Selected Summaries

Adjuvant chemotherapy in early breast cancer: Are we over-treating patients?

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SUMMARY

Adjuvant chemotherapy has been the standard of care for patients with early breast cancer (EBC) based on the studies of the National Surgical Adjuvant Breast and Bowel Project (NSABP). In the 2000s, it was realized that most EBC patients, especially those who are hormone-positive and lymph node-negative, are being over-treated, and clinical and histological features may not be enough to make decisions regarding adjuvant therapy. Paik *et al*. proposed a gene recurrence score (RS) in 2004 in their landmark paper called Oncotype DX based on 21 genes, which directly correlated with prognosis.[1] They also showed that patients with high RS benefit from chemotherapy.[2] Sparano *et al*. published their data on patients with low RS (1–10) and showed excellent survival with hormonal therapy alone.[3] The authors randomized around 6700 patients with early hormone-positive, lymph node-negative breast cancer into chemohormonal therapy and hormonal therapy alone with the objective of showing non-inferiority of hormonal therapy to the combination. The primary end-point was invasive disease-free survival (IDFS). After a median follow-up of 90 months, hormonal therapy was found to be non-inferior to chemohormonal therapy in the intention-to-treat as well as per-protocol analyses for all primary and secondary end-points. On exploratory analysis, chemohormonal therapy had IDFS benefit in women <50 years of age with an RS of >16. Thus, this trial established new RS cut-offs for offering chemotherapy, being >26 for women above 50 years of age and >16 for women <50 years of age.

COMMENT

We have certain reservations regarding the applicability of these results, especially in the Indian scenario. First, the median age of patients with breast cancer in India is around 47 years, which is a decade younger than that in the West.[4,5] Whether it reflects a real difference in disease biology or it is a result of the population distribution is debatable with no definitive data to this effect. Around half the Indian patients present with locally advanced or metastatic breast cancer compared to 30% in the West.[6] Various social factors responsible for this include difficult access to quality healthcare, and lack of awareness and a robust screening programme. It has been proposed that the biology of breast cancer is different in the Indian population with a higher number of triple-negative breast cancers (30% compared to 12%–15% in the West).[7] Whether there is heterogeneity with more number of luminal breast cancers among the hormone-positive subtype in India has not been explored but is postulated due to overall inferior outcomes for Indian women with breast cancer.[8] Thus, Oncotype DX is likely to benefit a smaller number of Indian patients at a high cost.

Second, there is a lack of data regarding the age distribution of RS. It is logical that the middle-age group, i.e. between 35 and 50 years, will be the most likely to benefit from this test. Age is an independent prognostic factor for survival in breast cancer with patients <35 years having an inferior overall survival after adjusting for other prognostic factors including the hormone receptor status.[9,10] These patients also tend to present with aggressive disease. Breast oncologists may not be comfortable in avoiding chemotherapy in this subset irrespective of RS until more data are available. On the other hand, we may be over-treating patients in the age group of 35–50 years who have an intermediate RS and chemotherapy maybe avoided in many such patients if the distribution of RS in this population is known.

Third, the RS cut-off value of 26 to offer chemotherapy to women >50 years of age may not be valid in the Indian setting due to the lower average age of diagnosis. An age of 40 years in the Indian setting may be the ideal dividing line; however, it will need validation in a prospective trial.

Conclusions

Although Oncotype DX has revolutionized the management of patients with EBC, breast oncologists must take into account the biology of the disease in a particular population along with other tumour- and patient-related factors before taking treatment decisions as the first-line setting to be the best chance to cure these patients. There is an urgent need to develop cost-effective alternatives for our resource-limited setting.

Conflicts of interest. None declared

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