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Clinicopathological features and survival of early stage breast cancer in northwest China: A population-based retrospective study of 1287 patients

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Keywords
Age subgroup; breast cancer; clinicopathological feature; molecular subtype; overall survival.

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Abstract

Background: Breast cancer (BC) displays different clinicopathological features and outcomes based on patient age, molecular subtype, and treatment. However, such features in BC patients in northwest China are unclear. This study investigated the clinicopathological features and overall survival (OS) of early stage BC patients using a population-based study.

Methods: Patients who were newly diagnosed with BC at the First Affiliated Hospital of Xi'an Jiaotong University between January 2001 and June 2012 were included. Clinicopathological features and OS were assessed.

Results: The median age of 1287 patients was 50 years, with an average tumor size of 2.65 cm. Additionally, 42.7% were luminal A, 25.6% luminal B, 9.3% Her2 overexpression, and 17.7% triple negative. The cut-off age was 35 years, and young patients (< 35) tended to have larger tumors, ≥ 4 positive lymph nodes, grade 2 or 3 histology, non-luminal types, high Ki67, and poor outcomes. Patients with luminal A tumors showed moderate features: 50.6% had tumors < 2 cm, 56.7% had negative lymph nodes. Patients with Her2 overexpression tumors showed aggressive features and the poorest survival (5-year OS 67.6%). Patients with triple negative tumors were the youngest (average 48.4 years), but had the largest proportion of grade 3 histology and poor outcomes.

Conclusion: Our results are consistent with those in other provinces in China, but showed an earlier age at diagnosis and more aggressive pathological features compared to developed countries. Additionally, each molecular subtype showed specific features and different survival outcomes.

Introduction

Breast cancer (BC) is the most frequently occurring cancer in women around the world.[1] According to 2012 GLOBOCAN statistics,[2] 1.67 million women were diagnosed with BC worldwide, with 522 000 related deaths, an increase of nearly 18% from 2008. Data from China also demonstrated the highest incidence (268.6/100 000) and a high mortality (70.7/100 000) rates in women of all ages in 2015. BC is a common cancer with a significant upward trend in age-standardized incidence rates and mortality,[3] and has therefore become a major public health problem worldwide.

In order to administer proper preventive measures and treatment for BC, information of clinical and pathological features is needed. Studies of BC patients in different countries, including the United States,[4,5] Switzerland,[6] Chile,[7] Iran,[8] India,[9] and South Korea,[10] have been conducted, however, with differing results. Differences in results exist even within the scope of China. For example, data from Guangzhou on molecular subtypes showed 31.1% patients with luminal A and 43.5% luminal B tumors, while results from Wuhan were 24% and 39%, respectively.[11,12] These differences may be a result of race, economy, education, and policy, among other aspects. Therefore, data from other regions cannot provide information for a specific area. The present study aimed to investigate the clinicopathological features and survival of early BC patients in northwest China, which has rarely been covered in previous studies, in order to contribute a solution to this public health problem.

Methods

Data source

Data was obtained from the First Affiliated Hospital of Xi'an Jiaotong University, and women who were newly diagnosed with BC between January 2001 and June 2012 were included. The exclusion criteria were: (i) patients with incomplete pathological records, without information of estrogen receptor (ER), progesterone receptor (PR), or human epidermal growth factor receptor 2(Her2) status; (ii) patients with a Her2 result of 2+ by immunohistochemistry, but without further assessment by fluorescence in situ hybridization (FISH); (iii) patients with other malignant disease that may influence survival; (iv) men with BC; (v) patients who had received neoadjuvant chemotherapy; and (vi) patients diagnosed with stage IV BC. A total of 1287 women were included in the present study and a database was established to process the data.

All procedures performed in studies involving human participants were in accordance with The Code of Ethics of the Declaration of Helsinki and the ethical standards of the institutional ethics committee of the First Affiliated Hospital of Xi'an Jiaotong University. All personal information was removed or disguised to ensure patient anonymity.

Pathological criteria

Records were collected from the Pathology Department of the First Affiliated Hospital of Xi'an Jiaotong University, and were examined by at least two experienced pathologists, along with puncture or surgery biopsy samples. Tumor staging was based on 7th American Joint Committee on Cancer system. Pathological type and histological grade were determined using the World Health Organization classification. ER, PR, Her2 status, and Ki67 proliferation index were assessed by immunohistochemistry. Based on the criteria of the 2007 American Society of Clinical Oncology/College of American Pathologists scoring system, ER or PR were considered positive when > 10% cells were stained in the nucleus. Her2 status was graded from 0 to 3+. Zero and 1+ were regarded as Her2 negative, and 3+ as positive. When a tumor presents with Her2 2+, further assessment by FISH is recommended. A quantitative test of the Ki67 index has been conducted since 2009 in our hospital, and after communication with pathologists, prior records were regarded as > 14% when marked positive.

Tumors were classified into four subtypes based on ER, PR, Her2, and Ki67 status. Because data was incomplete for Ki67, hormone receptor positive tumors with unknown Ki67 were categorized as luminal A with positive ER, and the remainder were categorized as luminal B. The four types were thus categorized as follows: (i) luminal A: ER or PR positive, Her2 negative, Ki67 < 14% or negative, and ER positive, any PR status, Her2 negative, unknown Ki67; (ii) luminal B: ER or PR positive, Her2 negative, Ki67 ≥ 14%, and ER or PR positive, Her2 positive, unknown Ki67 but cannot be categorized as luminal A; (iii) Her2 overexpression: ER negative, PR negative, Her2 positive; and (iv) triple negative (TN): ER, PR and Her2 were negative.

Statistical methods

Patients were divided into subgroups based on age or molecular type. A Pearson's chi-squared (χ^2) test was performed to determine the differences in clinicopathological factors between the groups. Overall survival (OS) was defined as the time from diagnosis of BC to the time of death from any cause or loss of contact. Patients were followed until last known follow-up, death, or to December 31, 2013, whichever occurred first. Cumulative survival probabilities (OS rates) were calculated using Kaplan–Meier curves. Multiple-factor analysis was conducted by Cox proportional hazards model. Statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). All statistical tests were two-tailed, and $P < 0.05$ was considered significant.

Results

Baseline clinicopathological features and treatment

A total of 1287 BC patients were included in the study. The patients' baseline features and treatment methods used are presented in Table 1.

The median age at diagnosis was 50 years, and most patients were aged between 40 and 60 years. With regard to pathological features, the average tumor size was 2.65 cm (range 1.31–3.99 cm). Small tumors were rare: only seven tumors were < 0.5 cm, while 95 tumors were 0.5–1 cm. More than half (55.4%) of the patients had negative ipsilateral axillary lymph nodes, but 21.0% patients had tumor metastasis in

> 4 lymph nodes. Most of the patients (42.7%) had luminal A tumors, followed by luminal B (25.6%), TN (17.7%), and only 120 patients (9.3%) had tumors with Her2 overexpression.

All 1287 patients underwent surgery at the time of diagnosis, followed by treatment: 57% of patients were administered adjuvant chemotherapy, 13.8% adjuvant radiotherapy, and 22.4% endocrine therapy.

Clinicopathological features of different age groups

To investigate the relationship between clinicopathological features and patient ages, all patients were divided into groups: Table 2 represents the distribution of five age groups, Table 3 represents the 35 year cut-off.

Patients aged < 30 had the largest tumors at > 5 cm, while those aged > 60 years had relatively smaller tumors. No trend was observed in tumor size by age group, but a majority of the patients in each age group had tumors ranging from 2 cm to 5 cm (< 30 = 47.6%, 30–39 = 54.9%, 40–49 = 49.5%, 50–59 = 54.9%, > 60 = 50.5%). In regard to tumor stage, in each age group > 70% patients had stage I or II tumors, and this result did not vary greatly between the groups (< 30 = 76.2%, 30–39 = 76.8%, 40–49 = 80.2%, 50–59 = 72.6%, > 60 = 79.2%). A significant difference was observed in terms of histology ($P < 0.001$). Patients aged 50–59 had the largest proportion (10.4%) of well-differentiated tumors. By contrast, more patients in the 30–39 age group displayed grade 3 disease (65.8%). In addition, a statistical difference was observed between molecular subtypes and age ($P = 0.001$). Patients aged ≥ 60 had more luminal A tumors (52.7%), while those aged 40–49 had more luminal B tumors (31.4%). In contrast, patients aged < 30 had fewer luminal type tumors (28.1%) than any other group, while the highest proportion of tumors with Her2 overexpression was observed in the 50–59 age group (11.9%).

Table 3 illustrates the comparison between patients aged < 35 and ≥ 35. Although patients aged < 35 made up only 6.0% of the total sample, large tumors were more common in this subgroup (2.80 cm vs. 2.64 cm). Younger patients had fewer negative lymph nodes (49.3% vs. 55.8%), metastasis in ≥ 4 (26.0% vs. 20.7%) lymph nodes, tended to have late stage and poorly differentiated tumors (although these results were not statically significant at $P = 0.39$ and $P = 0.15$, respectively) and more TN tumors (23.4% vs. 22.3%; $P = 0.84$).

Clinicopathological features of different molecular subtypes

Each molecular subtype had specific pathological features; the data is summarized in Table 4. Luminal type tumors were moderate. Most luminal A tumors were ≤ 2 cm, with negative lymph node metastasis, and displayed 52.6% grade 1 and 2 histology. In comparison, luminal B tumors were the smallest on

Table 1 Baseline features and treatment of 1287 breast cancer patients, northwest China, 2001–2012

Characteristics	All (n = 1287)
Age at diagnosis (years)	
Median age	50 (42–59)
Menopausal status	
Premenopausal	608 (47.2%)
Postmenopausal	613 (47.6%)
Unknown	66 (5.1%)
Family history	
Yes	30 (2.4%)
No	1257 (97.6%)
Tumor size, cm	
Average size	2.65 ± 1.34
T ≤ 2	574 (44.6%)
T ≤ 0.5	7
0.5 < T ≤ 1	95
1 < T ≤ 2	472
2 < T ≤ 5	669 (52.0%)
T > 5	44 (3.4%)
Lymph node status	
0	713 (55.4%)
1–3	304 (23.6%)
4–9	159 (12.4%)
≥ 10	111 (8.6%)
AJCC stage	
Stage I	353 (27.4%)
Stage II	642 (49.9%)
Stage III	292 (22.7%)
Tumor grade	
1	84 (6.5%)
2	485 (37.7%)
3	718 (55.8%)
Molecular subtypes	
Luminal A	549 (42.7%)
Luminal B	330 (25.6%)
Her2 overexpression	120 (9.3%)
Triple negative	288 (17.7%)
Ki67	
< 14%	302 (23.5%)
≥ 14%	399 (31.0%)
Unknown	586 (45.5%)
Adjuvant chemotherapy	
No	553 (43.0%)
Yes	734 (57.0%)
Regimen	
Contains anthracycline but not taxanes	249 (33.9%)
Contains taxanes but not anthracycline	25 (3.4%)
Based on anthracycline with taxanes	437 (59.6%)
Unknown	23 (3.1%)
Adjuvant radiotherapy	
Yes	178 (13.8%)
No	569 (44.2%)
Unknown	540 (42.0%)
Endocrine therapy	
Yes	288 (22.4%)
No	236 (18.3%)
Unknown	763 (59.3%)

AJCC, American Joint Committee on Cancer.

Table 2 Clinicopathological features of 1287 breast cancer patients grouped by age, northwest China, 2001–2012

Characteristics	< 30 21 (1.6%)	30–39 193 (15.0%)	40–49 414 (32.2%)	50–59 346 (26.9%)	≥ 60 313 (24.3%)	*P*
Menopausal status						< 0.001
Yes	0	5 (2.6%)	49 (11.8%)	248 (71.7%)	311 (99.4%)	
No	21 (100%)	175 (90.7%)	339 (81.9%)	71 (20.5%)	2 (0.6%)	
Unknown	0	13 (6.7%)	26 (6.3%)	27 (7.8%)	0	
Tumor size, cm						0.15
Average size	2.70 ± 1.68	2.91 ± 1.65	2.58 ± 1.25	2.69 ± 1.26	2.52 ± 1.29	
T ≤ 2	9 (42.9%)	75 (38.9%)	197 (47.6%)	145 (41.9%)	148 (47.3%)	
2 < T ≤ 5	10 (47.6%)	106 (54.9%)	205 (49.5%)	190 (54.9%)	158 (50.5%)	
T > 5	2 (9.5%)	12 (6.2%)	12 (2.9%)	11 (3.2%)	7 (2.2%)	
Lymph node status						0.25
0	12 (57.1%)	96 (49.7%)	245 (59.2%)	175 (50.6%)	185 (59.2%)	
1–3	4 (19.1%)	52 (26.9%)	88 (21.3%)	88 (25.4%)	72 (23.0%)	
4–9	3 (14.3%)	31 (16.1%)	47 (11.3%)	50 (14.5%)	28 (8.9%)	
≥ 10	2 (9.5%)	14 (7.3%)	34 (8.2%)	33 (9.5%)	28 (8.9%)	
AJCC stage						0.28
Stage I	6 (28.6%)	46 (23.8%)	124 (30.0%)	84 (24.3%)	93 (29.7%)	
Stage II	10 (47.6%)	102 (52.8%)	208 (50.2%)	167 (48.3%)	155 (49.5%)	
Stage III	5 (23.8%)	45 (23.2%)	82 (19.8%)	95 (27.4%)	65 (20.8%)	
Tumor grade						< 0.001
1	1 (4.7%)	6 (3.1%)	10 (2.4%)	36 (10.4%)	31 (9.9%)	
2	14 (66.7%)	60 (31.1.%)	180 (43.5%)	102 (29.5%)	129 (41.2%)	
3	6 (28.6%)	127 (65.8%)	224 (54.1%)	208 (60.1%)	153 (48.9%)	
Molecular subtype						0.001
Luminal A	8 (28.1%)	72 (37.3%)	170 (41.1%)	134 (38.7%)	165 (52.7%)	
Luminal B	6 (28.6%)	57 (29.5%)	130 (31.4%)	83 (24.0%)	54 (17.3%)	
Her2 overexpression	2 (9.5%)	18 (9.3%)	29 (7.0%)	41 (11.9%)	30 (9.6%)	
Triple negative	5 (23.8%)	46 (23.9%)	85 (20.5%)	88 (25.4%)	64 (20.4%)	
Ki67						0.004
< 14%	4 (19.0%)	31 (16.1%)	98 (23.7%)	74 (21.4%)	95 (7.4%)	
≥ 14%	6 (28.6%)	69 (35.7%)	133 (32.1%)	119 (34.4%)	72 (23.0%)	
Unknown	11 (52.4%)	93 (48.2%)	183 (44.2%)	153 (44.2%)	146 (46.6%)	

AJCC, American Joint Committee on Cancer.

average, with 51.5% negative lymph nodes, and the highest proliferation index. Her2 overexpression tumors were the largest on average, had the highest percentage of ≥ 4 positive lymph nodes, and the most stage III and grade 1 histology. Most TN patients had stage II, poorly differentiated 2–5 cm tumors.

Survival

The median follow up was 33 months (range 3–134). The three-year OS rate for these early stage breast cancer patients was 95.0%, and five-year OS was 90.8%.

Figure 1 shows the survival curves categorized by the five age groups. The youngest group displayed the poorest prognosis. Figure 2 shows the survival curves grouped by the cut-off age: patients aged < 35 exhibited statistically significantly poorer five-year OS at 78.4%, compared to the ≥ 35 age group at 98.4% ($P = 0.02$).

Survival curves according to different molecular subtypes are summarized in Figure 3. Four separate curves were represented by $P < 0.001$. The five-year OS rate in each group was: luminal A 97.3%, luminal B 94.1%, Her2 overexpression 67.6%, and TN 66.5%. In pairwise comparison, luminal A or B had statistically different prognoses compared to the Her2 or TN groups ($P < 0.005$), but the difference in outcomes between Her2 and TN patients was not significant ($P = 0.152$).

Cox regression analysis of the predictors, including age, tumor stage, histology grade, molecular subtype, and Ki67 index was conducted. After adjusting for the influence of other factors, tumor stage ($P = 0.012$) and molecular subtype ($P = 0.014$) were significant survival predictors. Age at diagnosis, histological grade, and Ki67 index did not affect OS ($P = 0.466$, $P = 0.172$, and $P = 0.312$, respectively.)

Discussion

Breast cancer is a heterogenetic cancer that exhibits varied clinicopathological features and survival between different age groups, races, and regions. Keegan *et al.* analyzed 5605 women aged 15–39 and illustrated higher proportions of HR+/HER2+, triple-negative, and stage III/IV, high-grade

Table 3 Clinicopathological features of 1287 breast cancer patients grouped by age, northwest China, 2001–2012

Characteristics	< 35 77 (6.0%)	≥ 35 1210 (94.0%)	*P*
Menopausal status			< 0.001
Yes	1 (1.3%)	612 (50.6%)	
No	66 (85.7%)	542 (44.8%)	
Unknown	10 (13.0%)	56 (4.6%)	
Tumor size, cm			0.45
Average size	2.80 ± 1.37	2.64 ± 1.34	
T ≤ 2	29 (37.7%)	545 (45.0%)	
2 < T ≤ 5	45 (58.4%)	624 (51.6%)	
T > 5	3 (3.9%)	41 (3.4%)	
Lymph node status			0.58
0	38 (49.3%)	675 (55.8%)	
1–3	19 (24.7%)	285 (23.5%)	
4–9	13 (16.9%)	146 (12.1%)	
≥ 10	7 (9.1%)	104 (8.6%)	
AJCC stage			0.39
Stage I	16 (20.8%)	337 (27.8%)	
Stage II	41 (53.2%)	601 (49.7%)	
Stage III	20 (26.0%)	272 (22.5%)	
Tumor grade			0.15
1	1 (1.3%)	83 (6.9%)	
2	32 (41.6%)	453 (37.4%)	
3	44 (57.1%)	674 (55.7%)	
Molecular subtype			0.84
Luminal A	33 (42.8%)	516 (42.7%)	
Luminal B	21 (27.3%)	309 (25.5%)	
Her2 overexpression	5 (6.5%)	115 (9.5%)	
Triple negative	18 (23.4%)	270 (22.3%)	
Ki67			0.15
< 14%	11 (14.3%)	291 (24.0%)	
≥14%	27 (35.1%)	372 (30.8%)	
Unknown	39 (50.6%)	547 (45.2%)	

AJCC, American Joint Committee on Cancer.

tumors.[13,14] Engels *et al.* conducted a study of women aged > 65 years at the time of diagnosis and reported more early stage tumors in the luminal subtypes, and more stage III tumors in the ERBB2, basal, and unclassified subtypes.[15] The present study, which included 1287 patients, analyzed BC features and outcomes between different ages and molecular types, in BC patients in Xi'an, a region few previous studies have examined.

Baseline clinicopathological features of breast cancer

The median age at diagnosis of the patient sample in this study was 50 years, similar to previous studies of Hubei (50 years),[12] Sichuan (47 years),[16] and Guangzhou (47.5 years),[11] indicating that age at diagnosis did not vary greatly within China. When compared to other countries, the age at diagnosis in China was younger. Nguyen *et al.*[5] reported a median age of 55 in Boston, Yi *et al.*[4] observed a similar result of 56 years in an Asian population, Robles-Castillo *et al.*[17] reported 53.6 years in Mexico and Vasconcelos *et al.*[18] reported 56.4 years in German patients. Ethnicity may be a reason for this difference; however, the screening practice cannot be ignored. Effective screening can result in diagnosis at an earlier age without causing overdiagnosis, and should be pursued by clinicians.

Much attention has been paid to small sized tumors in recent years, because T1a,bN0 tumors generally present with a good prognosis. Information from large population databases of untreated T1a,bN0M0 patients demonstrated relatively low cancer-related mortality rates at 15 years (< 10%).[19] Vaz-Luis *et al.* examined data of 4113 women with T1a,bN0M0 BC between 2000 and 2009 from the National Comprehensive Cancer Network Database.[20] Gang Sun *et al.* examined the data of 132 patients with T1aN0M0 and 378 with T1bN0M0 BC in a single center from 2005 to 2010.[21] In the present study, five out of 1287 patients were diagnosed with T1aN0M0 and 65 with T1bN0M0. Our sample of data covering 10 years only yielded 70 patients with T1a,bN0 tumors, reflecting a lack of screening and awareness of self-checking in women in northwest China. If we can discover tumors earlier, we can expect better survival with less treatment. Clinicians

Table 4 Clinicopathological features of 1287 breast cancer patients grouped by molecular subtypes, northwest China, 2001–2012

	Luminal A 549 (42.7%)	Luminal B 330 (25.6%)	Her2 overexpression 120 (9.3%)	Triple negative 288(17.7%)	P
Average age	51.4 ± 3.4	49.0 ± 5.9	57.9 ± 5.5	48.4 ± 8.1	
Menopausal status					< 0.001
Yes	247 (45.0%)	192 (58.2%)	44 (36.7%)	125 (43.4%)	
No	245 (44.6%)	125 (37.9%)	66 (55.0%)	137 (47.6%)	
Unknown	57 (10.4%)	13 (3.9%)	10 (8.3%)	26 (9.0%)	
Tumor size, cm					< 0.001
Average size	2.93 ± 1.09	1.94 ± 1.25	3.02 ± 1.56	2.96 ± 0.96	
T ≤ 2	278 (50.6%)	148 (44.8%)	43 (35.8%)	105 (36.5%)	
2 < T ≤ 5	261 (47.6%)	169 (51.2%)	68 (56.7%)	171 (59.3%)	
T > 5	10 (1.8%)	13 (4.0%)	9 (7.5%)	12 (4.2%)	
Lymph node status					0.07
0	311 (56.7%)	170 (51.5%)	59 (49.2%)	173 (60.1%)	
1–3	129 (23.5%)	83 (25.2%)	25 (20.8%)	67 (23.3%)	
4–9	71 (12.9%)	41 (12.4%)	22 (18.3%)	25 (8.7%)	
≥10	38 (6.9%)	36 (10.9%)	14 (11.7%)	23 (7.9%)	
AJCC stage					0.01
Stage I	174 (31.7%)	82 (24.8%)	26 (21.7%)	71 (24.7%)	
Stage II	259 (47.2%)	165 (50%)	57 (47.5%)	161 (55.9%)	
Stage III	116 (21.1%)	83 (25.2%)	37 (30.8%)	56 (19.4%)	
Tumor grade					< 0.001
I	16 (2.9%)	13 (3.9%)	45 (37.5%)	10 (3.5%)	
II	273 (49.7%)	135 (40.9%)	16 (13.3%)	61 (21.2%)	
III	260 (47.4%)	182 (55.2%)	59 (49.2%)	217 (75.3%)	
Ki67					< 0.001
< 14%	255 (46.4%)	5 (1.5%)	9 (7.5%)	33 (11.5%)	
≥ 14%	0	249 (75.5%)	48 (40.0%)	102 (35.4%)	
Unknown	294 (53.6%)	76 (23.0%)	63 (52.5%)	153 (53.1%)	

AJCC, American Joint Committee on Cancer.

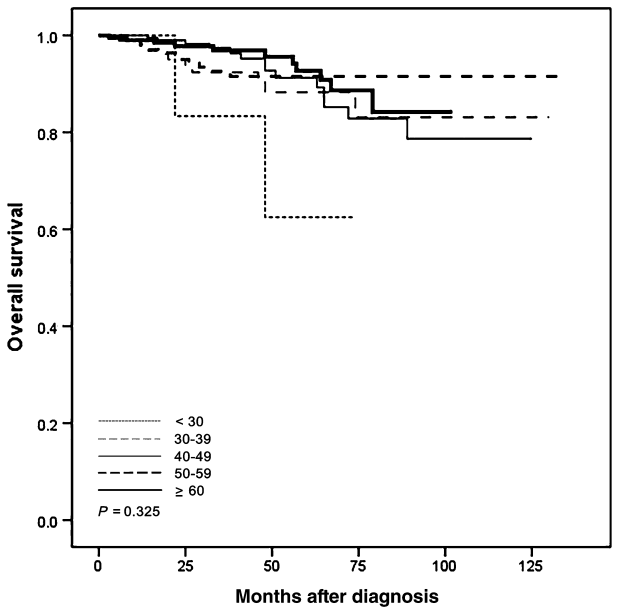

Figure 1 Overall survival curves of breast cancer patients (n = 1287) grouped by age groups, northwest China, 2001–2012.

and policy makers need to provide greater education to the public in order to effect earlier BC diagnosis.

Ki67 has become an important pathological biomarker in routine clinical practice, and can improve the accuracy of pathological models to determine distant BC recurrence.[22] Although our quantitative data was incomplete, our Ki67 results statistically different between age groups, similar to previous studies, indicating that the recommended cut-off value of 14% was meaningful and suitable.

Clinicopathological features of different age groups

The definition of "young" BC patients is not uniform throughout the world; however, we defined 35 years as a significant turning point for our study, and our results were consistent with those from other countries.[23,24] Although only 6.0% of patients were aged < 35 in the present study, aggressive features in this subgroup were observed: younger patients tended to have larger tumors, metastasis in > 4 lymph nodes, grade 2 or 3 histology, non-luminal types, and higher Ki67. In line with the results of previous studies based on foreign patients[23–25] and other provinces of

China,[26,27] younger patients were more often in advanced stage, with lower rates of ER positive expression, higher histological grades, and greater peritumoral vascular invasion. Figure 2 displays the poorer prognosis in younger patients, which has also been observed in clinical work and reported by previous studies.[28,29]

Clinicopathological features of different molecular subtypes

Previous studies have demonstrated the distribution of each molecular subtype in different populations. Our results were similar to those of the Sun Yat-Sen University Cancer Center:[11] Luminal A and B types 68.3% versus 74.6%, Her2 overexpression 9.3% versus. 9.0%, and TN 17.7% versus 16.5%, respectively. Two studies from India demonstrated fewer luminal types: luminal A 43.8% and 34%, luminal B 14.8% and 18%, Her2 overexpression 16.1% and 18%, TN 25.3% and 25%.[30,31] Data from Switzerland[6] and Germany[18] included more patients with luminal types, especially luminal A, which seemed to offer a better prognosis. These differences might be explained by the different definitions of ER, PR, and Ki67 positive; the sensitivity of pathological test methods; and ethnic differences.

Regarding the relationship between age and molecular subtype, the luminal A type was more common in older patients, while middle-aged patients tended to have luminal B, and younger patients were more likely to have TN tumors. In the present study, each molecular subtype had its own specific features. Luminal A type showed moderate features, more than half of the patients had tumors < 2 cm, no lymph node metastasis, and relatively well-differentiated histology, consistent with previous studies and observations in clinical work.[6,11,30,31] Luminal B tumors occurred in younger patients than luminal A tumors and more premenopausal patients, consistent with findings of Cherbal *et al.* and Cheng *et al.*[32,33] However, luminal B presented the smallest average size (1.94 cm), similar to 1.96 cm in a European population,[6] but smaller than 3.1 cm in Wuhan[12] and 2.7 cm in Berlin.[18] The Her2 overexpression group presented aggressive features: the largest size, the highest proportion of patients with ≥ 4 positive lymph nodes (30.0%), most patients in late stage (49.2%), and poorly-differentiated tumors (49.2%). Xue *et al.* reported similar results in 5809 patients, with 33.1% having > 4 positive lymph nodes, 35.6% with stage III tumors, and 66.3% with grade 3 histology, offering a poor prognosis.[11] Data from TCGA and METABRIC databases also showed poorer outcomes in patients with Her2 overexpression.[34] The TN group was the youngest of the four types, with an average age of 48.4 years. Previous studies have reported average ages of 42.3 to 51 years, indicating a trend in younger patients.[5,11,32,33,35] Another significant feature was that the TN group had the largest proportion of poorly-differentiated tumors. Nguyen *et al.* reported that 88% of grade 3 tumors in an American population were TN tumors.[5] Kumar *et al.* reported 64.3% in an Indian population.[31] All of these findings indicate that TN displays invasive behavior and a poor prognosis.

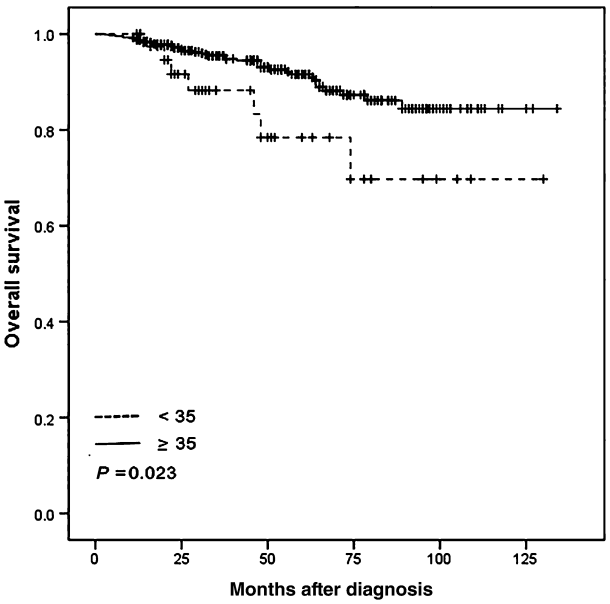

Figure 2 Overall survival of breast cancer patients (n = 1287) grouped by cut-off age, northwest China, 2001–2012.

Treatment of breast cancer

We included 879 (68.3%) hormone receptor positive women in our study, but only 285 (32.4%) were treated with endocrine therapy in any phase of their treatment. This proportion is much lower than in Chengdu[16] and Guangzhou,[11] at 54.4% and 69.8%, respectively, let alone the proportion from developed countries.[36] This result may be explained by a loss of data during follow-up or the fact that some patients did not realize that oral drugs were endocrine agents. Additionally, the use of non-standard treatment cannot be ignored, as patients were not advised to take endocrine agents after previous treatment. Although there are different opinions of how long endocrine therapy should be continued and the choice of drugs, clinicians need to be aware of indications for endocrine therapy.

Trastuzumab, a targeting drug, is strongly recommended for Her2 positive patients. Trastuzumab was indicated as adjuvant chemotherapy for 164 patients in our study sample, but only 10 patients were actually treated with trastuzumab. This may be explained by the fact that our data covered a period when trastuzumab was progressively being introduced into clinical practice and was not covered by medical insurance, as such, economic factors may have influenced the

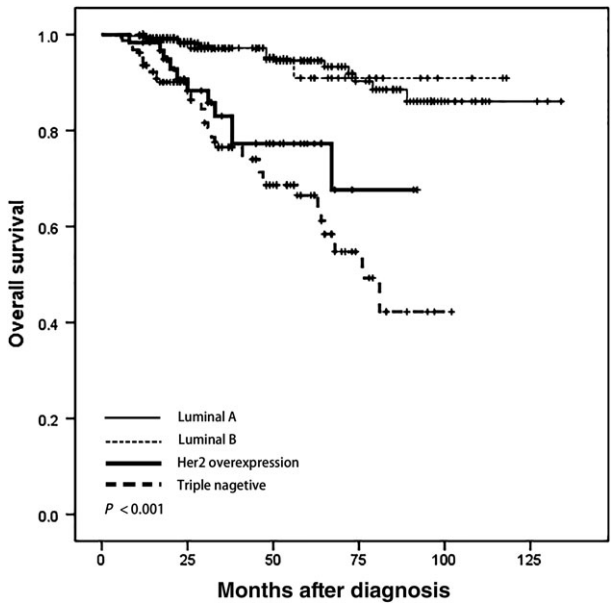

Figure 3 Overall survival curves of breast cancer patients (n = 1287) grouped by molecular subtypes, northwest China, 2001–2012.

decision to a large extent in the northwest district, and it may indicate a lack of cooperation between doctors with different specialties. During the past two years, charity events have publicized trastuzumab, resulting in an increase in use. Two studies are currently underway in Nv Wa and Jing Wei, covering multiple medical centers in China and our hospital is one of the centers providing data of patients administered trastuzumab for late period treatment.

Short-term survival analysis

The majority of patients in our study were diagnosed in recent years, and as a result the median follow-up was 33 months. The five-year OS rate was 91.0%, mainly because of the exclusion of patients with stage IV disease. Kaplan–Meier curves in Figures 1 and 2 show that younger patients had significantly poorer OS rates than older women. Survival curves grouped by molecular subtypes demonstrated similar results to previous reports.[16,30,34]

The results of multivariate regression indicated that tumor stage and molecular subtype were predictors of OS in the present study, which has also been demonstrated by other studies.[15] Therefore, it is important to divide patients into different subgroups, which could guide treatment and reexamination processes.

There were some limitations to the present study. First, as a retrospective study including 10 years of patient data, some data was missing, resulting in inaccuracies when grouping. Second, ER and PR positive were initially defined with a cut-off value of 10%, but were altered to 1% now, and as such, tumors with positive staining between 1% and 9% might be defined as HR negative here. Third, more patients were diagnosed in recent years, resulting in a relatively short follow-up time. A longer follow-up period would ensure greater data capture.

This retrospective study included 1287 early BC patients from a single medical center located in northwest China, which reflects the real world clinicopathological features, treatment, and survival of BC. Our results are consistent with those from other provinces of China, including age at diagnosis, average tumor size, distribution of stage and molecular subtypes, and OS rates. However, when compared to data from developed countries, the present study showed an earlier age at diagnosis, fewer small sized tumors, more stage III tumors, and more patients with Her-2 and TN types. Each molecular subtype has its own specific features and survival, which were also considered a predictor of OS, indicating the importance of considering such features when choosing groups and treatment strategies. Overall, this retrospective study analyzed the clinicopathological features, treatment, and survival of early BC patients, reflecting the situation of diagnosis and treatment in Xi'an over the past 10 years.

Disclosure

No authors report any conflict of interest.

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