cally for proliferation markers MIB1 (Ventana) and p34 CDC2 (Biogenex, San Ramon, CA). Patients were followed for a mean of 61 months (range 1–164 months).

Results: There were 63 (54%) node negative and 65 (56%) node positive cases. On univariate analysis MIB1 (p 0.002) and p34 CDC2 (p = 0.001) overexpression, HER-2/neu gene amplification and lymph node positive status (p < 0.0001) predicted disease related death.

HER-2/neu gene amplification correlated with lymph node metastasis (p = 0.001) and also predicted disease related death in lymph node negative patients (p = 0.029).

In multivariate analysis of combined lymph node negative and lymph node positive patients, HER-2/neu amplification (p = 0.04) and lymph node positive status independently predicted disease related death.

Conclusions: MIB1 and p34 CDC2 proliferation marker overexpression, HER-2/neu oncogene amplification and lymph node metastasis all predict disease related death in breast cancer, with HER-2/neu amplification and lymph node status independently predicting outcome. HER-2/neu amplification by FISH predicts disease related death in breast cancer independent of lymph node status.

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473   POSTER

Prognostic factors in human breast cancer

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A variety of new prognostic factors for breast cancer have been advocated, however their potential for identifying the time of relapse or the patient survival are still uncertain. In order to estimate the prognostic impact of different parameters we evaluated breast infiltrating ductal cancer specimens from 150 patients with a maximum 15 and a mean 9.4 years follow up by means of flow cytometry DNA analysis (DNA Index and S-phase fraction), the immunohistochemical assessment of Her/neu, Cathepsin D expression and the evaluation of the AgNORs through argyrophilic method.

55% of cases proved aneuploid with DNA Index between 1.1 and 2.42, whereas 45% of cases proved diploid. SPF, obtained to diploid cases only, was higher than median value (8.4%) in 37% of cases while 52% of cases showed the AgNOR value higher than cutoff value (9.5). Her/neu overexpression was detected in 34% of the cases, whereas 38% proved Cathepsin D positive.

The data obtained in our study carried out by univariate analysis, confirm the prognostic value of the individual indexes. As a matter of fact, cancer patients with DNA aneuploid, High SPF, Her/neu overexpression, high Cathepsin D levels and AgNOR exceeding 9 present a shorter DFS. The DNA Index is a highly significant prognostic parameter (rs = 0.56, p < 0.001) and also is the only factor able of discriminating node negative patients. The multivariate Cox model shows that DNA Index is the most important prognostic fact (coeff. = 2.74). We conclude that the data obtained from DNA flow cytometry, associated with other parameters, can be of great importance for the decision at the level aggressiveness of adjuvant therapy for a individual patients.

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474   POSTER

Axillary node involvement in T₁ breast cancer in pre-menopausal Chinese

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Purpose: Chinese Breast Cancer have some differences from that of western country, one of that is that half of the patients are ages between 35–50, The aim of the study is to assess the frequency of axillary rode involvement in T_1 breast cancer in young female, and to correlate the risk of nodal involvement in Chinese.

Methods: The study population consisted of 197 cases who were treated with modified radical mastectomy in our hospital from 1990 to 1995. All patients were T_1 lesion and age younger than 50. The lymph nodes all were classified to level I, II, III and Rotter's node. The number of dissected node were greater than 10. None of them has axillary recurrence in the follow up period. We analyzed patient's age, tumor size, axillary lymph node status, histologic grade, lymph vessel emboli, hormone receptor status, and P53 expression with immunochemical stain and flow cytometry.

Results: 1. T_1 breast cancer have a 27.92% risk of axillary LN involvement in premanupasl Chinese (24.14% for tumor 1 cm or smaller). 2. Patients

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younger than 50 years old are less likely to have positive lymph rode than older (P:0.038).

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475   POSTER

The local recurrence after breast conserving surgery: The prognosis and the diagnosis

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Purpose: To study the relationship between local recurrence after breast conserving surgery and the distant metastases.

Material and Methods: Between January 1981 and December 1989, 409 patient with invasive breast were treated with conservative surgery and radiation therapy, with actuarial follow-up of 12 years. Life tables were computed by the actuarial method and the comparisons of the distribution of length of time to local recurrence and distant metastases were made with the summary χ^2 test. The follow-up programme conducted a clinical exploration mammogram, echography and cytological punctures under echographic control.

Results: The overall actuarial survival rate at 12 years was 86%, with a 12 years distant metastases free of 64% and 12 years actuarial breast recurrence free rate of 78%. The 10 years actuarial distant metastases free rate in patients without local recurrence was 82%, in the patients who developed a local recurrence the rate was only 42% (p < 0.01). The patients who developed local recurrence within 4 years of original diagnosis, 33% developed distant metastases, in contrast the patients who developed later breast relapses only 9.5% developed distant metastases (p < 0.05).

Conclusion: The local recurrence after breast conserving surgery is associated with a distant metastases. The early local recurrence is a predictor factor of distant metastases.

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476   POSTER

Significance of soluble interleukin-2 receptors and natural killer cells in breast cancer

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Purpose: The aim of this study was to assess whether sIL-2r levels and/or percentage of natural killer (NK) cells were correlated with the pathologic stage and grade of tumors in breast cancer patients.

Methods: The study group consisted of 32 consecutive female patients undergoing surgery for breast cancer. The average age was 58 years. Sixteen patients underwent radical mastectomy, 13 had quadrantectomy with axially lymph node dissection and 3 had tumorectomy. Serum sIL-2r using the ELISA technique and NK cell count using flow citometry were determined prior to surgery. Tumor stage was recorde according the AJCC/UICC classification.

Results: Average sIL-2r levels was 1431 pg/ml. There was no significant correlation between sIL-2r levels and tumor stage or grade. However the sIL-2r were significantly higher in pts with ductal vs. those with lobular carcinoma and in pts with recurrent tumors of the same initial histotypo vs those who had primary and recurrent tumors of different histotypes. The NK cell count was significantly increased in in high grade tumor and there were inverse correlations between NK cell count and tumor size and the presence of lymph node metastasis. There was no correlation between sIL-2r levels and NK cell count.

Conclusion: These data show high sIL-2r levels may indicate breast tumor recurrence and tumor extension may be inversely correlated with NK cell count.

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477   POSTER

Thymidylate synthetase levels in breast cancer: A predictor for early prognosis and outcome of adjuvant chemotherapy

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Purpose: Thymidylate synthetase (TS) plays an essential role in the synthesis of DNA. The levels of TS were concluded to be indicators for early prognosis and retrospectively the outcome of adjuvant chemotherapy in breast cancer.

Method: TS levels were measured within tumors by TS binding assays in 47 female primary breast cancer patients excluding stage IV patients operated on from July 1993 to October 1995. TS levels were compared between patients with early recurrence and disease free patients within three years. These patients were classified into two groups by TS levels (high TS group vs low TS group). Disease free survival rates were compared between these groups statistically.

Result: TS levels ranged from 1.0 pmol/g to 30.8 pmol/g (mean:10.3 pmol/g). TS levels in twelve patients with early recurrence were significantly higher (17.7 ± 7.4 pmol/g) than those in 35 disease free patients (7.3 ± 6.1 pmol/g) (p = 0.0002). The high TS group (TS ≥ 10 pmol/g) and the low TS group (TS < 10 pml/g) consisted of 17 and 30 patients respectively. Age, TNM stage, histological characteristics, nodes status and ER status were not significantly different between these groups. The three year disease free survival rate of the high TS group was significantly poorer than that of the low TS group (47% vs 90%, p < 0.0001). Moreover in 22 patients with four or more positive nodes, the high TS group's survival rate was significantly poorer than the low TS group. In 19 advanced patients who had received adjuvant chemotherapy such as CMF or CEF, the mean TS level of six patients with cancer recurrence was 14.5 pmol/g which was higher than that of 13 patients with no recurrence (8.2 pmol/g).

Conclusion: The TS level is an important indicator for early prognosis in patients with breast cancer. The outcome of adjuvant chemotherapy in advanced patients will be expected for patients in the low TS group.

478   POSTER

A proposed prognostic factor for node-negative invasive breast carcinomas: Evaluation based on the intraductal component, particularly the presence of comedo-type necrosis

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Purpose: Node-negative invasive breast carcinomas relatively have a good prognosis with some exception. The aim of this study was to correlate their prognoses with some morphological features based on the intraductal component.

Methods: Ninety-four patients with node-negative invasive breast carcinoma with the intraductal component were classified into two types: the com () type included tumors which showed little or none of necrosis in the intraductal component, and the com (+) type included tumors which had a significant comedo-type necrosis. The Kaplan-Meier method was used to calculate disease-free survival. Moreover, in tumor specimens from 82 patients, the expression of p53, c-erbB-2, and Ki-67 protein was examined by immunohistochemistry.

Results: Disease-free survival was significantly poorer in the com (+) type than in the com () type (p = 0.007). The expression of p53 and c-erbB-2 was found in only 2 (4.2%) and 1 (2.1%) of 47 com () cases, respectively, whereas it was observed in 16 (45.7%) and 15 (42.9%) of 35 com (+) cases, respectively. High expression of MIB-1 was seen in 20 (42.4%) of 47 com () cases and 28 (80%) of 35 com (+) cases. The chi-square test showed a significant correlation between com type and each expression of p53, c-erbB-2 and MIB-1 (p < 0.0001, p < 0.0001, p = 0.0015).

Conclusion: These results suggest that the presence of comedo-type necrosis is associated with a biologically aggressive phenotype, and thus the subclassification of com (+) or com (−) types can be useful as a prognostic factor in node-negative invasive breast carcinoma.

479   POSTER

Relationship between tumor shrinkage and changes kinetic cell activity after primary chemotherapy (PC) in breast cancer (BC) patients

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Ki67 labelling index (LI) was evaluated immunohistochemically in tumor specimens obtained before and after PC in 145 patients with T2-4, N0-1, M0 primary BC submitted to a median of 3 cycles of either CMF regimen (days 1,8 every 28) or single agent epirubicin (120 mg/m2, every 21 days).

Tumor shrinkage greater than 50% was obtained in 112 patients (72.8%), 38 of them being complete responders (24.7%). PC significantly decreased the Ki67 LI: median 16% (range 1–90%), 7% (0–55%), before and after PC respectively. More than 50% decrease in Ki67 expression significantly correlated with tumor response (either complete or partial) both in univariate and multivariate analysis. Changes in cell kinetic activity, however, did not parallel with tumor regression in 22 patients. In addition a great proliferation activity (>15% of Ki67 positive cells) have been observed in 19 residual tumor of responding patients. Elevated KI67 LI at post-chemotherapy residual BC was found to be significantly related with short disease free interval (65% vs 85% DFI at 5 years). To conclude reduction in kinetic cell activity as a whole correlated but did not always match with the clinical response. Elevated kinetic cell activity after PC was related to poor prognosis. All these data suggest that the proliferation activity may be a useful toll that in addition with tumor response can discriminate early BC patients who would benefit from the cytotoxic treatment from those who would not.

480   POSTER

Relationship between estrogen receptor (ER) status in primary breast cancer (BC) specimens and serum CA 15-3 levels at first relapse of disease

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It has been shown a strict relationship between CA 15-3 concentration and ER expression in the cytosol of both primary and metastatic BC specimens. In newly diagnosed (BC), CA 15-3 serum levels are influenced by the disease extent (DE). We recorded data from 430 BC patients between October,88 and April, 97.260 patients (61%) were ER+ at diagnosis. At relapse, 278 (65%) had 1 organ involved, 118 (27%) 2 organs involved, and 34 (8%) >2; dominant sites of recurrence were 26% in liver, 32% in lung, 28% in bone and 14% in soft tissue. CA 15-3 overall sensitivity was 61%. Supranormal CA 15-3 levels were found in 183/260 patients (70%) with ER+ primary BC as compared to 78/170 patients (46%) with ER− ones (X2 p <.0001). CA 15-3 sensitivity parallelled the DE (assessed according to Swenerton, 1979). However, in patients with limited DE, elevated CA 15-3 levels were found in 71/123 (58%) with ER+ primary BC and in 18/70 (26%) with ER− primary tumors (X2 p <.0001), the corresponding percentages were 84% vs 57% (p < .001) in patients with intermediate overall tumor load and 84% vs 58% (p = n.s.) in those with elevated DE. ER status, DE and the presence of pleural effusion were independent variables predicting for CA 15-3 supranormal values according to a multivariate logistic regression analysis. The relationship between CA 15-3 supranormal rate at first relapse of disease and ER expression at diagnosis suggests that the steroid hormone receptor status might be a stable phenotype in BC patients. These data also suggest that the capability of CA 15-3 to early detect the disease relapse might be confined to patients with ER+ primary BC.

481   POSTER

Prognosis of 56 male breast cancers – Comparison with females

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Purpose: Due to a very low incidence rate of male breast cancer the prognostic factors are not so clear. Sometimes poorer than in females prognosis is suspected.

Methods: A study of 56 male and 952 female breast cancers was carried out and survivals were assessed in uni-, and multivariate analysis.

Results: Overall 5 and 10-year survivals of males treated by radical surgery were 71.6% and 38.9% (respectively). Lymph node status hardly influenced prognosis (81.5% N0 patients survived 5 years compared with 65% N+ patients). In multivariate Cox analysis only grading and lymph node status were independent factors which influenced males' survival. Relative risk of death was over 4 times higher for grade III tumours and near 3 times higher for males with metastatic axillary lymph nodes. An additional comparison of identical male and female breast cancer groups (pN0) showed marginally significant (p = 0.08) differences in survival. At 5th and 10th year, 82.3% and 69.1% (respectively) women were alive compared with 54.1% and 45% men. When multivariate Cox analysis was performed in the whole breast cancer group of patients, sex did not predict survival,