Triple-negative breast cancer types exhibit a distinct poor clinical characteristic in lymph node-negative Chinese patients

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Abstract. Comparative studies on the clinical features and outcomes of triple-negative subgroups to human epidermal growth factor receptor-2 (HER-2) overexpression, and luminal A and B subgroups in lymph node-negative breast cancer patients, are important to correctly evaluate clinical prognosis. A total of 1132 Chinese breast cancer patients were enrolled in a retrospective analysis. We characterized and identified prognostic information in the triple-negative subgroup [estrogen receptor (ER)-, progesterone receptor (PR)- and HER-2-negative] and compared that to HER-2 overexpression, and the luminal A and B subgroups. By using immunohistochemical staining, the triple-negative subgroup showed 17% (193/1132) in the whole group. However, HER-2 overexpression, and the luminal A and B subgroups were 11.2, 47.9 and 23.9%, respectively. Tumors in the triple-negative subgroup showed a higher histological grade (P=0.025) and lower invasive ductal carcinoma (P=0.007), compared to the three subgroups. More patients in the luminal A subgroup had received adjuvant chemotherapy (P=0.007). The difference of disease-free survival rates among the four subgroups was significant (P=0.0001). The P-value for overall survival was 0.0598. No significant difference among the four subgroups in lymph node-positive and non-chemotherapy breast cancers was found. From our data the poor clinical outcomes were independent of age, histological grade, tumor size, lymph nodal status, chemotherapy and clinical stages. Our data suggest that the triple-negative subgroup exhibits a distinct poor clinical outcome, especially in lymph node-negative Chinese breast cancer patients.

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Introduction

Breast cancer represents a heterogeneous group of tumors that are diverse in biological behaviors, outcomes and responsiveness to therapy. Breast cancer is the most common cancer among women in Shanghai, mainland China. To improve patient outcome, we need to accurately distinguish the subgroups of breast carcinoma with poor prognosis. A number of biological markers have been reported to evaluate the prognosis of breast cancer patients. Estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER-2) have been widely accepted as prognostic markers and therapeutic targets (1,2). Breast cancers can be classified into five major groups according to gene expression profiling by a new high throughput technology. HR (hormone receptor)-negative tumors are composed of three main subtypes: basal-like, HER-2 overexpression and normal-like. HR-positive tumors consist of the luminal A and B subtypes (3-10). The basal-like subtype is characterized by HR-negative and HER-2 overexpression (triple-negative subgroup) and basal cytokeratin (CK5/6, CK14 and CK17) or epidermal growth factor receptor (EGFR)-positive. It has been demonstrated that the majority (80-90%) of clinically determined triple-negative breast cancer types are included in the basal-like subtype (10-12). It is suggested that clinical behaviors of the triple-negative subgroup and basal-like breast cancer should be similar. Therefore, the standard biomarkers and immunohistochemical staining can be used to accurately classify the triple-negative subgroup or basal-like breast cancer types. A number of studies have been published describing the triple-negative breast cancer subgroup compared to the other subgroups (13-16). Racial disparities in breast cancer with regard to incidence, stage, treatment and mortality have also been well documented (16-19). However, few studies focus on the Chinese population. It has been reported that there is no difference in the survival rate of Chinese, Filipino and Caucasian women (20). In this study, we first evaluated the prognostic information on a special triple-negative subgroup of lymph node-negative Chinese breast cancers

compared to HER-2 overexpression, and the luminal A and B subgroups.

Patients and methods

Patients. A total of 1614 consecutive breast invasive carcinoma cases from January 2000 to December 2002 were admitted into the files of the Department of Breast Surgery of the Cancer Hospital affiliated to Fudan University (the former Cancer Hospital affiliated to Shanghai Medical University). We selected patients who were diagnosed with invasive breast cancer and had complete information of ER, PR and HER-2 status, of which 1132 were eligible. The records came from the database established by our department, containing >10,000 records, including detailed information of the date of diagnosis, age, menopausal status at diagnosis, tumor size, pathological data, nodal status as well as systematic therapeutic records (surgery, chemotherapy, endocrine therapy, radiation treatment and target therapy), as well as the date and type of relapse, and date and cause of succumbing to the disease. The histological grade was determined for each case according to the Scarff-Bloom-Richardson system (21). The clinical stage was classified according to the TNM classification of the International Union Against Cancer (UICC).

Immunohistochemical staining. ER, PR and HER-2 status were determined on representative paraffin sections of each tumor by using immunohistochemical staining (IHC). It was performed one week after the patient underwent surgery. ER and PR antibodies were purchased from Dako (clones ER 1D5 and PR 636). The two antibodies were evaluated by an avidin-biotin-peroxidase complex (ABC) assay as described by Shimada *et al* (22). ER and PR were considered as positive in breast cancer cells if the positive nuclei number was >10%. The cytoplasmic staining was ignored (23). Overexpression of the HER-2 protein was evaluated using a monoclonal antibody (Dako, Clone PN2A) and a peroxidase-antiperoxidase (PAP) technique. Positive HER-2 was defined as a complete membrane staining in >10% of tumor cells (24). It was divided into a qualitative scale from 0 to 3+, according to the criteria of a HercepTest. Scores 0 and 1 were negative, and scores 2 and 3 were positive (25). The pathological and IHC outcomes were diagnosed under an Olympus light microscope with x10 and x40 magnifications by two independent pathologists in the Department of Pathology of the Cancer Hospital at Fudan University. According to Carey *et al* (26), the triple-negative breast cancer subgroup was defined as ER-, PR- and HER-2-negative. However, the HER-2 overexpression subgroup was ER^-, PR^- and $HER2^+$, the luminal A subgroup ER^+ and/or PR^+ and $HER2^-$ and the luminal B subgroup ER^+ and/or PR^+ and $HER2^+$.

Statistical analyses. The follow-up period was defined as the time from surgery to the last observation for censored cases or until relapse/death events occurred. During July 2007, disease-free survival was defined as the time between the date of the primary treatment (surgery or neoadjuvant chemotherapy) to the date of first recurrence of the disease at a local, regional or distant site; the diagnosis of a second cancer; and succumbing without evidence of cancer. Overall survival was defined as the time between the date of the primary treatment to the date of succumbing to the disease for any reason in July 2007. The postoperative relapse-free and overall survival rate were subtracted from the Kaplan-Meier estimate and the difference between the survival curves was compared by means of the log-rank test. The correlations between categorical variables were analyzed by the χ^2 test while continuous variables were analyzed by one way analysis of variance (ANOVA). Cox's proportional hazard model was used to identify the independent predictors for overall and disease-free survival. A two-sided P-value <0.05 or ≤ 0.05 was considered statistically significant. We conducted the statistical analysis with the SPSS 12.0 software program (SPSS Inc., Chicago, USA).

Results

Patient characteristics. The clinical and pathological characteristics are shown in Table I. The mean age of the patients was 53 years, and 87.7% of the patients had a tumor size of <5 cm. Most patients (84.6%) received adjuvant chemotherapy and half of the regimen used was anthracycline-based. Endocrine therapy was received by ~37% of the patients. Among the 1132 invasive carcinomas [ER^+ 694 (61.3%); ER^- 438; PR^+ 587 (51.9%); PR^- 545; $HER2^+$ 397 (35.0%) and $HER2^-$ 735 cases], 193 (17%) cases were classified as the triple-negative breast cancer subgroup. The proportion of $HER2^+$, and the luminal A and B groups was 11.2, 47.9 and 23.9%, respectively. In the triple-negative subgroup, patients had a mean age of 50.9 years (range 28-73). The majority (84.0%, 163/193) of the tumors were invasive ductal carcinoma of non-special type (NST). Of the tumors, 31.5% were classified as histological grade 3 with 115 individuals being node-negative and 77 node-positive (1 patient was without lymph node information). After radical or modified radical mastectomy or breast conservatory therapy, patients received adjuvant systemic therapy according to previously accepted practice guidelines.

Difference between the triple-negative group and other groups. Table I shows the main features of the triple-negative breast cancer subgroup compared to the three subgroups as regards the different clinicopathological variables and biomarkers used in the current study. The mean age at diagnosis of the triple-negative subgroup was younger than that of the other subgroups (P=0.018). Approximately 49% of women with triple-negative breast cancer were diagnosed before the age of 50, whereas 42% of women in the other subgroups were diagnosed in the age range. Patients in the triple-negative subgroup were more likely to have histological grade 3 tumors (P=0.025). Of the patients in the triple-negative group, 31.5% were grade 3. The proportion of invasive ductal carcinoma was 84.5% in the triple-negative subgroup, which was less than that of the three subgroups (P=0.007). We also found that the luminal A subgroup had fewer patients who received adjuvant chemotherapy (P=0.007).

Clinical outcomes. The clinical outcome of the cases has been followed-up regularly. The last update was in July 2007. The median follow-up from the original diagnosis until analysis is

Table I. Clinical and histopathological features of the triple-negative group vs. HER2+, and the luminal A and B phenotypes.

Variable	All cases (%)	Triple negative (%)	HER2% (%)	Luminal A (%)	Luminal B (%)	Chi/F	P-value[a]
No. of cases	1132 (100.0)	193 (17.0)	127 (11.2)	542 (47.9)	270 (23.9)		
Age (years), mean	53.0±10.6	50.9±10.0	51.9±8.9	53.5±11.2	52.1±10.5	3.373	0.018
Age						4.381	0.223
≤50	552 (48.8)	104 (53.9)	54 (42.5)	259 (47.8)	135 (50.0)		
>50	580 (51.6)	89 (46.1)	73 (57.5)	283 (52.2)	135 (50.0)		
Tumor size						5.420	0.144
<5 cm	993 (87.7)	169 (87.6)	105 (82.7)	486 (90.1)	233 (86.3)		
≥5 cm	139 (12.3)	24 (12.4)	22 (17.3)	56 (9.2)	37 (13.7)		
UICC stage						5.991	0.112
I-II	863 (76.2)	143 (74.1)	89 (70.1)	429 (79.2)	202 (74.8)		
III	269 (23.8)	50 (25.9)	38 (29.9)	113 (20.8)	68 (25.2)		
Grade						9.378	0.025
1-2	821 (75.9)	124 (68.5)	91 (72.8)	407 (79.3)	199 (75.7)		
3	261 (24.1)	57 (31.5)	34 (27.2)	106 (20.7)	64 (24.3)		
Surgery						0.945	0.815
MRM	701 (61.9)	119 (61.7)	77 (60.6)	343 (63.3)	162 (60.0)		
Other	367 (38.1)	74 (38.3)	50 (39.4)	199 (36.7)	108 (40.0)		
Pathological type						12.017	0.007
IDC	1004 (88.7)	163 (84.5)	118 (92.9)	472 (87.1)	251 (93.0)		
Non-IDC	128 (11.3)	30 (15.5)	9 (7.1)	70 (12.9)	19 (7.0)		
Lymph node status						3.867	0.276
Negative	634 (56.3)	115 (59.9)	65 (51.2)	311 (57.7)	143 (53.2)		
Positive	493 (43.7)	77 (40.1)	62 (48.8)	228 (42.3)	126 (46.8)		
Untested	5	1	0	3	1		
Chemotherapy						12.111	0.007
Yes	958 (84.6)	165 (85.5)	118 (92.9)	441 (81.4)	234 (86.7)		
No	174 (15.4)	28 (14.5)	9 (7.1)	101 (18.6)	36 (13.3)		
Radiotherapy						1.295	0.730
Yes	178 (15.7)	33 (17.1)	17 (13.4)	82 (15.1)	46 (14.8)		
No	954 (84.3)	160 (82.9)	110 (86.6)	460 (84.9)	224 (85.2)		
Endocrine therapy						120.154	0.000
Yes	419 (37.0)	22 (11.4)	17 (13.4)	263 (48.5)	117 (43.3)		
No	713 (63.0)	171 (88.6)	110 (86.6)	279 (51.5)	153 (56.7)		
ER						NA	NA
Negative	438 (38.7)	193 (100)	127 (100)	80 (14.8)	38 (14.1)		
Positive	694 (61.3)	0 (0)	0 (0)	462 (85.2)	232 (85.9)		
PR						NA	NA
Negative	545 (48.1)	193 (100)	127 (100)	143 (26.4)	82 (30.4)		
Positive	587 (51.9)	0 (0)	0 (0)	399 (73.6)	188 (69.6)		
HER-2						NA	NA
Negative	735 (64.9)	193 (100)	0 (0)	542 (100)	0 (0)		
Positive	397 (35.1)	0 (0)	127 (100)	0 (0)	270 (100)		
Outcome[b]							
Follow-up, median (range), months	45 (1-91)						
5-year DFS	80.1%	72.4%	74.6%	84.0%	80.5%		0.0001
5-year OS	86.5%	81.3%	86.1%	88.1%	87.9%		0.0598

[a]Comparing the four types using the χ^2 test and [b]log-rank test. MRM, modified radical mastectomy and IDC, invasive ductal carcinoma.

Table II. Overall and disease-free survival rates of the triple-negative group vs. HER-2 overexpression, and the luminal A and B phenotypes in different clinicopathological subgroups.

	Disease-free survival		Overall survival	
	Log-rank	P-value	Log-rank	P-value
Age				
≤50	11.28	0.0103	8.73	0.0331
>50	12.06	0.0072	4.12	0.2458
Size				
<5 cm	13.22	0.0042	5.07	0.1669
≥5 cm	7.99	0.0463	4.46	0.2155
Chemotherapy				
Yes	20.18	0.0002	7.06	0.0702
No	2.84	0.4172	1.61	0.6581
Stage				
I-II	7.97	0.0467	2.27	0.5190
III	10.23	0.0107	4.06	0.2458
Lymph node				
Negative	23.53	0.0000	13.67	0.0034
Positive	3.29	0.3495	0.38	0.9437
Grade				
1-2	9.74	0.0209	3.44	0.3290
3	8.72	0.0332	3.74	0.2912

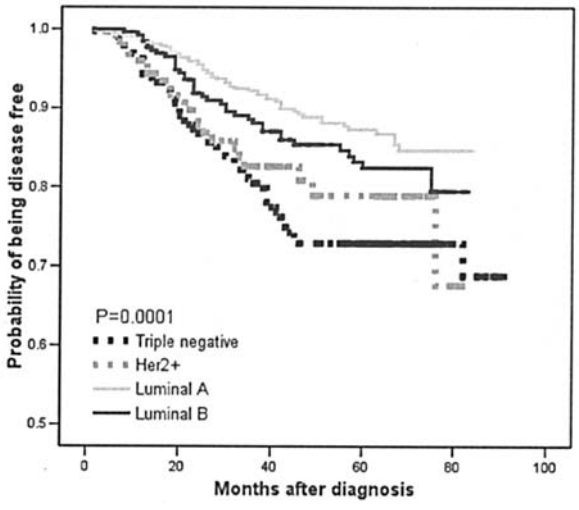

Figure 1. Kaplan-Meier estimates for disease-free survival based on the triple-negative, HER2+, and the luminal A and B phenotypes.

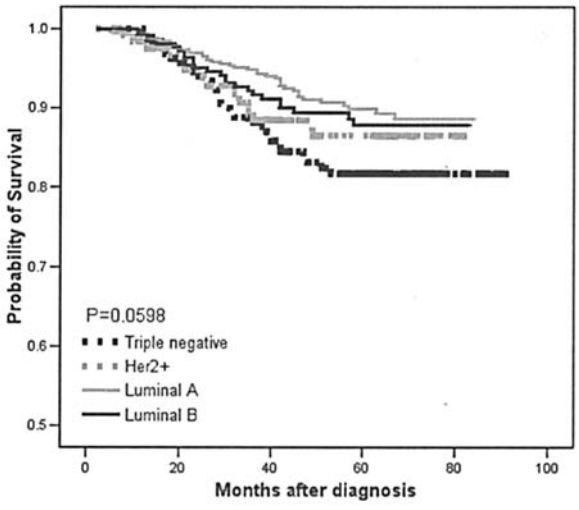

Figure 2. Kaplan-Meier estimates for overall survival based on the triple-negative, HER2+, and luminal A and B phenotypes.

45 months (range 1-91). During follow-up, 968 (85.5%) cases were disease-free with no relapse or metastasis. A total number of 164 (14.5%) patients developed recurrence or metastasis, with 115 (10.2%) patients succumbing due to the primary disease.

The triple-negative phenotype was associated with the development of recurrence and distant metastasis (25.4 versus 17.3, 10.1 and 14.1%, respectively; P=0.000). Patients with triple-negative breast cancer types were more likely to have death risk than patients with other subtypes (15.7 versus 10.2, 7.6 and 9.3%, respectively; P=0.008). Kaplan-Meier survival analyses were carried out to compare the clinical outcomes (Figs. 1 and 2). The difference of disease-free survival rates between the four groups was significant (P=0.0001). The difference among the four groups was not significant when overall survival was compared. There was a trend toward statistical difference. The P-value for overall survival was 0.0598. We performed subgroup analyses using the Kaplan-Meier survival analyses as well (Table II).

Table III. Cox's univariate and multivariate proportional hazard models associated with disease-free survival.

	Univariate		Multivariate	
	HR (95.0% CI)	Sig.	HR (95.0% CI)	Sig.
TN vs. non-TN	1.886 (1.348-2.637)	0.000	1.985 (1.415-2.786)	0.000
Age	0.833 (0.612-1.134)	0.246	0.722 (0.524-0.996)	0.047
Lymph node	0.256 (0.182-0.361)	0.000	0.392 (0.248-0.619)	0.000
Chemotherapy	0.886 (0.599-1.311)	0.546	0.676 (0.448-1.021)	0.063
Tumor size	0.389 (0.270-0.559)	0.000	0.882 (0.586-1.328)	0.547
Stage	0.210 (0.154-0.286)	0.000	0.428 (0.277-0.661)	0.000
Grade	0.474 (0.346-0.649)	0.000	0.561 (0.408-0.773)	0.000

A Cox model, including age at diagnosis (≤50 vs. >50); grade (1, 2 vs. 3); nodal status (negative, positive); tumor size (<5 vs. ≥5 cm); chemotherapy (yes, no); and stage (I, II vs. III). TN, triple-negative; HR, hazard ratio; CI, confidence interval and Sig., significance.

Table IV. Cox's univariate and multivariate proportional hazard models associated with overall survival.

	Univariate		Multivariate	
	HR (95.0% CI)	Sig.	HR (95.0% CI)	Sig.
TN vs. non-TN	1.670 (1.102-2.532)	0.016	1.567 (1.028-2.388)	0.037
Age	0.750 (0.513-1.097)	0.138	0.704 (0.474-1.047)	0.083
Lymph node	0.224 (0.145-0.345)	0.000	0.408 (0.223-0.748)	0.004
Chemotherapy	0.660 (0.425-1.025)	0.064	0.484 (0.303-0.772)	0.002
Tumor size	0.293 (0.193-0.444)	0.000	0.751 (0.470-1.200)	0.231
Stage	0.159 (0.108-0.233)	0.000	0.334 (0.189-0.587)	0.000
Grade	0.379 (0.260-0.552)	0.000	0.485 (0.331-0.712)	0.000

A Cox model, including age at diagnosis (≤50 vs. >50); grade (1, 2 vs. 3); nodal status (negative, positive); tumor size (<5 vs. ≥5 cm); chemotherapy (yes, no); and stage (I, II vs. III). TN, triple-negative; HR, hazard ratio; CI, confidence interval and Sig., significance.

The prognostic outcomes of the triple-negative subgroup were significantly worse in lymph node-negative breast cancer patients. However, there was no significant difference in the outcomes among the triple-negative, HER2$^+$, and luminal A and B subgroups in the lymph node-positive and non-chemotherapy breast cancer patients.

Univariate and multivariate analysis of prognostic factors influencing patient survival. By using the univariate analysis, the triple-negative subgroup had an increased likelihood of recurrence or metastasis in breast cancer (HR, 1.886; 95% CI, 1.348-2.637; P=0.000). Cox's multivariate proportional hazard model was used to adjust for age, grade, tumor size, nodal status, chemotherapy and stage. The risk of recurrence or metastasis from breast cancer remained higher for the triple-negative group (HR, 1.985; 95% CI, 1.415-2.786; P=0.000; Table III). Women with triple-negative breast cancer were associated with poorer overall survival independent of age, grade, tumor size, nodal status, chemotherapy and stage (HR, 1.567; 95% CI, 1.028-2.388; P=0.037; Table IV). Therefore, age, nodal status, grade and stage were found to be independent prognostic factors.

Prognostic value of the different markers in triple-negative breast cancer. In the overall series of the triple-negative breast cancer subgroup, survival analyses showed that tumor size, nodal status and the UICC stage were inversely associated with disease-free and overall survival. Only tumor grade was inversely associated with disease-free survival (Table V).

Discussion

The prognostic evaluation and treatment decisions on breast cancer patients have been influenced by many parameters, currently including lymph node (LN) status, tumor size, tumor grade, expression of steroid factor receptors and HER-2 (27,28). However, the clinical course of any individual patient with breast carcinoma is still difficult to be predicted. Furthermore, the heterogeneity of breast cancer has been proven at the gene expression level. Studies demonstrated that the molecular classification provided new parameters to make individualized treatment decisions and usefully distinguish breast cancer types into intrinsic subgroups with specific clinical outcomes. The basal-like breast cancer has been the

Table V. Association between prognostic variables and outcome in the triple-negative tumors.

	Disease-free survival		Overall survival	
	Log-rank	P-value	Log-rank	P-value
Age	0.02	0.882	0.05	0.820
Tumor size	15.28	0.002	13.31	0.004
Stage	32.08	0.000	28.43	0.000
Grade	8.74	0.013	5.65	0.060
Lymph node	33.05	0.000	30.47	0.000
Chemotherapy	0.29	0.590	1.15	0.283

most noteworthy study object associated with poor clinical outcomes (8,10,12,29). It was likely to reflect associations with a high proliferative capacity, high histological grade and lack of therapeutic targets since those tumors expressed a low level of ER/PR and did not express HER-2 (30-33). It is of note that a very similar classification of breast cancer types has now been characterized using immunohistochemistry (IHC) to analyze patterns of protein expression in paraffin-embedded sections. A number of protein biomarkers (e.g. ER, PR, HER-2, HER-1 and basal cytokeratins) have been used to stratify breast cancer types into different subgroups (11,30). However, a limited number of studies have investigated the prevalence of intrinsic subgroups by HER-1 and basal cytokeratin IHC staining in different races. The markers are not routinely stained for breast tumors in the clinic. The prevalence of the triple-negative breast cancer is easily detected because ER, PR and HER-2 IHC staining are routinely applied in various pathology laboratories. According to previous studies (10-12,26), 80-90% of the triple-negative subgroup can be classified as basal-like breast cancer. In the present study, we used the triple-negative subgroup as a surrogate for basal-like breast cancer.

The luminal A group affects at least half of all patients in most races. The prevalence of triple-negative tumors already published was diverse, with 11.2% in a study population from Canada (13), 12.5% according to a population-based study from the California cancer registry (15), 16.3% in a series of patients in the United Kingdom (14), 26% in conservatively managed patients in the USA (34), and 31% in a Korean study (35). In a Japanese study (16), the prevalence of triple-negative tumors was 10%, which was lower than in other studies. In our study, among Chinese patients, the proportion of triple-negative was 17% when compared to other countries. It appears that a lower prevalence of triple-negative breast tumors and a higher prevalence of luminal A breast tumors contributes to a favorable prognosis. The Carolina study (26) indicated that the African-American breast cancer patients may have a worse prognosis due to the high proportion of triple-negative breast tumors, but we still cannot conclude whether the socio-economic environment and inadequate treatment would influence their prognosis. Breast cancers in different races have a different biological identity, which may reflect genetic influences on the clinical outcome of patients. Although our data were not population-based, it is the first study describing the triple-negative and other subgroups among Chinese breast cancer patients.

The clinical and pathological features of the triple-negative subgroup were similar to those of basal-like breast cancer. The correlations among younger age, grade 3 morphology, largely ductal, stage, larger tumor size, axillary node involvement and triple-negative tumors have been widely reported (36,37). Our study was supported by previous studies. A so-called 'normal' breast subtype has been identified as having similar gene expression patterns to the basal-like signature (7,8). It was concluded that most but not all of the triple-negative characterized breast cancers include the basal-like subgroup. According to the definition of Nielsen *et al* (11), basal-like carcinomas were ER, PR and HER-2-negative and basal cytokeratin (CK5/6 and CK17)-positive and showed highly significant associations with high expression of HER-1, vimentin, c-kit, P-cadherin, FHIT and p63 proteins, and high mutation rates of p53 and BRCA-1 (11,12,26,29,38-41). We carried out an additional study (data not shown) to compare breast cancer patients using the characterization of CK5/6- and CK17-positive and -negative in an overall 112 series of triple-negative breast cancer types. This study will provide further supporting evidence for the prognostic importance of basal cytokeratin expression in triple-negative breast cancers. This subgroup has a very poor prognosis in CK5/6-or CK17-positive. Except for the CK5/6 and CK17 proteins, the tumor size, stage, grade and nodal status proved to be useful prognostic markers in a set of our triple-negative.

Triple-negative breast cancer types are associated with aggressive clinical outcome. Our results were consistent with previous studies of breast cancer which demonstrated that age, nodal status, grade and stage are independent prognostic factors. Furthermore, in our study, the clinical outcome was significantly different among the four intrinsic IHC subgroups. The triple-negative subgroup was identified as having the worst prognosis compared to other subgroups, including $HER2^+$ patients. When the cases were stratified into lymph node-positive and -negative groups, we found that survival was not significantly different among the triple-negative, $HER2^+$, and the luminal A and B subgroups in the lymph node-positive group (43.7% of the cases). However, the triple-negative subgroup was one of the most important markers of prognostic value in the lymph node-negative group (56.3% of cases). Breast cancer patients with lymph node-

positive definitely have a poor prognosis and no relationship to the triple-negative or non-triple-negative subgroup. The former may add important prognostic information particularly in the lymph node-negative tumors. Therapies targeting ER or HER-2 genes are not expected to be effective on triple-negative breast cancer types because this subgroup typically does not express any such proteins. Currently there is no specific systemic regimen for triple-negative breast cancer. It remains unclear which agent induces the best response. Platinum agents show activities in the BRCA-1 DNA repair of defective tumors. Evidence is needed for the use of special combination or sequential regimens in the future.

In conclusion, the classification system based on antibodies and IHC staining allows us to evaluate the clinical prognosis and outcomes of Chinese breast cancer patients. Using the three standard biomarkers ER, PR and HER-2, the triple-negative category showed a distinct poor clinical characteristic especially in lymph node-negative Chinese breast cancer patients. This classification system can be used as a tool for deciding on novel therapeutic options for breast cancer patients. We need to target the aggressive triple-negative subgroup of breast cancers to reduce incidence and mortality rate.

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