Re: Frequency and Cost of Chemotherapy-Related Serious Adverse Effects in a Population Sample of Women With Breast Cancer

In a recent article, Hassett et al. (1) suggested that chemotherapy-related serious adverse effects among younger women with breast cancer may be more common than reported by large clinical trials. To confirm this finding, we estimated the frequency of chemotherapy-related serious adverse effects among all incident breast cancer cases (n = 3317) that occurred between January 1999 and December 2002 in the female population (aged 69 years or younger) of Milan, Italy. For all patients, information about pathological staging, surgical treatment, radiotherapy, and chemotherapy were available. Information about the starting date and the type of drug used for chemotherapy administered within the 12 months following breast cancer diagnosis was derived, such that all prescriptions (prescribed between January 1999 and December 2003) with their Anatomical, Therapeutic, Chemical
therapeutic subgroup coded L01 were identified.

For each patient, hospitalizations for chemotherapy-related serious adverse effects occurred after breast cancer diagnosis (defined with the same methodology used by Hassett et al.) and preexisting comorbidities (chosen by adapting the Elixhauser list) (2) were identified from the hospital discharge registry. The hospital where primary treatment was given was identified and categorized according to the number of breast cancer patients treated there during the study period. Finally, for each patient, a full breast screening history was derived.

To control for potential bias related to use of chemotherapy, the propensity score was estimated using logit values from a stepwise logistic regression model that included age at diagnosis, type of surgery, pathological staging, comorbidities, volume of hospital activity, and screening history. Then, each treated patient was randomly matched with one not treated and having the same propensity score using the caliper matching method (3). Proportional hazard models were fitted by computing hazard ratios (HRs) and the corresponding 95% confidence intervals (95% CI).

A total of 847 breast cancer patients (25.5% of the patients studied) received chemotherapy. Discriminatory analysis identified young age, advanced pathological stage, access to a hospital with a high volume of activity, nonadherence to a screening program, and mastectomy as independent predictors of access to chemotherapy. Overall, 129 (15.2%) of the patients treated with chemotherapy had chemotherapy-related serious adverse effects. The percentage of patients experiencing individual categories of side effects were as follows: infection/fever (51.1%), neutropenia/thrombocytopenia (65.5%), anemia (5.6%), constitutional symptoms (0.4%), electrolyte disorders (0.8%), nausea/emesis/diarrhea (0.6%), thrombophlebitis/deep venous thrombosis (0.2%), and malnutrition (1.1%). Using the propensity score–matched approach, a statistically significant association between the experience of a chemotherapy-related serious adverse effect and chemotherapy was found (HR = 3.30, 95% CI = 2.22 to 4.89). Analysis of individual chemotherapy-related serious adverse effects showed a statistically significant association for infection/fever (HR = 2.76, 95% CI = 1.46 to 5.24), anemia (HR = 3.64, 95% CI = 1.74 to 7.63), and neutropenia/thrombocytopenia (HR = 5.25, 95% CI = 2.57 to 10.72). We estimated an average hospitalization expenditure of 12 000 Euros for each subject who experienced at least one chemotherapy-related serious adverse effect.

Our results, derived from a large population–based study that included incident breast cancer patients aged 69 or younger, confirm the conclusion of Hassett et al. that the impact and costs of chemotherapy-related serious adverse effects are larger than predicted from clinical data. An intriguing result of our study is the stage-independent associations observed between access to chemotherapeutic treatment and both nonadherence to the breast cancer screening program and admission to a hospital that does not specialize in cancer. This finding suggests that the differences in the risk of chemotherapy-related serious adverse effects could be due to different attitudes to prevention (cultural factors) and different skill in managing chemotherapeutic protocols and adverse events (institutional factors).

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REFERENCES

(2) Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8–27.

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