20   ORAL

The effect of treatment interruptions in the postoperative irradiation of breast cancer

N.S. Bese, P.A. Sut, A. Ober. *Istanbul University, Cerrahpasa Medical School, Radiation Oncology Department, Istanbul, Turkey*

Purpose:; To determine the outcome of the treatment interruptions in the postoperative irradiation of breast cancer, 853 patients treated in the years 1990-1999 inclusive were retrospectively analysed.

Materials and methods: Median age was 49 years(21-87). The median follow-up was 69 months(7-166). The most common histpathologic diagnosis was invasive ductal carcinoma (80%). Tumour distrubition by pathologic T stage was:T1; 38%, T2; 51%, T3; 7%, T4; 2%, TX;2%. Locally advanced breast cancers who received neoadjuvant chemotherapy were not included. Fivehunderedandfortysix (64%) patients were treated with mastectomy and 307(36%) patients were treated with breast conserving surgery; 20(2%) patients did not have axillary dissection. There were no axillary lymph node involvement in 268(31%) patients, 1-3 lymph nodes were positive in 300(36%), 4 and more lymph nodes were positive in 265(31%) patients. All of the patients had treatment with a Co60 unit or 4 MV x-rays. All patients with breast conserving surgery had breast irradiation. Chest wall irradiation were given to the patients who had axillary involvement.T3 and T4 tumours had chest wall irradiation regardless of axillary status. Lymphatic fields were selected due to the number of involved nodes. The dosage and treatment details will be presented. Patients are grouped due to the duration of treatment interruption. Grouping will be given in detail. Only the groups who had statistically significant results are mentioned in the abstract. Group A had 348(41%) patients who had no treatment break or interruptions of 7 days or less. Group B had 505(59%) patients who had treatment interruptions of 8 days or more. Locoregional control(LC), overall survival(OS), and disease free survival(DFS) rates were estimated by Kaplan-Meier method. Multivariate analyses were done by Cox model testing the parameters age, menauposal status, T stage, grade, histopathologic subgroups, axillary status, type of surgery, systemic treatment and duration of radiotherapy interruption.

Results: For all patients LC, OS and DFS for 5 years were 95%, 78%, 65% respectively and 10 years rates were as follows; 87%, 62%,54%. LC control rates for group A for 5 and 10 years were 94% and 90% respectively and it were 89% and 86% for group B. The difference was statistically significant (p=0,0196). OSS rates for group A for 5 and 10 years were 82% and 64% respectively, and it were 74% and 60% for group B (p=0,0267). DFS rates for group A for 5 and 10 years were 67% and 58% respectively and it were 63% and 52% for group B(p=0,05). In multivariate analyses treatment interruptions of 8 days or more and premenauposal status had appeared to be independent adverse prognostic factors on LC(p=0,036 and p=0,004, respectively).

Conclution: This retrospective study shows that treatment interruptions of 8 days or more during postoperative irradiation of breast cancer had adverse effects on outcome of treatment

21   ORAL

Histologic type of local recurrence and prognostic significance in breast conservation vs. mastectomy in invasive breast cancer: A 20-year update of a randomized trial

M. Nielsen, M. Blichert-Toft, S. Møller, M. Overgaard, F. Rank, H.T. Mouridsen. *Danish Breast Cancer Cooperative Group, Rigshospitalet, DBCG sec. 7003, Copenhagen, Denmark*

Aim: The main objectives are to analyse the histologic pattern of local recurrence in breast conserving therapy (BCT) vs. mastectomy (M) and to address the prognostic significance related to histologic type of local failure.

Material and methods: During 1983-1989 the Danish Breast Cancer Cooperative Group, DBCG, conducted a randomized trial, DBCG 82-TM, comparing BCT with M. A total of 1142 patients with invasive breast cancer were accrued and allocated to either type of surgery. The patients were followed until 2002 allowing up to 20 years of observation. Data set covering conventional patient- and tumour characteristics as well as type of surgery and adjuvant regimens were registered. Clinical records and histologic slides underwent revision. In case of a local failure within the ipsilateral breast (BCT) or chest wall (M) a discrimination was made between a true local recurrence vs. a new primary tumour. Further, a distinction was carried out between local relapse as a first event or a second event following regional and / or distant disease.

Results: Regarding local recurrence as a first event, the analysis revealed that true recurrence predominated as local failures in M versus

new primaries in BCT. Outcome measures indicate that true recurrence as a first event bears a worse prognosis compared with new primaries. Crude local recurrence rate amounted to 10% by at least 1o years of observation in either type of surgery. In BCT new primaries constituted 57% of local failures, while the figure in M reached 10%. Overall survival was 58% and did not differ significantly between BCT vs. M by 20 years of observation. Further details of the analysis will be presented.

Conclusion: It is concluded that the histologic local recurrence pattern regarding a first event differs between BCT and M and that outcome measures indicate a worse prognosis in true recurrence vs. new primaries. Overall survival in the trial did not differ significantly between BCT vs. M by 20 years of observation.

22   ORAL

Total tumour tissue levels of tissue inhibitor of metalloproteinases-1 as a prognostic marker in breast cancer: an EORTC validation study of 2984 patients.

A. Schrohl[1], M.N. Holten-Andersen[1], M.P. Look[2], H.A. Peters[2], J.G.M. Klijn[2], N. Brünner[1], J.A. Foekens[2]. [1] *The Royal Veterinary and Agricultural University, Inst. for Pharmacology and Pathobiology, Frederiksberg C, Denmark;* [2] *Erasmus MC -Daniel der Hoed, Josephine Nefkens Institute, Rotterdam, The Netherlands*

Background: Today, prognostic stratification of breast cancer patients with the aim of planning appropriate treatment for every patient is based on classical prognostic parameters: Lymph node status, tumour size, grade of malignancy, age, and hormone receptor status. Still, prognostic stratification is not complete, which results in over-treatment of a large number of patients.

We have previously demonstrated that total tumour tissue levels of tissue inhibitor of metalloproteinases-1 (TIMP-1) are associated with prognosis in patients with primary breast cancer. Furthermore, we have shown that TIMP-1 may be useful as a prognostic marker in combination with plasminogen activator inhibitor type-1 (PAI-1). The present study aims at validating these findings and has been conducted as an EORTC collaboration.

Materials and Methods: The study includes 2984 patients with primary breast cancer, 51% of whom were lymph node-negative and 49% lymph node-positive. The median age of the patients was 57 years. By use of an established TIMP-1 enzyme-linked immunosorbent assay (ELISA), total levels of TIMP-1 were measured in cytosol extracts of tumour tissue from the patients. Prior to measuring TIMP-1 in the extracts, the ELISA was thoroughly validated. Levels of urokinase-type plasminogen activator (uPA) and PAI-1 have previously been determined in these tumour tissue extracts.

Results: Levels of total TIMP-1 in the tumours showed a log-normal distribution (median 14.0 ng/mg protein, range 0-336 ng/mg). Univariate survival analysis showed a significant relationship between higher levels of tumour tissue TIMP-1 (continuous log-transformed variable) and poor prognosis with regard to recurrence-free as well as to overall survival (p<0.001). By use of isotonic regression analysis, we chose a cut-point to classify tumours as TIMP-1-low or TIMP-1-high. High levels of TIMP-1, then, were significantly associated with both recurrence-free and overall survival. In a multivariate model including uPA and PAI-1, TIMP-1 was significantly associated with shorter recurrence-free survival both when included as a continuous log-transformed variable (p=0.003) and when included as a dichotomised variable using the above-mentioned cut-point (p=0.002).

Conclusions: This study validates the findings of our first study demonstrating an association between total tumour tissue levels of TIMP-1 and prognosis in patients with primary breast cancer. Furthermore, it confirms that TIMP-1 may be useful as a prognostic marker in combination with PAI-1. By conducting the present study, we have added substantial positive information on the use of TIMP-1 as a prognostic marker in breast cancer and have made the first attempt to an identification of a cut-point for dividing tumours into TIMP-1-high and TIMP-1-low ones.

23   ORAL

Factors influencing the number of sentinel lymph nodes removed in breast cancer

A. Goyal, R.E. Mansel. *University of Wales College of Medicine, Department of Surgery, Cardiff, United Kingdom*

Background: The purpose of this analysis was to determine factors associated with the removal of multiple sentinel lymph nodes (SLNs) and whether removal of multiple SLNs results in a lower false-negative rate.

Methods: In the ALMANAC audit phase, 31 surgeons in 17 centres throughout the UK operated on 842 breast cancer patients. The SLN was