surgery from 1986 to 1995. Premenopausal women were treated with adjuvant ovarian ablation by irradiation and postmenopausal women with adjuvant Tamoxifen for 5 years. Steroid receptors contents were determined prospectively by the classical biochemical DCC method, while HER2 gene amplification was determined retrospectively by CISH in 134 women whose archival paraffin tissue samples were retrieved.

Results: One hundred and thirty four patients whose HER2 status was determined (66 premenopausal and 68 postmenopausal) of median age of 51 years (range 35−76), were followed for median 11.8 years (range 0.9−19). Eleven (8.21%) patients were node negative with grade 3 BC and 125 (93.28%) had 1−3 positive nodes irrespective of tumor grade. Median disease free interval was 12.3 years (95% CI 10–17.8); median BC specific survival (BCSS) was 16.2 years (95% CI 13-Inf) and overall survival (OS) was 15.2 years (95% CI 12.1-Inf). HER2 gene amplification (CISH+) were noted in 21 (15.67%), while 113 (84.33%) had no HER2 gene amplification (CISH−). There was no significant difference in the risk for disease relapse [HR 1.25 (95% CI 0.678–2.29), p = 0.489], death from BC [HR 1.21 (95% CI (0.608–2.42), p = 0.591], and death from any cause [1.19 (0.637–2.23), p = 0.590] between CISH+ and CISH− subgroup. Cox regression analysis showed that only ER-/PgR+ status was an independent favorable risk factor for BCSS [HR 8.29 (95% CI 1.14–60.24, Wald test p = 0.028)] and OS [HR 7.51 (95% CI 1.31–68.97, Wald test p = 0.0009)]. Comparison between premenopausal and postmenopausal subgroups with CISH+ BC showed a trend toward longer OS in premenopausal women (Log rank test χ^2_1= 3.302, p = 0.069), while the OS difference in CISH− group reached statistical significance in premenopausal women (Log rank test χ^2_1= 4.849, p = 0.028). However, there was no difference in BCSS between premenopausal and postmenopausal subgroups regardless of HER2 status.

Conclusion: Our results did not show that positive HER2 status had a significant influence on disease outcome in early SR-positive breast cancer patients treated with adjuvant endocrine therapy only.

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Clinicopathological implications of cyclin B1, cdc2, p16 and p53 expression in breast cancer

J.H. Kim[1], D.H. Kim[2], S.W. Chae[2], J.H. Sohn[2], C.K. Yom[1], S.Y. Kim[3], Y.L. Park[1]. *[1]Kangbuk Samsung Hospital Sungkyunkwan University School of Medicine, Surgery, Seoul, Korea; [2]Kangbuk Samsung Hospital Sungkyunkwan University School of Medicine, Pathology, Seoul, Korea; [3]Soonchunhyang University College of Medicine Cheonan Hospital, Surgery, Cheonan, Korea*

Backgound: Cell cycle prgression is governed by cooperation of specific cyclin and cyclin-dependent kinase (Cdk) at G1-S and G2-M checkpoint and the cell cycle deregulation plays a major role in carcinogenesis of human cancers. Therefore, the evaluation of cell cycle proteins is important. The molecular mechanism responsible for initiation and progression of breast cancers are largely unknown. The aim of this study was to analyze the cyclin B1, cdc2, p16 and p53 tumor suppressor gene in breast cancers.

Materials and Methods: Tumor samples were obtained from 98 patients with breast carcinomas. To investigate the role of cyclin B1, cdc2, p16 and p53 in the pathogenesis and prgression of breast carcinomas, 98 cases of breast cancers were examined for the expression of cyclin B1, cdc2, p16 and p53 by immunohistochemical method. The correlation of cyclin B1, cdc2, p16 and p53 expression with various clinicopathological findings was also analyzed.

Results: Cyclin B1, cdc2, p16 and p53 were diffusely expressed in 55 cases (56.1%), 52 cases (53.1%), 57 cases (58.2%) and 68 cases (69.4%) out of 98 cases studied, respectively. In normal breast tissues, cyclin B1, cdc2, and p16 were weakly expressed and p53 was not expressed. The overexpression of cyclin B1, cdc2, p16 and p53 in breast cacner were noted. The correlation between the loss of expression of cyclin B1, cdc2 and distant metastasis was noted (p < 0.05). The correlation between the expression of cdc2 and infiltrative tumor border pattern was noted (p < 0.05). In addition, the overexpression of cdc2 and p53 were correlated with histologic high grade carcinomas (p < 0.05).

Conclusions: Cyclin B1 and cdc2 appeared to be involved in the genesis or progression of breast cancers. In addition, overexpression of cdc2 and p53 may play important roles in progression into high grade group in patient of breast carcinomas. Deranged overexpression of cyclin B1, Cdk, p16 and p53 may play an important role in human breast carcinogenesis.

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Changes in nutrition parameters among women with early breast cancer

A. Stanislawek[1], L. Wolanski[1]. *[1]Medical University of Lublin, Chair of Social Health Care, Lublin, Poland*

Material and Methods: 127 blood samples from women with diagnosed breast cancer were collected. Received results were compared to control group (n = 35) of healthy women with the similar age (middle age 55 years old) and from the similar region. Further data (weight, height, other diseases) were received from the hospital documentation (patients with breast cancer) and directly from other patients. Received data were calculated statistically by using tests t-Student and U Mann-Whitney.

Results: The average level of TC in analyzed patients with breast cancer was 228.03 mg/dl with variability factor (v) 20%, which was significantly more than in control group (204.7 mg/dl, v=19%), p < 0.01. Over 76% of women with breast cancer had the level of TC in serum higher than 200 mg/dl and 8% of them had the level of TC higher than 300 mg/dl. The average level of HDL in blood serum of women with breast cancer was 58.66 mg/dl (v=27.75%), and in general population of women with similar age it equaled 63 mg/dl (v=16%), p < 0.05. The average level of LDL in blood serum among women with breast cancer was 142.35 mg/dl (v=29.05%) vs. 117.4 mg/dl (v=32%), p < 0.01 among women from control group. The average level of TGC in blood serum of women with breast cancer was 134.94 mg/dl (v > 35%) and the average level of TGC in general population of women was 119.2 mg/dl, p > 0.05 (statistically not significant). The BMI of women with breast cancer was similar to the general population of women with the same age group and from the same region. It was respectively 27.52 kg/m^2 and 27.31 kg/m^2 (v < 35%, p > 0.05).

The women were also divided into groups dependently of malignancy of the cancer (G). However, there were no statistic significance when comparing BMI, TC, HDL, LDL in women with breast cancer of G1, G2, and G3 malignancy, the average values of some studied parameters tended to change. The average level of TGC in blood serum in women with grade G3 breast cancer was 131.09 mg/dl vs. 143.06 mg/dl in women with breast cancer in grade G2. The average BMI of women with G3 breast cancer was 27.06 kg/m^2 vs. 27.26 kg/m^2 in women with G2 breast cancer. Unfortunately, the group of women with G1 breast cancer was too small to compare it to other groups.

Conclusions: The nutrition parameters like TC, HDL and LDL could the possible risk factors in breast cancer.

The level of TGC in blood serum and BMI could be helpful in the risk of malignancy of breast cancer.

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Relationship between hormone receptors, MIB-1 index and serum tumour markers CEA and CA 15−3 in patients with pT1−2 breast cancer

F. Lumachi[1], S.M.M. Basso[2], B. Marzano[2], M. Bonamini[2], E. Milan[2], G.B. Chiara[2]. *[1]University of Padova, Surg & Gastroenterol Sciences, Padova, Italy; [2]U.O. Chirurgia I, S. Maria degli Angeli Hospital, Pordenone, Italy*

Background: CEA and CA 15−3 are the best investigated serum tumor markers in breast cancer (BC) patients. The aim of this study was to find relationship between serum CEA and CA 15−3 and prognostic markers, such estrogen receptor (ER), progesterone receptor (PGR), and tumor proliferation rate index measured by MIB-1 index, in women with pT1−2 breast cancer.

Patients and Methods: Preoperative measurement of serum CEA and CA 15−3 was obtained from 301 women (median age 61.2 years, range 28−85 years) with confirmed BC, who underwent curative surgery. The removed tumor tissue was routinely processed for ER and PGR using a quantitative standard immunoenzymatic method, while the immunostaining of Ki-67 antigen was performed using the monoclonal antibody MIB-1.

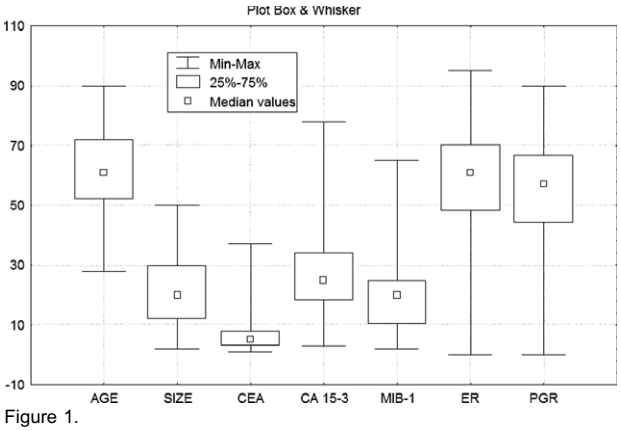

Figure 1.

Results: The results (age of the patients [61.2±12.9 years], size of the tumor [20.7±10.2 mm], CEA [6.3±5.0 ng/mL], CA 15−3 [26.1±12.4 U/mL],

MIB-1 [21.6%], ER [58.8%], and PGR [54.4%]), expressed as median values, are reported in Figure 1. There was a significant relationship between (1) size and both age (R = 0.16, p = 0.005) and ER (R = −0.15, p = 0.011), (2) CEA and CA 15−3 (R = 0.19, p < 0.001), (3) PGR and ER (R = 0.52, p < 0.001), and (4) an inverse relationship between PGR and age (R = −0.15, p = 0.008), size (R = −0.23, p < 0.001), and MIB-1 (R = −0.15, p = 0.009). A weak correlation (R = 0.11, P = 0.046) between age and CEA was also found.

Conclusions: There was no relationship between preoperative serum tumor markers CEA and CA 15−3, and routine prognostic markers ER, PGR and MIB-1, which mainly inversely correlate with age of the patients, and size of the tumor.

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Prognostic factors in Mexican young women with breast cancer

V. Pérez Sánchez[1], G. Delgado Velazquez[1], T.A. Vela Chavez[1], D. Almaguer Casados[1], A. Maldonado Hector[1], E. Bargallo Rocha[2], O. Arrieta Rodriguez[3]. *[1]Instituto Nacional de Cancerología, Patologia, Mexico D.F, Mexico; [2]Instituto Nacional de Cancerología, Cirugía de Tumores Mamarios, Mexico D.F, Mexico; [3]Instituto Nacional de Cancerología, Investigación, Mexico D.F, Mexico*

Background: Many epidemiologic studies have demonstrated that younger women with breast cancer have a worse survival than older women, which may potentially be related to more aggressive tumor biology. We studied the prognostic factors in Mexican young women with breast cancer.

Materials and Methods: Retrospective study of 136 Mexican women under 40 years with breast cancer (BC). We assessed inmunohistochemistry (IHC) studies for estrogen receptor (ER), progesterone receptor (PR), the results were scored by HScore previously described. HER-2/neu were scored positive with score 3 and score 2 was amplified by FISH with HER-2/neu CEP 17 probes (ratio $\geqslant$2.2). Clinical and pathologic features and survival were compared. Data were analyzed with the statistical package SPSS 17.

Results: Mean age was 36 years. Ductal carcinoma was observed in 87% of cases, lobular carcinoma 10.3% and others 2.2%. The percentage of stage I was 10.3%, stage II 35.3%, stage III 44.1%, stage IV 10.3%. RE was positive in 47.1% of tumors, RP 39%, HER2neu 22.8%. Tumors with HSCORE $\geqslant$200 for ER were 5.9% and PR 6.6%. High histological grade was related with tumors RE negative (p = 0.01) and RP negative (p = 0.046). Triple negative cancers (TPN) were 31% (IC95% 27.3–34.5). Median follow-up was 37.6 months. Overall 5-year and 10-year survival (OS) rates were 83.8% and 69.9% respectively. Factors associated with OS decreased in univariate analysis were advanced stage (p = 0.05), RE negative (p = 0.05), RP negative (p = 0.004), age <30 (p = 0.001), TPN (p = 0.007). After multivariate anlysis only age <30 (p = 0.001) was revealed to be independent factor for OS. The OS in patients with tumors HScore >200 was 100%.

Conclusions: TPN tumors are frequent in these patients (31%). Age <30 years is considered the only independent factor of bad prognosis in mexican women under 40 years with breast cancer.

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QuantiGene 2.0® assay for measurement of ER and PR in breast cancer

B.J. Chae[1], J.M. Paik[2], Y.J. Seo[3], W.C. Park[1], B.J. Song[1], J.S. Kim[4], S.J. Oh[5], S.S. Jung[1], A. Lee[6], S. Park[7]. *[1]Catholic University of Korea, Surgery, Seoul, Korea; [2]Catholic University of Korea, Surgery, Bucheon, Korea; [3]Catholic University of Korea, Surgery, Suwon, Korea; [4]Catholic University of Korea, Surgery, Uijeongbu, Korea; [5]Catholic University of Korea, Surgery, Incheon, Korea; [6]Catholic University of Korea, Pathology, Seoul, Korea; [7]Catholic University of Korea, Oncology, Seoul, Korea*

Intoroduction: Estrogen receptor (ER) and progesterone receptor (PR) status has been used as an indicator of endocrine responsiveness and as a prognostic factor for breast cancer. At present, IHC assessment of ER and PR is recommended as standard method. However, unfortunately interlaboratory variability with IHC assessment of ER, PR is relatively high in clinical practice. The QuantiGene 2.0® assay has lower interlaboratory variability and could measure amount of RNA directly without a reverse transcription step and polymerase chain reaction process. To evaluate the utility of QuantiGene 2.0® assay for assessment of ER and PR as an alternative to immunohistochemistry (IHC), we compared disease free survival according to the quantitative expression level of ER and PR between IHC method and QuantiGene 2.0® assay method.

Materials and Methods: 171 patients who underwent breast cancer surgery between January 2003 and December 2006 were collected at Seoul St. Mary's Hospital, the Catholic University of Korea. IHC and QuantiGene 2.0® assay was done for assessment of ER and PR. Cox-proportional hazard analysis was done and concordance between IHC and QuantiGene 2.0® assay for assessment of ER and PR was evaluated.

Results: Between IHC and QuantiGene 2.0® assay result of assessment for ER and PR both were well correlated (kappa value was 0.110 and 0.115 respectively). Disease free survival difference according to the expression level of ER was not significant in both IHC and QuantiGene 2.0® assay (p-value = 0.263, 0.514 respectively). In contrast, Disease free survival difference according to the expression level of PR was statistically significant in both group (p-value = 0.001, 0.045 respectively).

Conclusion: Although, we did not show the superiority, QuantiGene 2.0® assay for quantitative assessment of ER, PR showed similar results for response to treatment compared with IHC. So, our data for validation to the treatment response could support that QuantiGene 2.0® assay might be worthwhile alternative of IHC which is considered standard for evaluation of ER and PR.

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HER2/neu receptor positivity and its correlation with other prognostic and predictive factors of breast cancer

A. Tsiftsoglou[1], D. Dragoumis[1], A. Mourgela[1], A. Assimaki[1]. *[1]St Luke's Hospital, Department of General Surgery/Breast Division, Thessaloniki, Greece*

Background: There is consistent evidence in the literature, that overexpression of HER2/neu is associated with a worse clinical course in both node-positive and node-negative breast cancer patients. The objective of this study was to explore the relationship between HER2/neu receptor positivity and estrogen receptor status (ER), progesterone receptor status (PR), grade, tumor size, axillary nodal involvement and age in female breast cancer.

Materials and Methods: During 2005–2008, 346 consecutive female patients with invasive breast carcinoma, 307 ductal and 39 non-ductal, in which HER2/neu overexpression has been evaluated, were reviewed retrospectively. Each patient was further assessed for ER, PR, histological grade, tumor size, nodal status and age at diagnosis. Immunohistochemistry (IHC) was used to define ER, PR and HER2/neu expression status. HER2/neu was scored positive, if a 3+ immunostaining intensity result was found or amplified gene expression was present on fluorescence in situ hybridization (FISH). Statistical analysis (Chi-square and Levene's T-test) was performed using the SPSS software (Statistical Package for the Social Sciences − version 15.1). P-value of less than 0.05 was considered significant.

Results: The observed frequencies were significantly higher between HER2/neu overexpression and high tumor grade (p = 0.002), positive nodal status (p = 0.017), large tumor size (p = 0.007), ER negative (p < 0.001) and PR negative (p < 0.001) receptors in our series.

Conclusions: In summary, in this study of 346 cases of infiltrating breast carcinomas a statistically significant association was established between HER2/neu overexpression and histological grade, tumor size, ER, PR and nodal status. No statistically significant association was found between HER2/neu receptor positivity in relation to histological type and patients' age at presentation.

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Typical medullary carcinoma of the breast: experience of a single institution

I. Faustino[1], Y. Shvets[1], J. Loureiro[2], C. Leal[2], R. Soares[1], R. Couto[1], D. Pereira[1], S. Sousa[1], N. Afonso[1], H. Rodrigues[1]. *[1]Portuguese Oncology Institute − Porto, Medical Oncology, Oporto, Portugal; [2]Portuguese Oncology Institute − Porto, Pathology, Oporto, Portugal*

Background: Typical medullary carcinomas (TMC) of the breast account for less than 10% of all invasive breast cancers. Despite their aggressive histological features (hormonal receptors (HR) negative and grade 3), the prognosis of these tumours is generally favourable.

The aim of this retrospective study was to evaluate clinical and pathologic features, overall (OS) and disease free survival (DFS) in a population with TMC.

Methods: We reviewed all cases of TMC admitted at Instituto Português de Oncologia-Porto, between January/1985 and August/2009. We characterised TMC in terms of clinical and histopathological factors. Outcome was evaluated for OS and DFS, which were illustrated with Kaplan-Meier plots.

Results: We identified 29 cases of TMC. The average age was 54 (range from 23 to 82) years old; 62.1% were treated with modified radical mastectomy and 37.9% with conservative surgery; 65%, 55.2% and 24.1% undergo adjuvant chemotherapy, radiotherapy and hormonotherapy, correspondingly; 24.1% were stage I and 62% were stage II; 86.2% were