

Treatment patterns and outcomes according to age among older patients with early breast cancer: a retrospective study

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Abstract

Background:

Breast cancer is increasingly diagnosed in older adults because of population aging; however, evidence supporting perioperative chemotherapy in patients aged ≥ 75 years remains limited. Real-world treatment patterns and their association with clinical outcomes in this population have not been well characterized. This study aimed to evaluate age-related differences in perioperative treatment patterns and clinical outcomes among older patients with early breast cancer in routine clinical practice.

Methods:

We retrospectively reviewed 171 patients aged ≥ 65 years with stage I–III breast cancer who underwent surgery in 2007–2016 and met institutional indications for perioperative chemotherapy. Patients were grouped as 65–74 years or ≥ 75 years. Clinicopathological characteristics, treatment patterns, disease-free survival (DFS), overall survival (OS), breast cancer-specific survival (BCSS), and prognostic factors were analyzed.

Results

Compared with patients aged 65–74 years, those aged ≥ 75 years were less likely to receive chemotherapy (4.3% vs. 56.4%; $P < 0.001$), anti-HER2 therapy, or radiotherapy, whereas use of hormone therapy was similar. Tumor stage and receptor subtype distributions did not differ between groups. Five-year DFS ($P = 0.3311$) and BCSS ($P = 0.175$) were comparable, although OS ($P = 0.0466$) was lower in patients aged ≥ 75 years. Multivariable analysis identified age ≥ 75 years, stage III disease and high nuclear grade and/or Ki-67 as independent prognostic factors for OS.

Conclusions

Despite substantially lower use of perioperative chemotherapy in patients aged ≥ 75 years, disease-free and breast cancer-specific survival were comparable between the age groups. Since only three patients aged ≥ 75 years received chemotherapy, these findings should not be interpreted as evidence regarding chemotherapy efficacy. Rather, they describe real-world treatment patterns in older Japanese patients with early breast cancer and support an individualized approach to treatment consistent with current guideline recommendations.

BACKGROUND

Breast cancer (BC) is the most commonly diagnosed cancer among women worldwide, with approximately 2.3 million new cases reported in 2022 (1). In Japan, where one of the world's most rapidly aging population resides, individuals aged ≥ 65 years account for approximately 30% of the total population and the proportion of older patients with breast cancer continues to increase (2). Although adjuvant systemic therapy has substantially improved the prognosis of early-stage BC, evidence supporting chemotherapy in older adults, particularly those aged ≥ 75 years, remains limited. Older patients are underrepresented in prospective clinical trials. Consequently, treatment decisions are often based on chronological age rather than robust evidence, whereas frailty, comorbidities, life expectancy, and patient preferences substantially influence chemotherapy use (3).

In older patients with BC, the 2022 edition of the Japanese Breast Cancer Society Clinical Practice Guidelines for Breast Cancer considers standard chemotherapy a valid perioperative chemotherapy option (4). Nonetheless, evidence-based use of chemotherapy in older patients with early-stage BC is limited (5). Although previous studies have evaluated the efficacy of adjuvant chemotherapy in selected older patients (6), because they involved selected trial populations rather than real-world

patients, little is known about how chemotherapy is used in routine clinical practice among Japanese patients aged ≥ 75 years and whether age-related differences in treatment patterns are associated with clinical outcomes.

Therefore, this study aimed to evaluate age-related differences in perioperative chemotherapy use and clinical outcomes in older Japanese patients with early BC treated in routine clinical practice. By examining both treatment patterns and oncologic outcomes, we sought to determine whether age-related variations in treatment were associated with differences in survival.

METHODS

Ethical approval

All procedures involving human participants in this study were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. This study was approved by the Research Ethics Committee of Tokyo Women's Medical University (Approval No. 2021–0065). Informed consent was waived by the Ethics Committee due to the retrospective study design, and an opt-out approach was implemented in accordance with the institutional ethics policy.

Study design

This retrospective single-center cohort study included all patients aged ≥ 65 years with stage I–III BC who underwent curative surgery at Yachiyo Medical Center between January 2007 and December 2016 and met our institutional criteria for perioperative chemotherapy. Patients were classified into two age groups (65–74 years and ≥ 75 years). Clinical data were obtained from electronic medical records. Patients were followed until death, the last clinical follow-up, or December 31, 2021, whichever occurred first.

Inclusion and exclusion criteria

Eligibility for chemotherapy was defined as meeting one or more of the following criteria, excluding cases with an infiltration diameter of ≤ 0.5 cm: 1) infiltration diameter ≥ 5 cm, 2) lymph node metastasis, 3) nuclear grade ≥ 3 or Ki-67 $\geq 30\%$, 4) positive vascular invasion, 5) estrogen receptor (ER)-negative or progesterone receptor (PgR)-negative, and 6) human epidermal growth factor receptor 2 (HER2)-positive.

Tumors were evaluated using preoperative needle biopsy or histological examination of surgical specimens. ER and PgR status were determined by immunohistochemical staining of tissue sections and were evaluated based on the staining results. If $\geq 10\%$ of cells were positive, the tumor was considered ER-positive. HER2 expression was assessed by first examining protein levels using immunohistochemistry (IHC), with an IHC score of 3+ considered positive. Cases with an IHC score of 2+ were evaluated for gene amplification using fluorescence in situ hybridization. Even if an ER-positive or PgR-positive patient met at least one other criterion (PgR-negative or ER-negative, respectively), the patient was considered a candidate for chemotherapy. Exclusion criteria were stage IV disease at diagnosis, recurrent breast cancer, bilateral breast cancer, ductal carcinoma in situ (DCIS), referral after surgery performed at another institution, and incomplete clinicopathological data.

Chemotherapy regimen and assessment

The indication for perioperative chemotherapy was determined by the treating breast surgeons according to the institutional treatment policy based on the contemporaneous Japanese Breast Cancer Society Clinical Practice Guidelines. Before surgery, patients were evaluated using computed tomography (CT), ultrasonography, and fine-needle aspiration cytology of the lymph nodes. Treatment decisions were individualized after consideration of clinicopathological factors, including tumor stage, lymph node status, hormone receptor status, HER2 status, histological grade, and estimated risk of recurrence, together with patient age, performance status, comorbidities, and patient preference. Chemotherapy regimens included

anthracycline-based therapy (epirubicin plus cyclophosphamide), anthracycline followed by taxane (paclitaxel or docetaxel), taxane-based therapy (docetaxel plus cyclophosphamide), and oral tegafur-uracil (UFT). Regimens were selected according to recurrence risk, patient fitness, and the prevailing standard of care during the study period.

Data collection

Patient demographic and clinicopathological characteristics, treatment information, and follow-up data were retrospectively extracted from the electronic medical records. Collected variables included age at surgery, tumor size, pathological stage, lymph node status, histological type, nuclear grade, ER status, HER2 status, Ki-67 index, lymphovascular invasion (LVI), perioperative chemotherapy, endocrine therapy, anti-HER2 therapy, radiotherapy, recurrence, survival status, cause of death, and follow-up duration. Missing data were handled using available-case analysis; patients with missing values for a given variable were excluded only from analyses involving that variable, and no imputation of missing values was performed.

Statistical analyses

Categorical variables were compared using Fisher's exact test or the chi-square test, as appropriate. Continuous variables were compared using the Student's t-test after confirming normality. Disease-free survival (DFS) was defined as the time from surgery to the first occurrence of breast cancer recurrence or death from any cause. Overall survival (OS) was defined as the time from surgery to death from any cause, and breast cancer-specific survival (BCSS) as the time from surgery to death due to breast cancer. Patients were considered lost to follow-up if they discontinued follow-up at our institution within 5 years after surgery and no subsequent information on recurrence or survival was available in the institutional medical records. These patients were censored at the date of their last documented clinical visit in the survival analyses. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Multivariable analyses were performed using the Cox proportional hazards model. Covariates included age, chemotherapy, ER status, HER2 status, lymph node status, pathological stage, LVI, and high-proliferative tumors (defined as nuclear grade 3 and/or Ki-67 ≥30%), which were selected based on their established clinical relevance and previously reported prognostic significance in early breast cancer. Missing data were handled using available-case analysis; patients with missing values for a given variable were excluded only from analyses involving that variable, and no imputation was performed. The proportional hazards assumption was assessed before fitting the Cox proportional hazards model and was confirmed to be satisfied. A two-sided P value <0.05 was considered statistically significant. All statistical analyses were performed using JMP Pro 14 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Patient characteristics

From January 2007 to December 2016, 244 patients with BC aged ≥65 years underwent surgery at Tokyo Women's Medical University Yachiyo Medical Center. Among them, 171 (70.1%) had an indication for perioperative chemotherapy. The number of patients aged 65–74 years was 101 (59.1%), whereas 70 (40.9%) were aged ≥75 years. Table 1 shows the characteristics of the two groups. Compared with patients aged 65–74 years, those aged ≥75 years more frequently had lobular carcinomas (1.9% vs. 7.3%) and special histologic types (7.0% vs. 16.7%) rather than invasive ductal carcinomas. No differences were observed in tumor stage, invasive diameter, lymph node metastasis, ER, PgR, HER2, nuclear grade, Ki-67, or vascular invasion. Mastectomy was significantly more frequent among patients aged ≥75 years (44.5% vs. 64.3%; P=0.0107). Chemotherapy (56.4% vs. 4.3%; P<0.0001) and anti-HER2 therapy (25.7% vs. 10.0%; P=0.0008) were administered significantly less often; however, no difference was observed in the use of hormone therapy (64.4% vs. 72.9%; P=0.326). Among patients who received chemotherapy, anthracycline-based regimens predominated in the 65–74-year group, whereas only three patients aged ≥75 years received chemotherapy (one EC followed by a taxane, one taxane-alone regimen, and one UFT regimen). Radiotherapy was also administered significantly less often (50.5% vs. 22.9%; P<0.0001).

Table 1. Characteristics of patients

Category	65–74 years	≥75 years	P*
	n=101(%)	n=70(%)	
Median Follow-up period, month (range)	82 (7–163)	61.5 (0–162)	<0.0001
Loss to follow-up within 5 years	7 (6.9)	11 (15.7)	0.0683
Median Age, years (range)	69 (65–74)	79 (75–93)	<0.0001
Sex			
Female	99 (98.0)	69 (98.6)	0.784
Male	2 (2.0)	1 (1.4)	
Stage			
I	24 (23.8)	24 (34.3)	0.3251
II	62 (61.4)	37 (52.9)	
III	15 (14.8)	9 (12.8)	
T			
T1	48 (45.5)	36 (51.4)	0.6085
T2	38 (37.6)	22 (31.4)	
T3	4 (4.0)	5 (7.2)	
T4	13 (12.9)	7 (10.0)	
N			
N0	49 (48.5)	38 (54.2)	0.4577
N1	52 (51.5)	32 (45.8)	
Histology			
Ductal	144 (91.1)	73 (76.04)	0.0006
Lobular	3 (1.9)	7 (7.29)	
Other	11 (6.96)	16 (16.67)	
Receptor subtype			
ER positive	64 (63.4)	49 (70.0)	0.3659
ER negative	37 (36.6)	21 (30.0)	
PgR positive	38 (37.6)	23 (32.9)	0.5214
PgR negative	63 (62.4)	47 (67.1)	
HER2 positive	28 (28.7)	17 (24.3)	0.967
HER2 negative	71 (70.3)	41 (58.6)	
Unknown	1 (10.0)	12 (17.1)	
Nuclear grade			
1	38 (37.6)	23 (32.9)	0.892
2	31 (30.7)	22 (31.4)	

3	30 (29.7)	24 (34.3)	
Unknown	2 (2.0)	1 (1.4)	
Ki-67			
<30%	51 (50.5)	37 (52.9)	0.2943
≥30	7 (6.9)	9 (12.9)	
Unknown	43 (42.6)	23 (34.3)	
Vascular invasion			
Yes	34 (33.7)	33 (47.1)	0.1084
No	45 (44.5)	25 (35.7)	
Unknown	22 (21.8)	12 (17.2)	
Surgery			
Bp	56 (55.5)	40 (35.7)	0.0107
Bt	45 (44.5)	56 (64.3)	
Chemotherapy			
Administered ^{\$}	57 (56.4)	3 (4.3)	<0.0001
Not administered	44 (43.6)	67 (95.7)	
Chemotherapy regimen			
Anthracycline → taxane	28	1	
Anthracycline only	20	0	
Docetaxel + cyclophosphamide	6	0	
Taxane only	0	1	
Tegafur–uracil (UFT)	3	1	
Anti-HER2 therapy			
Administered	26 (25.7)	7 (10.0)	0.008
Not administered	75 (74.3)	63 (90.0)	
Hormone therapy			
Administered	65 (64.4)	51 (72.9)	0.326
Not administered	36 (49.5)	54 (77.1)	
Radiotherapy			
Administered	51 (50.5)	16 (22.9)	0.0002
Not administered	50 (49.5)	54 (77.1)	

^{\$}n = 19 patients (65–74 years, n = 18; ≥75 years, n = 1) underwent preoperative chemotherapy. n = 41 patients (65–74 years, n = 39; ≥75 years, n = 2) underwent postoperative chemotherapy. Bt, mastectomy; Bp, partial mastectomy. * Significance level was set at P < 0.05.

Patient outcomes

The median follow-up period was 71 months (range: 7–163 months). The proportion of patients who were lost to follow-up within 5 years after surgery was higher in the ≥ 75 -year group (11/70, 15.7%) than in the 65–74-year group (7/101, 6.9%), although the difference did not reach statistical significance ($P = 0.0683$). For recurrence events, among patients aged 65–74 years, 11 (19.0%) who underwent chemotherapy and eight (18.6%) who did not had recurrence. In patients aged ≥ 75 years, recurrence occurred in two (66.7%) who underwent chemotherapy and 13 (19.4%) who did not. For deaths, among patients aged 65–74 years, 11 (19.0%) patients who underwent chemotherapy and seven (16.3%) who did not died. Among patients aged ≥ 75 years, one (33.3%) died among those who underwent chemotherapy, and 17 (25.4%) died among those who did not undergo chemotherapy (Table 2).

Table 2. Outcome of chemotherapy treatment in older adults with early breast cancer

Category	65–74 years		≥ 75 years	
	CTx	No CTx	CTx	No CTx
	N=58 (%)	N=43 (%)	N=3 (%)	N=67 (%)
Disease-free survival				
No recurrence	43 (74.1)	32 (74.4)	1 (33.3)	43 (64.2)
Recurrence	11 (19.0)	8 (18.6)	2 (66.7)	13 (19.4)
Unknown	4 (6.9)	3 (7.0)	0 (0)	11 (16.4)
Overall survival				
Survival	42 (72.4)	32 (74.4)	2 (66.7)	39 (58.2)
Death during follow-up	11 (19.0)	7 (16.3)	1 (33.3)	17 (25.4)
Death due to breast cancer	8 (13.8)	4 (9.3)	1 (33.3)	10 (14.9)
Death due to other causes	3 (5.2)	3 (7.0)	0 (0)	7 (10.4)
Unknown	5 (8.6)	4 (9.3)	0 (0)	11 (16.4)

CTx; chemotherapy.

No difference was observed in the 5-year DFS between those aged 65–74 years (81.7%) and those aged ≥ 75 years (70.8%; $P=0.3311$). The 5-year OS was 85.4% for those aged 65–74 years and 78.1% for those aged ≥ 75 years, and the prognosis was worse for those aged ≥ 75 years ($P=0.0466$). Nonetheless, no difference was observed in the 5-year BCSS between those aged 65–74 years (89.3%) and those aged ≥ 75 years (86.6%; $P=0.175$) (Figure 1).

On univariable analysis, stage III or higher was a risk factor for OS. For DFS, lymph node metastasis, stage III or higher, and nuclear grade 3 or Ki-67 ≥ 30 were poor prognostic factors. On multivariable analysis, age, stage III or higher, vascular invasion, and nuclear grade 3 or Ki-67 ≥ 30 were independent prognostic factors for OS. Nuclear grade 3 or Ki-67 ≥ 30 was an independent prognostic risk factor for DFS. Furthermore, no significant difference was observed according to the presence or absence of chemotherapy (Tables 3 and 4).

Table 3. Univariable analysis of potential prognostic factors for overall and disease-free survival

Potential prognostic factor	Overall survival		Disease-free survival	
	HR (95% CI)	P*	HR (95% CI)	P*
Age	1.93 (0.99–3.79)	0.0524	1.40 (0.70–2.77)	0.3382
Chemotherapy	0.90 (0.44–1.74)	0.75	1.14 (0.56–2.23)	0.7169
ER	0.76 (0.39–1.54)	0.4271	0.82 (0.41–1.34)	0.5749
HER2	0.62 (0.23–1.42)	0.537	0.59 (0.22–1.34)	0.4649
≥T2	1.83 (0.94–3.72)	0.0755	1.91 (0.96–3.98)	0.0664
≥N1	1.20 (0.62–2.34)	0.5791	2.21 (1.10–4.71)	0.0254
Stage ≥2	1.25 (0.61–2.81)	0.5579	1.89 (0.84–5.05)	0.131
Stage ≥3	2.51 (1.11–5.16)	0.0288	3.69 (1.73–7.41)	0.0013
Ly≥1 and/or V≥1	1.79 (0.80–4.24)	0.1307	1.85 (0.89–4.02)	0.1229
NG3 and/or Ki-67≥30	2.02 (1.04–3.93)	0.0392	2.36 (1.18–4.71)	0.0467

*The significance level was set at $P < 0.05$. Bold font indicates significant values. HR, hazard ratio; CI, confidence interval; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; NG, nuclear grade; Ly, lymphatic invasion; V, vascular invasion.

Table 4. Multivariable Cox regression analyses for overall and disease-free survival

Potential prognostic factor	Overall survival		Disease-free survival	
	HR (95% CI)	P*	HR (95% CI)	P*
Age	2.44 (1.11–5.74)	0.0274	1.70 (0.75–3.81)	0.1946
Chemotherapy	1.10 (0.45–2.71)	0.8297	0.97 (0.40–2.33)	0.9505
ER	0.63 (0.27–1.45)	0.2707	0.64 (0.26–1.56)	0.3262
HER2	0.48 (0.17–1.20)	0.2982	0.53 (0.18–1.32)	0.429
≥N1	1.12 (0.52–2.39)	0.7687	1.92 (0.85–4.51)	0.1207
Stage ≥3	2.91 (1.09–7.32)	0.0334	3.49 (1.44–8.27)	0.0047
Ly≥1 and/or v≥1	1.48 (0.63–3.66)	0.3632	1.42 (0.65–3.22)	0.5945
NG3 and/or Ki-67≥30	2.58 (1.22–5.45)	0.047	2.36 (1.30–6.33)	0.0303

*Significance level was set at $P < 0.05$. Bold font indicates significant values. HR, hazard ratio; CI, confidence interval; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; NG, nuclear grade; Ly, lymphatic invasion; V, vascular invasion.

In patients aged ≥75 years, no significant difference in DFS was observed, despite the high proportion of patients who did not receive chemotherapy (Figure 2).

DISCUSSION

This study demonstrated substantial age-related differences in perioperative treatment patterns among older Japanese patients with early BC. Despite broadly similar clinicopathological characteristics, patients aged ≥75 years were considerably less likely to receive perioperative chemotherapy, anti-HER2 therapy, and radiotherapy than those aged 65–74 years.

Nevertheless, DFS and BCSS were comparable between groups. Therefore, treatment decisions in patients aged ≥ 75 years appeared to be influenced by patient-related factors beyond tumor characteristics, including physiological reserve, treatment tolerance, and competing health risks. Although chronological age has traditionally influenced treatment decisions, current evidence consistently emphasizes that age alone should not determine eligibility for systemic therapy (7). Instead, treatment decisions should integrate tumor biology, physiological reserve, comorbidities, cognitive function, functional status, estimated life expectancy, treatment tolerance, and patient preference (8). Accordingly, recent recommendations from the International Society of Geriatric Oncology, the American Society of Clinical Oncology, and the Japanese Breast Cancer Society advocate individualized treatment strategies supported by comprehensive geriatric assessment whenever feasible (3, 4, 9). The marked reduction in chemotherapy use among patients aged ≥ 75 years, despite similar tumor characteristics, as observed in our study, suggests that clinicians incorporated these patient-related factors into treatment selection. Although comprehensive geriatric assessment was not routinely performed during the study period, our findings reflect routine clinical decision-making before geriatric assessment became widely integrated into BC management.

Here, multivariable analysis identified age ≥ 75 years, pathological stage III or higher, and highly proliferative tumors (nuclear grade 3 and/or Ki-67 $\geq 30\%$) as independent prognostic factors for overall survival. These findings suggest that both chronological age and tumor characteristics independently influence prognosis in older patients. Therefore, treatment decisions should not rely on chronological age alone but should also take pathological stage and tumor biology into account. Although the benefit of perioperative chemotherapy could not be directly evaluated because only a small number of patients aged ≥ 75 years received chemotherapy, these high-risk clinicopathological features may help identify patients who are appropriate candidates for perioperative systemic therapy. Overall, the optimal role of adjuvant chemotherapy in older patients remains controversial because high-quality evidence is limited (5). Older adults have historically been underrepresented in randomized clinical trials (8), resulting in uncertainty regarding the balance between efficacy and toxicity in this population. Several retrospective studies have suggested that selected older patients derive survival benefit from adjuvant chemotherapy, particularly those with high-risk biological features such as triple-negative or HER2-positive disease (10). Conversely, other observational studies have demonstrated only modest improvements in DFS, with little or no benefit in OS after adjustment for competing causes of death (11, 12). These discrepancies probably reflect differences in patient selection, tumor biology, treatment intensity, and baseline health status across studies. Recently, the ASTER 70s randomized trial provided important prospective evidence regarding chemotherapy in older women with hormone receptor-positive, HER2-negative early BC who were considered to have genomic high-risk disease. In that study, adding chemotherapy to hormone therapy did not significantly improve OS, although certain secondary endpoints suggested potential benefit in selected patients. Rather than supporting universal omission of chemotherapy, the ASTER 70s trial reinforced the importance of careful patient selection and individualized decision-making in older adults (13). Similarly, despite the markedly lower use of chemotherapy among patients aged ≥ 75 years in our cohort, BCSS did not differ significantly between the age groups. Our findings are broadly consistent with this evolving evidence and further support an individualized approach rather than routine administration or omission of chemotherapy based solely on chronological age.

This study has several strengths. First, it provides real-world data regarding treatment patterns and long-term outcomes in older Japanese patients with early breast cancer, a population that remains underrepresented in prospective clinical trials. Second, the relatively long follow-up enabled evaluation of clinically relevant outcomes, including disease-free and breast cancer-specific survival. Finally, all patients were treated and followed using relatively consistent institutional protocols, allowing a uniform assessment of treatment patterns and outcomes. Consequently, our findings complement evidence from clinical trials by providing insight into age-related treatment patterns encountered in routine clinical care.

Importantly, our findings should not be interpreted as evidence that perioperative chemotherapy provides no benefit for patients aged ≥ 75 years. Only three patients in this age group received chemotherapy, precluding meaningful treatment-specific comparisons. Additionally, analyses according to chemotherapy regimen were not feasible because of the limited number of treated patients in the ≥ 75 -year group. Therefore, the absence of a statistically significant survival difference should be interpreted cautiously. Rather, our findings describe real-world treatment patterns and their associated outcomes in routine clinical practice during the study period.

Some limitations should also be acknowledged. First, this was a retrospective, single-center study and was therefore subject to selection bias and unmeasured confounding. Second, the very small number of patients aged ≥ 75 years who received chemotherapy limited the statistical power for treatment-specific analyses. Third, comprehensive geriatric assessment was not routinely performed during the study period, and important patient-related factors such as frailty, cognitive function, and functional status could not be evaluated. Finally, subgroup analyses by intrinsic molecular subtype were limited by sample size, although treatment benefit is known to differ among molecular subtypes. The higher proportion of patients lost to follow-up in the ≥ 75 -year group may have reduced the precision of survival estimates and should be considered when interpreting the absence of significant differences in breast cancer-specific survival between the age groups.

As populations age globally, optimizing treatment selection for patients aged ≥ 75 years is an increasingly important challenge. Our findings offer contemporary evidence on treatment patterns in Japanese clinical practice and support individualized treatment decisions that consider both tumor biology and patient fitness. Future prospective multicenter studies incorporating comprehensive geriatric assessment, molecular subtype, treatment toxicity, quality-of-life measures, and patient-reported outcomes are needed to optimize treatment selection for older adults with early BC.

CONCLUSIONS

This study demonstrated substantial age-related differences in perioperative chemotherapy use among older Japanese patients with early breast cancer. Because only three patients aged ≥ 75 years received chemotherapy, the findings should not be interpreted as evidence regarding chemotherapy efficacy. Rather, they provide real-world evidence on treatment patterns and associated clinical outcomes and support individualized treatment decision-making for older patients.

Abbreviations

BC, breast cancer; DCIS, ductal carcinoma in situ; CI, confidence interval; CT, computed tomography; CTx, chemotherapy; BCSS, breast cancer-specific survival; DFS, disease-free survival; OS, overall survival; ER, estrogen receptor; PgR, progesterone receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IHC, immunohistochemistry; NG, nuclear grade; LVI, lymphovascular invasion.

Declarations

Ethics approval and consent to participate

All data were collected in accordance with the protocol approved by the local ethics committee at Tokyo Women's Medical University (Shinjuku, Tokyo, Japan; no. 2021-0065). Requirement for informed consent was not applicable, owing to the retrospective nature of the study.

Consent for publication

Not applicable, as this study was a retrospective study that used data from medical records

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by NJ, YS, TN, and SA-T. The first draft of the manuscript was written by NJ; all authors commented on earlier versions of the manuscript. All authors read and approved the final manuscript.

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References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74:229-63. doi:10.3322/caac.21834
2. Annual Report on the Ageing Society [Summary] FY2024 chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www8.cao.go.jp/kourei/english/annualreport/2024/pdf/2024.pdf
3. Biganzoli L, Battisti NML, Wildiers H, McCartney A, Colloca G, Kunkler IH, et al. Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG). *Lancet Oncol.* 2021;22:e327–40. doi:10.1016/S1470-2045(20)30741-5.
4. Terada M, Ito A, Kikawa Y, Koizumi K, Naito Y, Shimoi T, et al. The Japanese Breast Cancer Society Clinical Practice Guidelines for systemic treatment of breast cancer, 2022 edition. *Breast Cancer.* 2023;30:872–84. doi:10.1007/s12282-023-01505-x.
5. Battisti NML, Biganzoli L. Systemic therapy for early breast cancer in older adults: current status and prospects. *Curr Opin Oncol.* 2021;33:574–83. doi:10.1097/CCO.0000000000000768.
6. Giordano SH, Duan Z, Kuo YF, Hortobagyi GN, Goodwin JS. Use and outcomes of adjuvant chemotherapy in older women with breast cancer. *J Clin Oncol.* 2006;24:2750–6. doi:10.1200/JCO.2005.02.3028.
7. Schmidt M, Loibl S. Chemotherapy in older patients with early breast cancer. *Breast.* 2024;78:103821. doi:10.1016/j.breast.2024.103821.
8. Sung WWY, Sharma K, Chan AW, Al Khaifi M, Oldenburger E, Chuk E. A narrative review of the challenges and impact of breast cancer treatment in older adults beyond cancer diagnosis. *Ann Palliat Med.* 2024;13:1521–9. doi:10.21037/apm-24-90.
9. Bergerot CD, Temin S, Verduzco-Aguirre HC, Aapro MS, Alibhai SMH, Aziz Z, et al. Geriatric assessment: ASCO global guideline. *JCO Glob Oncol.* 2025;11:e2500276. doi:10.1200/GO-25-00276.
10. Pal SK, Mortimer J. Adjuvant chemotherapy for older adults with breast cancer: making the standard a standard. *Womens Health (Lond).* 2009;5:481–4. doi:10.2217/whe.09.43.
11. Jueckstock J, Kasch F, Jaeger B, Schramm A, Janni W, Scholz C. Adjuvant therapeutic decisions in elderly breast cancer patients: the role of chemotherapy in a retrospective analysis. *Arch Gynecol Obstet.* 2015;292:1101–7. doi:10.1007/s00404-015-3728-8.
12. Morita M, Shimomura A, Tokuda E, Horimoto Y, Kawamura Y, Ishizuka Y, et al. Is adjuvant chemotherapy necessary in older patients with breast cancer? *Breast Cancer.* 2022;29:498–506. doi:10.1007/s12282-021-01329-7.

13. Brain E, Mir O, Bourbouloux E, Rigal O, Ferrero JM, Kirscher S, et al. Adjuvant chemotherapy and hormonotherapy versus adjuvant hormonotherapy alone for women aged 70 years and older with high-risk breast cancer based on the genomic grade index (ASTER 70s): a randomised phase 3 trial. *Lancet*. 2025;406:489–500. doi:10.1016/S0140-6736(25)00832-3.

Figures

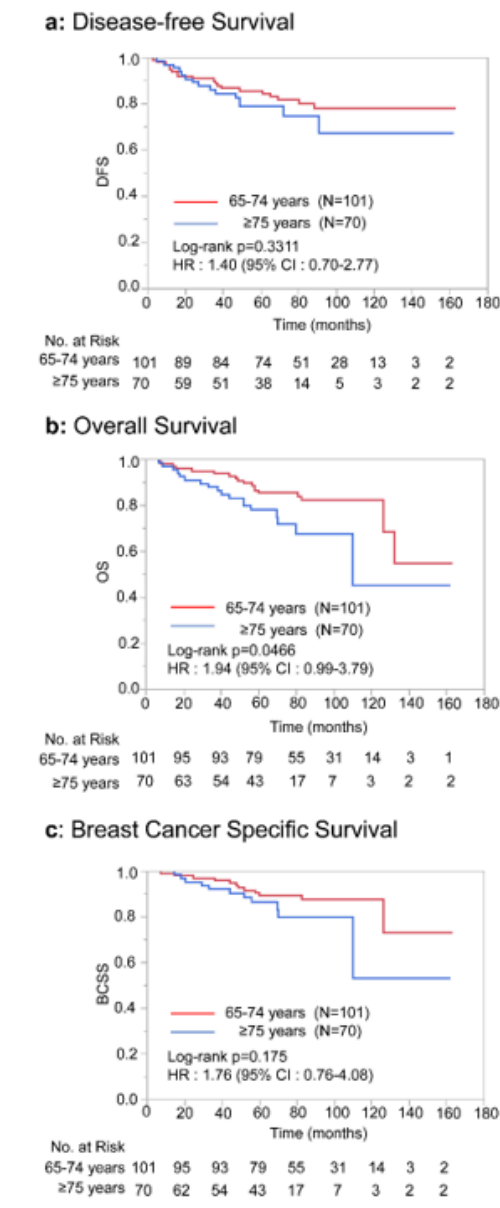
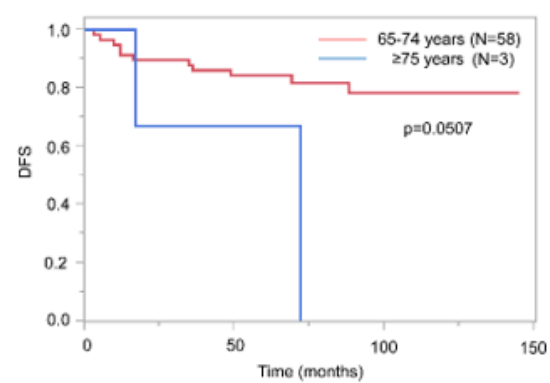


Figure 1
Kaplan–Meier curves with 95% confidence interval (CI).

(a) disease-free survival (DFS; log-rank P=0.3311), (b) overall survival (OS; log-rank P=0.0466), and (c) breast cancer-specific survival (BCSS; log-rank P=0.175).

(a) Chemotherapy and (b) non-chemotherapy groups.

a: Chemotherapy



b: No Chemotherapy

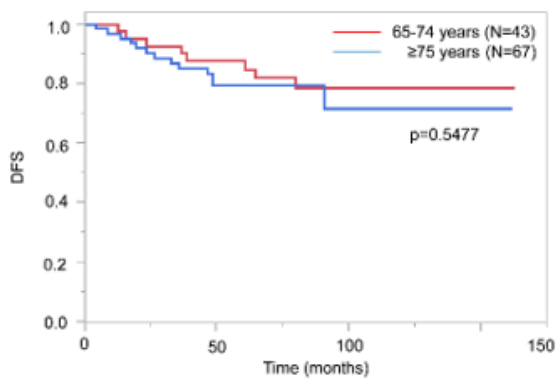


Figure 2

Kaplan–Meier curves with 95% confidence interval (CI) for disease-free survival (DFS).

(a) Chemotherapy and (b) non-chemotherapy groups.