

Editorial

Prognostic Factors in Early Breast Cancer

Breast Cancer is the commonest female malignancy. About 250,000 women die of this disease every year throughout the world. The over all 5 year survival for patients with Breast Cancer is approximately 75%. However, of the 5 year survivors a further 17% will die of their disease in the next 5 years¹.

If the clinician has an indication of the potential prognosis for a patient with Breast Cancer, he or she can then counsel her appropriately and target those with a poorer prognosis who would benefit from adjuvant systemic therapy; conversely the patients with a good prognosis can be spared additional therapy.

The natural history of Untreated Breast Cancer was reported by Bloom in 1962^{2,3}. The median survival from the onset of symptoms was 2.7 years; 18% survived to 5 years and only 4% to 10 years. This provides a baseline against which different prognostic factors and response to treatments can be judged.

The prognosis for patients with Breast Cancer will depend on many factors, which can be broadly divided into two categories: Tumour-related and patient-related factors.

TUMOUR-RELATED PROGNOSTIC FACTORS

Tumour Size

Increasing tumour size is associated with an increased likelihood of Axillary Lymph node metastases, as well as higher risk of recurrence and death. The report from the Surveillance, Epidemiology and End Result Program of the National Cancer Institute, analysed data from 24740 breast cancer patients⁴, showed that the 5-year survival rate was 99.2% for patients with tumours <0.5 cm, decreasing to 82.2% for patients with tumours >5 cms. The incidence of positive axillary lymph nodes metastases steadily increased from 20.6% in patients with small tumours (<0.5cm) to 70.1% for patients with tumours >5 cms.

Lymph Node Status

Axillary Lymph Nodes Status is probably the best predictor of Prognosis; Survival decreases in presence of Axillary metastases and worsens as the number of involved nodes increases. Between 40 and 50% of patient, with tumour evident on clinical examination have axillary node involvement⁵, although clinical examination

of the axilla is notoriously inaccurate in the predication of axillary node metastases, with false-positive rate of 25-29% and false-negatives in the region of 27-32%^{6,7}. The 10-year survival is directly related to the presence or absence of axillary nodal metastases. Several series have reported 10-year survival of 65-80% for node-negative patients and 25-48% for node-positive patients. The prognosis is related to the number of nodes involved. Haagensen⁸ found that the 10-year survival was 63% for patients with 1-3 nodes involved, compared to 27% if greater than 4 nodes were involved.

Tumour Histopathology

Tumour grade is statistically significant prognostic factor for overall survival. High grade tumours carry a worse prognosis than lower grade tumours. Davis¹⁰ reported the overall survival as 86% for grade I, 70% for grade II and 57% for grade III. Peritumoral lymphatic emboli are associated with poorer survival in node-negative patients, but the significance of lymphatic invasion for node-positive patients is less certain. Vascular invasion is also associated with poor prognosis. Lobular carcinomas generally carry a better prognosis than ductal carcinomas. Tubular, cribriform and mucinous carcinomas have a favourable prognosis with medullary carcinomas placed in a moderate group.

Steroid Hormone Receptors

Estrogen-receptor positive tumours have a better prognosis than estrogen-receptor negative tumours. Disease-free survival was improved by 8-10% for ER-positive patients¹¹. Positive progesterone receptors are stronger predictor of survival than positive ERs¹².

Cell Kinetics and Ploidy

DNA ploidy was unable to provide independent prognostic information, but there is evidence for an independent prognostic role for S-phase fraction. High S-phase fraction has association with shorter relapse-free survival and reduced overall survival. Patients with aneuploid tumours have a poorer prognosis than those with diploid tumours¹³.

C-ERL B2

Tumours expressing the proto-oncogene C-ERL B2 and tumours with high levels of **Cathepsin D** have been associated with a worse prognosis^{14,15}. Tumours with **Epidermal growth factor receptor-positive** have been associated with a poorer prognosis¹⁶. **PS2** a protein, when

present in a tumour, has been associated with a longer disease-free and overall survival¹⁷.

PATIENT-RELATED FACTORS

Young age, obesity, resection of the tumour at certain stages of the menstrual cycle and psychological trauma have been associated with a worse prognosis in some but not in all studies. Pregnant women with Breast Cancer tend to present at a more advanced stage but when stage is taken into account they do not have a worse outlook.

Prognostic Index

The preceding discussion details the many factor which govern the prognosis for a patient with Breast Cancer. The problem for the clinician is how to interpret this information and get an overall picture of the prognosis in order to council the patient and be able to make rational decisions about adjuvant therapy. Haybittle¹⁸ and Todd¹⁹ outlined a prognostic index which they described as :

$$\text{Prognosis} = 0.2 \times \text{Size of the tumour (cm)} + \text{stage} + \text{grade}$$

The score gives prognosis as good (<3.4), moderate (3.4-5.4) and poor (>5.4).

Good prognosis correlates with a 5-year survival of 88% compared to 69% for the moderate group, and 21% for the poor prognosis group. A patient with Breast Cancer will have good prognosis if she is Node-Negative, grade I tumour less than 20 mm in diameter, whose score was below 3.

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