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The Effect of Adjuvant Treatment Preferences on Survival in Elderly Patients (≥65 Years) with Early-stage Breast Cancer

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ABSTRACT

Objective: The optimal management of early-stage breast cancer in elderly patients remains challenging due to age-related comorbidities, limited life expectancy, and underrepresentation in clinical trials. This study aimed to evaluate the impact of adjuvant treatment preferences on survival outcomes in women aged 65 years and older with early-stage, node-negative, hormone receptor-positive, human epidermal growth factor receptor 2-negative breast cancer.

Material and Methods: In this retrospective cohort study, 157 patients aged ≥65 years who underwent surgery between 2003 and 2022 were analyzed. Patients were categorized into two groups according to adjuvant treatment strategy: chemotherapy (CT) followed by hormonal therapy (HT), or HT alone. Clinicopathological characteristics, comorbidities, relapse-free survival (RFS), and overall survival (OS) were compared between groups. Survival outcomes were assessed using Kaplan-Meier analysis, and prognostic factors were evaluated using univariate and multivariate Cox proportional hazards regression models, including clinically relevant variables.

Results: Of the 157 patients, 49 (31.2%) received CT followed by HT, and 108 (68.8%) received HT alone. Patients treated with HT alone were significantly older and had smaller tumors and earlier-stage disease. Despite these favorable tumor characteristics, OS was significantly lower in the HT group compared with the CT group (p=0.003). No significant difference in RFS was observed between the groups (p=0.782). In multivariate analysis of OS, age [hazard ratio (HR): 1.17; 95% CI: 1.08-1.26; p<0.001] and multicentricity (HR: 6.51; 95% CI: 2.16-19.64; p=0.001) were independently associated with worse survival, while the treatment group was not independently associated with survival after adjustment. In multivariate analysis of RFS, age (HR: 1.24; 95% CI: 1.10-1.39; p<0.001) and the Charlson comorbidity score (HR: 2.07; 95% CI: 1.04-4.14; p=0.038) were independently associated with recurrence.

Conclusion: In elderly patients with early-stage hormone receptor-positive breast cancer, survival outcomes appear to be influenced more strongly by age and comorbidity burden than by treatment choice alone. While HT is frequently preferred, adjuvant CT may still be considered in carefully selected patients. A personalized, multidisciplinary approach is essential to optimize treatment decisions in this population.

Keywords: Breast cancer; aged; adjuvant chemotherapy; hormone therapy; comorbidity; survival

INTRODUCTION

Breast cancer (BC) is the most frequently diagnosed malignancy among women, and its incidence increases steadily with advancing age, particularly in countries with aging populations.[1] Despite this growing burden, elderly patients remain markedly underrepresented in clinical trials, resulting in limited high-level evidence to guide treatment decisions in this population.[2] Consequently, management strategies for older patients often rely on retrospective data and clinical judgment rather than standardized, evidence-based recommendations.

BC in elderly women is commonly characterized by more favorable biological features, including higher hormone receptor positivity, lower histological grade, and reduced proliferative activity.[3,4] While these characteristics are generally associated with better oncologic outcomes, their prognostic advantage may be offset by age-related factors such as comorbid conditions,

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reduced physiological reserve, and decreased tolerance to systemic therapies.[5,6] As a result, overall survival (OS) in older patients is frequently influenced not only by cancer-related factors but also by competing causes of mortality.

Treatment decision-making for older patients with BC is complex and extends beyond tumor biology. Factors such as life expectancy, functional status, comorbidity burden, and patient preference play a central role in selecting optimal therapy.[6,7] Although surgery remains the cornerstone of curative treatment in early-stage disease, adjuvant systemic therapy is often de-escalated in older patients. Endocrine therapy is frequently preferred due to its favorable toxicity profile, particularly in patients with hormone receptor-positive tumors and significant comorbidities.[8,9] However, reliance on endocrine therapy alone—especially in patients who are otherwise fit—may raise concerns regarding potential undertreatment. However, these patients have been shown to experience higher rates of regional recurrence, often necessitating delayed surgical interventions later in life.[10,11]

Radiotherapy and breast-conserving surgery (BCS) are also less frequently used among older adults, even when clinically indicated. Previous randomized trials have demonstrated that radiotherapy can be safely omitted in selected low-risk older patients following BCS without compromising OS.[12,13] Nevertheless, treatment omission outside well-defined low-risk groups may contribute to suboptimal outcomes.

Adjuvant chemotherapy (CT) is particularly underutilized in elderly patients across all disease stages. Population-based studies have consistently shown a sharp decline in CT use with increasing age, independent of tumor stage or risk profile.[14,15] This trend may reflect concerns regarding toxicity, comorbidities, and limited life expectancy, but also result in the exclusion of potentially beneficial therapy for carefully selected, fit older patients.

Given these challenges, there remains a need to better understand the impact of adjuvant treatment choices on survival outcomes in elderly patients with biologically favorable BC. This study aimed to evaluate the association between adjuvant treatment strategies—CT followed by hormonal therapy (HT) versus HT alone—and survival outcomes in women aged 65 years or older with early-stage, node-negative, hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative BC.

MATERIAL AND METHODS

Study Design and Patient Selection

This retrospective cohort study included women aged 65 years or older who were diagnosed with early-stage, node-negative, hormone receptor-positive, HER2-negative BC and who underwent primary surgical treatment between 2003 and 2022. Patients were identified through institutional medical records.

Patients with lymph node-positive disease were excluded, as adjuvant CT is routinely recommended in this group. In addition, patients who received neoadjuvant CT (NAC) were excluded to allow accurate evaluation of preferences for adjuvant treatment. After applying these criteria, a total of 157 patients were included in the final analysis.

Ethics committee approval was obtained from the University of Health Sciences Türkiye, Antalya Training and Research Hospital Scientific Research Ethics Committee (approval number: 8/3, date: 08.05.2025).

Treatment Groups

Patients were categorized into two groups according to the adjuvant systemic treatment received following surgery:

1. patients who received CT followed by HT, and

2. patients who received HT alone.

The choice of adjuvant treatment was based on tumor characteristics, patient age, comorbidities, and clinician judgment at the time of treatment.

Data Collection and Variables

Clinical and pathological data were collected retrospectively and included age, tumor size, pathological stage, histological subtype, tumor grade, Ki-67 proliferation index, E-cadherin status, tumor localization, multicentricity, type of surgery, receipt of radiotherapy, and adjuvant systemic therapy.

Comorbidities were assessed using the Charlson comorbidity index; individual comorbid conditions such as diabetes mellitus (DM), hypertension, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), and cerebrovascular disease (CVD) were recorded.

Outcome Measures

The primary outcome of the study was OS, defined as the time from the date of surgery to death from any cause or to the last follow-up. The secondary outcome was relapse-free survival (RFS), defined as the time from surgery to the first documented local, regional, or distant recurrence or last follow-up.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as medians with interquartile ranges, and categorical variables were presented

as frequencies and percentages. The Mann-Whitney U test was used to compare continuous variables between treatment groups, while categorical variables were compared using the Pearson's chi-square test or Fisher's exact test, as appropriate.

Survival curves for OS and RFS were estimated using the Kaplan-Meier method and compared with the log-rank test.

Univariate Cox proportional hazards regression analyses were performed to identify factors associated with OS and RFS.

For OS, two multivariate Cox regression models were constructed. In Model 1, variables with a p-value <0.05 in the univariate analysis were included. In Model 2, clinically relevant variables were included irrespective of univariate significance to better account for potential confounding.

For RFS, a multivariate Cox regression model was constructed, including clinically relevant variables irrespective of univariate significance, in line with the approach used for Model 2 in the OS analysis.

Given the limited number of events, the multivariate models may be prone to overfitting, and the results should be interpreted with caution.

A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 157 patients aged 65 years and older who underwent surgery without prior NAC were included in the analysis. Among them, 49 patients (31.2%) received adjuvant CT followed by HT, while 108 patients (68.8%) received HT alone.

The median age was significantly higher in the HT group than in the CT group (82 vs. 73 years; p<0.001). Tumor size was significantly larger in patients who received CT (median 2.5 cm vs. 1.9 cm; p=0.001). Regarding stage distribution, stage IA disease was more common in the HT group (61.1%), whereas stage IIA disease was more common in the CT group (59.2%; p=0.004). Baseline clinicopathological characteristics are summarized in Table 1.

TABLE 1: Baseline clinicopathological characteristics of the study population.

	Total (n=157)	Chemotherapy (n=49)	Hormonal therapy (n=108)	p-value
Age, years, median	80.0 (10.0)	73.0 (12.0)	82.0 (11.8)	**<0.001**[a]
65-70	13 (8.3)	13 (26.5)	0 (0.0)	**<0.001**[b]
≥70	144 (91.7)	36 (73.5)	108 (100.0)	
Stage, n (%)				
1A	84 (53.5)	18 (36.7)	66 (61.1)	**0.004**[b]
2A	62 (39.5)	29 (59.2)	33 (30.6)	
2B	6 (3.8)	2 (4.1)	4 (3.7)	
3B	5 (3.2)	0 (0)	5 (4.6)	
Tumor size (median)	2.0 (1.3)	2.5 (1.4)	1.9 (1.0)	**0.001**[a]
Grade, n (%)				
1	25 (18.0)	8 (17)	17 (18.5)	0.150[c]
2	100 (71.9)	31 (66)	69 (75)	
3	14 (10.1)	8 (17)	6 (6.5)	
E-cadherin, n (%)				
Negative	14 (21.5)	5 (21.7)	9 (21.4)	1.000[b]
Positive	51 (78.5)	18 (78.3)	33 (78.6)	
Histology, n (%)				
Invasive ductal carcinoma	108 (68.7)	28 (57)	80 (74)	0.885[c]
Invasive lobular carcinoma	19 (12.1)	5 (10.2)	14 (13)	
Others	30 (19.1)	16 (32.6)	14 (12.9)	
Ki-67, n (%)				
<20%	79 (61.2)	24 (54.5)	55 (64.7)	0.261[c]
≥20%	50 (31.8)	20 (45.5)	30 (35.3)	

TABLE 1: Continued.				
	Total (n=157)	Chemotherapy (n=49)	Hormonal therapy (n=108)	p-value
Tumor localization, n (%)				
Upper outer quadrant	66 (42.0)	19 (38.8)	47 (43.5)	0.378[b]
Upper inner quadrant	44 (28.0)	11 (22.4)	33 (30.6)	
Lower outer quadrant	32 (20.4)	14 (28.6)	18 (16.7)	
Lower inner quadrant	13 (8.3)	5 (10.2)	8 (7.4)	
Retroareolar	2 (1.3)	0 (0)	2 (1.9)	
Multicentricity, n (%)				
No	141 (89.8)	43 (87.8)	98 (90.7)	0.577[b]
Yes	16 (10.2)	6 (12.2)	10 (9.3)	
Surgery, n (%)				
BCS	55 (37.9)	18 (37.5)	37 (38.1)	0.940[c]
MRM	90 (62.1)	30 (62.5)	60 (61.9)	
Radiotherapy, n (%)				
No	107 (68.2)	25 (51)	82 (75.9)	**0.002**[c]
Yes	50 (31.8)	24 (49)	26 (24.1)	
Charlson comorbidity score		5.0 (2.0)	5.0 (2.0)	0.980[a]
DM, n (%)				
No	98 (62.4)	31 (63.3)	67 (62)	0.883[c]
Yes	59 (37.6)	18 (36.7)	41 (38)	
HT, n (%)				
No	75 (47.8)	23 (46.9)	52 (48.1)	0.888[c]
Yes	82 (52.2)	26 (53.1)	56 (51.9)	
CVD, n (%)				
No	155 (98.7)	48 (98)	107 (99.1)	0.528[b]
Yes	2 (1.3)	1 (2)	1 (0.9)	
CAD, n (%)				
No	136 (86.6)	47 (95.9)	89 (82.4)	**0.021**[c]
Yes	21 (13.4)	2 (4.1)	19 (17.6)	
Hyperlipidemia, n (%)				
No	152 (96.8)	48 (98)	104 (96.3)	1.000[b]
Yes	5 (3.2)	1 (2)	4 (3.7)	
COPD, n (%)				
No	141 (89.8)	41 (83.7)	100 (92.6)	0.096[b]
Yes	16 (10.2)	8 (16.3)	8 (7.4)	
Hormonal therapy, n (%)				
Anastrazol	107 (70.4)	28 (63.6)	79 (73.1)	0.105[b]
Letrozol	40 (26.3)	15 (34.1)	25 (23.1)	
Exemestan	1 (0.7)	1 (2.3)	0 (0)	
Tamoxifen	4 (2.6)	0 (0)	4 (3.7)	
Relapse, n (%)				
No	144 (91.7)	46 (93.9)	98 (90.7)	0.756[b]
Yes	13 (8.3)	3 (6.1)	10 (9.3)	

TABLE 1: Continued.

	Total (n=157)	Chemotherapy (n=49)	Hormonal therapy (n=108)	p-value
Mortality, n (%)				
Alive	123 (79.4)	46 (95.8)	77 (72)	**0.001**[c]
Dead	32 (20.6)	2 (4.2)	30 (28)	
Chemotherapy				
CA	14 (29.2)			
Weekly paclitaxel	3 (6.3)			
TC	15 (31.3)			
CA+T	8 (16.7)			
EC	4 (8.3)			
CEF+T	3 (6.3)			
Carboplatin+T	1 (2.1)			

[a]: Mann-Whitney U test, [b]: Fisher's Exact test, [c]: Pearson chi-square test. BCS: Breast-conserving surgery; MRM: Modified radical mastectomy; DM: Diabetes mellitus; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; CVD: Cerebrovascular disease; CAD: Coronary artery disease; CA: Doxorubicin plus cyclophosphamide; T: Paclitaxel; TC: Docetaxel plus cyclophosphamide; EC: Epirubicin plus cyclophosphamide; CEF: Cyclophosphamide, epirubicin, and 5-fluorouracil.

Tumor grade and Ki-67 proliferation index did not differ significantly between treatment groups, indicating comparable tumor biology across cohorts (Table 1). N o significant differences were observed in histological subtype, E-cadherin status, tumor localization, multicentricity, or surgical approach.

Treatment Characteristics

Modified radical mastectomy (MRM) was performed in 62.1% of patients, while BCS was performed in 37.9%. Adjuvant radiotherapy was administered significantly more frequently in the CT group than in the HT group (49.0% vs. 24.1%; p=0.002).

Among patients receiving CT, the most commonly used regimens were docetaxel plus cyclophosphamide (TC) (31.3%) and doxorubicin plus cyclophosphamide (29.2%), followed by other anthracycline- or taxane-based combinations.

None of the patients in this cohort underwent genomic risk assessment using assays such as Oncotype DX or MammaPrint.

Comorbidities

Hypertension (52.2%) and DM (37.6%) were the most frequently observed comorbidities in the overall cohort. CAD was significantly more prevalent in the HT group than in the CT group (17.6% vs. 4.1%; p=0.021). Other comorbid conditions, including COPD, CVD, and hyperlipidemia, were similarly distributed between the groups. Despite differences in age and comorbidity profiles, the median Charlson comorbidity score was 5 in both treatment groups (p=0.980) (Table 1).

Survival Outcomes

During follow-up, disease relapse occurred in 13 patients (8.3%); there was no statistically significant difference in relapse rates between the CT and HT groups (6.1% vs. 9.3%; p=0.756). A total of 32 patients (20.6%) died during the study period. Mortality was significantly higher in the HT group compared with the CT group (28.0% vs. 4.2%; p=0.001) (Table 1).

Kaplan-Meier analysis demonstrated a median OS of 172.3 months [95% confidence interval (CI): not reached (NR)] for the entire cohort. The 2 years and 5 years OS rates were 92.7% and 80.1%, respectively. OS was significantly longer in the CT group than in the HT group (log-rank p=0.003). Median OS was NR in the CT group, whereas in the HT group it was 172.3 months (95% CI: 81.87-262.72) (Table 2).

The median RFS was NR in both treatment groups. The 2 years and 5 years RFS rates for the entire cohort were 98% and 90%, respectively. No significant difference in RFS was observed between the treatment group arms (log-rank p=0.782) (Table 2).

Prognostic Factors

In univariate Cox regression analysis for OS, tumor stage, tumor size, and multicentricity were significantly associated with an increased risk of death. Stage IIIB disease was associated with the highest mortality risk [hazard ratio (HR): 9.52; 95% CI: 2.64-34.28; p=0.001], and multicentric disease was also associated with poorer OS (HR: 2.70; 95% CI: 1.01-7.20; p=0.047). Tumor grade, histology, Ki-67 proliferation index, type of surgery, receipt of radiotherapy, and Charlson comorbidity score were not significantly associated with OS (Table 3).

Two multivariate Cox regression models were constructed for OS. In Model 1, which included variables selected based on univariate analysis, multicentricity emerged as an

independent predictor of mortality (HR: 2.99; 95% CI: 1.10-8.09; p=0.031) (Table 4).

To better account for potential confounding, Model 2 included clinically relevant variables irrespective of univariate significance. These variables included treatment group, age, tumor size, stage, radiotherapy, Charlson comorbidity score, CAD, and multicentricity.

TABLE 2: Overall survival and relapse-free survival outcomes.

OS (months)	Median (95% CI)	p-value
Overall	172.30 (NR)	
Treatment		
Chemotherapy	-	0.003
Hormonal therapy	172.30 (81.87-262.72)	
RFS (months)	**Median(95% CI)**	**p-value**
Overall	-	
Treatment		
Chemotherapy	-	0.782
Hormonal therapy	-	

Survival analyses were performed using the Kaplan-Meier method, and survival curves were compared using the log-rank test. A p-value <0.05 was considered statistically significant. CI: Confidence interval; OS: Overall survival; RFS: Relapse-free survival.

TABLE 3: Univariate Cox regression analysis for overall survival.

OS	Univariate	
	HR (95% CI)	p-value
Stage (ref: 1A)		**0.007**
2A	1.31 (0.61-2.79)	0.482
2B	2.08 (0.27-15.97)	0.481
3B	9.52 (2.64-34.28)	**0.001**
Tumor size	1.29 (1.04-1.59)	**0.018**
Grade (ref: 1)		0.240
2	0.67 (0.27-1.67)	0.398
3	1.63 (0.46-5.71)	0.445
E-cadherin (ref: negative)	0.50 (0.12-2.02)	0.334
Histology (ref: others)		0.774
Invasive ductal carcinoma	0.77 (0.35-1.68)	0.515
Invasive lobular carcinoma	1.05 (0.34-3.17)	0.931
Ki-67 (ref: <20%)	1.57 (0.66-3.72)	0.297
Multicentricity (ref: no)	2.70 (1.01-7.20)	**0.047**
Surgery (ref: BCS)	0.87 (0.39-1.93)	0.744
Radiotherapy (ref: no)	0.50 (0.20-1.22)	0.130
Charlson comorbidity score	1.4 (0.90-1.70)	0.182
p<0.001, -loglikelihood=260.45		

HR: Hazard ratio; CI: Confidence interval; BCS: Breast-conserving surgery; OS: Overall survival.

In Model 2, age (HR: 1.17; 95% CI: 1.08-1.26; p<0.001) and multicentricity (HR: 6.51; 95% CI: 2.16-19.64; p=0.001) were independently associated with worse OS. The treatment showed a trend toward improved survival with CT, but this did not reach statistical significance after adjustment (HR: 3.61; 95% CI: 0.79-16.45; p=0.097). Tumor size, stage, radiotherapy, Charlson comorbidity score, and CAD were not independently associated with OS (Table 5).

The results of Model 2 were considered the primary findings of the study. Given the limited number of events, these findings should be interpreted with caution due to the risk of overfitting.

For RFS, univariate analysis did not identify any clinical or pathological variables significantly associated with recurrence (Table 6).

A multivariate Cox regression model for RFS was subsequently fitted, including clinically relevant variables regardless of univariate significance. In this model, age (HR: 1.24; 95% CI: 1.10-1.39; p<0.001) and Charlson comorbidity score (HR: 2.07; 95% CI: 1.04-4.14; p=0.038) were independently associated with worse RFS. Treatment group and tumor-related variables were not significantly associated with recurrence (Table 7).

Given the limited number of relapse events (n=13), these findings should be interpreted with caution.

DISCUSSION

The incidence of BC continues to rise with advancing age, and management of older adults remains challenging due to age-related comorbidities, competing mortality risks, and limited representation in clinical trials. In this retrospective study, we evaluated the impact of adjuvant treatment strategies on survival outcomes in women aged 65 years and older with early-stage, node-negative, hormone receptor-positive, HER2-negative BC.

Our findings demonstrate a clear preference for endocrine therapy alone in the elderly population, consistent with previous reports showing declining use of adjuvant CT with increasing age.[14,15] Patients treated with HT alone were older and had smaller tumors and earlier-stage disease, reflecting a tendency to avoid CT in those perceived to have lower oncologic risk. Tumor grade and Ki-67 proliferation index were comparable between treatment groups, suggesting that treatment selection was influenced predominantly by age and comorbidity considerations rather than intrinsic tumor biology.

Despite more favorable clinicopathological characteristics, the HT group had significantly lower OS. This observation should be interpreted with caution, as it likely reflects differences in

TABLE 4: Multivariate Cox regression analysis for overall survival (Model 1: univariate-based model).

OS	Multivariate HR (95% CI)	p-value
Stage (ref: 1A)		**0.035**
2A	0.85 (0.32-2,12)	0.744
2B	0.36 (0.01-7.45)	0.509
3B	5.27 (0.92-30.07)	0.061
Tumor size	1.35 (0.91-2.01)	0.130
Multicentricity (ref: no)	2.99 (1.10-8.09)	**0.031**

HR: Hazard ratio; CI: Confidence interval; OS: Overall survival.

TABLE 5: Multivariate Cox regression analysis for overall survival (Model 2: fully adjusted model).

OS	Multivariate HR (95% CI)	p-value
Hormonal therapy (ref: chemotherapy)	3.61 (0.79-16.45)	0.097
Age	1.17 (1.08-1.26)	<0.001
Tumor size	1.13 (0.81-1.57)	0.470
Radiotherapy (ref: no)	1.13 (0.42-3.03)	0.806
Charlson comorbidity score	1.13 (0.76-1.70)	0.548
CAD	1.91 (0.67-5.42)	0.226
Multicentricity (ref: no)	6.51 (2.16-19.64)	0.001
Stage	1.09 (0.58-2.03)	0.797

HR: Hazard ratio; CI: Confidence interval; CAD: Coronary artery disease; OS: Overall survival.

TABLE 6: Univariate Cox regression analysis for relapse-free survival.

RFS	Univariate HR (95% CI)	p-value
Stage (ref: 1A)		0.306
2A	1.82 (0.55-5.97)	0.322
2B	4.67 (0.53-40.60)	0.162
3B	4.20 (0.48-36.35)	0.192
Tumor size	1.21 (0.91-1.62)	0.178
Grade (ref: 1)		0.055
2	0.29 (0.06-1.33)	0.114
3	2.04 (0.41-10.23)	0.382
E-cadherin (ref: negative)	29.18 (0.00-)	0.649
Histology (ref: others)		0.739
Invasive ductal carcinoma	1.54 (0.51-4.66)	0.437
Invasive lobular carcinoma	-	0.981
Ki-67 (ref: <20%)	2.81 (0.79-10.01)	0.109
Multicentricity (ref: no)	0.82 (0.11-6.36)	0.855
Surgery (ref: BCS)	0.80 (0.22-2.85)	0.735
RT (ref: no)	0.68 (0.18-2.47)	0.559
Charlson comorbidity score	1.63 (0.97-2.73)	0.064

HR: Hazard ratio; CI: Confidence interval; BCS: Breast-conserving surgery; RT: Radiotherapy; RFS: Relapse-free survival.

TABLE 7: Multivariate Cox regression analysis for relapse-free survival.

RFS	Multivariate HR (95% CI)	p-value
Hormonal therapy (ref: chemotherapy)	0.79 (0.20-3.13)	0.733
Age	1.24 (1.10-1.39)	<0.001
Tumor size	1.16 (0.71-1.91)	0.550
Radiotherapy (ref: no)	0.84 (0.21-3.34)	0.800
Charlson comorbidity score	2.07 (1.04-4.14)	0.038
CAD	0.51 (0.09-2.85)	0.441
Multicentricity (ref: no)	3.10 (0.33-29.11)	0.322
Stage	1.04 (0.42-2.60)	0.927

HR: Hazard ratio; CI: Confidence interval; RFS: Relapse-free survival; CAD: Coronary artery disease.

baseline health status and competing risks of mortality rather than a direct causal effect of treatment choice.

Although CT appeared to be associated with improved OS in unadjusted analyses, this effect was no longer statistically significant after adjustment for clinically relevant variables. In the fully adjusted model, age and multicentricity emerged as independent predictors of mortality. These findings highlight the potential impact of confounding by indication and suggest that the observed differences in OS between treatment groups may largely reflect baseline patient characteristics rather than a direct treatment effect. They also underscore the importance of careful patient selection, indicating that treatment decisions in elderly patients should not rely solely on chronological age but should also incorporate the comorbidity burden and overall functional status.

In line with prior population-based studies, a substantial proportion of elderly BC patients die from non-cancer-related causes, most commonly cardiovascular disease.[5,7,16] Supporting this finding, CAD was significantly more prevalent in the HT group in our cohort. However, CAD was not independently associated with OS in multivariate analyses. This finding suggests that, while comorbid conditions may influence treatment selection and baseline risk, they may not act as independent prognostic factors in this setting.

RFS did not differ significantly between treatment groups, indicating comparable disease control regardless of the choice of adjuvant systemic therapy. The low recurrence rate observed across the cohort likely reflects the favorable biological profile of hormone receptor-positive, node-negative disease. These findings suggest that, in carefully selected elderly patients, omission of CT may not adversely affect recurrence risk, although overall outcomes remain influenced by non-oncologic factors.

Consistent with these observations, multivariate analysis of RFS demonstrated that neither treatment group nor tumor-related variables were independently associated with recurrence. Instead, age and comorbidity burden, as reflected by the Charlson comorbidity score, emerged as significant predictors. These findings highlight the dominant role of patient-related factors in determining outcomes among elderly patients with BC. However, given the limited number of relapse events, these results should be interpreted with caution.

Surgical and radiotherapy patterns in our study also reflect real-world practice in elderly patients.[17,18] MRM was performed more frequently than BCS, and radiotherapy was underutilized, particularly in patients receiving HT alone. Previous randomized trials have demonstrated that radiotherapy can be safely omitted in selected low-risk elderly patients without compromising OS.[12,13] Given that a large proportion of our cohort met these low-risk criteria, the observed treatment patterns may be clinically justified.

In our study, radiotherapy was not independently associated with either OS or RFS in multivariate analyses. However, this finding should be interpreted cautiously, as differences in radiotherapy use between treatment groups and the retrospective nature of the study may still contribute to residual confounding.

Among patients who received CT, anthracycline- and taxane-based regimens were most commonly used, consistent with standard practice. The frequent use of TC aligns with evidence supporting its favorable efficacy-toxicity balance in older patients, particularly those with cardiovascular risk factors.[19,20] These findings suggest that adjuvant CT can be safely administered to selected elderly patients when guided by careful clinical assessment.

These findings provide insight into real-world treatment patterns and outcomes in elderly patients with early-stage BC and may help inform clinical decision-making in this population. Given the retrospective design, non-randomized treatment allocation, and the absence of frailty and performance status measures, residual confounding by indication likely persists and should be considered when interpreting the results.

Study Limitations

Several limitations of this study should be acknowledged. First, the retrospective, and single-center design introduces potential selection bias, and treatment allocation was not randomized.

Second, the absence of performance status measures, such as Eastern Cooperative Oncology Group, represents an important limitation, as frailty and functional capacity are key determinants of treatment selection among elderly patients and may have contributed to residual confounding by indication. In this context, prospective studies and real-world registries integrating Comprehensive Geriatric Assessment tools are warranted to better individualize and standardize adjuvant treatment decisions in older patients with BC.

Third, the absence of genomic risk assessment tools, such as multigene assays, limited the ability to further refine risk stratification for recurrence. During the study period, genomic risk assessment tools were not reimbursed by our national social security system, and their high out-of-pocket costs limited their routine use. Consequently, adjuvant treatment decisions were primarily based on clinicopathological factors and tumor biology, which remains common practice in our setting. This limitation reflects disparities in access to certain oncological approaches between developed and developing countries, and it may have influenced treatment selection and risk stratification within this cohort. In contemporary clinical practice, the routine integration of genomic assays may further refine risk stratification and help identify a more selective subgroup of older patients who are likely to benefit from adjuvant CT.

Fourth, the relatively small number of relapse events may have reduced the statistical power to identify independent predictors of recurrence. In addition, given the relatively low number of outcome events, particularly for RFS, the multivariate models may be prone to overfitting, which could limit the robustness of the identified associations. Although multivariate analyses were performed to adjust for clinically relevant variables, residual confounding cannot be fully excluded.

Fifth, the lack of quantitative estrogen and progesterone receptor expression data limited our ability to capture biological heterogeneity within hormone receptor-positive disease. Treating hormone receptor positivity as a binary variable may obscure clinically relevant differences, as tumors with low receptor expression may exhibit more aggressive behavior and differential responses to systemic therapies. Future studies that incorporate quantitative measurements of receptor expression are needed to refine treatment selection in this population.

Finally, cause-specific mortality data were not available, precluding a detailed analysis of cancer-related versus non-cancer-related deaths.

Despite these limitations, this study provides real-world data on adjuvant treatment patterns and outcomes in an understudied elderly BC population.

CONCLUSION

This study highlights the importance of individualized adjuvant treatment strategies in elderly patients with early-stage, node-negative, hormone receptor-positive, HER2-negative BC. While endocrine therapy alone is commonly preferred due to its favorable tolerability profile, our findings suggest that treatment selection should be guided primarily by patient-related factors rather than by treatment modality alone.

Importantly, survival outcomes in this population appear to be strongly influenced by age, comorbid conditions, and competing risks of mortality, rather than by cancer-related factors alone. Therefore, treatment decisions should not be based solely on chronological age but should integrate tumor characteristics, comorbidity burden, functional status, and life expectancy within a multidisciplinary framework. Such an approach may help optimize outcomes while minimizing both undertreatment and overtreatment in this heterogeneous patient population.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the University of Health Sciences Türkiye, Antalya Training and Research Hospital Scientific Research Ethics Committee (approval number: 8/3, date: 08.05.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: E.U., D.K.S., Design: E.U., D.K.S., Data Collection or Processing: E.U., Analysis or Interpretation: D.K.S., Literature Search: E.U., Writing: E.U.

Conflict of Interest: No conflict of interest was declared by the authors.

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