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# Operation with less adjuvant therapy for elderly breast cancer



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## ABSTRACT

**Background:** The standard of care for elderly women with breast cancer remains controversial. The aim of this study was to clarify the management of elderly breast cancer patients who undergo surgery.

**Materials and methods:** This retrospective single-center cohort study included 2276 breast cancer patients who underwent surgery between 1993 and 2014. The patients were divided into three groups according to age:  $\leq 64$  y (young), 65–74 y (older), and  $\geq 75$  y (elderly).

**Results:** The elderly had more advanced stage disease at diagnosis (stage III and IV, 16.2%, 17.5%, and 22.1% for the young, older, and elderly groups, respectively). The elderly were more likely to undergo mastectomy (43.3%, 41.4%, and 50.7%, respectively), omit axillary operation (0.6%, 1.1%, and 9.3%, respectively), and skip radiotherapy after breast-conserving surgery (93.1%, 86.8%, and 29.1%, respectively). Endocrine therapy was widely used in all the groups (94.4%, 93.8%, and 90.1%, respectively), but frequency of chemotherapy was lower in the elderly regardless of hormone receptor (HR) status (40.8%, 25.5%, and 9.3% in HR(+), 87.2%, 75.3%, and 39.5% in HR(–), respectively). Although the locoregional recurrence rate was higher in the elderly (4.2%, 3.4%, and 7.0% at 5 y, respectively;  $P = 0.028$ ), there were no differences among groups in distant metastasis-free survival or breast cancer-specific survival.

**Conclusions:** Although elderly patients had more advanced stages of cancer and received less treatment, there were no differences in survival. Omission of axillary dissection, radiation, and chemotherapy after operation may be an option for breast cancer patients aged  $\geq 75$  y.

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## Introduction

Breast cancer is the most common malignant disease among women in the world. The incidence has been increasing substantially in Japan and other Asian countries over the past 3 decades, and it has a high incidence in the United States and Europe.<sup>1-3</sup> In Asia including Japan, breast cancer incidence peaks among women in their 40s, whereas it peaks among women in their 60s in the United States and Europe.<sup>1,4</sup> Despite the difference in median age at diagnosis, the number of breast cancer patients is increasing in Japan due to a rapid increase in the number of elderly individuals. The population that is aged over 65 y accounted for 9.1% of the total in 1980, 19.9% in 2005, and it is estimated to reach 31.8% by the year 2030.<sup>5,6</sup>

Although the number of elderly patients with breast cancer is increasing, knowledge about the possible differences in the biology and clinical outcomes of elderly cases of breast cancer that should reflect management according to age remains limited. Currently, treatment for elderly women with breast cancer is largely extrapolated from data derived from trials that enrolled younger patients; thus, the standard of care for elderly breast cancer patients is far from being established.<sup>7</sup> Several reports demonstrated that elderly breast cancer patients are less likely to undergo surgery, radiation, or chemotherapy.<sup>8-11</sup> Although studies consistently show that older women are undertreated for breast cancer, the impact of undertreatment on breast cancer survival among older women remains controversial.<sup>10</sup> Furthermore, little has been reported on the management of elderly breast cancer patients in Asian countries.

The aim of this study was to clarify the management of elderly breast cancer patients who underwent surgery and to investigate any effect of management choice on their outcomes.

## Patients and methods

The study included 2276 patients with breast cancer referred for surgery at Yokohama City University Medical Center between May 1993 and June 2014. Data on patient medical history, histopathologic factors of the breast cancers, and management including surgery, radiation, and systemic treatment (hormonal therapy or chemotherapy) were recorded. This study was approved by the Institutional Review Board of Yokohama City University, Kanagawa, Japan.

Estrogen receptor (ER) level, progesterone receptor level, human epidermal growth factor 2 (HER2) status, and Ki-67 labeling index were evaluated pathologically using the invasive component of the tumor. Hormonal receptor status was evaluated via immunohistochemistry as described previously.<sup>12-14</sup> HER2 testing was performed via immunohistochemistry and/or *in situ* hybridization as previously reported.<sup>15</sup> The Ki-67 labeling index was evaluated in the highest immunoreactivity fields and was recorded as 0%-100% as recommended.<sup>16</sup>

We defined the nomenclature of the operations as the following: mastectomy (including radical, modified radical, or

simple mastectomy), breast-conserving surgery (BCS, including lumpectomy, segmental resection, wide resection, quadrantectomy, or partial mastectomy), or immediate reconstructive surgery with skin (and nipple) sparing mastectomy. For axillary lymph nodes, sentinel lymph node biopsy using dye and/or radioisotope methods, and/or complete axillary lymph node dissection was performed.<sup>17</sup>

The patients who underwent BCS were recommended to receive adjuvant radiation therapy to the remaining breast tissue.<sup>18</sup> The patients with pT3-T4 tumors and/or  $\geq 4$  positive axillary nodes were recommended to receive radiation therapy according to clinical practice guidelines.<sup>17,19-22</sup>

For patients with invasive ductal carcinoma, adjuvant systemic therapy was administered according to the estimated risk of recurrence. The adjuvant chemotherapy regimens included anthracycline-based regimens such as AC (doxorubicin and cyclophosphamide), CAF (cyclophosphamide, doxorubicin, and 5-fluorouracil [5FU]), CEF (cyclophosphamide, epirubicin, and 5FU), taxane-containing regimens such as TC (docetaxel and cyclophosphamide), docetaxel/3w or paclitaxel/w; CMF (cyclophosphamide, methotrexate, and 5FU), and oral 5FU alone. Endocrine treatments were mainly selective estrogen-receptor modulators, such as tamoxifen and toremifene, or aromatase inhibitors such as anastrozole, exemestane, and letrozole.

The statistical analysis was conducted using the SPSS 22.0 for Windows software (SPSS Inc, Chicago, IL). Correlations among the clinicopathologic parameters and age groups were evaluated via Tukey-type multiple comparison analyses with the chi-square and Mantel test. Patient outcomes were assessed in terms of disease-free survival (DFS). Survival distributions were estimated using the Kaplan–Meier method. Differences were compared using the log-rank test.  $P < 0.05$  was considered statistically significant.

## Results

### Pathologic characteristics by age group

Of the 2276 women in our study population, 1632 (71.7%) were aged below 64 y (young), 400 (17.6%) were between 65 and 74 y (older), and 244 (10.7%) were aged older than 75 y (elderly). The patients' characteristics are summarized in Table 1. The elderly patients had larger and more advanced tumors, but no significant difference was observed among groups in terms of lymph node involvement. Because of the increased frequency of larger tumors, the elderly patients had significantly advanced stage disease at diagnosis (stages III and IV, 16.2%, 17.5%, and 22.1%, for the young, old, and elderly groups, respectively;  $P < 0.001$ ).

There were no differences in estrogen receptor positivity by age (77.0%, 74.1%, and 77.0%, respectively), but there were fewer patients aged 65-74 y with progesterone receptor-positive tumors (67.8%, 59.8%, and 67.7%, respectively;  $P = 0.060$ ) and fewer HER2-positive tumors in patients aged  $\geq 65$  y (14.0%, 9.1%, and 8.0%, respectively;  $P = 0.003$ ). Thus, there were more luminal and fewer HER2 subtypes among the older and elderly patients than among the young patients.

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