Results: There are 230 (16.9%) women with an ER−ve PR−ve breast cancer and 20 (1.5%) women with an ER−ve PR+ve tumour; the other 1108 patients (81.6%) have ER+ve tumours. Compared with women with a ER−ve PR−ve tumour, patients with ER−ve PR+ve breast cancer are younger (mean age 48.45 years vs 55.03 years; P=0.037) and more likely premenopausal (78.9% vs 34.3%). Such tumours are larger (39.05 mm vs 27.66 mm) and more likely of lobular type (20% vs 7.8%; P=0.002). Tumours in the ER−ve PR+ve category are less likely grade 3 (60% vs 86.1%, P=0.002), more frequently lymph node positive although not statistically significant (50% vs 38%; P=0.291) and more frequently overexpress HER-2/neu especially in the non-lobular type breast cancers (62.5% vs 35%; P=0.028).

Conclusion: ER−ve PR+ve breast cancers are less likely grade 3, appear more often in younger and premenopausal women and express more frequently HER-2/neu compared with the ER−ve PR−ve phenotype. Our findings suggest ER−ve PR+ve breast cancers have typical characteristics separating them from other breast cancers.

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Expression analysis of VEGF-C in breast cancer – correlates with expression of LYVE-1 gene and some prognostic factors

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Background: Metastatic spread of cancer cells is a major risk factor linked to the clinical prognosis. Despite of numerous clinicopathological studies on VEGF-C and LYVE-1 expression in various malignancies, little studies have investigated the correlation between them and its relationship with other prognostic factors in human breast cancer. The aim of this study was to assess the expression levels of VEGF-C and LYVE-1 gene and protein in human breast cancer, and to compare the correlation between these factors, to analyes the the expression of VEGF-C protein and VEGF-C, LYVE-1 mRNA to compare related data with clinico-pathological findings, to consider as valuable prognostic factor of VEGF-C in breast cancer patients.

Material and Methods: RT-PCR was carried on VEGF-C, LYVE-1 mRNA drawn from three adjacent normal breast tissue, MCF-7 breast cancer cell line and 39 breast cancer tissues and imunohistochemical staining to detect the expression of VEGF-C protein on 39 cancer tissues and 5 benign tissues using well preserved paraffin embedded blocks. Clinico-pathological findings were reviewed for menopausal status, axillary nodal status, lymphatic invasion by tumor cells, hormonal status, p53, c-erbB2, retrospectively. **Results:** RT-PCR analysis revealed the expression of VEGF-C mRNA in 23 of 39 (60.0%) and LYVE-1 mRNA in 19 of 39 (48.7%). The expression of VEGF-C mRNA was positive in all cases except one in LYVE-1 mRNA positive group, this revealed good correlation between two genes. The expression of VEGF-C and LYVE-1 mRNA did not significantly correlate with expression of VEGF-C protein. Immunohistochemical analysis revealed but VEGF-C protein is expressed only in breast cancer cells, specific VEGF-C staining was evident in 10 of 39 (25.6%). There was no significant correlation between VEGF-C, LYVE-1 mRNA expression and other prognostic variables. However, VEGF-C protein expression was negative in the group of premenopausal status, positive estrogen receptor, negative c-erbB2, statistical significantly.

Conclusions: VEGF-C seems to have a significant role in the mechanisms of lymphatic spread of breast cancer cells, the expression of its protein may help to evaluate the patient's prognosis.

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Oxidative stress products and soluble adhesion molecules in patients with breast cancer

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Backgrounds: Identification of clinically useful prognostic markers and markers of activity could contribute to the improvement of therapy of patients with breast cancer, mainly to the identification of subgroups of patients in higher risk of formation of metastases and early detection of relapses of the disease. In patients with breast cancer oxidative stress may modify membrane lipids which may then become the target of some autoantibodies. Some receptors (including EGF receptor and apo1/Fas) and adhesion molecules (standard and/or variant CD44 and P-selectin) may detach from the surface of tumor cells and increased levels of their soluble forms may be also identified in sera.

Methods: In our study serum levels of soluble EGF receptor, soluble standard and variant CD44 (CD44s and CD44v6, respectively), soluble P-selectin, soluble Apo-1/Fas, advanced oxidation protein products (AOPP), advanced glycation end-products (AGEs), pregnancy associated plasma protein (PAPP-A) and IgG and IgM anticardiolipin antibodies (ACA) were studied in 76 patients (pts) with newly diagnosed mostly non-metastatic breast cancer (3 pts in stage 0, 37 pts in stage I, 18 pts in stage IIA, 12 patients in stage IIB, 4 patients in stage III and 2 patients in stage IV) and compared with 8 age-matched healthy women.

Results. Patients with breast cancer had significantly higher serum levels of soluble standard form of CD44 (CD44s, 581.5±281.1 vs. 406.4±48.9 ng/ml, p<0.05), but not soluble variant form most common on breast cancer cells (CD44v6, 171.4±48.4 vs. 160.1±48.3 ng/ml, p=n.s.). Serum levels of soluble P-selectin (248.1±137.0 vs. 125.5±32.0 ng/ml, p<0.05) and serum levels of soluble Apo-1/Fas (852.9±1593 vs. 541.5±124.5 pg/ml, p<0.05) were also significantly increased in patients with breast cancer. Concerning the markers of oxidative stress patients with breast cancer had higher AOPP (93.6±46.8 vs. 68.5±23.1 μmol/l, p<0.05), but there was no difference in AGEs, PAPP-A and IgM and IgG ACA. We were not able to find any significant difference in serum levels of soluble EGF receptor (3.2±3.1 vs. 3.6±2.0 ng/ml, p=n.s.). None of measured parameters was able to discriminate the patients with different stages of breast cancer.

Conclusions: Patients with breast cancer (including those in early stages of the disease) may have increased serum levels of some soluble adhesion molecules (sCD44s, sP-selectin), markers of apoptosis (sApo-1/Fas) and oxidative stress (AOPP). Further follow-up should demonstrate the response of these markers to hormonal therapy/chemotherapy and putative prognostic significance of increased levels of these markers in order to improve the current possibilities to monitor the activity of the disease and to predict its outcome.

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A new look at the prognostic value of the presence of estrogen, progesterone and epidermal growth factor receptors in breast cancer tissue of women patients

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The aim of the study was to evaluate the influence of the presence or absence in tumours of estrogen (ER), progesterone (PR) and epithelial growth factor receptors (EGFR) on the survival of women with breast cancer. The receptors were determined by biochemical radiocompetitive methods. In order to analyse disease-free survival (DFS) and overall survival (OS) we applied Cox's proportional hazard model, in which we analysed both the presence of receptors and clinical and morphological parameters of survival.

The tumour size, metastatic lymph nodes and the presence of cancer infiltrations outside lymph nodes were negative prognostic factors. The mean relative risk (RR) were between 1.50 and 3.91.

The table presents the influence of 8 different variants of receptor status of breast cancer tissue on the survival of the patients.

No of patients n=184	Variables				DFS		OS	
				Significance	RR Exp(B)	Significance	RR Exp(B)
	ER	PR	EGFR	0.0074		0.0394	
28	+	+	+	0.0855	0.45	0.0248	0.22
9	−	+	−	0.4783	0.63	0.1895	0.26
64	+	+	−		1.00		1.00
11	−	−	−	0.9297	1.07	0.6914	1.16
11	−	+	+	0.5020	1.46	0.0516	3.16
33	+	−	−	0.0350	2.14	0.0454	2.56
21	−	−	+	0.0337	2.23	0.0712	2.32
7	+	−	+	0.0332	3.31	0.0383	3.95

Our results suggest, that both disease free survival and overall survival is directly related to the concomitant presence or absence of ER, PR and EGFR in breast cancer. It was found that patients with receptor status ER+PR+EGFR+ ER− PR+EGFR−; ER+PR+EGFR−; and ER− PR− EGFR− had better parameters of DFS and OS (RR for DFS or OS were between 0.22–1.16). The patients with receptor status: ER− PR+EGFR+; ER+PR− EGFR−, ER− PR− EGFR+ and ER+PR− EGFR+ presented a more aggressive disease course (RR for DFS and OS were between 1.46 – 3.95).

The presence of EGFR in breast cancer tissue is not always a negative prognostic factor for survival. It's coexistence with ER and PR is related to the best survival parameters (the group ER+PR+EGFR+, RR for DFS – 0.45 and for OS – 0.22).