The complete results and possible explanation of these differences will be presented.

PP-6-4 Prognostic Significance of Obvious Peritumoral Emboli in 2692 Primary Operable Breast Carcinoma

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The prognostic significance of obvious peritumoral emboli (OPE) was evaluated in 2692 consecutive operable infiltrating ductal carcinoma of the breast operated and monitored at our institution between 1975 and 1992 (50.2% N− and 49.8% N+). OPE were assessed in routine practice and defined by the presence of neoplastic emboli within unequivocal vascular lumina including both lymphatic spaces and blood capillaries lined by recognizable endothelial cells adjacent to but outside the margins of the carcinoma. The frequency of OPE was 33.8% (19.6% in N−, 49% in N+). In univariate analysis OPE were related to tumour size ($p < 0.0001$), lymph node stage ($p < 0.0001$) and histologic grade ($p < 0.0001$); they were statistically significant with respect to survival (OS): $p < 10^{-29}$, disease-free survival (DFS): $p < 1.7 \times 10^{-13}$ and metastasis-free survival (MFS): $p < 10^{29}$. In multivariate analysis in the N− group, OPE were the most predictive factor for MFS ($p = 7.1 \times 10^{-7}$) before size and grade, and for survival ($p = 1.9 \times 10^{-3}$) after tumor size. In the N+ group OPE were the first predictive factor for local recurrence ($p = 4.1 \times 10^{-7}$).

In conclusion this study confirm with a very simple routine approach the prognostic significance of emboli in breast carcinoma. This is particularly interesting in the N− group to select a subset of patients at high risk, for a possible adjuvant therapy.

PP-6-5 Does Semi-Quantitative Evaluation Improve the Prognostic Value of Histological Grade in Breast Carcinoma: Comparison of Scarff-Bloom-Richardson (SBR) and Elston-Ellis (EE) Grading Systems in a Series of 825 Cases with a Follow-Up of 10 Years

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The respective prognostic value of two grading schemes was compared in a retrospective series of 825 patients treated between 1981 and 1988 for a small invasive carcinoma with conservative surgery and radiation therapy. Histological grade was assessed using the criteria developed by SBR and those recently proposed by EE. In addition, the exact number of mitotic figures per 10 high power field was recorded. Our results showed a strong unbalanced distribution of cases with a majority of Grade I cases (61% according to SBR, 50% according to EE) and a low number of Grade III cases (16% according to SBR, 4% according to EE). However, univariate and multivariate analysis showed that both histological grades were strongly correlated to overall and metastasis free survival. Despite the improvement of EE grading scheme in defining more precisely the morphological features, its prognostic value, in this series, was not better than SBR grading's. The number of mitotic figures was unexpectedly low, which could explain these results. We suggest that the mitotic score threshold are too high considering the small tumor sizes or, that due to the retrospective nature of the study, the technical conditions were less than optimal to properly assess the number of mitotic figures.

PP-6-6 The Prognostic Importance of Tumour Grade in Lymph Node Positive Breast Cancer

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Lymph node status is an important prognostic factor in primary breast cancer. However, considerable prognostic heterogeneity exists such that offering adjuvant systemic therapy to all lymph node positive patients may overtreat a low risk subgroup.

We reviewed the results of 636 patients aged < 70 years treated between 1973 and 1988 with histologically proven lymph node positive breast cancer. No patients received adjuvant systemic therapy.

On univariate analysis histological tumour grade and number of lymph nodes involved were found to be significant prognostic variables ($p < 0.01$). Patient age, menopausal status, oestrogen receptor and tumour size were not significant. In a second representative subgroup of 158 tumours MIB 1, S-phase fraction and erbB-2 were analysed. MIB-1 and S-phase fraction were significant prognostic variables on univariate analysis. On multivariate analysis for survival, tumour grade was the most important factor predicting for survival in the entire group and for the second subgroup.

The 15 year survival and average annual probability of death from breast cancer for lymph node positive grade I patients (n = 87) was 59% and 3.9%/year respectively. This shows that histological grade identifies a group of women who, although lymph node positive, have a 60% chance of surviving 15 years. This is similar to survival in breast cancer patients who are lymph node negative.

PP-6-7 Automated Grading in a Prognostic Index

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The Nottingham prognostic index (NPI) for primary operable breast cancer (NPI = (0.2 × tumour size) + lymph-node stage + histological grade), validated with 15 year survival analysis, remains a powerful clinical tool which defines three subsets of patients with different chances of dying from breast cancer (good, moderate, and poor prognostic groups partitioned by NPI score: < 3.4, 3.4–5.4, > 5.4 respectively). Grade contributes significantly toward NPI scoring but is a semi-objective variable. Quantitative measurement of histological tumour grade derived from automated analysis offers less subjective assessment and potential substitution of conventional techniques. Putative substitutes for grade: MIB1 labelling, cell morphometry (CAS™ image analysis), and proliferative index (PI = % SPF + % G2M) (flow cytometry) were measured on tumour tissue from 102 patients with primary operable breast cancer (median follow-up, 144 months) who received no adjuvant therapy. Multivariate analysis generated a simple (3 level) grade substitute, G^n = 0.02 (MIB1 + standard deviation of nuclear size + PI), weighted by NPI score frequency. A new prognostic index, NPI^n = (0.4 × tumour size) + (0.6 × lymph-node stage) + G^n, defined three subgroups whose survival curves superimposed the corresponding curves generated by the standard NPI. An automated score, G^n, can substitute for histological grade in an established prognostic index.

PP-6-8 Prediction of Tumor Response to Neoadjuvant Chemotherapy in Operable Breast Cancer

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The value of parameters obtained by fine-needle cytopunctures for the prediction of chemosensitivity was evaluated in 105 large operable primary breast carcinoma ((T2 ≥ 30 mm-T3, N0-N1-N2, PEV0-PEV1) treated with AVCMF (3 cycles) or FEC (4 cycles) before surgery. Cytopunctures were studied: before treatment for cytologic nuclear grading (in 2 groups) and S-phase fraction (SPF: 2 groups) by image cytometry; and after one cycle of chemotherapy for cytomorphologic and cell-kinetic changes. 13 patients showed pathologic complete regression (pCR), 26 were scored partial regression (with concordant clinical ≥ 50%, mammographic and histologic findings) and 59 showed no regression. Objective tumor regression and overall pCR were significantly related to high grade, high SPF, and to cytomorphologic and dramatic cell kinetic changes. Univariate analysis showed that high grade and high-SPF remained bad prognostic factors for metastasis free survival (MFS: $p = 0.005$ and $p = 0.003$, respectively; median follow up = 38.5 months). However, the subgroup of patients with pCR experienced a better clinical course (MFS, $p = 0.04$). The Cox model selected 3 variables: node positive, high S-phase and initial tumor size for MFS. At present the subgroup of pCR did not emerge from the Cox model possibly due to its small number of patients.

POSTER PRESENTATIONS

PP-6-9 Prognostic Significance of Epidermal Growth Factor Receptor and Estrogen Receptor in Advanced Breast Cancer

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The Epidermal Growth Factor Receptor EGFR is a specific glycoprotein transmembrane receptor that is believed to be a functional entity constituting

to their autocrine control of breast cancer growth. In a prospective study, we examined the response of 66 recurrent or metastatic breast cancer cases to therapy on the basis of the primary tumor EGFR status and ER status. Twenty eight patients received hormonal therapy in the form of tamoxifen and 38 received CEF (patients that had visceral metastasis or failure to previous hormonal therapy). The median age was 45.5 y. in the hormonal group (range 30 to 65) and that in the chemotherapy group was 42 y (range 29 to 65). RR was 60.7% and 68.4% in the hormonal and chemotherapy groups respectively. In the group receiving hormonal therapy, 83.3% of the ER +ve cases responded while 30.8% of ER −ve cases responded. Also, 73.7% of EGFR −ve cases responded compared to 0% of the EGFR +ve cases. In the group receiving chemotherapy 94.4% of ER +ve cases responded while 58.3% ER −ve cases did, also, 90.5% of EGFR −ve cases responded while only 55.6% EGFR +ve did. Follow up was done for a period of 3.5 years. Time to progression and overall survival for patients treated with hormonal therapy or chemotherapy stratified by EGFR and ER was calculated. In conclusion, EGFR status appears to be useful marker for lack of response to endocrine therapy and chemotherapy giving complementary information to ER.

PP-6-10 Diabetes Mellitus — A Prognostic Factor in Breast Cancer?

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A retrospective study, including 752 patients with breast cancer showed a highly significant correlation ($p < 10^{-5}$) between diabetes mellitus (DM) and metastatic disease. In order to confirm these interesting data, we carried out a prospective study including 747 patients with breast cancer. Documented were tumorrelated data like tumor growth, nodal involvement, histolagical grading, rezeptorstatus, patientrelated data like age, menopausal status and the body mass index (BMI), data about the carbohydrate metabolism (fasting and postprandial blood sugar and plasma insulin).

Results: There was no difference between patients with and without DM related to tumor growth, nodal involvement, grading and rezeptor status. Patients with DM were older and had a higher BMI than patients without DM. In contrast to the results of the retrospective study metastatic disease was not correlated with DM. According with the results of the retrospective stuy were highly significant correlations between tumor growth, nodal involvement and grading with metastatic disease.

Conclusion: The classical risk factors (tumor growth and nodal involvement predominate in the first years after primary therapie. The possible risk factor DM seems to be of importance later. The time of observation in the prospective study is with 24 months significantly shorter compared with the retrospective study with 50 months.

PP-6-11 Prognostic Significance of P53 Protein Accumulation in Male Breast Cancer (MBC)

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p53 abnormalities are frequently (20–40%) reported in female breast cancer (FBC) and often correlated with poor prognosis. Relatively few are the studies on its expression and mutation and correlation with prognosis in MBC. However, while some data (ASCO 1994, 1276) indicate that MBC rarely overexpress p53 protein, others support that it is similar to the female (Cancer 1995, 75, 2233). Twenty-nine consecutive non metastatic MBC were studied for prognostic factors (size, nodes, grading, ER, PgR, Ki-67 L.I./PCNA) and (in 21 pts) for monoclonal mouse anti-human p53 protein (DAKO-p53, D07) on formalin-fixed-embedded tissue sections. Staining was assessed by the number of cells and the intensity of the cells staining. Positivity was considered when > 20% of cells stained. The median pt age was 65 years; there were 23 infiltracting ductal (79.3%), 3 1obular (10.3%), 2 tubular (6.9%) and 1 apocrine (3.4%); 17 (58.6%) pts have LN involvement. All pts underwent mastectomy (radical in 24 pts). Of the 21 pts, 6 (28.6%) were positive for p53 and there was a trend for p53 positivity to be N+ and ER − and no correlation for size, grading and Ki-67 L.I. For the entire group five- and 10-year Kaplan-Meier time to progression rates were 45% and 30% and overall survival 55% and 40% respectively. No significant differences in DFS and OS were found with respect to size (p = 0.46; p = 0.35), grading (p = 0.54; p = 0.24), ER (p = 0.64; p = 0.23), PgR (p = 0.54; p = 0.11) and p53 (p = 0.83; p = 0.49) while at 5-year follow-up, node and Ki-67 L.I. negative group had a statistically significant higher DFS (p = 0.02) and OS (p = 0.007) than the positive group. At 10-year only the Ki-67 L.I. was predictive of DFS (p = 0.027) and OS (p = 0.007). At least in this series the incidence of p53 positivity is concordant with the FBC and, moreover, our data did not provide the p53 a useful predictor of disease-specific-and overall survival. Nodes and Ki-67 L.I. were significant predictors in worse survival.

PP-6-12 Histopathological Characteristics of Ductal Carcinoma in Situ (DCIS) of the Breast. A Comparison before and after the Introduction of Mammographic Screening

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The incidence of DCIS has increased from a few percent up to and over 20% of all breast cancers since mammographic screening started.

Aim: To investigate if there is any morphological differences between pre-screening respectively post screening DCIS.

Material: Patients operated at the University Hospital in Lund, 1978–1982 (pre-screening) 36 cases and 1990–1994 (post screening) 97 cases were included.

Method: Pre-screening as well as post screening DCIS were retrospectively and blindly evaluated by one pathologist (11) according to a previously presented standardised protocol using the original hematoxylin-erythrosin stained slides.

Results: There were no statistically significant differences in histopathological pattern considering aggressive characters as comedo head type, nuclear grade III, necrosis and diffuse growth pattern between pre and post-screening DCIS.

Conclusion: DCIS detected before and after the introduction of mammographic screening showed similar histopathological patterns. The results suggest that screening detected DCIS has similar malignant potential as non-screening detected DCIS.

PP-6-13 Significance of Some Morphological Signs for Treatment Results in Breast Cancer T1-2N0M0 Patients

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836 T1-2N0M0 breast cancer patients were operated by the modified radical mastectomy or by the breast conserving operations +/− irradiation. Majority of patients (646) was not undergone to any adjuvant treatment. Disease free survival (DFS) and overall survival (OS) were estimated by Kaplan Meier life table method, the significance of the differences was evaluated by means of the log rank test and considered significant at $p < 0.05$. Results. Patients with ductal and lobular cancer had identical course of disease, but both groups had significantly lower DFS in comarison with rare forms (mucous, papillary, medullary and tubular invasive cancer) patients group. Decreasing of the risk of disease relapse were reviewed in mucous cancer – in 1.2 times, in medullary cancer – in 1.6 times, in papillary cancer – in 2.3 times, and in tubular cancer – in 2.4 times in comparison with the hole patients group. Presence of the tumor cells in a lymphatic or in a blood vessels was a factor of a bad prognosis. DFS and OS in this patients group are decreased significantly, and risk of relapse was increased in 1.8 times. The 1-st grade of ductal cancer was a factor of the good prognosis, the curves of DFS and OS were significantly higher, than in patients groups with 2-nd and 3-d grade, the risk of disease relapse was 2.1 times lower. Early breast cancer can beseparated in some groups with different prognosis by means of morphological investigation.

PP-6-14 32P Relative Uptaking by a Tumor (32PRUT) is a Factor of Prognosis in Breast Cancer (BC) Patients

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The use of needleform semiconductor beta-detector has given the possibility to measure 32PRUT by intratissual technique, this 32PRUT in an o... more than one was measured on a tumor surface. 32PRUT was detected in primary tumor of 130 BC patients. 55 T1-2N0-1M0 patients were operative