Treatment and survival outcomes in older women with primary breast cancer: A retrospective propensity score-matched analysis

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Purpose: Changes in biological features and functional status make management decisions in older women with primary breast cancer complicated. We aimed to provide an overview of the clinicopathological characteristics and survival outcomes of older breast cancer patients based on the current treatment strategies.

Methods: Female patients diagnosed with primary invasive breast cancer at Fudan University Shanghai Cancer Centre from 2008 to 2016 were included. Patients were divided into a younger group (<65 years) and older group (≥65 years). Propensity score matching was utilised to generate balanced cohorts.

Results: A total of 13,707 patients met the study criteria. Compared with younger patients, older patients had a higher Charlson Comorbidity Index (p < 0.001), less lymph node metastasis (p = 0.009), more advanced tumour stage (p = 0.038), and a larger proportion of estrogen receptor-positive (p < 0.001) and epidermal growth factor receptor 2-negative (p < 0.001) tumours. Older patients were likely to receive mastectomy and axillary lymph node dissection in addition to a lower proportion of adjuvant chemotherapy. Adjuvant chemotherapy (HR [hazard ratio] 0.69, p = 0.039) was independently correlated with better overall survival in the older patients. This survival benefit (HR 0.58, p = 0.041) was confirmed in matched cohorts. Among the older patients with larger tumours (HR 0.48, p = 0.038) and more lymph node involvement (HR 0.44, p = 0.040), adjuvant chemotherapy was associated with a significant survival benefit.

Conclusion: Older breast cancer patients showed less aggressive biological characteristics, intensive surgical and moderate medical preferences. The addition of adjuvant chemotherapy should be considered for older patients, especially for patients with large tumours and more lymph node involvement.

1. Introduction

Female breast cancer has the highest cancer incidence and is the fourth major cause of cancer mortality among women in China [1]. Data indicate that patients aged 60 years or older account for 30% of all breast cancer cases and 46% of all deaths [2]. According to qualified data from the National Central Cancer Registry (NCCR) of China, 31.30% of patients with breast cancer were aged 60 years or older in 2015; by 2030, the proportion of newly diagnosed breast cancer cases in those aged ≥65 years is expected to be 41.37% [3]. A similar pattern was identified in patients aged ≥65 years [4]. Research reported a shift in the age composition of breast cancer towards older age groups in China, with an increasing median age at diagnosis [5]. Furthermore, the mortality rate was found to increase in older patients according to NCCR data. Compared with younger patients, patients over the age of 60 years have a considerably higher rate of breast cancer mortality, suggesting that older women may obtain little benefit from advances in breast cancer diagnosis and treatment [3]. Therefore, research on different treatment patterns between younger and older patients would help us to identify the factors causing these disparities in mortality and develop strategies to eliminate them. However, most existing studies concentrate on age-specific incidence and mortality in China.

Previous research reported notable differences in tumour pathological features between younger and older individuals with breast cancer. Older patients were found to have a larger proportion of estrogen receptor (ER)- and human epidermal growth factor receptor 2 (HER2)-

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negative tumours [6–8]. Studies also demonstrated that older patients tended to develop tumours with less aggressive characteristics than their younger counterparts [9–12]. Moreover, studies indicated that comorbidities, toxicity tolerance, functional status, and life expectancy played increasingly essential roles in treatment decisions with ageing [13], which makes decision-making for older patients increasingly complicated [14].

According to treatment guidelines from the National Comprehensive Cancer Network (NCCN), the European Society of Breast Cancer Specialists (EUSOMA), and the International Society of Geriatric Oncology (SIOG), management decisions for breast cancer patients should not depend on their chronological age [15,16]. Instead, therapeutic strategies for older women with breast cancer should consider ageing-related changes in functional status, comorbidities, mental health, and social standing. Geriatric assessment has been recommended as a supplement to oncology assessment for guiding therapeutic interventions in older patients [17,18]. Regarding the detrimental effects on functional status, toxicity, and poor tolerance to chemotherapy, consideration must be given to whether the advantages of surgery and treatment will outweigh the risks for these patients. Based on the available evidence, surgical intervention remains the main option for older individuals and is equally recommended in younger patients. Moreover, a Cochrane review and another retrospective study reported that primary endocrine therapy (PET) had equivalent survival outcomes to surgery in patients aged 70 years and older with ER-positive tumours, while the progression-free survival was worse for PET [19,20]. Recently, a multicentre, prospective study comprising 3416 patients aged ≥70 years further confirmed that surgery was oncologically superior to primary endocrine therapy [21].

Studies have indicated that older patients with comorbidities or poor functional status are less likely to receive chemotherapy [13,22,23]. Moreover, little research has been conducted to investigate the benefits of adjuvant chemotherapy (ACT) in controlled groups of older breast cancer patients, while the available data show inconsistent results. Muss et al. [24] suggested that older women aged 50–69 years with lymph node (LN)-positive breast cancer receiving ACT had a significant reduction in breast cancer mortality and recurrence, while the reduction was progressively diminished with increasing age in patients older than 70 years. Based on the Surveillance, Epidemiology, and End Results (SEER) program dataset, another research demonstrated that ACT was associated with a survival benefit in patients with ER-negative, LN-positive breast cancer, whereas this improvement in survival was not observed among patients with ER-positive disease [25]. Recently, a retrospective study comprising 16,062 patients with triple-negative breast cancer (TNBC) demonstrated that the survival benefit of chemotheraphy persisted for LN-negative and LN-positive patients, and even patients with high comorbidity scores [26]. Moreover, study reported survival benefits of ACT in older patients with ER-negative disease, while its detrimental impact on quality of life was resolved after 18 months [27,28]. Given that older women have historically been underrepresented in many breast cancer clinical trials, evidence regarding optimal treatment in older women is scarce, especially for patients in China.

In this study, we compared the differences in clinicopathological characteristics between older (≥65 years) and younger (<65 years) patients and assessed the effectiveness of current therapies on overall survival in older breast cancer patients.

2. Material and methods

2.1. Patients

Female patients diagnosed with primary invasive breast cancer between January 2008 and December 2016 at Fudan University Shanghai Cancer Centre (FUSCC) were enrolled. Patients with bilateral tumours, incomplete comorbidity records, incomplete pathological assessment and follow-up data, those who received neoadjuvant therapy, and those who did not receive any treatment were excluded. A total of 13,707 breast cancer patients met the study criteria and were included in the study (Supplemental Fig. 1). Based on the age at diagnosis, 12,004 patients were assigned to the younger group (<65 years), and 1703 patients were assigned to the older group (≥65 years).

2.2. Data extraction

The patients’ demographic, clinicopathological, and treatment data were retrospectively collected by medical record review, which was based on the dataset established by department of cancer prevention in FUSCC. Charlson Comorbidity Index (CCI) score was utilised for quantification of comorbidity, which was calculated based on the severity of the comorbidities documented in the hospital information system [29]. Survival status of patients was extracted from department of clinical statistics of FUSCC based on medical records or telephone follow-up records. Overall survival (OS) was defined as time from primary diagnosis to patient death related to any cause or the last follow-up.

2.3. Clinicopathological characteristics

Given the significant correlation between a CCI score of 3 and therapeutic options and survival outcomes reported in previous studies [30–33], 3 was chosen as the cut-off score for the CCI. CCI scores of 0, 1–2, and ≥3 corresponded to patients with no, few, and major comorbidities, respectively. All pathological variables were determined according to the same guidelines at any time point. Histological subtype was identified using the 2003 and 2012 World Health Organization (WHO) histological classification criteria. The staging of the tumour and axillary LNs were categorized using the 2002 and 2010 American Joint Committee on Cancer (AJCC) Tumor Node Metastasis (TNM) staging criteria. Pathological tumour (pT) and LN (pN) stage was evaluated by pathological assessment after surgery. ER and PR status were identified using immunohistochemistry (IHC). HER2 positivity was defined as IHC 3+ or amplification by fluorescence in situ hybridization (FISH). Accordingly, tumours were divided into four molecular subtypes: (I) luminal A-like (ER- and/or PR-positive, HER2-negative, Ki-67 ≤20%); (II) luminal B-like (ER- and/or PR-positive, HER2-negative, Ki-67 >20%); (III) HER2-positive (HER2-positive and ER- and/or PR-negative, or HER2-positive and ER- and/or PR-positive); and (IV) triple-negative (negative for ER, PR, andHER2).

2.4. Statistical analysis

The Chi-square test was used to compare the clinicopathological data in the younger and older groups. OS was analysed by the Kaplan–Meier method and compared with the log-rank test. Correlated factors of survival were explored with multivariate analysis using Cox proportional hazards. Factors that were considered clinically significant were included in the multivariate model. We used 1:1 propensity score matching (PSM) without replacement to balance the significant variables between groups. For survival analysis between the younger and older groups, matching was based on CCI score, molecular subtype, pT stage, pN stage, type of breast and axillary surgery, and receipt of chemotherapy. For survival analysis between patients with and without ACT, matching was based on age, CCI score, molecular subtype, pT stage, pN stage, and type of breast and axillary surgery. A p-value <0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS version 25.0.

3. Results

3.1. Patients

A total of 13,707 patients with invasive breast cancer were involved...
in this study. Based on age at diagnosis, 12,004 patients were assigned to the younger group (≤65 years) and 1703 patients were assigned to the older group (≥65 years) (Table 1). The data indicated that older women had higher CCI scores (p < 0.001), fewer LN metastases (p = 0.009), and less advanced tumour stage (p = 0.038) than younger women. Invasive ductal carcinoma not otherwise specified (NOS) was the most common histological subtype in both groups, while older patients had a higher percentage of lobular carcinoma NOS and other subtypes (p < 0.001). Older patients had a higher proportion of ER-positive (p < 0.001) and HER2-negative (p < 0.001) tumours. Furthermore, compared with younger patients, luminal A-like and luminal B-like tumours accounted for a substantially higher proportion in older patients (p < 0.001). There was no statistically significant difference in tumour size, PR status, or distant metastasis between the two groups.

### Table 1

Comparison of clinicopathological characteristics of breast cancer patients between the younger (≤65 years) and older groups (≥65 years).

| Characteristics                        | Older group (≤65 years) | Younger group (≥65 years) | P value |
|----------------------------------------|------------------------|---------------------------|---------|
| No. of patients                        | 1703                   | 12,004                    |         |
| Age at diagnosis, median (quartiles, years) | 69 (65–92) | 49 (18–64) | <0.001 |
| CCI score                              |                        |                           | <0.001 |
| 0                                      | 995 (58.4)             | 10,488 (87.4)             |         |
| 1–2                                   | 554 (32.5)             | 1,434 (11.9)              |         |
| ≥3                                     | 154 (9.0)              | 82 (0.7)                  |         |
| pT stage                               |                        |                           | 0.111   |
| T0                                     | 1 (0.01)               | 9 (0.1)                   |         |
| T1                                     | 1000 (58.7)            | 6999 (58.3)               |         |
| T2                                     | 672 (39.5)             | 4650 (38.7)               |         |
| T3/T4                                  | 20 (1.1)               | 253 (2.1)                 |         |
| Tx                                     | 10 (0.59)              | 93 (0.8)                  |         |
| pN stage                               |                        |                           | 0.009   |
| N0                                     | 1117 (65.6)            | 7366 (61.4)               |         |
| N1, N2                                 | 486 (28.5)             | 3868 (32.2)               |         |
| N3                                     | 89 (5.2)               | 695 (5.8)                 |         |
| Nx                                     | 11 (0.7)               | 75 (0.6)                  |         |
| M stage                                |                        |                           | 0.360   |
| M0                                     | 1685 (98.9)            | 11,845 (98.7)             |         |
| M1                                     | 18 (1.1)               | 159 (1.3)                 |         |
| pTNM stage                             |                        |                           | 0.038   |
| I                                      | 772 (45.3)             | 5140 (42.8)               |         |
| II                                     | 694 (40.8)             | 4882 (40.7)               |         |
| III                                    | 219 (12.9)             | 1823 (15.2)               |         |
| IV                                     | 18 (1.0)               | 159 (1.3)                 |         |
| Histological type                      |                        |                           | <0.001  |
| Invasive ductal carcinoma NOS          | 1296 (76.1)            | 9016 (75.1)               |         |
| Invasive ductal carcinoma NOS with DCIS| 279 (16.4)             | 2568 (21.4)               |         |
| Lobular carcinoma NOS                  | 67 (3.9)               | 256 (2.1)                 |         |
| Others                                 | 61 (3.6)               | 164 (1.4)                 |         |
| ER status                              |                        |                           | <0.001  |
| Positive                               | 1311 (77.0)            | 8762 (73.0)               |         |
| Negative                               | 392 (23.0)             | 3242 (27.0)               |         |
| PR status                              |                        |                           | 0.504   |
| Positive                               | 1151 (67.6)            | 7824 (65.2)               |         |
| Negative                               | 552 (32.4)             | 4180 (34.8)               |         |
| HER2 status                            |                        |                           | <0.001  |
| Positive                               | 301 (17.7)             | 3436 (28.0)               |         |
| Negative                               | 1402 (82.3)            | 8568 (71.4)               |         |
| Molecular subtypes                     |                        |                           | <0.001  |
| Luminal A-like                         | 604 (35.5)             | 3492 (29.1)               |         |
| Luminal B-like                         | 587 (34.5)             | 3528 (29.4)               |         |
| HER2-positive                          | 301 (17.7)             | 3436 (28.0)               |         |
| Triple-negative                        | 211 (12.3)             | 1548 (12.9)               |         |

Abbreviations: CCI, Charlson Comorbidity Index; pT stage, pathological tumor stage; pN stage, pathological lymph node stage; M, distant metastases; NOS, not otherwise specified; DCIS, ductal carcinoma in situ; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

#### 3.2. Management patterns

After excluding patients with distant metastases at diagnosis, there were 1685 (98.9%) and 11,845 (98.7%) breast cancer patients initially treated with surgery in the older and younger groups, respectively. Data indicated that elderly patients had a higher rate of mastectomy and lower rate of breast-conserving surgery (BCS) (p < 0.001). For axillary evaluation, older patients were inclined to directly undergo axillary lymph node dissection (ALND) or not have axillary surgery (p < 0.001). Additionally, most of the younger patients received ACT, whereas more than one-half of the older patients did not receive ACT (p < 0.001). Among the patients undergoing ACT, older individuals were less likely to receive regimens containing anthracycline and tended to be administered capecitabine alone (Table 2).

Endocrine therapy was administered to 88.99% (1270/1427) and 88.50% (8531/9639) of the patients with ER- and/or PR-positive tumours in the older and younger groups, respectively. Among the patients with HER2-positive tumours, 44.18% (133/301) of the older patients and 63.65% (2187/3436) of the younger patients received targeted therapy.

#### 3.3. Survival analysis

The median follow-up time was 68.12 months for the entire study cohort. A total of 2088 patients were matched perfectly after PSM between the older and younger patients (Supplemental Table 1). The older patients showed a significantly worse OS compared with younger patients (HR 2.16 [95% CI 1.60–2.92], p < 0.001) (Supplemental Fig. 2). Multivariate Cox analysis suggested that the risk of poor OS substantially increased with age. In older patients with a CCI score ≥3, advanced pT and pN stage, luminal B-like, HER2-positive, and TNBC subtype were correlated with poorer OS. ACT was significantly correlated with improved OS. Nevertheless, the type of breast and axillary surgery were not statistically correlated with OS (Table 3).

#### Table 2

Therapeutic options for breast cancer patients are primarily treated with surgery.

| Variables                        | Older group (N = 1685) | Younger group (N = 11,845) | P value |
|----------------------------------|------------------------|-----------------------------|---------|
| Breast surgery                   | 258                    | 15.32                       | 2464    | 20.80 |
| Mastectomy                       | 1423                   | 84.45                       | 9095    | 76.78 |
| With                              | 3                      | 0.18                        | 286     | 2.42  |
| Without breast surgery           | 1                      | 0.06                        | 0       | 0.00  |
| Axillary surgery                 |                        |                             |         |
| SLNB only                        | 690                    | 40.95                       | 5005    | 42.25 |
| SLNB + ALND                      | 145                    | 8.61                        | 1330    | 11.23 |
| ALND                             | 825                    | 48.96                       | 5474    | 46.21 |
| Without axillary surgery         | 25                     | 1.48                        | 36      | 0.30  |
| Adjuvant chemotherapy            |                        |                             | <0.001  |
| With                              | 36                     | 20.53                       | 6645    | 56.09 |
| Without breast surgery           | 346                    | 79.47                       | 3355    | 43.91 |
| Anthracycline                     | 72                     | 4.27                        | 7       | 0.06  |
| Capecitabine only                | 25                     | 1.48                        | 36      | 0.30  |
| Others                           | 25                     | 1.48                        | 36      | 0.30  |
| Without chemotherapy             | 25                     | 1.48                        | 36      | 0.30  |
| Missing                          | 1                      | 0.06                        | 0       | 0.00  |

Abbreviations: SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.

a The type of surgery that patients primarily received.

b Patient was diagnosed with occult breast cancer and did not receive breast surgery.
Table 3
Multivariable Cox survival analysis in older patients (≥65 years) who received surgery as initial treatment.

| Variables          | Hazard ratio (95% CI) | P value |
|--------------------|-----------------------|---------|
| Age at diagnosis (years) |                       |         |
| 65-69 (ref)        | –                     | –       |
| 70–74              | 1.79 (1.29–2.49)      | 0.001   |
| 75–79              | 1.80 (1.22–2.69)      | 0.003   |
| 80–84              | 4.36 (2.69–7.08)      | <0.001  |
| ≥85                | 6.04 (2.99–15.96)     | <0.001  |
| CCI score          |                       |         |
| 0–2                | –                     | –       |
| 1–2                | 1.10 (0.82–1.48)      | 0.524   |
| ≥3                 | 1.69 (1.15–2.48)      | 0.007   |
| pT stage           |                       |         |
| pT0/pT1 (ref)      | –                     | –       |
| pT2                | 1.37 (1.03–1.81)      | 0.027   |
| pT3                | 2.86 (1.36–5.99)      | 0.005   |
| pN stage           |                       |         |
| pN0 (ref)          | –                     | –       |
| pN1/pN2            | 2.06 (1.51–2.80)      | <0.001  |
| pN3                | 5.00 (3.18–7.83)      | <0.001  |
| Molecular subtypes |                       |         |
| LUMinal A-like (ref) | –                     | –       |
| LUMinal B-like     | 1.47 (1.04–2.08)      | 0.059   |
| HER2-positive      | 2.10 (1.40–3.16)      | <0.001  |
| Triple-negative    | 2.35 (1.52–3.64)      | <0.001  |
| Breast surgery     |                       |         |
| Mastectomy (ref)   | –                     | –       |
| Breast-conserving surgery | 1.00 (0.64–1.56) | 0.991   |
| Auxiliary surgery  |                       |         |
| Sentinel lymph node biopsy (ref) | – | –       |
| Axillary lymph node dissection | 1.32 (0.95–1.83) | 0.996   |
| Without axillary surgery | 1.58 (0.65–3.84) | 0.312   |
| Adjuvant chemotherapy | –                     | –       |
| No (ref)           | –                     | –       |
| Yes                | 0.69 (0.49–0.98)      | 0.039   |

Abbreviations: ref, reference; CCI, Charlson Comorbidity Index; pT stage, pathological tumor stage; pN stage, pathological lymph node stage; HER2, human epidermal growth factor receptor 2.

3.4. Survival analysis after propensity score matching

We further verified the effect of ACT in a matched cohort. After PSM, 224 patients with ACT and 224 patients without ACT were matched successfully (Table 4). Patients receiving ACT showed improved OS compared with those who did not receive ACT (HR 0.58 [95% CI 0.35–0.96], p = 0.041) (Fig. 1). Subgroup analysis suggested that chemotherapy was beneficial in patients with low tumour stage (HR 0.46 [95% CI 0.29–0.70], p = 0.01) and in patients with HER2-negative tumours and low LN involvement (HR 0.48 [95% CI 0.24–0.76], p = 0.003) (Fig. 2). However, no significant improvement in survival was observed in patients from different age groups, CCI scores, and molecular subtypes.

Table 4
Balanced statistics of patients aged over 65 years with or without adjuvant chemotherapy (ACT) after propensity score matching.

| Variables          | Pre-matching | Post-matching | P value |
|--------------------|--------------|--------------|---------|
| Age at diagnosis (years) |              |              |         |
| 65-69 (ref)        | 496          | 379          | <0.001  |
| 70–74              | 738          | 42.0         | 0.68     |
| 75–79              | 130          | 262          | 0.52     |
| 80–84              | 37           | 151          | 0.15     |
| ≥85                | 9            | 65 (7.2)     | 0.33     |
| CCI score          |              |              |         |
| 0                  | 0.000        | 0.000        | 1.000   |
| 1–2                | 218          | 212          | 0.99     |
| 3–5                | 58           | 158          | 0.18     |
| pT stage           |              |              |         |
| pT0/pT1 (ref)      | –            | –            | –       |
| T1                 | 327          | 606          | 1.000   |
| T2                 | 332          | 282          | 0.87     |
| T3                 | 13           | 14 (1.6)     | 0.09    |
| pN stage           |              |              |         |
| pN0 (ref)          | –            | –            | –       |
| pN1/pN2            | 314          | 734          | 0.001   |
| pN3                | 68           | 12 (1.3)     | 0.09    |
| Molecular subtypes |              |              | 0.478   |
| LUMinal A-like     | 229          | 337          | 71 (31.7) |
| LUMinal B-like     | 237          | 308          | 98 (48.3) |
| HER2-positive      | 125          | 147          | 22 (9.8) |
| Triple-negative    | 81           | 110          | 22 (9.8) |
| Breast surgery     |              |              | 0.001   |
| Breast-conserving surgery | 68     | 176          | 24 (10.7) |
| Mastectomy         | 604          | 726          | 200 (100) |
| SLNB               | 183          | 463          | 112 (50.0) |
| ALND               | 487          | 419          | 112 (50.0) |

Abbreviations: CCI, Charlson Comorbidity Index; ACT, adjuvant chemotherapy; pT stage, pathological tumor stage; pN stage, pathological lymph node stage; HER2, human epidermal growth factor receptor 2; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.

4. Discussion

In the present study, we demonstrated significant differences in clinicopathological characteristics and treatment patterns between older women and their younger counterparts with primary invasive breast cancer. Our data suggested that ACT was independently correlated with an apparent survival benefit in patients aged ≥65 years.

Retrospective studies reported that ageing not only increased the incidence of comorbidities but also influenced the clinicopathological features of breast cancer patients [6-8,11]. Our result indicated that older patients tended to be diagnosed with less aggressive tumours at a less advanced stage, which included a higher proportion of ER-positive, HER2-negative tumours and less LN involvement. Although previous studies suggested that older women were more likely to have large tumours [34-36], no significant difference in tumour size was identified between the two groups in our study. A possible explanation might be the development and promotion of breast cancer screening in recent decades. The most common histological subtype of invasive breast cancer in our cohort was ductal carcinoma. Moreover, we identified a lower percentage of ductal carcinoma and higher percentage of lobular carcinoma, a special type of invasive breast cancer. Similar trends in the incidence of different histological types were reported by Albrektsen.
et al. [37] and Fisher et al. [38].

Despite the recent application of new surgical techniques, including BCS, sentinel LN biopsy, and breast reconstruction, we reported higher rates of mastectomy in patients older than 65 years compared with studies from developed areas [39–43]. This status of therapeutic options was consistent with recent research based on 110 hospitals in China [44]. One possible explanation might be that older patients were more conservative due to extensive tension and anxiety about cancer, which was attributed to their poor functional status and comorbidities [45,46]. In addition, older patients focused less attention on cosmetic outcomes and were more inclined to undergo mastectomy to avoid radiotherapy after BCS [44]. However, surgery remains the standard treatment option in older patients with operable breast cancer [15,22] and was reported to be correlated with a survival benefit in patients older than 80 years [47,48]. Considering the passive clinicopathological features, surgical trends in the elderly are quite aggressive in China. According to the results of the NASBP B-06, BCS plus radiotherapy was considered an alternative to mastectomy [49]. Furthermore, based on SEER data, no differences in survival between older breast cancer patients who underwent mastectomy and BCS were identified in the functional status-controlled groups [50]. Similarly, our data indicated that surgical

type did not influence survival outcomes in older patients. Overall, the surgical practices of the breast in China were quite different from those in developed countries, which indicated that implementation of consensus and guidelines for breast cancer needs further promotion in addition to a potential insufficiency in evidence-based decision-making in elderly individuals.

ALND was more prevalent in older patients than younger patients, even in cases with less LN metastasis. However, omission of axillary surgery or substitution by other adjuvant therapy options in certain groups of elderly patients has been proven to be safe. IBCSG 10–93, a randomised-controlled trial, identified no improvement in disease-free survival or OS in patients aged ≥60 years with clinically node-negative operable breast cancer after addition of ALND [51]. Similarly, an Italian study indicated no survival benefit from ALND in women aged 65–80 years after 15 years of follow-up [52]. Consistently, we found that type of axillary surgery was not associated with significantly better OS. Given that SLNB was effective in pathologic nodal staging and cancer control and was associated with a significant decline in arm morbidity [53–55], it is a rational alternative to ALND in elderly patients. Altogether, our results suggest a conservative attitude of older patients towards SLNB and insufficient consultation of current evidence by surgeons and patients during the treatment decision-making process in older patients in current clinical practice.

ACT was independently correlated with a decreased risk of mortality in elderly breast cancer patients. However, our data reported a lower proportion of ACT among older patients, which was consistent with earlier studies [25,56–59]. One possible explanation might be that the comorbidities, geriatric syndromes, frailty, and limited life expectancy become more serious with ageing, which leads to progressively poorer acceptance of standard chemotherapy. However, based on the balanced cohorts in the current study, ACT was found to be associated with better OS. Subgroup analysis further indicated that patients with large tumour size and more LN involvement could benefit from ACT. In addition, an increased incidence of single capecitabine application was identified in elderly patients. According to the results of the CALGB 49907 study, standard chemotherapy is superior to capecitabine monotherapy in terms of relapse-free survival and OS, especially in older patients with hormone receptor-negative disease [23,60]. Moreover, compared with
standard chemotherapy, the advantage of capecitabine on quality of life during treatment was found to be equivalent at 1 year [61].

The major limitation of the present study was caused by the nature of retrospective studies, which made selection bias inevitable regarding patients’ options for postoperative treatment. As the cancer centre with more than 2000 breast cancer patients diagnosed and hospitalised every year since 2010, a large proportion of elderly patients are from other cities in China [5,62]. However, due to a lack of convenience and socioeconomic problems, elderly patients are inclined to return to the local area for subsequent adjuvant treatment and regular follow-up. In addition, based on the experience of surgeons at the clinic, older patients had a relatively passive attitude towards standard treatment. Therefore, a higher percentage of missing records on complete pathological assessment, complete follow-up data, and therapeutic information were identified in older patients. Therefore, the cohort of the current study may not be sufficient to reflect the pathological and therapeutic features of all elderly Chinese patients with breast cancer. Moreover, a large proportion of older patients were excluded from our analysis because they were diagnosed with ductal carcinoma in situ, which lead to an even lower proportion of patients aged ≥65 years in the current study. Without the specific cause of death, we can only analyse OS instead of breast cancer-specific survival, which would provide better assessment of therapeutic benefits in elderly patients. Regarding postoperative therapy, the completion status of endocrine and targeted therapy was absent in many patients, and intermittent adherence or discontinuance of the regimens led to inadequate data for survival analysis among patients with or without endocrine and targeted therapy. Moreover, due to the lack of geriatric assessment, we utilised age and CCI score to broadly assess the functional status of patients based on the retrospectively collected data regarding comorbidities. Previous studies reported that age was significantly correlated with poorer survival outcomes, and optimal therapeutic strategies varied based on the age of elderly patients [36,63]. Therefore, age-stratified studies concentrating on the treatment of elderly patients should be conducted in China. All the limitations of the present study should be taken into consideration, and randomised-control studies are needed to further confirm our findings.

5. Conclusions

We provided a brief overview of the distinct clinicopathological features, more aggressive surgical choices, and moderate chemotherapy preferences of breast cancer patients aged ≥65 years compared with their younger counterparts. Our results support the administration of ACT, especially in older patients with large tumour size and LN involvement.

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Conflicts of interest

The authors declare that they have no conflict of interest.

Ethics approval

The study was conducted following the Declaration of Helsinki (as revised in 2013). This research has been approved by the Medical Ethics Committee of Fudan University Shanghai Cancer Centre. Informed consent has been waived by the ethics committee as this retrospective research poses no risk to patients.

Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Yuting Sang. The first draft of the manuscript was written by Yuting Sang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

None.

Acknowledgments

Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2022.09.001.

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