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POSTER

The effects of prognostic factors on the first recurrence patterns of breast cancer

H. Turna¹, M. Ozguroglu¹, G. Demir¹, N. Mandel¹, S. Ilvan², Z. Calay², E. Buyukunal¹, S. Serdengeci¹. ¹Cerrahpasa Medical Faculty Istanbul University, Medical Oncology, Istanbul, Turkey; ²Cerrahpasa Medical Faculty Istanbul University, Pathology, Istanbul, Turkey

Background: The aim of the study was to determine the effect of clinical and pathological prognostic factors on recurrence patterns and survival rates of patients with breast cancer whom were followed up at the Medical Oncology department of Cerrahpasa medical Faculty of Istanbul University during years between 1980 and 2002.

Materials and Methods: The files of 1624 patients with breast cancer were retrospectively analysed. Mean age, menopausal status and clinical stage of patients, pathological subtypes, axillary lymph node involvement, tumor grade, hormonal receptor status, perineural and lymphatic invasion, perinodal invasion and c-erbB2 expression patterns were determined. First recurrence patterns, site of systemic recurrences, recurrence free and overall survival times of patients were analysed.

Results: The 5 year survival rates were found to be 94.6% and 26.2% in patients with stage I and IV disease respectively. The higher TNM stage of the disease, age under 35 ($p=0.0001$), estrogen ($p=0.014$) and progesterone receptor negativity ($p=0.003$), axillary lymph node involvement ($p=0.0001$), perinodal invasion ($p=0.0001$), lymphatic ($p=0.005$), perineural ($p=0.0229$) and c-erbB2 ($p=0.0056$) positivity were found to be the prognostic factors affecting adversely the disease free survival in univariate analysis. Axillary lymph node involvement ($p=0.0023$) and progesterone receptor negativity ($p=0.022$) were found to be associated with systemic metastases rather than local recurrence as the first recurrence pattern. Progesterone receptor positivity predicts systemic metastases to bone and soft tissue rather than visceral organ involvement and patients who have cranial and leptomeningeal involvement during the first recurrence have a tendency to have progesterone receptor negative tumors ($p=0.028$). In multivariate analysis, c-erbB2 positivity ($p=0.0001$), axillary lymph node involvement ($p=0.006$), age under 35 ($p=0.008$), progesterone receptor negativity ($p=0.082$), perinodal invasion ($p=0.025$) were found to be the independent adverse prognostic factors.

Conclusions: The progesterone receptor status has a greater effect than estrogen receptor on the first recurrence patterns and systemic metastases sites of patients with breast cancer.

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POSTER

Update of survival and prognostic factors of triple-negative breast cancer in Thailand

C. Rojratsirikul¹, K. Jaisthaporn², P. Pornprasertthuk³, T. Sinthusake⁴, A. Cheirsilpa⁴. ¹Princess Mahachakri Sirindhorn Medical Center, Surgery, Nakhon Nayok, Thailand; ²National Cancer Institute, Medicine, Bangkok, Thailand; ³Lopburi cancer institute, Medicine, Lopburi, Thailand; ⁴Maha Vajiralongkorn Cancer Center, Medicine, Patumthanee, Thailand

Background: To study survival and prognostic factor of triple negative breast cancer (TNBC) which has never been reported in Thailand.

Methods: We retrospectively reviewed 116 patients who were classified as having TNBC. The all of them came from 4 public hospitals and 3 private hospitals in Bangkok between January 2000 and March 2009. The patient characteristics, tumor characteristics, and treatment outcomes had been collected, then mapping with demographic data, staging, and treatment outcome.

Results: The median follow up time was 47.5 months (range, 24–72 months). 116 patients were classified as having triple-negative breast cancer. Among these, 66 patients (56.9%) had premenopausal status and 50 patients (43.1%) had postmenopausal status. 88 patients were classified as having early breast cancers (13 in stage I/11.2%, 46 in stage IIA/39.66%, and 28 in stage IIB/24.14%) and 28 patients were classified as having locally advanced breast cancers. The majority of cases ($n=105$) were invasive ductal carcinoma. None of them were graded as well differentiated. Eleven of them had vascular involvement. Treatment regimens were as follows: 99 patients underwent surgery followed by adjuvant chemotherapy, 17 patients received neo-adjuvant therapy, and 51 patients received postoperative radiation. During a median follow-up time of 4 years, 8 patients experienced relapse, of which 2 were local relapses and 6 were distant relapses (brain and lung metastasis). At the end of the study, 106 of 116 are not metastasis till the censored date (31 March 2009). The 5 years disease free overall survival (DFS) is 76.68% (95%CI: 57.17 to 88.16). Hazard ratio for locally advanced to early breast is 2.45 (95%CI: 0.58 to 10.38). The 5-year survival rate was 63.77% (95%CI: 20.07 to 88.16) for locally advanced and 80.77% (95%CI: 58.40 to 91.87) for early breast cancer. The patients with vascular/perineural involvement

had increased risk of relapse ($p=0.005$). Cell type grading between locally advanced and early cancer was significantly different ($P<0.005$).

Conclusion: Triple-negative breast cancer is an aggressive disease with relatively poor survival. We found that one who had vascular and perineural involvement associated with short term survival and cell type grading has significant correlation with staging of disease. Unfortunately, there is no significance of outcome among both stages in this study. Therefore, we would like to concluded that vascular and perineural involvement might be poor prognostic factor in this our data.

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Predictive factors of response to neoadjuvant 3-weekly epirubicin (EPI) plus docetaxel (DOC) chemotherapy (CT) in locally advanced breast cancer (LABC): a prospective phase II trial

M.R. Strada¹, M. Frascaroli², R. Palumbo¹, A. Bernardo¹, L. Villani³, M. Scelsi³, I. Jedrychowska², D. Albanese², C. Teragni¹, G. Bernardo¹.

¹Clinica del lavoro Fondazione Salvatore Maugeri, Medical Oncology II, Pavia, Italy; ²Clinica del lavoro Fondazione Salvatore Maugeri, Rehabilitative Oncology, Pavia, Italy; ³Clinica del lavoro Fondazione Salvatore Maugeri, Unit of Pathology, Pavia, Italy

Background: A prospective phase II trial was designed to verify the activity and safety of 3-weekly EPI/DOC primary CT in LABC and to identify predictor factors of response. The primary end point was the complete pathological response (pCR), defined as no invasive breast carcinoma in breast an axillary nodes after primary CT.

Patients and Methods: Consecutive patients (pts) referring at our Centre with newly diagnosed, histologically proven LABC were enrolled. Primary CT consisted of EPI 75 mg/m² plus 75 mg/m² given as i.v. infusion on day 1 of 3-week cycles.

Results: Fifty-two pts were treated: median age 46 years (range 29–59); median tumor size was 4.5 cm (range 3–9) by clinical examination and 4.2 cm by ultrasonography (range 2.5–8); 47 pts had invasive ductal, 5 invasive lobular carcinoma; ER– status in 14 pts; PgR– in 22 pts; triple negative: 7 pts; HER2/neu overexpression (IHC 3+ or FISH+) in 13 pts. A minimum of 3 cycles of CT was administered (median 4, range 3–6). Treatment compliance was good and no dose reduction was required; 12 cycles were delayed by one week because of hematological toxicity (WHO grade 3/4 neutropenia in 14% of cases, 2 case of febrile neutropenia) and G-CSF support was given in 3 pts. Grade 1 cardiotoxicity occurred in 2 pts at the 4th cycle and in 3 additional pts at the completion of adjuvant CT; other non haematological toxicities were within grade 1–2. All 52 pts underwent surgery without delay; breast conserving surgery was performed in 24/29 candidate pts; 5 pts preferred total mastectomy. The clinical overall response rate (ORR) was 86% (95% CI: 77–94), with 21 (40%) complete responses (CR); the sonographical OOR was 96% (95% CI: 87–98) with 7 CRs (13%). A pCR (ypT0) with negative axillary lymph nodes was confirmed in 10 pts (19%) and additional 4 pts had *in situ* lesions only in breast tissue (ypDCIS), with an overall pCR rate of 25%. There was no case of progressive disease. Among clinical and tumour characteristics evaluated as potential predictors of pCR, ER status and HER2/neu overexpression resulted significantly correlated with pCR in univariate analysis ($p=0.04$ and 0.02 , respectively); in multivariate analysis triple-negativity and ER-negativity showed an independent relationship with pCR.

Conclusions: Our data show that 3-weekly EPI/DOC primary CT is very active and well tolerated in patients with LABC, also producing an interesting high percentage of pCR in triple negative tumours.

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Columnar cell lesions are the early precursors of some forms of invasive breast carcinoma – a new genetic map for the evolutionary pathway of low nuclear grade breast neoplasia (LNGBN) family

T.M.A. Abdel-Fatah¹, D.G. Powe¹, M. Lambros², D. De Biase², K. Savage², A. Mackay², J.S. Reis-Filho², I.O. Ellis¹. ¹University of Nottingham, Histopathology, Nottingham, United Kingdom; ²Institute of Cancer Research, The Breakthrough Breast Cancer Research Centre, London, United Kingdom

Background: There is evidence to suggest that a number of low nuclear grade invasive breast cancers (LNGBC) and putative precursor lesions may consist in a family of interrelated lesions. The aim of this study is to identify the molecular genotypic profile of lesions belonging to LNGBN.

Material and Methods: 15 LNGBCs and matched coexisting columnar cell lesions (CLLs, ductal carcinoma in situ (DCIS) and lobular neoplasia (LN) were microdissected and subjected to high-resolution array-comparative genomic hybridization (aCGH), single nucleotide polymorphisms (SNPs) analysis, and loss of heterozygosity analysis. Results were validated using

fluorescence and chromogenic in situ hybridisation and immunohistochemistry.

Results: We observed that at the genetic level, lesions from the same patient displayed remarkably similar patterns of genetic aberrations (Spearman's correlations 0.55–0.89; $p < 0.00001$). All CLLs, low grade DCIS, LN and their matching invasive carcinoma harboured gain/amplification of 1q31–32 and loss of 16q12, 16q21 and 16q23. In addition to the aberrations found in CCLs, in situ and matching invasive components displayed additional genetic aberrations at 16p13.3, 13q34, 20q13.33, 11q13.1–q14.1, 17q25.3, 19p13.3, 7p22.2, 8q24.3, 9q34.3, 14q32.33, 5p15.33 and 10q25.3 and losses on 10q22, 8p, 11q24–25, 15q11.2, 17p11.2, 9p11.2 and Xq. Amplification of cyclin D1 was detected by CISH in ILCs and their matching LN and FEA lesions.

Conclusion: Our results provide strong circumstantial evidence to suggest that CCLs are the earliest morphologically identifiable non-obligate precursors of more advanced lesions in the LNGBN family and that that loss of 16q and gain 1q are the earliest genetic changes in this family of lesions that lead to the activation of the 'luminal' pathway.

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POSTER

Can we use age-dependent changes of enzymes activity in benign disease as poor prognostic factors?

B. Borzenko¹, H. Bakurova¹, O. Verkhova¹, Y. Zhebelenko¹, T. Zhuravel¹, O. Shatova¹, Y. Tursunova¹, I. Zinkovich¹. ¹Donetsk National Medical University, Biochemistry, Donetsk, Ukraine

Background: Mastopathy – benign disease of a breast, developed by a hyperplasia (by pathological growth) of a tissue gland. Risk factors for breast cancer are age, hormones level modification of the females and benign disease, such as mastopathy. It is known the direct interaction between metabolism of thymidine – precursor of DNA and rate of proliferation processes. Thus, as marker of proliferation was chosen any enzymes of thymidine exchange – thymidine kinase (TK) and thymidine phosphorylase (TP). Moreover TK correspond to the index of cellular proliferation.

The aim – to compare activity of TK and TP in blood serum of healthy women, patients with mastopathy and breast cancer from I to IV stages.

Materials and Methods: Blood serum of healthy persons, patients with mastopathy and patients with cancer of mammary gland. Age of surveyed groups 40–60 years. The activity of TK was defined by radioisotop method, TP – spectrophotometrically.

Table. TK and TP activity healthy women and women with pathology

| Diagnosis | Healthy women n = 16 | Mastopathy n = 32 | Breast cancer T ₁ N ₀ M ₀ n = 17 | T ₂ N ₀ M ₀ n = 22 | T ₃ N ₁ M ₀ n = 52 | T ₄ N ₂ M _x n = 39 |
|-------------------------------------|-------------------------|----------------------|---|--|--|--|
| Thymidine kinase (nMol/mg*h) | 3.14±0.55 | 3.58±0.29 | 3.82±0.01 | 3.98±0.03 | 4.28±0.28 | 4.94±0.14 |
| Thymidine phosphorylase (nMol/mg*h) | 23.76±2.30 | 17.82±2.0 | 19.80±0.66 | 18.48±1.01 | 15.18±1.98 | 9.90±0.70 |

$p < 0.05$

Results: In comparison with healthy group (table), the level of TP activity was reduced at mastopathy. Upon T₁N₀M₀ the activity is TP is lower than normal (like mastopathy), but TK activity was enhanced that can be responsible for some increase in DNA biosynthesis in case of such pathology. The obtained dates about the increase of TK activity and decrease of TP activity at a mammary gland cancer according to a stage of cancer. This shift (simultaneously increasing of TK and decreasing of TP) indicates about more intensively proceeding processes of a proliferation at tumour pathology.

Conclusions: Thus, a similar metabolic displacement during mastopathy and breast cancer may be one of the endogenous factors of malignancy. The biochemical test of determination of TK and TP activity in blood serum of patients with mastopathy, we propose to use in early diagnostic of breast cancer.

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POSTER

Intraoperative ultrasound guided occult lesion localization in early stage breast cancer surgery

N. Ilic¹, N. Frlleta Ilic¹, J. Juricic¹, J. Banovic¹, J. Tripkovic¹, D. Krnic¹, L. Grandic¹, D. Ilic¹. ¹University Surgical Hospital, Thoracic Surgery Department, Split, Croatia

Objective: Different methods are used in detecting non-palpable breast lesions. We present our experience in intraoperative ultrasound guided occult lesion localization in early breast cancer surgery.

Methods: Retrospective analysis of clinical, surgical, pathological and oncological data on 168 patients with non-palpable breast cancer lesions treated in University Surgical Hospital Split, Croatia, within five years time period. 88 (52%) patients had their lesions preoperatively labelled with blue-dye or hook wire, and intraoperative ultrasound hand-held probe was used in localizing occult breast lesion in other 80 (48%) patients. Definitive surgical and adjuvant treatment was carried out due to pathological findings.

Results: All the patients had their non-palpable breast lesion detected and surgically removed under local or general anesthesia. Tissue specimen obtained using intraoperative hand-held ultrasound probe was easier to localize and surgically assessed. In the same time such tissue specimen was much more accurate to temporary and definitive pathological findings. Operative time was shortened using intraoperative US but without statistically significance. There were no intraoperative or postoperative complications due to detection method used.

Conclusions: Intraoperative ultrasound guided breast surgery allows detecting of occult early breast cancer lesions with high accuracy and safety.

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POSTER

Is mammographic breast density a breast cancer risk factor in women with BRCA mutations?

K. Passaperuma¹, E. Warner¹, K.A. Hill¹, A. Gunasekara², M.J. Yaffe³.

¹Sunnybrook Cancer Center, Department of Medical Oncology, Toronto, Canada; ²Sunnybrook Cancer Center, Department of Imaging Research, Toronto, Canada; ³Sunnybrook Cancer Center, Department of Medical Biophysics, Toronto, Canada

Background: Increased mammographic breast density is well-recognized as a breast cancer risk factor in the general population. However, it is unclear whether it is a risk factor in women with BRCA mutations. We present the results of a correlative study investigating the relationship between breast density and breast cancer incidence in women with BRCA mutations.

Methods: The study population consisted of women ages 25 to 65 with BRCA1 or BRCA2 mutations enrolled in a single-centre high-risk breast cancer screening trial of annual breast mammography, MRI, and ultrasound, and semiannual clinical breast examination. Using a computer-aided technique (Cumulus), quantitative percentage density (PD) was measured for each participant on her first study mammogram by a single investigator blinded to the clinical outcome. For women with prior breast cancer, the contralateral breast was used for density measurement.

Results: Between 11/97 and 03/08, 462 women (mean age at first study mammogram = 44; 245 with BRCA1 mutations and 217 with BRCA2 mutations) were screened and 50 breast cancers were diagnosed (33 invasive ductal, 1 invasive lobular, 1 microinvasive, 3 DCIS with microinvasion, 12 DCIS only). Density was not measured in 40 women of whom 4 developed cancer (2 invasive ductal, 1 invasive lobular, 1 DCIS) because the baseline mammogram could not be digitized or located. Mean PD (± SD) for the 376 women who did not develop breast cancer was 34% (23) compared to 31% (21) for 46 women who developed cancer ($p = 0.51$, two-sample Wilcoxon rank sum test). Logistic regression model of breast cancer incidence and PD revealed an odds ratio of 0.99 (± 0.01) for a 1-unit increase in PD ($p = 0.44$).

Age-adjusted odds ratio for a 1-unit increase in PD was 1.00 (± 0.01, $p = 0.83$). Results were similar when BRCA1 and BRCA2 mutation carriers were analyzed separately, as well as when women who developed DCIS without invasion were excluded from the analysis.

Conclusions: Increased mammographic breast density is not associated with higher breast cancer incidence in women with BRCA mutations. Therefore, breast density should not be considered a factor for these women in decision-making regarding prophylactic surgery or chemoprevention.

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POSTER

“Competition on Clinical Mass Spectrometry Based Proteomic Diagnosis” based on serum protein profiling for the detection of breast cancer

W.E. Mesker¹, B.J. Mertens², Y.E.M. van der Burg³, A.M. Deelder³, R.A.E.M. Tollenaar¹. ¹Leiden University Medical Center, Surgery, Leiden, The Netherlands; ²Leiden University Medical Center, Medical Statistics, Leiden, The Netherlands; ³Leiden University Medical Center, Biomolecular Mass Spectrometry, Leiden, The Netherlands

Background: Detection of breast cancer at early stage can increase a patient's five-year disease-free survival rate. Mammography is currently the gold standard for screening purposes. This method is non-invasive and highly specific but low sensitivities have been reported. Especially for younger women with a familial or genetic predisposition mammography