

for uPA is 0.709 (95% C.I. 0.616–0.791), and for PAI-1 is 0.731 (95% C.I. 0.639–0.81) which shows good discriminatory efficacy. Limit values obtained by ROC analysis were 0.92 for uPA, and for PAI-1 1.44 ng/mg protein.

Curves of survival were obtained by Kaplan-Meier analysis. Survival curves of 72 patients with uPA ≤ 0.92 and 41 patients with uPA > 0.92 ng/mg proteins showed statistically significant difference ($P < 0.001$). Statistical probability of difference in curves of 62 patients with PAI-1 ≤ 1.44 and 51 patients with PAI-1 > 1.44 ng/mg protein ($P < 0.001$) is the same. Correlation coefficient of uPA and PAI-1 is 0.714 ($P < 0.0001$).

Our research confirmed prognostic significance of both parameters.

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POSTER

Associated changes of lipid peroxidation and transglutaminase activity in the evolution of breast tissue to cancer

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Background: Lipid peroxidation and tissue transglutaminase (tTG) have been independently implicated in tissue damage associated with several disease including breast cancer. We have investigated lipid peroxidation products, such as malondialdehyde (MDA) and 4-hydroxy-nonenal (HNE)-protein adducts, and tTG activity in tissues from breast surgical specimens to study the evolution from the normal to the cancerous tissue.

Methods: We have collected breast tissues from surgical specimens affected by primary invasive ductal breast carcinomas (C), fibroadenoma (F) and atypical ductal hyperplasia (H). The samples were obtained during surgical resection, directly frozen in liquid nitrogen and stored at -80°C until use. The tissue was suspended in hypotonic buffer Tris-HCl 10mM, EDTA 0.1mM and MgCl_2 5mM, PMSF 90 μM , 2- β mercaptoethanol 0.1mM (pH 7.5). The suspensions were homogenized by a Ultradurax T25 basic, then they were centrifuged at 13,000 rpm for 10 min. Biorad protein assay, spettrofluorimetric analyses of HNE-proteins adducts and tTG activity were conducted on the supernatants. The quantitation of the fluorescence intensity at 360 nm excitation/430 nm emission was taken as an indirect measure of the HNE-protein adduct (AFU/mg protein). The pellets were added of 500 μl urea 6M, SDS 8.1% buffer. After mixing the samples were centrifuged at 15,000 rpm for 15 min and 100 μl of supernatants were used for the TBA test in buffer TCA 15%, TBA 0.3%, HCl 0.12 N.

Results: The MDA levels and HNE-protein adducts of normal tissues obtained from specimens affected by breast cancer were compared with benign breast disease. In the breast cancer the values were respectively 60 ± 5 nmol/g and 2.2 AFU/mg protein while in the normal tissue belonging to specimens with atypical ductal hyperplasia the values were 30 ± 2.5 nmol/g and 79 ± 4.5 AFU/mg protein. In the control group represented by fibroadenoma affected one the values were 12.4 ± 1.6 nmol/g and 11.5 AFU/mg protein. The tTG activity increased only in normal tissues obtained from specimens affected by breast cancer.

Conclusion: Oxidative stress can damage many biological molecules; indeed, proteins and DNA are more significant targets than are lipids, and lipid peroxidation often occurs late in the injury process. In fact HNE-protein adducts increased in precancerous tissue, while higher MDA values are shown in cancer tissue damage. We speculated that these biochemical parameters together with the tTG activity may be a diagnostic index for cancer research.

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Prediction of axillary lymph node status in breast cancer patients by the presence of cancer emboli in the primary tumor's vessels

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Objective: To identify the presence of vascular emboli of breast cancer histologic specimens and validate its significance for the axillary lymph node (LN) involvement.

Methods: Two hundred and twenty-four patients with invasive breast cancer, who underwent modified radical mastectomy or breast-conserving surgery and standard axillary dissection (level I and II) at the Metaxa Memorial Anticancer Hospital the last 3 years, were assessed for the presence of cancer emboli in at least one vascular structure, irrelevantly of the size of the vessel. Then we applied chi-square test and logistic regression analysis (univariate and multivariate analysis) for the evaluation of the statistical association between the vascular invasion and the number of the metastatic infiltrated LN. In the present study the 224 patients, which participated, had a tumor size until 3 cm. We excluded patients with larger tumors owing to their likelihood of positive LN (74%).

Results: Vascular invasion (VI) was seen in 29.9% of 127 and 54.6% of 97 patients with ≤ 2 cm and > 2 cm tumors respectively. 81.5% of the patients with VI and tumors ≤ 2 cm had axillary lymph node metastases, compared with 35.9% of patients without VI. Also for tumors > 2 cm 77.3% of patients with VI had at least one positive LN, compared with 52.2% of patients without VI.

Conclusions: By multivariate analysis axillary lymph node metastases are significantly related to VI (p-value: < 0.001 for tumors ≤ 2 cm and p-value < 0.05 for tumors > 2 cm). The absence of VI can be considered as a favourable prognostic factor for the axillary status.

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PAI-1 and PAI-2 as predictive factors in breast cancer

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Introduction: The prognostic value of PAI-1 and PAI-2 in breast cancer has already been confirmed. However, the factors that predict the response to therapy are even more important. The latest observations made in the patients with operable breast cancer have shown that PAI-1 may have predictive value in breast cancer.

Aim: To evaluate the correlation between PAI-1 and PAI-2 measured in primary tumor and the efficacy of systemic therapy with cytostatics and hormonal therapy in advanced breast cancer.

Patients and methods: The patients treated for advanced disease with chemotherapy (ChT) (CMF, vepeside, taxane or platinum-based) or hormonal therapy (HT) (tamoxifen or aromatase inhibitors) were included in the study. PAI-1 and PAI-2 values were determined in the primary tumor using ELISAs (American Diagnostica Inc.; CT). High and low levels of PAI-1 as well as PAI-2 were dichotomized using median value for PAI-1 and optimal cut-off level for PAI-2. Those who achieved complete or partial response by RECIST were considered responders, whereas in patients treated by HT, stable disease for more than six months (mo) was also regarded as response. Differences in response were calculated using chi-square test, time to progression (TTP) was presented by Kaplan-Maier curves and differences in TTP calculated by log rank test.

Results: In 45 patients treated by HT, a higher response rate, though statistically not significant, was observed in the patients with high PAI-1 levels compared to the patients with low PAI-1 levels (60% vs. 50%). In these, prognostically unfavourable group of patients, the median TTP was even longer compared to the group of patients with low PAI-1 levels (6.7 vs. 4.1 mo; p=NS). A slightly better response to treatment was observed in the patients with low PAI-2 levels (56% vs. 44.4; p=NS). However, no difference in TTP was observed. The correlation between the PAI-1 and PAI-2 levels and the efficacy of ChT was estimated in 144 patients. The patients with low PAI-1 levels responded better to ChT compared to the patients with high levels of PAI-1 (52.8% vs. 46.2%; p=NS). However, no difference in TTP was observed. A better response to chemotherapy was observed in the patients with low PAI-2 levels (49.1% vs. 38.9%; p=NS). In these, prognostically unfavourable group of patients, also a longer median TTP was observed (6.3 vs. 5.7 mo), this difference was just over the limit of statistical significance (p=0.095).