Lung Cancer

32 P

CORRELATIONS BETWEEN DNA PLOIDY AND IMMUNOPHENOTYPE OF LYMPHOCYTES FROM MALIGNANT PLEURAE EFFUSIONS.

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Lymphocytes populations and DNA ploidy were analysed in 30 pleural effusions (12 nonmalignant and 18 malignant) by the use of flow DNA cytometry.The percentage of lymphoctes T, B, NK, cytotoxic, helper & activated was estimated . The changes in lymphocyte populations and DNA ploidy were compared in both malignant and benign pleural effusions. Malignant pleural effusions were divided into two groups according to aneuploid DNA contents. It was observed that DNA contents in malignant cells had no influence on lymphocyte B, cytotoxic & NK cells count. However, in pleural effusions with aneuploid population, the numbers of lymphocytes T, helper & activated were lower than in benign effusions.

The results of this study may suggest that immunological response is decreased in malignant environment with aneuploid cells population.

33 P

A MODEL TO ASSESS COST-EFFECTIVENESS OF PROPHYLAXIS OF FEBRILE NEUTROPENIA.

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Reported incidences of febrile neutropenia in cancer patients undergoing chemotherapy vary widely according to cancer site, chemotherapy regimen, patient characteristics and definition of febrile neutropenia. Human Colony Stimulating Factors are effective in reducing the rate or duration of febrile neutropenia allowing more intensive chemotherapy, but they are expensive. The economic consequences of prophylaxis with HCSFs reported in the literature vary from cost savings to high added costs. Guidelines for the use of primary prophylaxis with HCSF have recommended that this should be restricted for patients with an expected incidence of febrile neutropenia of > 40%.

We developed a simple decision analytical model to assess the cost-effectiveness of prophylaxis of febrile neutropenia under various assumptions about the expected incidence of febrile neutropenia, effectiveness and cost of prophylaxis, cost of febrile neutropenia, and potential impact of prophylaxis on quality of life and life expectancy. The model was applied to lung cancer using data from the literature and from EORTC clinical trials.

The model illustrates some main principles of economic evaluation and can be used to assess the cost-effectiveness of prophylaxis of febrile neutropenia taking into account the best availaible information on expected toxicity and associated costs with various chemotherapy regimens.

34 P

BLOOD VESSEL INVASION BY TUMOR CELLS AND TUMOR ANGIOGENESIS COULD PREDICT RECURRENCE IN RESECTED NON SMALL CELL LUNG CANCER

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Traditional parameters such as tumor size, histology, hilar and mediastinal lymph nodes involvement have been identified as prognostic factors of natural history of completely resected lung cancer. New factors including tumor proliferative activity have been evaluated in the research setting, but at the moment their prognostic significance in resected lung cancer is not identified. Therefore controversy continues as to whether tumor proliferative index provides more useful clinical information than traditional prognostic parameters.

We investigated parameters like proliferative activity, fibrosis and necrosis, mitotic count, intratumoral and peritumoral blood or lymphatic vessel invasion by tumor cells and neoangiogenesis in 125 consecutive patients with non small cell lung cancer and who underwent operation between January 1990 and December 1993. Seventy-four were in stage I, 13 in stage II and 38 in stage III; 52 were adenocarcinoma, 55 squamous cell carcinoma, 11 adeno-squamous cell carcinoma and 7 indifferentiated large cell carcinoma. Fourteen patients in stage III had previous neoadjuvant chemotherapy with 3 cycles of mitomycin, cisplatin and vinblastine (MPV) and after underwent surgery. Median follow-up of the entire group is 3.4 years.

Fifty-three patients in stage I (71.6%) are still alive and free of disease; eight patients (61.5%) in stage II and 20 (52.6%) in stage III are alive respectively. Eleven patients (78.6%) who had previous chemotherapy and complete resection are alive and free of disease at a median follow-up of 22 months. By multivariate analysis the disease-free survival seems to be influenced by blood vessel invasion by tumor cells and neoangiogenesis expecially for patients in stage I and in stage III for neoadjuvant group. In this latter group exists a correlation between fibrosis grade, presence of inflammatory peritumoral reaction and survival.

Preliminary data of our study show a correlation between either the density of microvessels or the blood vessel invasion in histologic sections and the recurrence of disease. Furthermore our results suggest that the presence of concomitant fibrosis and inflammatory infiltration could be an important factor for better clinical out-come althought longer follow-up is needed to assess the impact of this multimodality evaluation.

35 O

DOES NEOADJUVANT MPV (MITOMYCIN C, CISPLATIN, VINBLASTINE) CHEMOTHERAPY INCREASE THE RISK OF BRONCHOPLEURAL FISTULAS?

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Encouraging results have been reported with neoadjuvant chemotherapy and radio-chemotherapy in the treatment of stage III non small cell lung cancer (NSCLC). However, the risk of postoperative morbidity, particularly bronchopleural fistulas (BPFs) seems to be increased after the treatment. Nevertheless, an in-depth pathophysiological analysis of the relationship between neoadjuvant treatment and postoperative morbidity is still lacking. At our Department from November 1990 to August 1995 57 stage III NSCLC patients (36 stage IIIa and 21 stage IIIb) underwent MPV neoadjuvant chemotherapy. Mean age was 56 years (range 39-68). Major response was observed in 44 patients (77%)and treatment-related mortality was 4%. Following chemotherapy, 31 of the patients underwent surgical treatment. Complete resection of all residual tumor in the primary site and lymph nodes could be performed in 84% (26/31) patients. The overall complete resection rate was 46% (26/57); 66% of the patients in stage IIIa and 9.5% of the patients in stage IIIb. The median follow-up for the 57 patients that have completed the chemotherapy treatment is 20 months (5 to 57). Twenty-eight patients are still alive (49%)and 29 died as a result of disease progression; 17 out of the 26 patients who had complete resection are still alive and 9 of them died because of disease progression (median follow-up 27 months). No postoperative morbidity or mortality were observed.There were no BPFs or clinically evident mitomycin-related pulmonary toxicity. Microscopic examination of resected bronchial specimens was performed to evaluate chemotherapy-related histological findings. A slight evidence of microvascular trombosis and submucosal fibrosis was found. In contrast, in a control group of patients submitted to preoperative radiotherapy (5000 cGy), microvascular trombosis and submucosal fibrosis were more marked. This could partially explain the higher incidence of postoperative BPFs reported after high-dose radiotherapy than with MPV chemotherapy. In our experience MPV neoadjuvant chemotherapy has been associated with favourable response and resection rates, with limited treatment-related bronchial damage and absence of BPFs. Although further studies are needed, this approach seems to be preferable to radio-chemotherapy in the treatment of stage III NSCLC.