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Original Article

Molecular subtypes of breast cancer with pathological features prevalent in Zhuang and Han ethnic groups in China: a study of 990 patients

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Abstract: To compare the difference of molecular types and clinical pathological characteristics of breast cancer between Zhuang and Han ethnic groups of patients, and to provide improved treatment regimens for individuals with breast cancer. 278 cases of Zhuang women with breast cancer and 712 cases of Han female breast cancer patients were selected and divided into four molecular subtypes according to expression of 4 immunohistochemical (IHC) markers: estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER-2) and Ki-67. Then they were divided into the 4 subtypes, which were Luminal A type, Luminal B type, HER-2 over-expression type and the Triple negative type, and these were analyzed and compared with clinical and pathological features. The molecular subtypes of the Zhuang and Han patients were mainly Luminal B, but the difference was not statistically significant ($P > 0.05$). However, there were several clinical parameters that were found to be statistically different between the Zhuang and Han patients in the 4 subtypes classified including family history of breast cancer, the number of births, incidence of tumor position and tumor diameter as well as differences in the operation mode, endocrine therapy and in the proportion of patients receiving chemotherapy ($P < 0.05$). There are differences in molecular classification and clinical pathological features between the Zhuang and Han female patients with breast cancer, and a better understanding of these differences can provide guidance for improved individual treatment of breast cancer.

Keywords: Breast cancer, immunohistochemical, molecular subtype, clinical pathological characteristics, Zhuang, Han

Introduction

Breast cancer is one of the most common malignant tumors in elderly women and the incidence and mortality of breast cancer has been increasing in recent years [1]. The incidence and mortality of breast cancer are affected by many factors, such as age, race, heart factors, tumor size, grade, clinical stage and so on [2]. Clinical research on molecular typing of breast cancer has become increasingly important in recent years. In 2000, Perou et al pointed out that the clinical characteristics and prognosis of breast cancer patients with molecular subtypes are different [3]. There are several studies on molecular subtypes of breast cancer in China at present, but there is little research on the clinical and pathological features of different molecular subtypes of breast cancer among women in the Zhuang and Han ethnic nationalities. This study analyzed the clinical and pathological data, immunohistochemical (IHC) markers and molecular subtype of 278 cases of Zhuang female breast cancer, and compared these with 712 cases of breast cancer in Han women and aims to study breast cancer molecular typing and clinical pathological features of these two ethnic groups of females with a view to provide better clinical individual therapy.

Materials and methods

Patients and samples

Data were collected from patients attending the Affiliated Tumor Hospital of Guangxi Medical University between 2010 January 1 to 2013 December 31. All were treated after surgery after being diagnosed with breast cancer. 990

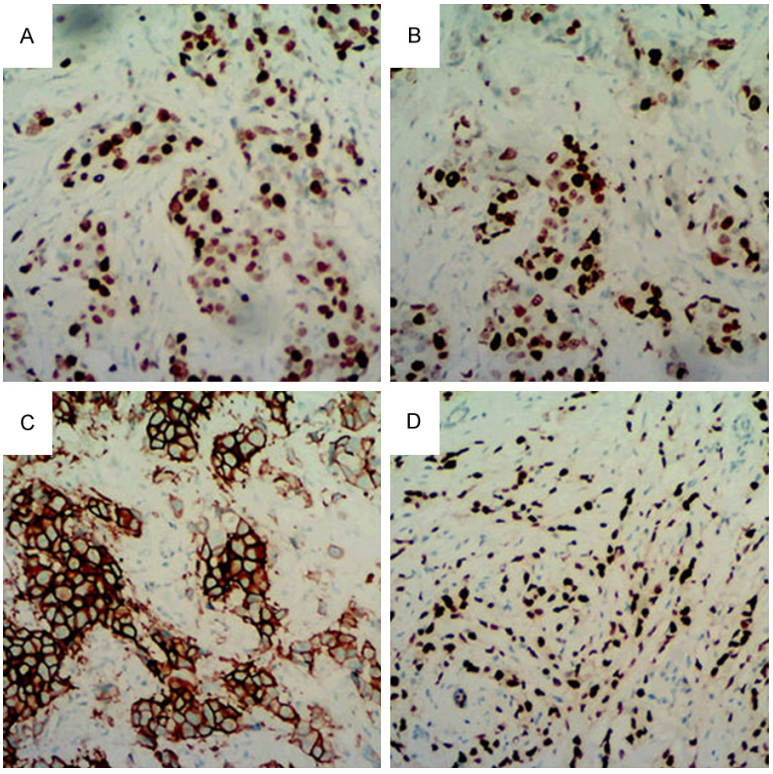

Figure 1. Immunohistochemical staining of four protein positive expression in breast cancer tissue sections (× 100). A: ER; B: PR; C: HER-2; D: Ki-67.

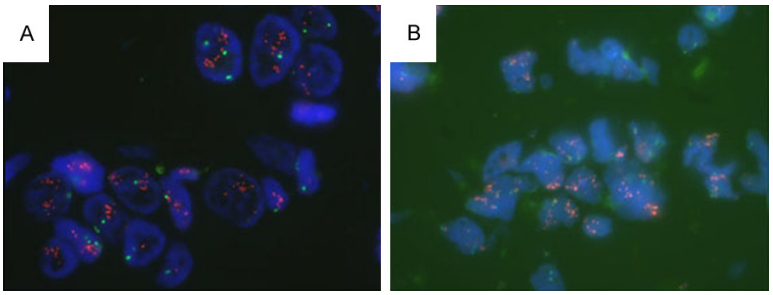

Figure 2. Positive HER2 gene amplification was detected by fluorescent in situ hybridization (FISH) (× 1000). Red signals represent the HER2 gene probe, and green dots indicate the CEP17 reference probe. (A and B).

patients with complete clinical and pathological data were included in this study and the proportion of Zhuang and Han ethnic groups was 1:2.5 with 278 cases of Zhuang women with breast cancer aged 27 to 75 years (the median age of 44 years) and 712 cases of breast cancer in Han women aged 24-78 years (median age of 48 years).

Inclusion criteria

(1) a clear diagnosis of breast cancer in female Zhuang and Han patients after surgical treatment with complete clinical data, including general situation, pathological diagnosis, surgical approach and treatment plans; (2) a complete four IHC markers diagnosis with results of: ER, PR, HER-2 and Ki-67 expression in samples obtained from these patients; (3) before surgery these patients received no radiotherapy, chemotherapy, endocrine or other treatments.

Molecular subtypes of breast cancer

According to the results for the four IHC markers (ER, PR, HER-2, Ki-67), four molecular subtypes were identified. Estrogen receptor (ER) and progesterone receptor (PR) were positive for more than 1% of tumor nuclei; human epidermal growth factor receptor 2 (HER-2) positive was classed as of +++ (where > 10% of the tumor cell membrane showing high strength complete coloring) or ++ (where > 10% of the tumor cells was incomplete and weak to moderate strength cell membrane staining or less than or equal to 10% of the tumor cells showing strong and intact cell membrane coloring. However, if there was a FISH detection HER-2/CEP17 ratio of ≥ 2 or HER-2 gene copy number was ≥ 6), a negative HER-2 (classified as 0) was returned, a + result was allocated where; Ki-67 was positive is equal or more than 14% in tumor nuclear staining and negative for < 14% [4] (**Figures 1** and **2**).

Using the classification outlined in the 13th St. Gallen International Breast Cancer Conference, four molecular subtypes were delineated: (1) Luminal A type: ER+ and (or) PR+, HER-2- and Ki-67 < 14%; (2) Luminal B type: ① ER+ and (or) PR+, HER-2- and Ki-67 ≥ 14% ② ER+ and (or) PR+, HER-2+, any level of Ki-67; (3) HER-2

Table 1. Distribution of different molecular subtypes of breast cancer in Zhuang and Han nationalities. The percentages are given in parentheses

Ethnic	Luminal A	Luminal B	HER-2 over-expression	Triple negative	X^2	*P*-value
Zhuang (n=278)	64 (23.0)	151 (54.3)	35 (12.6)	28 (10.1)	5.522	0.137
Han (n=712)	207 (29.1)	338 (47.4)	81 (11.4)	86 (12.1)		

Table 2. General conditions of different molecular subtypes of breast cancer patients in Zhuang and Han nationalities. The percentages are given in parentheses

General condition parameter	Luminal A			Luminal B			HER-2 over-expression			Triple negative		
	Zhuang (64)	Han (207)	P	Zhuang (151)	Han (338)	P	Zhuang (35)	Han (81)	P	Zhuang (28)	Han (86)	P
Age (years)												
≤ 35	8 (12.5)	18 (8.7)	0.047	16 (10.6)	28 (8.3)	0.041	2 (5.7)	9 (11.1)	0.703	5 (17.9)	9 (10.5)	0.363
36-60	50 (78.1)	141 (68.1)		123 (81.5)	255 (75.4)		30 (85.7)	63 (77.8)		22 (78.6)	67 (77.9)	
> 60	6 (9.4)	48 (23.2)		12 (7.9)	45 (16.3)		3 (8.6)	9 (11.1)		1 (3.6)	10 (11.6)	
Family history												
Yes	0 (0)	1 (0.5)	1	1 (0.7)	6 (1.8)	0.586	0 (0)	1 (1.2)	1	3 (10.7)	0 (0)	0.014
No	64 (100)	206 (99.5)		150 (99.3)	332 (98.2)		35 (100)	80 (98.8)		25 (89.3)	86 (100)	
Number of birth												
0	2 (3.1)	8 (3.9)	0.716	8 (5.3)	18 (5.3)	0.836	0 (0)	4 (4.9)	0.029	0 (0)	3 (3.5)	0.607
1 or 2	54 (84.4)	180 (87)		115 (76.2)	264 (78.1)		32 (91.4)	56 (69.1)		23 (82.1)	72 (83.7)	
> 2	8 (12.5)	19 (9.1)		28 (18.5)	56 (16.6)		3 (8.6)	21 (25.9)		5 (17.9)	11 (12.8)	
Menstruation												
Premenopausal	44 (68.8)	107 (51.7)	0.016	102 (67.5)	194 (57.4)	0.034	21 (60)	49 (60.5)	0.96	18 (64.3)	45 (52.3)	0.269
Postmenopausal	20 (31.2)	100 (48.3)		49 (32.5)	144 (42.6)		14 (40)	32 (39.5)		10 (35.7)	41 (47.7)	
Occurrence site												
Left	26 (40.6)	120 (58.0)	0.031	66 (43.7)	166 (49.1)	0.314	12 (34.3)	45 (55.6)	0.04	19 (67.9)	51 (59.3)	0.803
Right	34 (53.1)	82 (39.6)		79 (52.3)	165 (48.8)		23 (65.7)	33 (40.7)		9 (32.1)	33 (38.4)	
Bilateral	4 (6.3)	5 (2.4)		6 (4)	7 (2.1)		0	3 (3.7)		0 (0)	2 (2.3)	

over expression type: ER-, PR-, HER+, any level of Ki-67; (4) Triple negative type: ER-, PR-, HER-, and Ki-67 any level [5].

Histological grading and clinical staging

The histological grading was recorded under the guidelines set by the WHO breast tumor pathology classification criteria. The clinical stage was delineated according to the 2009 Joint Committee on Cancer, American (AJCC) breast cancer staging standard (Seventh Edition) staging.

Statistics

SPSS17.0 statistical software was used for statistical analysis, Percentages were used for the description of the clinical data and the X^2 test or Fisher exact probability method was used for rates or data count, $P < 0.05$ was considered to be statistically significant.

Results

Distribution of different molecular subtypes of breast cancer patients in Zhuang and Han nationalities

In 990 cases of female breast cancer patients, the proportion of the Zhuang in the four kinds of molecular subtypes accounted for 64 cases (23%), 151 (54.3%), 35 cases (12.6%) and 28 cases of (10.1%). The proportion of the Han Chinese in the four subtypes accounted for 207 cases (29.1%), 338 cases (47.4%), 81 cases (11.4%), 86 cases (12.1%), of which the proportion of Luminal B in Zhuang was higher than in Han populations and the proportion of Luminal A in Zhuang was lower than in Han nationality, but differences in distribution in Guangxi of Zhuang and Han populations in different molecular subtypes showed no statistical significance ($P > 0.05$) (**Table 1**).

Table 3. Clinical and pathological features of different molecular subtypes of breast cancer between Zhuang and Han nationalities. The percentages are given in parentheses

Pathological features	Luminal A			Luminal B			HER-2 over-expression			Triple negative		
	Zhuang (64)	Han (207)	P	Zhuang (151)	Han (338)	P	Zhuang (35)	Han (81)	P	Zhuang (28)	Han (86)	P
Histological type												
Invasive ductal	47 (73.4)	182 (87.9)	0.027	138 (91.4)	310 (91.7)	0.909	30 (85.7)	76 (93.8)	0.224	21 (75.0)	78 (90.7)	0.047
Invasive lobular	3 (4.7)	7 (3.4)		3 (2)	7 (2.1)		0 (0)	0 (0)		2 (7.1)	1 (1.2)	
Intraductal	5 (7.8)	6 (2.9)		7 (4.6)	17 (5)		4 (11.4)	5 (6.2)		4 (14.3)	3 (3.5)	
Other	9 (14.1)	12 (5.8)		3 (2)	4 (1.2)		1 (2.9)	0 (0)		1 (3.6)	4 (4.6)	
Histological grade												
I	17 (26.6)	14 (6.8)	0	12 (7.9)	6 (1.8)	0.003	4 (11.4)	2 (2.5)	0.027	3 (10.7)	6 (7.0)	0.042
II	32 (50)	88 (42.5)		66 (43.7)	149 (44.1)		10 (28.6)	41 (50.6)		10 (35.7)	54 (62.8)	
III	15 (23.4)	105 (50.7)		73 (48.3)	183 (54.1)		21 (60)	38 (46.9)		15 (53.6)	26 (30.2)	
Tumor size (CM)												
≤ 2	19 (29.7)	62 (30)	0.725	32 (21.2)	83 (24.6)	0.657	1 (2.9)	14 (17.3)	0.046	0 (0)	20 (23.3)	0.005
3 to 5	37 (57.8)	111 (53.6)		91 (60.3)	200 (59.2)		28 (80)	48 (59.3)		23 (82.1)	57 (66.3)	
> 5	8 (12.5)	34 (16.4)		28 (18.5)	55 (16.3)		6 (17.1)	19 (23.5)		5 (17.9)	9 (10.5)	
Number of lymph nodes metastasis												
0	30 (46.9)	115 (55.6)	0.465	64 (42.4)	162 (47.9)	0.299	18 (51.4)	36 (44.4)	0.836	13 (46.4)	37 (43)	0.865
1 to 3	20 (31.3)	47 (22.7)		40 (26.5)	96 (28.4)		12 (34.3)	27 (33.3)		10 (35.7)	26 (30.2)	
4 to 9	9 (14.1)	33 (15.9)		33 (21.9)	51 (15.1)		3 (8.6)	11 (13.6)		3 (10.7)	14 (16.3)	
≥ 10	5 (7.8)	12 (5.8)		14 (9.3)	29 (8.6)		2 (5.7)	7 (8.6)		2 (7.1)	9 (10.5)	
Clinical stage												
I	17 (26.6)	38 (18.4)	0.04	12 (7.9)	53 (15.7)	0.044	3 (8.6)	10 (12.3)	0.937	3 (10.7)	15 (17.4)	0.533
II	27 (42.2)	121 (58.5)		78 (51.7)	181 (53.6)		26 (74.3)	54 (66.7)		19 (67.9)	44 (51.2)	
III	11 (17.2)	36 (17.4)		40 (26.5)	63 (18.6)		3 (8.6)	8 (9.9)		4 (14.3)	20 (23.3)	
IV	9 (14.1)	12 (5.8)		21 (13.9)	41 (12.1)		3 (8.6)	9 (11.1)		2 (7.1)	7 (8.1)	

General conditions of different molecular subtypes of breast cancer patients in Zhuang and Han nationalities

In the subtypes of luminal A and Luminal B, age of onset in less than 35 years and 36-60 years old, Zhuang accounts for a higher proportion than the Han nationality, although in Zhuang and Han nationalities there was a statistical significance in the age distribution ($P < 0.05$). There were statistical differences in the family history of breast cancer between the Zhuang and Han patients in the molecular subtype of Triple negative ($P < 0.05$), the proportion of Zhuang is higher than that in Han nationality. There is a statistical difference in the number of births between the Zhuang and Han patients in the molecular subtype of HER-2 over-expression ($P < 0.05$), the proportion of patients with one or two children of Zhuang is higher than the Han nationality, but the proportion of patients with more than two children of the Han is higher than the Zhuang nationality. Two groups of patients with differences in menstruation parameters in the luminal A and Luminal B were statistically significant ($P < 0.05$); with the Zhuang patients showing a higher premenopausal prevalence ratio than the Han, but Han patients the postmenopausal prevalence ratio is higher than in the Zhuang population. There is a statistical difference in the occurrence site between the Zhuang and Han patients in the molecular subtypes of Luminal A and HER-2 over-expression ($P < 0.05$), with the proportion of the Zhuang occurring in the right breast is much higher than in Han patients, but the proportion of the Han where the tumors occur in the left breast is much higher than Zhuang patients (**Table 2**).

Clinical and pathological features of different molecular subtypes of breast cancer patients between Zhuang and Han nationalities

In the subtypes of Luminal A and triple negative, the proportion of invasive ductal carcinoma of Han was higher than Zhuang patients, but the proportion of other cancer types of Han was lower than Zhuang, and the difference was statistically significant ($P < 0.05$). The differences of histological grading of different molecular subtypes of breast cancer patients in Zhuang and Han are also statistically significant ($P < 0.05$). In particular, the histological III grade of Han patients in the subtype of luminal is higher than Zhuang, but the histological III grade of Zhuang patients in the subtypes of HER-2 over-expression and triple negative were higher than in Han groups. In the subtypes of HER-2 over expression and Triple negative, the proportion of the Zhuang patients with tumor diameters of more than 2 cm were higher than in Han patients, and this difference is statistically significant ($P<0.05$). There is no significant difference in the number of lymph node metastases between the Zhuang and Han patients ($P > 0.05$). In the clinical stage of Luminal A and Luminal B, the proportion of time periods patients stay in clinical stages III+IV of Zhuang patients is higher than that in Han, but the proportion of time periods in clinical stages I+II of Han is higher than Zhuang, and the difference is statistically significant ($P < 0.05$) (**Table 3**).

The treatment of breast cancer patients with different molecular subtypes of Zhuang and Han nationalities

There are statistically significant differences in the operations performed on the Zhuang and Han patients in the Luminal A subtype ($P < 0.05$). In the Luminal A, the proportion of Han patients who received endocrine therapy was higher than Zhuang, and the difference is statistically significant ($P < 0.05$). There is a statistical difference in patients receiving chemotherapy between Zhuang and Han in subtypes of the Luminal B and Triple negative ($P < 0.05$), the proportion of the Han being higher than Zhuang. The difference of accepting radiotherapy between Zhuang and Han is statistically significant in the subtypes of Luminal B, HER-2 over-expression and Triple negative ($P < 0.05$), such that in the former two subtypes, the proportion of Zhuang accepting radiotherapy is higher Han, and in the latter subtype that the proportion of Han accepting radiotherapy is higher than Zhuang patients (**Table 4**).

Different molecular subtypes of breast cancer with recurrence and metastasis in Zhuang and Han patients

The difference of recurrence and metastasis between Zhuang and Han patients is statistically significant in the subtype of Luminal A ($P < 0.05$), which the proportion of Zhuang being higher in Han, and the most transformation of tumors is seen in the visceral areas (59.1% and

Table 4. The treatment of breast cancer patients with different molecular subtypes of Zhuang and Han nationalities. The percentages are given in parentheses

General parameters	Luminal A			Luminal B			HER-2 over-expression			Triple negative		
	Zhuang (64)	Han (207)	P	Zhuang (151)	Han (338)	P	Zhuang (35)	Han (81)	P	Zhuang (28)	Han (86)	P
Operation mode												
Radical	30 (46.9)	86 (41.5)	0.017	66 (43.7)	152 (45)	0.27	15 (42.9)	43 (53.1)	0.335	13 (46.4)	38 (44.2)	0.541
Conserving	12 (18.8)	35 (16.9)		24 (15.9)	71 (21)		7 (20)	11 (13.6)		9 (32.1)	21 (24.4)	
Resection	19 (29.7)	86 (41.5)		61 (40.4)	115 (34)		12 (34.3)	27 (33.3)		6 (21.4)	27 (31.4)	
Other	3 (4.7)	0 (0)		0 (0)	0 (0)		1 (2.9)	0 (0)		0 (0)	0 (0)	
Endocrine therapy												
Yes	46 (71.9)	193 (93.2)	0	93 (61.6)	213 (63)	0.763	1 (2.9)	2 (2.5)	1.000	2 (7.1)	4 (4.7)	0.98
No	18 (28.1)	14 (6.8)		58 (38.4)	125 (37)		34 (97.1)	79 (97.5)		26 (92.9)	82 (95.3)	
Chemotherapy												
Yes	51 (79.7)	151 (72.9)	0.279	124 (82.1)	303 (89.6)	0.021	33 (94.3)	75 (92.6)	1	21 (75)	79 (91.9)	0.042
No	13 (20.3)	56 (27.1)		27 (17.9)	35 (10.4)		2 (5.7)	6 (7.4)		7 (25)	7 (8.1)	
Radiotherapy												
Yes	30 (46.9)	107 (51.7)	0.501	81 (53.6)	148 (43.8)	0.044	31 (88.6)	33 (40.7)	0	9 (32.1)	51 (59.3)	0.012
No	34 (53.1)	100 (48.3)		70 (46.4)	190 (56.2)		4 (11.4)	48 (59.3)		19 (67.9)	35 (40.7)	
Targeted therapy												
Yes	0 (0)	0 (0)	-	14 (9.3)	23 (6.8)	0.341	2 (5.7)	10 (12.3)	0.457	0 (0)	0 (0)	-
No	64 (100)	207 (100)		137 (90.7)	315 (93.2)		35 (94.3)	71 (87.7)		28 (100)	86 (100)	

39.4%). The rate of visceral metastasis in Han patients is higher than Zhuang in the subtype of HER-2 over-expression, but the rate of visceral metastasis of Zhuang is higher than Han in the subtype of triple negative, but the differences are not statistically significant ($P > 0.05$) (**Table 5**).

Discussion

According to the American Cancer Society, breast cancer is the most common malignant tumor in elderly women and their statistics for 2014 show that the prognosis for new breast cancer cases is second only to lung cancer with respect to mortality [6]. Women with breast cancer in China show an upward trend, and the age when women contract the disease is getting younger. Breast cancer is different from other malignant tumors in that it appears to be heterogeneous in outcomes. The effect of treatment to the patient and the prognosis are not the same, even though the histological types and the treatment methods used are the same. Therefore, the molecular classification of breast cancer can provide an important basis for individualized treatment and prognosis. Some scholars first put forward the concept of molecular typing of breast cancer [3] in recent years with gene microarray technology being used to divide the breast cancer into 5 molecular subtypes. Studies and clinical trials have indicated that different molecular subtypes are closely related to clinical treatment and prognosis [7-9], and there are differences. Because the gene array requires a high level of technology and is relatively expensive, it is difficult to be widely used in the clinical setting. Currently, in clinics most treatments are administered on the basis of ER, PR, HER-2 and Ki-67 IHC results which is able to distinguish four subtypes of breast cancer, namely Luminal A, Luminal B, HER-2 over-expression and triple negative [5]. Studies have indicated that the genetic background of different ethnic groups is an important factor that affects the development of breast cancer [2], according to the analysis of the Zhuang and Han female patients with breast cancer molecular subtypes and clinical pathological features. This can provide a theoretical basis for individual therapy and prognosis judgment.

Many studies have indicated that there are differences in the molecular subtypes of breast cancer among different ethnic groups [10-12]. A study in the United States indicated that in white Caucasians and African Americans, the molecular subtype distribution proportions were 64%, 11%, 5%, 11% and 48%, 8%, 7%, 22% for Luminal A, Luminal B, HER-2 over-expression and triple negative respectively

Table 5. Different molecular subtypes of breast cancer with recurrence and metastasis in Zhuang and Hanpatients. The percentages are given in parentheses

General parameters	Luminal A			Luminal B			HER-2 over-expression			Triple negative		
	Zhuang (64)	Han (207)	P	Zhuang (151)	Han (338)	P	Zhuang (35)	Han (81)	P	Zhuang (28)	Han (86)	P
Recurrence and metastasis												
Yes	14 (21.9)	24 (11.6)	0.038	19 (12.6)	45 (13.3)	0.825	6 (17.1)	12 (14.8)	0.751	1 (3.6)	11 (12.8)	0.305
No	50 (78.1)	183 (88.4)		132 (87.4)	293 (86.7)		29 (82.9)	69 (85.2)		27 (96.4)	75 (87.2)	
The site												
Chest wall	3 (13.6)	4 (12.1)	0.197	2 (6.9)	2 (2.9)	0.655	0 (0)	2 (12.5)	0.641	0 (0)	0 (0)	1
Visceral	13 (59.1)	13 (39.4)		11 (37.9)	28 (41.2)		3 (42.9)	9 (56.3)		1 (100)	8 (47.1)	
Bone	2 (9.1)	11 (33.3)		10 (34.5)	19 (27.9)		2 (28.6)	3 (18.8)		0 (0)	6 (35.3)	
Lymph node	4 (18.2)	5 (15.2)		6 (20.7)	19 (27.9)		2 (28.6)	2 (12.5)		0 (0)	3 (17.6)	

[12]. The object of this study was to compare Zhuang female breast cancer patients and Han patients and in our study it was found that breast cancer with different molecular subtypes in Zhuang and Han populations showed no obvious regional difference in distribution. Some studies have indicated that Luminal A is the most common molecular subtype [13, 14] with Luminal B being a molecular variation of this subtype. On the contrary, our study shows that B Luminal is the major molecular subtype of breast cancer patients in Zhuang and Han nationalities and that Luminal A is a second molecular subtype. This is different to other research reports and may reflect the genetic background of racial differences and may also be due to the detection method used and the standards used for judging the cause of the disease. For example, different pathologists defined the methods and standards for Ki-67 detection differently. This study shows that the distribution of HER-2 over expression and Triple negative types as similar to that reported at home and abroad.

The results of this study show that the Zhuang and Han women of different molecular subtypes of breast cancer show differences with respect to age onset, menstruation, site, histological type, histological grade, clinical staging, surgical approach, endocrine therapy, recurrence and metastasis. The median age of Zhuang and Han patients was 44 years and 48 years old respectively. There were differences in both Luminal A and Luminal B incidence age with a younger, age of onset in Zhuang where it was mainly concentrated in 36-60 years of age. However, in western countries the age onset was mainly concentrated in the 60-70 year olds [12]. Studies have shown that closely related to the development and prognosis of breast cancer is the family histories, age of menarche, menstruation and childbirth [15]. Our study found differences in the family history of Zhuang and Han patients with the triple negative subtype. Differences were also found between the two nationalities in the number of births in HER-2 over expression, menstruation in the luminal type and this confirms that the different races and molecular subtypes of breast cancer are related to the occurrence, development and prognosis.

Studies have shown that the tumor size, histological grade, lymph node metastasis and clinical staging of breast cancer are closely related with treatment and prognosis [16] and most of the studies showed that the type of Luminal of breast cancer with slowprogression can be treated with endocrine therapy and follows a good prognosis. However, in the subtypes of HER-2 over expression and triple negative of breast cancer progression is quicker and there is a poor prognosis [17, 18]. Our study show that the difference of histological grade between Zhuang and Han patients in each subtype is statistically significant with the proportion of histological grade III of Han in the subtype of luminal is higher than the Zhuang, but the proportion of histological grade III of Zhuang in the subtypes of HER-2 over-expression and triple negative is higher than the Han, suggesting that the Zhuang women show a poorer prognosis. Tumor size is an independent factor for the prognosis of breast cancer with the greater the diameter of the tumor showing a worse prognosis [19]. Our study revealed that the differences of tumor size between Zhuang and Han patients in subtypes of HER-2 over expression and triple negative type are statistically

significant, Zhuang patients with tumor diameters of more than 2 cm being higher than in Han patients, suggesting that the prognosis of Zhuang breast cancer patients may be poor. The more number of lymph node metastases and late clinical stage indicates poor prognosis in breast cancer patients [20] and our study shows that the difference of the number of lymph node metastases in different molecular subtypes is not statistically significant, but in the clinical staging of luminal A and Luminal B, the proportion of Zhuang patients with stage III and IV was higher than that in Han, yet the proportion of Han patients with stage I/II was higher than in Zhuang patients. The difference is statistically significant, which suggests that the prognosis of Zhuang patients with breast cancer may be worse than Han.

Endocrine therapy is an important means of treatment in hormone receptor positive breast cancer and this have been showed to significantly improve the prognosis of patients and reduce the risk of death [21]. Trastuzumab is currently the targeted therapy of choice for HER-2/neu over-expression as a first-line drug with neoadjuvant chemotherapy plus trastuzumab being used to significantly improve the clinical cure rate [22]. Triple negative is the most popular subtype researched in recent years and it has a unique biological behavior and clinical pathological features. Thus subtype has a poor prognosis of breast cancer and is able to recur easily with distant metastases. Unfortunately, endocrine and targeted therapies work less well for this subtype with chemotherapy being the only effective treatment [23]. Our study found that the proportion of Zhuang patients who received endocrine therapy was significantly lower than Han in Luminal A subtype, the proportion of Zhuang patients who received chemotherapy was lower than Han in subtype of Luminal B and the proportion of Zhuang patients who accepted chemotherapy was significantly lower than Han in the subtype of triple negative. In our study of the subtype of HER-2 over-expression, the ratio of Zhuang patients who received Herceptin targeted therapy is lower than in Han. The probable reason for this discrepancy is that most of the Zhuang patients cannot afford the huge costs of Herceptin. Therefore, only a small portion of the population can make use of Herceptin and this may be an important factor to be considered when determining the reasons for the Zhuang having a worse prognosis than Han patients in the subtype of HER-2 over expression.

At the same time, this study found that the rate of recurrence and metastasis of Zhuang patient is much higher than Han in Luminal A subtype, especially respect to visceral metastasis. However, the rate of recurrence and metastasis in subtypes of HER-2 over-expression and triple negative showed no difference. At present, there is no research report to confirm this. One of the reasons may be that Zhuang patients were less likely to received endocrine therapy but there are likely to be other reasons which require further study.

In summary, there are differences of pathological features and prognosis in different molecular subtypes of breast cancer between Han and Zhuang patients with the Zhuang having an overall worse prognosis. Understanding these differences can lead to provide a more accurate treatment plan and prognosis for patients and guide an individualized comprehensive approach to treatment.

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Disclosure of conflict of interest

None.

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