	0.112	3.414	0.065	0.813	0.652	1.013
Breastfeeding (mo)	-0.009	0.011	0.665	0.415	0.991	0.97	1.013
History of family malignant tumors	0.346	0.311	1.238	0.266	1.413	0.768	2.599
History of benign breast surgery	-1.355	0.489	7.664	0.006	0.258	0.099	0.673
Gynecological diseases	-0.357	0.299	1.42	0.233	0.7	0.389	1.258
Thyroid disease	-0.156	0.305	0.261	0.609	0.856	0.471	1.555

ARTICLE HIGHLIGHTS

Research background

Breast cancer is the most common malignancy in women all around the world. According to the latest statistics in 2018, there were more than 2.08 million new breast cancer cases all around the world and more than 620000 deaths; the proportion of breast cancer deaths in women with cancer is 15%.

Research motivation

To retrospectively summarize and compare the disease history of patients with primary breast cancer and patients with benign thyroid tumors admitted to our hospital in the past 10 years to understand the clinicopathological characteristics and risk factors for primary breast cancer.

Research objectives

To investigate the clinical and pathological characteristics and risk factors for primary breast cancer and the Zhuhai to provide reference for prevention and screening of breast cancer.

Research methods

Through a retrospective case-control study, 149 patients with primary breast cancer diagnosed at the Department of Breast Medicine of Zhuhai Hospital of Guangdong Provincial Hospital of Traditional Chinese Medicine from January 2013 to March 2020 were included as a case group; they ranged in age from 26-95 years, with an average age of (48.20 ± 12.06) years. In addition, 165 patients with benign breast tumors admitted to Zhuhai Hospital of Guangdong Traditional Chinese Medicine Hospital from January 2019 to March 2020 were included as controls;, they ranged in age from 28-69 years, with an average age of (42.36 ± 7.7) years. SPSS22.0 statistical software was used for statistical analyses.

Research results

Invasive ductal cancer was the main type of invasive carcinoma. Breast cancer patients with stage I/II disease accounted for 69.2% of all cases. Luminal B was the most common molecular type, accounting for 62.4% of cases, of which 36.2% were HER2 negative and 26.2% were positive.

Research conclusions

This study found that distant metastasis at first diagnosis is more common among elderly women aged ≥ 60 years, that advanced age, late menarche, and late childbearing age are risk factors for the onset of primary breast cancer, and that a

surgical history of benign breast lesions is the primary protective factor against breast cancer.

Research perspectives

Further studies with large multicenter samples are needed.

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