Conclusion: LR after BCT is associated with higher DM risk and poor survival. Especially patients with LRs developed within two years after BCT are at high risk. Late recurrences with high mitotic count have the same poor prognosis as early recurrences. For these patients systemic adjuvant treatment after the occurrence of LR should be considered.

291 POSTER

Quantitation of c-erbB-2 in primary breast cancer allows identification of a further poor prognostic group

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C-erbB-2 amplification or high levels of overexpression are found in about 20% of breast cancers and these patients have a poor outcome. Using a quantitative radioimmunohistochemical method in frozen sections we have previously shown that c-erbB-2 is nearly always overexpressed in primary breast cancers with gene amplification accounting for a population with very high levels of expression.

Here we report on the application of radioimmunohistochemistry to measure the c-erbB-2 protein in a larger set of cases (n ≈ 179) with followup exceeding 5 years. Levels of expression in areas of tumour were expressed relative to normal breast tissue taken from frozen sections of reduction mammoplasties. Disease specific survival was assessed using Kaplan Meier life table analysis and log rank tests.

85% of tumours overexpressed c-erbB-2. 23% had greater than 15 times normal expression. These cases had a significantly poorer survival than the rest of the overexpressors ($p < 0.0001$). 15% of cases had lower c-erbB-2 expression compared to normal breast tissue. These patients also had a poorer prognosis than the non-amplified overexpressors ($p < 0.0001$).

Dividing patients according to the Nottingham prognostic index, those in NPI group 1 with between normal and amplified levels of c-erbB-2 expression had a 5-year survival of 92%. But only 79% of patients in this group with amplified or downregulated c-erbB-2 levels survived 5 years. Similarly, patients in NPI group 2 with between normal and amplified levels of c-erbB-2 expression had a 5-year survival of 66% while those with amplified or downregulated c-erbB-2 levels had a 5-year survival of only 29%. The corresponding figures for NPI group 3 were 29% and 20%.

Quantitative radioimmunohistochemical measurement of c-erbB-2 protein provides additional prognostic information and can identify high risk groups within NPI subgroups which may have treatment implications for these patients.

292 POSTER

Prognostic impact of extended extracapsular component (EEC) in involved lymph nodes (LN) in primary breast cancer (BC)

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The importance of the nodal status of BC patients (pts.) is clear, but rarely are the patterns of LN metastases regarded as prognostic indicator. Extracapsular spread of tumour cells in metastatic LN, called EEC, has been attributed to bad outcome. We prospectively studied the impact of EEC regarding disease-free survival (DFS), distant failure (MFS) and overall survival (OAS).

483 patients with primary, node positive, non metastatic, previously untreated BC underwent surgery including axillary dissection with a median of 16 removed LN (Range 2–46). The axillary LN were extensively examined and regular follow up-examinations carried out.

Mean observation time is 36 months. In 219 cases (45%) EEC was diagnosed. EEC is correlated with the number of LN metastases ($p < 0.001$), lymphangiosis in the primary tumour ($p = 0.002$) and the expression of plasminogenactivator inhibitor PAI-1 ($p = 0.002$). Pts. without EEC had a median of 2 positive LN (1 to 40) and pts. with EEC 5 (1 to 44). Treatment decision for endocrine or cytotoxic therapy was not different in pts. with or without EEC, but pts. with EEC received significantly more often anthracycline-containing regimens ($p < 0.001$) and radiation therapy ($p = 0.006$).

DFS, MFS and OAS after 5 years are 53%, 64% and 78% for pts. without EEC and 37%, 40%, 61% for pts. with EEC respectively. These differences are significant with p-values of 0.007 (DFS), 0.0001 (MFS) and 0.0003 (OAS). The significance disappears in subgroup analysis for LN (1–3 LN, 4–9 LN and 10+ LN), but in multivariate analysis EEC is significant with a RR of 1.6 (1.1–2.3). Pts. with EEC without anthracycline-containing chemotherapy show a worse 5-year MFS and OAS than pts. without EEC (22% vs. 63%, $p = 0.003$ and 50% vs. 76%, $p = 0.002$), while pts. with anthracyclines do not (52% vs. 55% and 60% vs. 67%, p = n. s.).

We conclude, that EEC due to its strong correlation with the number of involved LN might be no independent prognostic marker, but a surrogate for nodal involvement. EEC could perhaps be a predictive marker for bad outcome with chemotherapy without anthracyclines, but this finding has to be confirmed through prospective randomised trials.

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The study of breast cancer metastases to the specific group of the axillary lymph nodes

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Purpose: We have conducted the studies on the metastases to the specific groups of axillary lymph nodes in patients with breast cancer since 1994. The aim of these studies was also to examine the possibility to lessen the lymph-oedema on the side of the operation.

Methods: The studies have been performed on 52 patients with breast cancer of various degrees of clinical advancement T1N0M0, T2N0M0, T2N1M0 and T3N2M0. The lymph nodes located inferior to the axillary vein, externally to the thoraco-dorsalis bundle, and medially to the margin of the muscle latissimus dorsi were included into separate groups. The lymphatic vessels were visualised with blue dye administered before the operation in the region of the tumour and the skin superior to it.

Results: No metastases to this group of the lymph nodes were found. However, it was established that in this triangle there are vessels which drain away the lymph from the upper extremity and the shoulder region, the cutting of which without putting a clip extends the period of lymph-seroma drainage.

Conclusion: The surgical removal of these lymph nodes is by no means an effective treatment, and may increase the frequency of the upper extremity lymph-oedema.

294 PUBLICATION

Overexpression of p27 in relation to p53 and clinicopathologic variables in node-positive breast cancer

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Purpose: The aim of this study was to determine the prognostic implication of p27 in relation to p53 in breast cancer patients with lymph node metastases.

Methods: We retrospectively evaluated 100 breast cancer with positive lymph nodes in the period between 1986 and 1991. Immunohistochemical staining for p27 and p53 was performed on formalin-fixed, paraffin-embedded sections. The results were compared with clinicopathologic variables and outcomes. A nuclear staining over 50% was defined as high expression for p27, and p53 protein expression >10% was defined as positive.

Results: High expression of p27 was shown in 54. There was no correlation between p27 staining and age, menopausal status, nodal metastases, or tumor size, but high p27 correlated to positive estrogen receptor and p53(−). High expression of p27 was significantly associated with longer survival. No differences of survival and disease-free survival were shown between patients with p53(+) and p53(−). A multivariate analysis showed that the independent variables were p27 and lymph node metastases.

Results: The results indicated high expression of p27 was an independent factor associated with good prognosis. Accordingly p27 may be more important than p53 in making therapeutic decisions for patients with lymph node metastases.