

## Original Article

# A retrospective comparative study of clinicopathological features between young and elderly women with breast cancer

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**Abstract:** Objective: This is a retrospective study to compare the clinicopathological features between young and elderly women with breast cancer. Methods: Totally 181 young and 186 elderly breast cancer patients were analyzed and compared in respects of the histological subtype, tumor number and size, tumor location, histological grading, UICC-pTNM pathological staging, and lymph node metastasis status. Results: Our results showed that invasive ductal carcinoma was the most frequent histotype in young and elderly breast cancer patients. The second most frequent histological subtype was intraductal carcinoma in the young group, while the second leading histotype was invasive lobular carcinoma in the elderly group. No significant differences in tumor number and location were observed between the young and elderly groups. The percentage of patients with tumor size T3 (diameter > 5 cm) and the proportion of patients with histological grade III in the young group were significantly higher than the elderly group. For UICC-pTNM pathological staging, patients at stages 0-I and II in the young group were less than, while patients at stage III was more than, in the elderly group. In addition, the axillary lymph node metastasis rate and the numbers of axillary lymph node metastasis were elevated in the young group, compared with the elderly group. Conclusion: Breast cancer in young female patients is associated with increased aggressiveness and potential malignancy. Our findings might contribute to future diagnosis and treatment of breast cancer in young women.

**Keywords:** Breast cancer, clinical characteristics, retrospective comparative study, young and elderly females

## Introduction

Breast cancer is one of the most common malignancies in females, which is the second leading cause of cancer death throughout the world [1, 2]. The incidence of breast cancer has been increasing over the past decades [3, 4], especially in young women ( $\leq 35$  years old). Young breast cancer patients account for up to 4% in total breast cancer cases in Western countries [5, 6]. In Asia, the morbidity rate is as high as 9.5%-12% [7]. Even worse in China, the average onset age of breast cancer might be 8-10 years younger than that in Western countries [8], and the proportion of patients  $\leq 35$  years old has been reported to be 10%-15% [9].

Even though many studies have claimed that age is an independent prognostic factor for the breast cancer, it remains a controversial issue until now. However, in young female patients, breast cancer is likely to be of a more aggressive subtype, and prone to present at an advanced stage (either due to the aggressiveness

or delayed suspicion and/or diagnosis) [10]. In line with this, more loco-regional recurrences and distant metastases have been reported in young women with breast cancer, contributing to the poorer outcome of these patients [11].

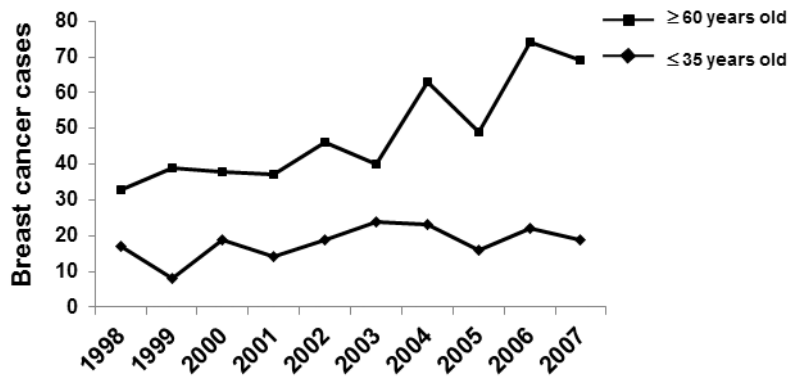
In this study, we retrospectively analyzed the clinicopathological features of 181 young breast cancer patients ( $\leq 35$  years old), in comparison with 186 elderly counterparts ( $\geq 60$  years old) admitted to Qilu Hospital, Shandong University from 1998 to 2007. Our study might provide evidence for the clinical diagnosis and treatment of breast cancer in young women.

## Materials and methods

### *Patients*

In total, 2537 patients with breast cancer were diagnosed and admitted to our hospital from Jan 1998 to Dec 2007. Among these patients, 181 cases (7.1%) were  $\leq 35$  years old at the time of diagnosis, and 488 cases (19.2%) were

## Retrospective analysis of breast cancer



**Figure 1.** Young ( $\leq 35$  years old) and elderly ( $\geq 60$  years old) breast cancer patients diagnosed and admitted to our hospital from 1998 to 2007.

$\geq 60$  years old. All these 181 young breast cancer patients were included in this study, with a median age of 27 years old (ranging between 19 and 35 years old). Another 186 elderly patients were randomly selected as the comparison group, with a median age of 73 years old (ranging between 60 and 85 years old). Prior written and informed consent were obtained from each patient in advance and the study was approved by the ethics review board of Shandong University.

### HE staining

Breast tissues were collected from these breast cancer patients. The tissue was fixed and embedded in paraffin, and then cut into 5- $\mu$ m sections. After deparaffinized and ethanol-rehydrated, these sections were stained with hematoxylin and eosin, and then observed with microscopy.

### Histological grading and pathological staging

Histological grading of breast cancer was performed with the criteria established by Elston and Eliis [12]. Pathological stage was determined according to the clinical staging system of the Union for International Cancer Control (UICC)-pTNM classification [13].

### Statistical analysis

SPSS 13.0 software was used for statistical analysis. The  $\chi^2$  test was performed for comparison.  $P < 0.05$  was considered statistically significant.

## Results

### Histological subtype

During the decade from 1998 to 2007, breast cancer patients diagnosed and admitted to our

hospital had significantly increased. There were 181 female patients  $\leq 35$  years old at the time of diagnosis, accounting for 7.1% of the total breast cancer patients (Figure 1). Among these young breast cancer patients, 7 cases were  $\leq 25$  years old (3.9%), 48 cases were between 26 and 30 years old (26.5%), and 126 cases were between 31 and 35 years old (69.6%).

Together with another 186 elderly cases, histological subtype of breast cancer was analyzed. As shown in Table 1, invasive ductal carcinoma is the most frequent histotype, in both the young and elderly groups, with 140 cases (77.3%) in the young group and 157 cases (84.4%) in the elderly group. In addition, the second most frequent histological subtype of breast cancer in the young group was intraductal carcinoma (15 cases, accounting for 8.3%), while the second leading histotype in the elderly group was invasive lobular carcinoma (7 cases, accounting for 3.8%). In the following sections, the tumor number and size, tumor location, histological grading, UICC-pTNM pathological staging, and lymph node metastasis status in these young and elderly breast cancer patients were analyzed and compared.

### Tumor number and size

The tumor number and size were analyzed and compared between the young and elderly groups. In the young group, there were 160 patients (88.4%) with single tumor, while there were 21 cases (11.6%) with multiple tumors. In the elderly group, there were 179 patients (96.2%) with single tumor, while there were only 7 cases (3.8%) with multiple tumors. On the other hand, the percentage of patients with tumor size T3 (diameter  $> 5$  cm) in the young group (12.7%) was significantly higher than that in the elderly group (5.4%) (Table 2;  $P < 0.05$ ). These results suggest that young breast cancer patients were prone to suffer from large-size tumors compared with the elderly patients.

### Tumor location

Our results showed that in the young group, the left breast was involved in 98 patients (54.1%),

**Table 1.** Analysis and comparison of breast cancer histological subtypes between the young and elderly groups

Histological subtypes	Young (%)	Elderly (%)
Invasive ductal carcinoma	140 (77.3%)	157 (84.4%)
Invasive lobular carcinoma	6 (3.3%)	7 (3.8%)
Intraductal carcinoma	15 (8.3%)	6 (3.2%)
Tubular carcinoma	1 (0.6%)	2 (1.1%)
Medullary carcinoma	3 (1.7%)	1 (0.5%)
Mucinous adenocarcinoma	7 (3.9%)	5 (2.7%)
Secretory carcinoma	1 (0.6%)	1 (0.5%)
Inflammatory breast cancer	2 (1.1%)	0 (0.0%)
Invasive cribriform carcinoma	0 (0%)	1 (0.5%)
Micro-invasive papillary carcinoma	2 (0.1%)	0 (0%)
Papillary carcinoma	1 (0.6%)	2 (1.1%)
Apocrine carcinoma	1 (0.6%)	0 (0%)
Mixed cancer	2 (0.5%)	4 (2.2%)

the right breast was involved in 81 patients (44.8%), and both sides were involved in only 2 patients (1.1%). In these young breast cancer patients, there were 110 cases (60.8%) with tumors located in the upper lateral quadrant, with 14 cases (7.7%) in the lower lateral quadrant, 29 cases (16.0%) in the upper medial quadrant, 6 cases (3.3%) in the lower medial quadrant, 15 cases (8.3%) in the nipples, and 7 cases (3.9%) in the areola area. On the other hand, in the elderly breast cancer patients, the left breast was involved in 93 patients (50.0%), and the right breast was involved in 93 patients (50.0%), while no cases were associated with both sides. Moreover, tumors were located in the upper lateral quadrant in 113 cases (60.8%), with the lower lateral quadrant in 14 cases (7.5%), the upper medial quadrant in 25 cases (13.4%), the lower medial quadrant in 5 cases (2.7%), the nipples in 21 cases (11.3%), and the areola area in 8 cases (4.3%). However, no significant differences in tumor location were observed between the young and elderly groups.

#### *Histological grading*

Histological grading of breast cancer was determined according to the criteria established by Elston and Elis, which was classified into grades I-III [12]. As shown in **Figure 2** and **Table 2**, in the young group, histological grading was as follows: 4 cases (2.9%), grade I; 97 cases (69.3%), grade II; and 39 cases (27.9%), grade

III. On the other hand, in the elderly group, there were 19 cases (12.1%) of grade I, 122 cases (77.7%) of grade II, and 16 cases (10.2%) of grade III. Significant differences were observed between the young group and the elderly group ( $P < 0.01$ ). These results indicate that, compared with the elderly patients, breast cancer in young patient was poorly differentiated, with high malignancy.

#### *UICC-pTNM pathological staging*

Pathological stage was determined with the clinical staging system of the UICC-pTNM classification [13]. As shown in **Table 2**, in the young group, UICC-pTNM staging was as follows: 32 cases (17.7%), stage 0-I; 89 cases (49.2%), stage II; and 60 cases (33.1%), stage III. In the elderly

group, there were 59 cases (31.7%) at the UICC-pTNM stage 0-I, 97 cases (52.2%) at stage II, and 30 cases (16.1%) at stage III. Significant differences were found between the young group and the elderly group ( $P < 0.01$ ). These results suggest that, there were obvious disease progression in young breast cancer patients, and most young patients were in the late or advanced stage at clinical diagnosis.

#### *Lymph node metastasis status*

Lymph node metastasis status was next investigated in these breast cancer patients. As shown in **Table 2**, there were 106 cases (58.6%) of axillary lymph node metastasis in young breast cancer patients, while 67 cases (36.0%) of axillary lymph node metastasis were found in elderly patients. The axillary lymph node metastasis rate in the young group was significantly higher than the elderly group ( $P < 0.01$ ). Moreover, the number of axillary lymph node metastasis in the young group was higher than the elderly group ( $P < 0.01$ ). These results suggest that the young breast cancer patients might be more prone to suffer from axillary lymph node metastasis.

#### **Discussion**

In recent years, the number of new-onset young cases has been increasing throughout the world. In USA, data from Surveillance, Epidemiology, and End Results show that breast cancer patients  $\leq 35$  years old and  $\leq 45$  years old

**Table 2.** Analysis and comparison of pathological characteristics between the young and elderly breast cancer patients

	Young (%)	Elderly (%)	P
Tumor diameter			0.029
≤ 2 cm	64 (35.4%)	81 (43.5%)	
> 2 cm, ≤ 5 cm	94 (51.9%)	95 (51.1%)	
> 5 cm	23 (12.7%)	10 (5.4%)	
Histological grading			0.0001
Grade I	4 (2.9%)	19 (12.1%)	
Grade II	97 (69.3%)	122 (77.7%)	
Grade III	39 (27.9%)	16 (10.2%)	
UICC-pTNM staging			0.0001
Stage 0-I	32 (17.7%)	59 (31.7%)	
Stage II	89 (49.2%)	97 (52.2%)	
Stage III	60 (33.1%)	30 (16.1%)	
Axillary lymph node metastasis			0.0001
Yes	106 (58.6%)	67 (36.0%)	
No	75 (41.4%)	119 (64.0%)	
Number of axillary lymph node metastasis			0.0001
0	75 (41.4%)	119 (64.0%)	
1-3	47 (26.0%)	37 (19.9%)	
4-9	28 (15.5%)	16 (8.6%)	
≥ 10	31 (17.1%)	14 (7.5%)	

account for 1.9% and 12.1%, respectively, of the total breast cancer patients in 2009 [14-16]. Young breast cancer patients might be associated with physiological challenges, including greater likelihood of mastectomy, premature menopause, and loss of fertility [17]. In some researches, diagnosis age ≤ 45 years old has been considered as an independent risk factor for the clinical outcome and prognosis of the disease [18]. On the other hand, others have shown that there are no significant differences in the 5-year overall survival rate by age in HR<sup>-</sup> patients and Her2<sup>+</sup> patients, compared with HR<sup>+</sup> patients, indicating a poor prognosis irrespective of age [19, 20].

In China, according to the Cancer Mortality Surveillance, the incidence of breast cancer in women has increased from 19.9/100000 in 2000 to 24.8/100000 in 2005 [21]. Up to 2011, female patients ≤ 45 years old represent 27.3% of the total breast cancer patients in China [22]. Beadle *et al.* [23] show that the recurrence rate at 10 years after breast-conserving surgery of breast cancer patients ≤ 35 years old is up to 19.8%. Moreover, Meng *et al.* [8] show that young breast cancer patients might

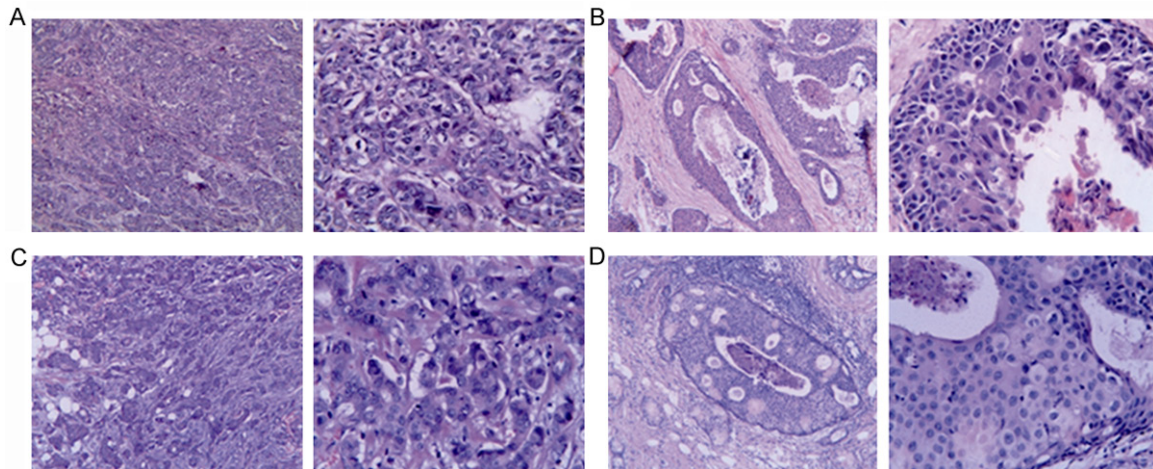
account for 5-13% of all the breast cancer cases over the same period. Esther *et al.* have first shown that molecular subtypes exhibit a different distribution and exert different prognostic effects in elderly breast cancer patients compared to young patients [21].

In this study, our results indicated that young women with breast cancer represented 7.1% of all the patients with breast cancer diagnosed and admitted to our hospital from 1998 to 2007. Moreover, in the young group, left breasts were more involved in breast cancer than right breasts, with only 2 cases associated with both sides. However, in the elderly

group, half the tumors were located in left breasts and the other half were in right breasts, with no cases involving both sides. In both the young and elderly groups, breast tumors were mainly located in the upper lateral quadrant, followed subsequently by the upper medial quadrant and the nipples. Gu *et al.* [24] suggest that the mean onset age of patients with breast tumors in both sides is significantly younger than the unilateral breast cancer patients, and the incidence of bilateral breast cancer is much higher in premenopausal females than postmenopausal females. The predilection sites of bilateral breast cancer are concentrated in tissues rich for glands and conduits, i.e., the upper lateral quadrant and the areola area.

According to the WHO 2003 guideline, breast cancer falls into 19 subtypes, including the invasive ductal carcinoma, invasive lobular carcinoma, and so on. Invasive ductal carcinoma is the most common breast cancer subtype. Yiangou *et al.* [25] and Jiang *et al.* [26] report that the invasive ductal carcinomas account for approximately 80% in breast cancer patients. A recent multi-center clinical study has found that breast cancer actually represents a certain





**Figure 2.** Histological grading and pathological staging of breast cancer patients. Histological grading and pathological staging of young (A, B) and elderly (C, D) breast cancer patients were performed on the basis of HE staining. Representative pictures indicated stage III invasive ductal carcinoma (A) (left,  $\times 100$ ; right,  $\times 400$ ; hereinafter the same) and intraductal carcinoma (B) in young patients, as well as stage II invasive ductal carcinoma (C) and intraductal carcinoma (D) in elderly patients.

definite proportion in young females [27]. Due to the high levels of estrogen in younger breast cancer patients, tumor cell invasion would be up-regulated. Therefore, young breast cancer patients might be at high risk of invasive ductal carcinoma, severe malignancy, and rapid disease progression [28]. In this study, both the young and elderly groups were dominated by invasive ductal carcinoma, which is consistent with previous studies.

Breast cancer tumor size, histological grading, pathological staging, and lymph node metastasis status are important prognostic factors. Studies have shown that histological grading of tumors is associated with the 5-year survival rate, and the higher histological grading might indicate the poorer prognosis [29]. On the other hand, Liu *et al.* [30] show that the 3-year (5-year) survival rate of young breast cancer patients with lymph node metastasis is 61.1% (25.0%), while the survival rate of young patients without lymph node metastasis is 100% (83.3%). A retrospective study from Zhou *et al.* [31] involving 484 breast cancer patients indicates that female patients between 41 and 50 years old are associated with the high incidence of breast cancer, and young patients always have large-size tumors. Our study showed that the percentage of patients with tumor size T3 (diameter  $> 5$  cm) and the proportion of patients with histological grade III in the young group are significantly higher than the

elderly group, which is in line with the study from Wang *et al.* [32]. For UICC-pTNM pathological staging, patients at stages 0 - I and II in the young group were less than, while patients at stage III was more than, in the elderly group. Furthermore, the axillary lymph node metastasis rate and the number of axillary lymph node metastasis were higher in the young group, compared with the elderly group.

Young breast cancer patients are always associated with high aggressive and adverse pathological features. The reasons might include 1) that the mammary glands are always huge and abundant in young females, which makes it difficult to detect tumors, resulting in misdiagnosis; 2) that vigorous metabolism in young females could contribute to rapid tumor growth and high metastasis rate; and 3) the poor vigilance of themselves and/or their physicians. It has been controversial whether age is an independent prognostic factor for the breast cancer [33, 34]. Based on our findings, we claim that age itself might not be one of the main prognostic factors for breast cancer, however it indeed is associated with increased aggressiveness and potential malignancy, on which more attention should be addressed in clinical diagnosis and treatment.

## Conclusions

In conclusion, our results showed that, compare with the elderly breast cancer patients,

young patients were characterized by large-size tumors, higher histological grades, more advanced UICC-pTNM stages, and elevated lymph node metastasis rates. Breast cancer in young female patients is associated with increased aggressiveness and potential malignancy. These findings might contribute to future diagnosis and treatment of breast cancer in young women.

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## Disclosure of conflict of interest

None.

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