COMPARISON OF SURVIVAL BENEFIT AND TOXICITY OF ADJUVANT CHEMOTHERAPY IN ELDERLY PATIENTS WITH BREAST CANCER

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Background

- The incidence and mortality of breast cancer increase with age. The higher mortality in elderly patients with breast cancer is primarily due to comorbidities, functional status, and the treatment preference of either the patients or clinicians.
- Older women with breast cancer benefit from standard adjuvant chemotherapy regimens, but they are often vulnerable due to multiple comorbidities and may easily suffer from chemotherapy toxicity. Consequently, older women with better functional status are more likely to receive chemotherapy, especially low-intensity regimens.
- The optimal use of adjuvant chemotherapy in older women with breast cancer remains a topic of ongoing discussion due to the lack of data and conflicting results.
- In this research, we sought to compare the survival benefits and toxicities of adjuvant chemotherapy regimens in elderly patients with breast cancer.

Methods

- We retrospectively reviewed 124 elderly patients aged 65 years or older with resectable breast cancer who were treated at a single center from March 2013 to December 2023.
- The patients had to receive neoadjuvant or adjuvant chemotherapy, including anthracycline, cyclophosphamide, or taxane.
- Patients were categorized into two groups based on their chemotherapy regimen. The high-intensity regimen (HIR) was defined as a three-drug combination of anthracycline, cyclophosphamide, and taxane, while the low-intensity regimen (LIR) was described as a two-drug combination, such as four cycles of anthracycline plus cyclophosphamide or taxane plus cyclophosphamide.

Results

- The median age was 69 years (range, 65-82 years). Stages II and III were present in 71 (57.3%) and 30 (24.2%) patients. Hormone receptor-positive plus HER2-negative and triple-negative statuses were found in 44 (35.5%) and 37 (29.8%) patients. Fifty patients (40.3%) received LIR, while 74 (59.7%) received HIR. The median follow-up time for survivors was 40.7 months (range, 4.6 to 125.6 months), and the 5-year overall survival (OS) estimate for all patients was 83.9% (95% CI 76.4–92.1).

Table 1. Characteristics of elderly patients with breast cancer according to chemotherapy regimen

Characteristics		Total	Regimen (n = 124)		
			LIR (n = 50)	HIR (n = 74)	*P*
Age (years, median)		69 (65-82)	69 (65-80)	70 (65-82)	
	< 75	106 (85.5)	43 (86.0)	63 (85.1)	.893
	≥ 75	18 (14.5)	7 (14.0)	11(14.9)	
ECOG PS	0–1	110 (88.7)	43 (86.0)	67 (90.5)	.433
	2–3	14 (11.3)	7 (14.0)	7 (9.5)	
BMI	< 28	93 (75.0)	39 (78.0)	54 (73.0)	.526
	≥ 28	31 (25.0)	11 (22.0)	20 (27.0)	
Age-adjusted CCI	≤ 3	96 (77.4)	41 (82.0)	55 (74.3)	.316
	> 3	28 (22.6)	9 (18.0)	19 (25.7)	
Medication	< 5	87 (70.2)	39 (78.0)	48 (64.9)	.117
	≥ 5	37 (29.8)	11 (22.0)	26 (35.1)	
Stage	I	23 (18.5)	23 (46.0)	0 (0.0)	.000
	II	71 (57.3)	26 (52.0)	45 (60.8)	
	III	30 (24.2)	1 (2.0)	29 (39.2)	
Type	HR+/HER2-	44 (35.5)	12 (24.0)	32 (43.2)	.030
	HR+/HER2+	18 (14.5)	7 (14.0)	11 (14.9)	
	HR-/HER2+	25 (20.2)	16 (32.0)	9 (12.2)	
	TNBC	37 (29.8)	15 (30.0)	22 (29.7)	
Treatment setting	Neoadjuvant	28 (22.6)	2 (4.0)	26 (35.1)	.000
	Adjuvant	96 (77.4)	48 (96.0)	48 (64.9)	
Adjuvant endocrine therapy	Yes	58 (46.8)	19 (38.0)	39 (52.7)	.107
	No	66 (53.2)	31 (62.0)	35 (47.3)	
HER2 targeted therapy	Yes	40 (32.3)	22 (44.0)	18 (24.3)	.021
	No	84 (67.7)	28 (56.0)	56 (75.7)	
Adjuvant radiotherapy	Yes	67 (54.0)	24 (48.0)	43 (58.1)	.268
	No	57 (46.0)	26 (52.0)	31 (41.9)	
Prophylactic long-acting G-CSF	Yes	81 (65.3)	31 (62.0)	50 (67.6)	.523
	No	43 (34.7)	19 (38.0)	24 (32.4)	

Table 2. Cox regression univariate and multivariate analyses of risk factors for disease-free survival

Univariate analysis	HR (95% CI)	*P*-value
Age ≥ 75 years	2.69 (1.12-6.46)	.026
BMI ≥ 28	2.18 (0.99-4.81)	.053
Age-adjusted CCI > 3	3.24 (1.47-7.15)	.004
Medication more than 5	2.11 (0.94-4.73)	.071
Stage III	2.00 (0.88-4.53)	.096
Multivariate analysis	**HR (95% CI)**	***P*-value**
Age ≥ 75 years	2.99 (1.16-7.70)	.023
Age-adjusted CCI > 3	2.31 (0.93-5.71)	.071

Table 3. Treatment response and adverse events of chemotherapy in elderly patients with breast cancer

Patients (%)	LIR (n = 50)	HIR (n = 74)
Recurrence	5 (10.0)	9 (12.2)
Any cause of deaths	5 (10.0)	12 (16.2)
TRAEs leading to dose reduction	3 (6.0)	31 (41.9)
TRAEs leading to discontinuation	6 (12.0)	10 (13.5)
TRAEs leading to deaths	1 (2.0)	5 (6.8)

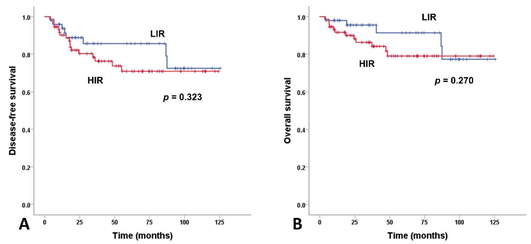

Figure 1. Disease-free survival (A) and overall survival (B) after perioperative chemotherapy in elderly patients with breast cancer according to chemotherapy regimen.

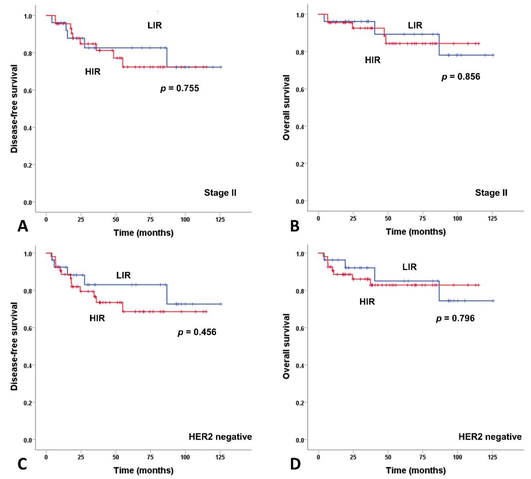

Figure 2. Disease-free survival (A, C) and overall survival (B, D) after perioperative chemotherapy in the subgroups of elderly patients with breast cancer according to chemotherapy regimen; Stage II (A, B) and HER2 negative (C, D).

- In univariate analyses, age ≥ 75, BMI ≥ 28, age-adjusted Charlson Comorbidity Index (CCI) > 3, taking more than 5 medications, and stage III were associated with disease-free survival (DFS). Multivariate analyses identified age ≥ 75 (HR, 2.99; *p*=0.023) and age-adjusted CCI > 3 (HR, 2.31; *p*=0.071) as significant risk factors.
- The 5-year estimated OS was 91.4% (95% CI 82.1–100.0) for patients receiving LIR and 79.0% (95% CI 68.6–90.9) for patients receiving HIR. The 5-year estimated DFS was 85.7% (95% CI 75.5–97.2) for patients receiving LIR and 70.9% (95% CI 59.7–84.3) for patients receiving HIR. There were no significant differences in survival outcomes between the two groups (DFS, *p*=0.323; OS, *p*=0.270).
- Treatment-related mortality occurred in 2.0% of patients on LIR and 6.8% on HIR. The incidence of recurrence was 10.0% in the LIR group and 12.2% in the HIR group. Notably, 41.9% of patients on HIR experienced a dose reduction in chemotherapy.
- In subgroup analyses, there were no significant differences between the LIR and HIR groups in either Stage II (DFS, p = 0.755; OS, p = 0.856) or HER2 negative patients (DFS, p = 0.456; OS, p = 0.796).

Conclusion

The HIR did not demonstrate superior survival outcomes compared to the LIR and was associated with greater treatment-related mortality and a higher incidence of chemotherapy dose reductions, indicating increased toxicity. These findings underscore the importance of careful consideration of individual risk factors when selecting HIR for elderly patients with breast cancer.

There are no relationships to disclose.