EL was a statistically significant independent factor with adjustment for various clinicopathologic parameters.

Conclusions: EL was a strong independent prognostic factor of breast cancer and these results were more evident under clinicopathologically more favorable conditions. Earlier diagnosis and active treatments are suggested as the main causes of superior survival in the women with higher EL.

Table: Univariate and multivariate analyses of overall survival according to clinicopathologic characteristics

	Univariate analysis			Multivariate analysis								
Characteristic	Cox's proportional hazard model			Biological model[a]			Treatment model[b]			Combined model[c]		
	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*	HR	95% CI	*P*
Education level, high vs low	0.759	0.709-0.812	<0.001	0.776	0.684-0.880	<0.001	0.804	0.743-0.870	<0.001	0.837	0.727-0.964	0.014
Age, >35 vs ⩽35	0.652	0.593-0.718	<0.001	0.628	0.527-0.748	<0.001				0.578	0.479-0.698	<0.001
Tumor size, >2 cm vs ⩽2 cm	3.064	2.829-3.320	<0.001	1.895	1.648-2.178	<0.001				1.613	1.369-1.900	<0.001
Node positivity, yes vs no	3.762	3.484-4.061	<0.001	2.648	2.292-3.058	<0.001				2.247	1.892-2.668	<0.001
Metastasis, yes vs no	12.024	10.720-13.487	<0.001	5.221	3.994-6.825	<0.001				4.413	3.156-6.170	<0.001
Hormone receptor, positive vs negative	0.501	0.466-0.540	<0.001	0.477	0.421-0.540	<0.001				0.546	0.444-0.671	<0.001
HER2, positive vs negative	1.345	1.234-1.465	<0.001	1.046	0.931-1.176	0.446				1.014	0.892-1.153	0.833
Histologic grade, 3 vs 1, 2	2.257	2.082-2.445	<0.001	1.665	1.463-1.894	<0.001				1.608	1.394-1.855	<0.001
Lympho-vascular invasion, yes vs no	2.537	2.280-2.821	<0.001	1.492	1.307-1.704	<0.001				1.475	1.268-1.716	<0.001
Body mass index, >25 vs ⩽25	1.109	1.031-1.193	0.005	1.021	0.902-1.157	0.740				1.104	0.962-1.266	0.159
Operation, mastectomy vs lumpectomy	2.799	2.558-3.062	<0.001				4.608	4.104-5.173	<0.001	2.816	2.346-3.380	<0.001
Radiation therapy, yes vs no	0.926	0.861-0.997	0.040				2.178	1.990-2.384	<0.001	1.498	1.289-1.739	<0.001
Chemo-therapy, yes vs no	1.629	1.473-1.802	<0.001				1.276	1.138-1.431	<0.001	0.779	0.599-1.015	0.064
Hormonal therapy, yes vs no	0.593	0.551-0.639	<0.001				0.613	0.566-0.663	<0.001	0.865	0.707-1.058	0.157

HR, hazard ratio; CI, confidence interval; HER2, human epidermal growth factor receptor 2. [a]Cox's proportional hazard model adjusted with nine factors including age, tumor size, node positivity, metastasis, hormonal receptor, HER2, histologic grade, lymphovascular invasion, and BMI. [b]Cox's proportional hazard model adjusted with four factors including operation, radiation therapy, chemotherapy and hormonal therapy. [c]Cox's proportional hazard model adjusted with all thirteen factors described above.

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Ki-67 as Predictive Biomarker for Systemic Chemotherapy in Breast Cancer

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Background: Biological markers that reliably predict clinical or pathological response to primary systemic therapy early during the course of chemotherapy may have considerable clinical potential. Aim of the study is to evaluate changes in Ki-67 (MIB-1) labeling index and apoptotic index (AI) before, during, and after neoadjuvant anthracycline chemotherapy in breast cancer.

Materials and Methods: Breast cancer tissue were collected from Grant Medical College and Sir J.J. Groups of Hospitals, Mumbai, India. Twenty-seven patients receiving neoadjuvant FEC (5-fluorouracil, epirubicin, and cyclophosphamide) chemotherapy for operable breast cancer underwent repeat core biopsy after 21 days of treatment.

Results: The objective clinical response rate was 56%. Eighty patients (31%) achieved pathological response by histopathological criteria; two patients had a near-complete pathological response. Increased day-21 AI was statistically significant predictor of pathological response ($p = 0.049$). A strong trend for predicting pathological response was seen with higher Ki-67 indices at day 21 and AI at surgery ($p = 0.06$ and 0.06 respectively).

Conclusion: The clinical utility of early changes in biological marker expression during chemotherapy remains unclear. Until further prospectively validated evidence confirming the reliability of predictive biomarkers is available, clinical decision-making should not be based upon individual biological biomarker profiles.

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Triple-negative Breast Cancer − Which Classical Prognostic Factors Can Help in Identifying Patients with Early Relapse?

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Background: Triple-negative breast cancer (TNBC) belongs to a poor prognostic group with the highest risk of relapse during the first few years after radical surgery. We investigated the influence of classical prognostic factors and adjuvant CHT (A-CHT) on 2-year prognosis in early TNBC pts treated at the Institute for Oncology and Radiology of Serbia (IORS).

Patients and Methods: We identified a group of 165 stage 1/2 TNBC pts diagnosed during 2006–2008 treated with radical surgery ± postoperative radiotherapy and A-CHT as per protocol. TN status was defined as IHC ER0−3/PR0−3/HER2:0−1 or IHC HER2:2+/CISH−. We analyzed the following prognostic factors: patients' age, menopausal status, medullar histology, tumor size, tumor grade, nodal status, HR/HER2 phenotype (ER0/PR0/HER2:0 vs. non-ER0/PR0/HER2:0) and A-CHT (anthracyclines vs. non-anthracyclines). Disease free survival (DFS) and overall survival (OS) were the main end points. Fisher Exact test, Pearson Chi-squared test and Log-rank test were used for statistical analysis.

Results: Median age of analyzed group was 58 years (range 26−84) and median follow-up was 24 months (range 3−56). Disease relapse experienced 31/165 (18.8%) pts, and 21/165 (12.7%) pts died, all from BC. Women ⩽50 years more frequently undergone subcutaneous mastectomy with immediate reconstruction ($p < 0.0001$) and received more frequently anthracycline − containing CHT ($p < 0.0001$) compared to women >50 years. Medullar BCs were more frequently associated with grade 3 tumors than non-medullar BCs ($p < 0.0001$). Breast conserving surgery was more frequently performed in pts with tumors ⩽2 cm compared to pts with tumors >2 cm ($p < 0.0001$) and in N0/N1−3 pts compared to N⩾4 pts ($p = 0.0003$). Grade 3 BCs were more frequently associated with ER0/PR0/HER2:0 phenotypes than grade 2 BCs ($p = 0.03$). Pts with N⩾4 more frequently experienced disease relapse than pts with N0/N1−3 ($p = 0$), especially bone and liver metastases ($p < 0.0001$ and $p = 0.0002$, respectively). There was no difference in DFS and OS in subgroups divided according to age, menopausal status, tumor histology, size and grade, HR/HER2 phenotype, and type of adjuvant CHT. N0/N1−3 pts subgroups had significantly better DFS (Log-Rank test; $p = 0$) and OS (Log-Rank test; $p = 0$) than N ⩾4 subgroup.

Conclusion: Nodal status was the only prognostic discriminator for 2-year outcome in pts with stage 1/2 TNBC.

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PR Negative Tumors ñ Prognosis and Results of Oncotype Dx

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Several studies demonstrated that breast cancers that are ER positive/PR negative carry a worse prognosis than ER/PR positive tumors if treated only by adjuvant hormonal therapy. In these studies PR was assessed by methods that measure protein content. Oncotype Dx measures mRNA expression. In clinical trials the discrepancy between IHC and RT PCR for the expression of PR was about 20%, but this was not assessed in a community setting. The meaning of high levels of PR mRNA without detectable PR protein is unclear. This discrepancy might result from technical issues or might be explained by a biological mechanism such as translational inhibition of PR by miRNA's.

We sought to verify the prognostic value of the expression of the progesterone receptor by IHC in women with early stage HER 2 negative, ER positive BC treated with systemic hormonal therapy only at our institution. Next, we aimed to characterize the results of Oncotype Dx in ER positive, PR negative HER 2 negative tumors.

Methods: 1st cohort: Files of consecutive patients with ER positive HER 2 negative tumors that were treated by adjuvant hormonal treatment during 2000–2006 were reviewed.

2nd cohort: The characteristics of PR negative tumors tested by Oncotype Dx during 2007–2011 were analyzed.