Proffered papers

Breast cancer—diagnostic and prognostic factors

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BREAST CANCER SURVIVAL AFTER ORAL CONTRACEPTIVE USE

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The aim of our study was to investigate the influence of a positive history of OC use on survival of breast cancer. The prognostic effect of an antecedent OC use was investigated in 471 breast cancer patients recruited between 1982 and 1986 as contribution to the WHO Collaborative Study of Neoplasia and Steroid Contraceptives using univariate (Kaplan-Meier/ logrank test)- and multivariate (Cox model) survival analyses.

297 (63%) patients had ever used OCs and 202 (43%) were long-term users. Sixty months after diagnosis OC users had a significantly increased overall survival ($P = 0.037$). The effect persisted after adjustment for other prognostic factors and was mainly attributed to women who had taken OCs four years or longer ($P = 0.025$). Comparing the survival dependent on duration of OC use (never, 1–48 months, $\geqslant$ 49 months) the most significant influence on survival was observed among long-term users with a rather expected worse prognosis.

These results suggest an effect of OC use on tumor biology during the preclinical course of the disease.

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PROGNOSTIC VALUE OF BONE MARROW BIOPSY IN OPERABLE BREAST CANCER PATIENTS AT THE TIME OF INITIAL DIAGNOSIS: RESULTS OF A 19-YEAR MEDIAN FOLLOW-UP

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From May 1975 until May 1980, 128 operable breast cancer patients clinical stage I–II had a core bone marrow biopsy (BMB) from the posterior iliac crest as a part of the routine diagnostic work-up at the time of initial diagnosis. The mean age of the patients was 56 years, range 26–93. Prior to this study, in 10 patients BMB (7.8%) were positive for tumor cells and in 118 negative by conventional histopathology. In 1995 we reexamined all BMB separately at two laboratories, using monoclonal antibodies against cytokeratins AE1–AE3, KL 1, CAM 5-2 (DPG), and DC10, BA17 (MCI). Micrometastases were detected totally in 17 patients (13.3%) at MCI and in 16 patients at DPG. Moreover, at MCI another 8 patients were classified as suspicious. Median follow-up was 19 years. All tumor cell-positive patients relapsed and deceased within 6 years of disease progression with evident osseous metastases. There were 3 survivors of the 8 patients with suspicious BMB: 2 with evident osseous and skin metastases, time to relapse 19 and 20 years respectively, and one patient was disease-free after 15 years of follow-up. The median overall survival was significantly shorter in tumor-cell positive patients being 1.9 years compared to 11.7 years in the BMB negative and BMB suspicious groups ($P < 0.0001$). BMB is useful in predicting the prognosis in patients with breast cancer clinical stage I–II.

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PROGNOSTIC SIGNIFICANCE OF UPA AND PAI-1 IN RELATION TO OTHER PROGNOSTICATORS FOR THE CLINICAL OUTCOME OF BREAST CANCER

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In a retrospective study, uPA and PAI-1 were assayed by enzyme-linked immunosorbent assay (ELISA) in detergent extracts prepared from 400 primary breast tumours. The patients were followed for a median of 9 years and for all patients relevant clinical findings were recorded.

We found a correlation between uPA/PAI-1 and classical prognostic factors such as number of lymph nodes involved, grade, tumour size, hormone receptor status and histology, but no correlation according to menopause or age.

Disease-free (DFS) and over-all survival (OS) were analyzed using a Cox's proportional hazard model. As cut-off point the median uPA and PAI-1 values were used. Breast cancer patients with high content of PAI-1 (>11.0 ng/mg protein) have an increased risk of relapse and death (RR: 1.74 (1.27–2.39), while high uPA (>4.3 ng/mg protein) had no impact.

Despite PAI-1's correlation to other prognosticators, PAI-1 retained its independent significance in the Cox-model in contrast to uPA.

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PROTEIN TYROSINE KINASE ACTIVITY IN 350 T1/T2, N0/N1 BREAST CANCER. PRELIMINARY RESULTS

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Protein tyrosine kinases (PTKs) play a major role in the transduction of the mitogenic signal and have been reported to be involved in cell proliferation, differentiation and transformation. PTKs can be subdivided into two major families: membrane associated PTKs consisting essentially of growth factor receptors (receptor tyrosine kinases or RTKs) and cytosolic PTKs involved in the transduction of mitogenic and differentiation signals. From January 1988 to January 1992, PTK activity was assayed in cytosolic fractions prepared from 350 T1–T2, N0–N1 M0, breast carcinomas. Enzymatic activity was measured using ^{32}P-ATP and poly-Glu-Tyr as an artificial substrate. According to our previously reported pilot study, we chose a cut-off value of 12 pmol ^{32}P incorporated min^{-1} mg^{-1} protein, corresponding to median value. We found positive PTK levels ($\geqslant$12 pmol/min/mg) to be correlated with the loss of differentiation according to Scarff-Bloom grade ($P < 0.001$), negative PR ($P = 0.003$) and ER status ($P = 0.004$). With a median follow-up of 30 months (0–90), patients with a positive PTK level and a positive axillary status presented a significantly smaller 3 year disease-free survival than the PTK negative ($\leqslant$12 pmol/min/mg) ones ($P = 0.07$). In Cox multivariate analysis including pT, pN, Scarff-Bloom grade, PR and ER, PTK activity does however not emerge as a prognostic factor.

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MEDULLARY CARCINOMA OF THE BREAST, HISTOPATHOLOGICAL AND CLINICAL CHARACTERISTICS

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We characterized 110 medullary breast cancers (MC), diagnosed according to a new definition, recently proposed by us. The criteria are: (1) predominantly syncytial growth pattern and no tubular component,