Original Study

Maintaining Dose Intensity of Adjuvant Chemotherapy in Older Patients With Breast Cancer

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Abstract

A suboptimal dose intensity of adjuvant chemotherapy has been associated with a poor prognosis in patients with early-stage breast cancer. We investigated the relative dose intensity (RDI) of modern adjuvant chemotherapy regimens in patients aged ≥ 65 years. An RDI of ≥ 85% was achieved in 177 of 281 included patients (63%). Better supportive care of risk groups might further optimize the RDI.

Introduction: Maintaining the relative dose intensity (RDI) of adjuvant chemotherapy at ≥ 85% has been associated with improved treatment outcomes in early-stage breast cancer (ESBC). Increasing evidence has suggested that patients aged ≥ 65 years can maintain the optimal RDI for standard chemotherapy regimens. The present study investigated the RDI of newer adjuvant chemotherapy regimens in this demographic. **Patients and Methods:** We retrospectively analyzed the data from 281 patients aged ≥ 65 years with a diagnosis of ESBC who had received adjuvant chemotherapy across 3 sites in Queensland, Australia from 2010 to 2015. The primary endpoint was the proportion of patients who had received an RDI of ≥ 85%. **Results:** The median age at diagnosis was 68 years (range, 65-85 years), with 36.3% aged > 70 years. The patient characteristics included tumor stage T3 or T4 in 17% and node-positive disease in 60%. The common chemotherapy regimens included docetaxel/cyclophosphamide (23%), 5-fluorouracil/epirubicin/cyclophosphamide plus docetaxel or paclitaxel (17%); Adriamycin/cyclophosphamide/weekly paclitaxel (38%); and docetaxel/carboplatin/trastuzumab (11%). Primary (15%) and secondary (54%) granulocyte colony-stimulating factor (G-CSF) was used. An RDI of ≥ 85% was achieved in 63% of the patients. Significant associations were noted between a reduced RDI and age ≥ 70 years ($P < .001$), Charlson comorbidity index ≥ 1 ($P = .043$), initial dose reductions ($P = .01$), secondary G-CSF use ($P = .45$), hospital admission ($P < .001$), and febrile neutropenia ($P = .007$). Treatment-related toxicities were the most common reason for noncompletion, with high rates of hospital admissions (46%) and febrile neutropenia (22%). **Conclusion:** Our findings suggest that patients aged ≥ 65 years with ESBC can maintain an optimal RDI with modern chemotherapy regimens. Appropriate geriatric assessment and the use of supportive measures such as G-CSF could better assist select groups to maintain an optimal dose intensity.

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Introduction

Breast cancer is the leading cause of cancer and the second leading cause of cancer-related deaths among Australian women. Its incidence increases with age, with 59% of new diagnoses occurring in patients aged ≥ 65 years and a median age at presentation of 61 years.[1] Although the prognosis of primary breast cancer has improved significantly in recent decades, that trend has been heavily skewed toward younger patients. According to the breast cancer

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Table 1 Patient Demographic Data and Treatments Used

Variable	Patients, n (%)
Gender	
Female	279 (99)
Male	2 (1)
BMI, kg/m^2	
< 25	84 (30)
≥ 25	197 (70)
Charlson comorbidity index	
< 1	178 (63)
≥ 1	103 (37)
ECOG performance status	
< 1	243 (87)
≥ 1	38 (13)
Tumor stage	
1-2	234 (83)
3-4	47 (17)
Simplified tumor type	
IDC	210 (75)
ILC	44 (16)
Other	27 (9)
Positive lymph nodes	
< 1	111 (40)
≥ 1	170 (60)
Hormone receptor status	
Positive	217 (77)
Negative	64 (23)
HER2 status	
Positive	65 (23)
Negative	216 (77)
Surgery	
Wide local excision	102 (36)
Mastectomy	179 (64)
Adjuvant external radiation therapy	
Yes	188 (67)
No	93 (33)
Neoadjuvant therapy	
Yes	21 (8)
No	260 (92)
Chemotherapy protocols used	
AC-wT	106 (38)
TC	64 (23)
FEC-D/FEC-T	48 (17)
TAC	8 (3)
TCH	30 (11)
Paclitaxel	12 (4)
FEC 100	8 (3)
Other	5 (1)

Abbreviations: AC-wT = Adriamycin, cyclophosphamide with weekly paclitaxel; BMI = body mass index; ECOG = Eastern Cooperative Oncology Group; FEC-D = 5-fluorouracil, epirubicin, cyclophosphamide, docetaxel; FEC-T = 5-fluorouracil, epirubicin, cyclophosphamide, paclitaxel; HER2 = human epidermal growth factor receptor 2; IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; TAC = docetaxel, doxorubicin, cyclophosphamide; TC = docetaxel, cyclophosphamide; TCH = docetaxel, carboplatin, trastuzumab (Herceptin).

mortality database compiled by the World Health Organization, women aged 50 and 69 years and those aged ≥ 70 years have experienced median improvements in mortality from 1989 to 2006 of 21% and 2%, respectively.[2] Recent studies have noted that a potential major reason for this comparatively poor prognosis among the elderly cohort is underusage of adjuvant chemotherapy in this patient group.[3,4] Older patients have been more likely to receive dose reductions and delays, reducing the overall relative dose intensity (RDI) of their treatment.[5]

Dose intensity refers to the measure of chemotherapy drug delivered per unit time (ie, mg/m^2/wk), and the RDI is defined as the received dose intensity relative to the reference dose intensity. The RDI is an important prognostic factor that reflects the degree of adherence to the recommended chemotherapy regimen and, by extension, the safety and tolerability of these treatments. The maintenance of the RDI at greater than a minimum optimal threshold of 85% has been shown to correlate with increased rates of disease-free survival and overall survival.[6-8] The reported data have suggested that a key cause of this age-based discrepancy in treatment was the historical consensus that adjuvant chemotherapy treatments are poorly tolerated by older patients compared with their younger counterparts. Several older studies reported significantly greater rates of toxicity and mortality associated with first- and second-generation adjuvant regimens among elderly breast cancer patients, leading to caution when prescribing chemotherapy in this demographic.[5,8-10] However, an increasing body of evidence has suggested that select older patients will tolerate a range of adjuvant chemotherapy regimens better than previously thought and will be capable of maintaining an optimal dose intensity.[11-14]

The primary aim of the present study was to assess whether patients aged ≥ 65 years who received adjuvant chemotherapy for early-stage breast cancer (ESBC) could maintain an RDI of ≥ 85%.

Materials and Methods

Subjects and Data Collection

A retrospective analysis was conducted of all patients aged ≥ 65 years who had undergone surgical resection for ESBC and received adjuvant chemotherapy across 3 sites in Queensland, Australia from 2010 to 2015. Patients receiving palliative intent treatment were excluded from the present study. The primary outcome measure was to assess the proportion of patients reaching a RDI of ≥ 85%. The secondary outcome measures age, body mass index (BMI), Charlson comorbidity index, chemotherapy protocol, the use of granulocyte colony-stimulating factor (G-CSF), and toxicity data and were assessed to determine their effect on the dose intensity. RDI was analyzed against disease recurrence and patient mortality. The human research ethics committee granted low-risk ethical approval (approval no. HREC/15/QRBW/320) for the present study, with the need for individual patient consent waived.

Dose Intensity

The RDI was calculated as the ratio of the actual dose intensity to the standard dose intensity. To calculate the standard dose intensity (mg/m^2/wk), the total chemotherapy dose standard to each protocol was divided by the standard duration of that protocol, including all planned cycles. To calculate the actual dose intensity, the total chemotherapy dose received by each patient during their treatment