

A Pretreatment Risk Model to Predict Dose Attenuation of Adjuvant Chemotherapy in Patients With Early-Stage Breast Cancer

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| Origin of Study | USA |
| Type of Study | MULTICENTER, RETROSPECTIVE COHORT STUDY |
| Objectives | Develop a predictive risk model to select patients at risk for compromised outcomes due to dose attenuation who would benefit from supportive interventions intended to facilitate chemotherapy delivery at full dose intensity |
| Study Design | Data were collected retrospectively between August 1997 and May 2000 from 20,799 patients and included pretreatment patient demographics and clinical characteristics, as well as detailed information about planned and delivered chemotherapy. |
| Patients | <p>Medical records from 20,799 patients treated with adjuvant chemotherapy for early-stage breast cancer were examined.</p> <p>Mean age was 52 years; 17% of the patients were ≥ 65 years of age. Forty-nine percent of the patients were postmenopausal.</p> |
| Observations | <p>Multivariate analyses based on fixed logistic regression models identified the following significant (all $P < 0.001$) predictors of a relative dose intensity $< 85\%$: age ≥ 65 years (odds ratio, 1.6), body surface area $> 2 \text{ m}^2$ (odds ratio, 1.7), CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) regimen (odds ratio, 3.6), CAF (cyclophosphamide, Adriamycin [doxorubicin], and 5-fluorouracil) regimen (odds ratio, 4.3), and a 28-day dosing schedule (odds ratio, 2.6).</p> <p>An unconditional (pretreatment) model was developed employing these factors to generate a composite score (0–4), and its predictive performance was assessed by ROC analysis (AUC = 0.737; $P < 0.0001$).</p> <p>Patients stratified by risk score were 0 points, 23.7%; 1 point, 34.9%; 2 points, 30.7%; 3 points, 9.8%; and 4 points, 0.8%. The probability of a relative dose intensity $< 85\%$ increased progressively with increasing risk score: 0, 24.7%; 1, 53.3%; 2, 71.4%; 3, 85%; and 4, 89.6% ($P < 0.0001$).</p> |
| Conclusions | A reliable tool to identify patients at increased risk for dose attenuation would be valuable to help clinicians avoid compromised chemotherapy by targeting appropriate supportive care to these patients. Results with a risk model developed for this purpose show that this approach is feasible and provides good performance that is likely to improve the cost-effectiveness of supportive measures. |
| Discussion | <p>A recent analysis of practice pattern data from more than 20,000 patients with early-stage breast cancer treated with adjuvant chemotherapy demonstrated dose attenuation to $< 85\%$ of reference standard dose intensity in more than half of all patients and almost two thirds of elderly (≥ 65 years) patients. Additional recent clinical trial results with dose-dense regimens support the importance of sustaining or even increasing dose intensity for maximizing long-term outcomes.</p> <p>Because long remissions and even cures are possible for early-stage breast cancer patients receiving adjuvant chemotherapy, substantial reductions in the relative dose intensity of adjuvant chemotherapy, which may compromise outcomes, are problematic. It is possible to construct a pretreatment risk model that will predict which patients are at risk for dose attenuation and thus might benefit from targeted use of colony-stimulating factors, according to this large multicenter study.</p> |

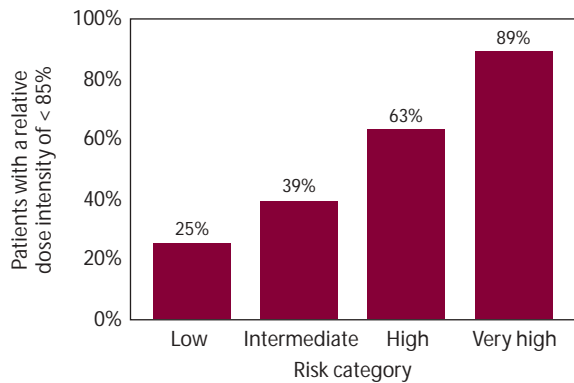
Prediction of Dose Attenuation of Adjuvant Chemotherapy in Patients With Early-Stage Breast Cancer

Investigators constructed a risk model based on a nationwide survey of 1,243 community oncology practices from August 1997 to May 2000. Data were collected on 20,799 patients treated with adjuvant chemotherapy for early-stage breast cancer.

The survey found that reduced relative dose intensity is common: More than half of the patients (56%) received a relative dose intensity < 85% of published reference standards, according to investigator Gary H. Lyman, MD, at the University of Rochester Medical Center, New York.

“Despite the risk of compromised outcomes, there was substantially reduced relative dose intensity in a large proportion of patients. It is likely that many of these dose attenuations were due to chemotherapy-induced neutropenia, which is known to result in dose delays and reductions,” Dr. Lyman said.

Incidence of Relative Dose Intensity < 85% by Risk Category



Multiple logistic regression analyses indicated that a greater risk of a relative dose intensity < 85% was associated with older age, higher body surface area, CAF and CMF chemotherapy, and a 28-day chemotherapy cycle ($P < 0.001$). Significantly lower risks were associated with more recent year of treatment and with primary prophylaxis with a colony-stimulating factor ($P < 0.001$).

A composite risk model was developed; it assigned 3 points each to age ≥ 65 years and body surface area $> 2 \text{ m}^2$, 7 points to CMF therapy, 8 points to CAF therapy, and 5 points to a 28-day cycle. Thus, patients could have a risk score of 0 to 26. Patients were then categorized as being at low risk if their score was 0, intermediate risk with a score of 1–5, high risk with a score of 6–12, and very high risk with a score of ≥ 13 points.

Dr. Lyman said that this and similar models, if validated prospectively, could be used to select patients for prophylactic colony-stimulating factor therapy, increase its cost-effectiveness, avoid overtreatment, and help to achieve optimal outcomes.

Key Points

- Over one half of patients with early-stage breast cancer who are receiving adjuvant chemotherapy are treated at a relative dose intensity < 85% of published reference standards.
- Factors placing patients at higher risk for a relative dose intensity < 85% include older age, higher body surface area, CMF or CAF chemotherapy, and a 28-day chemotherapy cycle.
- Patients treated in recent years and those receiving a primary colony-stimulating factor are less likely to have reduced relative dose intensities.
- Risk models can predict which patients are at higher risk and thus are candidates for targeted colony-stimulating factor therapy.

References

Agboola O, Crawford J, Dale D, Lyman GH; ANC Study Group. A pretreatment risk model to predict dose attenuation of adjuvant chemotherapy in patients with early-stage breast cancer. Poster presented at the 26th Annual San Antonio Breast Cancer Symposium; December 3–6, 2003; San Antonio, Tex. Abstract 642.

Agboola O, Crawford J, Dale D, Lyman GH; ANC Study Group. Most patients treated with adjuvant chemotherapy for breast cancer receive substantially reduced dose intensity. Poster presented at the 39th Annual Meeting of the American Society of Clinical Oncology; May 31–June 3, 2003; Chicago, Ill. Abstract 110. See page 50.