Breast cancer metastasis: mapping long term outcomes in Australia

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Characterising the ongoing but changing risk of relapse after breast cancer diagnosis improves surveillance planning and patient care

The high incidence of breast cancer and the enduring risk of relapse are major burdens for oncology care. Defining individual recurrence risk profiles would help optimise resource use when managing patients with breast cancer, but population-based outcomes datasets are unfortunately scarce.

In this issue of the *MJA*, Lord and colleagues[1] report long term outcomes for all women diagnosed with primary breast cancer in New South Wales during 2001 and 2002. The reported 14-year cumulative distant metastasis (DM) rate of 22.2% compares favourably with the 15-year recurrence rates of 41–53% after polychemotherapy and 33% after tamoxifen in the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) 2005 meta-analysis.[2] Clinical trials often recruit patients at higher risk and include local as well as distant metastases in the collaborative figures, factors that probably contribute to the higher rates in the EBCTCG report.

DM rates based on cancer registry data are rare because registries generally rely on biopsy data collected at relapse. A Canadian study found, however, that 29% of patients did not undergo biopsy at recurrence, rendering DM data in state registries very incomplete.[3] In this regard, the population-based study by Lord and colleagues, which drew on relapse data sources apart from biopsy reports, is all the more valuable. The authors noted that their overall findings were comparable with those of several other population-based studies, including the finding that the metastasis rate was stable from five years (for women diagnosed with localised breast cancer) or seven years (for those diagnosed with regional disease) after the primary breast cancer diagnosis. Later risk is probably driven by hormone receptor (HR)-positive cancers.[4]

The incidence of DM was markedly influenced by age in the study by Lord and colleagues; the rate in women under 40 years of age was almost twice that of older patients during the first five years after diagnosis, and their rates were similar thereafter.[1] This finding may be explained by a higher proportion of HR-negative tumours, associated with earlier relapse, in younger patients.[4] Further, genomic testing for HR-positive tumours in very young women has identified a higher prevalence of poor prognostic features, including homologous recombination deficiency and amplification-enriched subsets.[5] The influence of socio-economic status and remoteness on DM incidence was minor (however, few

patients were living in remote locations), providing reassurance that access to care is fairly equitable in NSW.[1]

The median breast cancer-specific survival of 28 months and 5-year survival of 29% reported by Lord and colleagues were impressive, particularly in view of the limited range of metastatic treatments available during 2001–2002. Survival was longer for women with HR-positive disease, as expected given its slower progression and the more numerous treatment options.[1] Shorter survival in younger patients could be related to more aggressive tumour subtypes, and in older patients to treatment options being constrained by comorbidity. Inferior survival for patients in regional areas may reflect more restricted services or different treatment philosophies; for instance, we have reported poorer survival rates for people with advanced cancer of various types in regional Western Australia, and that they received fewer lines of metastatic cancer therapy.[6]

The core strengths of the study by Lord and colleagues were the large number of women included, the whole population recruitment, and its drawing on multiple data sources to establish the DM date. This approach yielded robust data on DM-free survival and survival after DM detection not available in standard cancer registry reports.

An inevitable limitation, however, was the follow-up period required to define long term outcomes. A number of adjuvant therapies have been introduced in the meantime, including aromatase inhibitors and agents targeting human epidermal growth factor receptor 2 (HER2). Options for metastatic breast cancer management have expanded to an even greater degree.[7] The cited Munich Cancer Registry study found that 5-year relative survival increased from 80% to 94% over 35 years.[8] It would be expected that outcomes in NSW have also improved since 2002.

A more remediable limitation was the lack of biological subtype-specific data, which makes it difficult to apply the findings of Lord and colleagues to individual patients, as women with HR-positive, HER2-enriched, or triple negative tumours require quite different treatment protocols and have different natural outcomes. Consequently, their findings can be used for

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benchmarking outcomes for all women with breast cancer but not for specific patient groups. Most patients in the study would not have undergone HER2 testing, but HR testing was fully established in 2001–2002. Separate analyses of data for women with HR-positive and HR-negative tumours could illuminate the reasons for outcome differences by age and allow HR-specific prognoses over time, adding value to patient care.

Data of the type reported by Lord and colleagues could be used to benchmark locally audited results against national standards. Additionally, the detailed analysis of relapse risk over time could facilitate better prognosis and more intense monitoring of women at higher risk. No less important, as fear of recurrence is a cause of significant morbidity,[9] assuaging such concerns when risk is low would be beneficial.

Looking to the future, similar studies for establishing state and national standards are essential for identifying service inadequacies and ensuring best practice. Further, the continuing risk of late relapse for people with breast cancer, without effective targeted solutions, indicates that our knowledge of cancer dormancy is poor, and that more cyto-oncological research is needed in this area.

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