Abstract of dissertation thesis

Prognostic and Predictive Factors in Breast Cancer

The mRNA Expression of Selected Genes in Normal and Tumor Breast Tissue Samples and Theirs Clinical Value in Breast Cancer

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Background: The aim of this work was to describe and to evaluate possibilities of prognosis and prediction in breast cancer. Within the framework of this study-work we carry out a prospective clinical study. The aim of this prospective study was to detect mRNA MMP-7, p53 and TIMP-1 expression in normal and tumor breast tissue samples and to determine the clinical and prognostic significance of our results.

Prognosis and prediction: The tumor size, lymph node status, presence of distant metastasis, differentiation of the tumor, perivascular invasion, mitotic activity, expression of ER, PR and HER2 receptors are the basic prognostic factors in breast cancer. Age under/above 35 years was included among independent prognostic breast cancer factors in 2005. It is approved to use uPA/PAI to assess prognosis in node negative breast cancer patients. The hormone receptor status and HER-2 receptor status are the only two predictive markers associated with the target therapy. OncotypeDX analysis could be use to predict the disease recurrence interval of patients with estrogen positive and node negative breast cancer.

Patients and methods: 74 samples of breast cancer tissue were taken away from inpatients undergoing primary surgeries for breast cancer. 24 samples of normal breast tissue were taken away from inpatients undergoing plastic surgeries. Samples were verified and deep frozen till the mRNA expression was assessed by RT-PCR. Histopatological examinations include the assessment of final tumor histotype, grade of differentiation, hormonal receptor status and mitotic index. After surgery patients were treated according to the Czech Society of Oncology Recommendations and examined till death or till the first end of the study. Routine statistical methods were used for the statistical analysis.

Results: The expressions of p53, MMP-7 and TIMP-1 mRNA were statistically significantly higher in tumor tissue samples ($p < 0.001$) compared with normal breast tissue samples. The expression of all three markers was significantly higher in samples from patients with node negative (N0) and also with node positive (N+) breast cancer compared to normal breast tissue samples ($p < 0.001$). The expression of MMP-7 mRNA was significantly higher in estrogen negative samples ($p = 0.017$). Patients with high mRNA expression of MMP-7 (above median) had shorter disease free interval ($p = 0.017$). The expression of p53 mRNA significantly correlated with tumor grade. The lower the rate of cell differentiation is the lower the median of gene expression is. Patients with grade 1 have higher median expression of p53 than patients with grade 2 ($p = 0,032$). The expression of TIMP-1 did not correlate with any clinical and pathological features and the disease free interval. Gene expression values according to occurrence of progression in patient in 5 years after operation were not statistically significant.

Conclusion: Higher expression of MMP-7 mRNA in breast tumor tissue sample is associated with shorter disease free interval. We confirmed that the expression of MMP-7 is higher in estrogen negative breast cancer samples compared. The expression of MMP-7 mRNA is negative prognostic factor in early breast cancer. We didn´t document the prognostic role of expression of TIMP-1 and p53 mRNA in breast cancer.