325 Poster

The Correlation of Multifocality with Lymph Node Status in Patients with Breast Carcinoma

E. de Sousa[1], N.J. Bundred[1], R.K. Johnson[1]. [1]*University Hospital of South Manchester, The Nightingale Breast Unit, Manchester, United Kingdom*

Background: One of the factors used to predict breast cancer prognosis is tumour size. For staging of multifocal breast cancers, the current recommendation is to use the diameter of the largest tumour nodule of the highest grade, regardless of the number or size of additional nodules. This assumes that the metastatic potential of multifocal tumours is determined by the size of the largest nodule. As a result, the total tumour burden is potentially underestimated because additional, often sizeable nodules, are not included. We explored the relationship between tumour size and lymph node metastasis. Our objective was to compare multifocal tumours and same sized unifocal tumours, to assess whether there is an observed higher frequency of axillary lymph node metastasis.

Method: 126 patients with multifocal tumours were identified from the pathology database between January 2005 and December 2006. A control series of 1522 consecutive patients with unifocal invasive breast cancer obtained from our database between 1992 and 1999 was used for comparison. Differences in histological type, tumour grade and size, hormone receptor status and axillary lymph node metastasis between the multifocal and unifocal groups were analysed.

Results: Overall, multifocal tumours had a higher frequency of positive axillary lymph nodes compared to patients with unifocal lesions of the same size (49% vs. 30%, $p < 0.001$). Grade 1 tumours were more common in the unifocal group (25.7% vs. 13.5% $p < 0.001$) and grade 3 tumours were more common in the multifocal group (42.1% vs. 31.3%, $p = 0.001$).

Conclusion: Multifocal breast cancers are associated with increased axillary lymph node metastasis compared with unifocal breast cancers of identical size. An improved method of including the increased tumour burden presented in multifocal breast cancer in the future would enable more accurate assessment of metastatic potential.

326 Poster

Does Ethnicity and Social Deprivation Affect Length of Stay in Elective Breast Cancer Surgery?

A. Gunawardene[1], H. Brown[1]. [1]*City Hospital, Breast Surgery, Birmingham, United Kingdom*

Background: Benefits of breast cancer surgery being performed as day-case procedures include early mobilization, a timely return to the psychological support of the family for the patient, and more efficient utilization of hospital beds. It is therefore important to identify which breast cancer patients may or may not be suitable for day-case surgery. The aim of this study was to investigate whether patients' ethnicity and level of social deprivation affect their length of hospital stay.

Method: A retrospective analysis of 511 elective admissions for non-reconstructive breast surgery in a single unit in Birmingham, UK between January and December 2010 was carried out using data collected from hospital records and Index of Multiple Deprivation (IMD 2010) scores were derived from the patients' residential postcodes. All procedures for treatment of breast cancer at the unit were routinely planned as day-cases or 23 hour admission. For patients having more than one procedure during the twelve month period, only the index admission was included. Chi squared and t-test were used with univariate and multivariate regression analysis and $p < 0.05$ was taken to be statistically significant.

Results: 406 patients were included in the study of which, 318 (78.3%) were 'White', 38 (9.4%) were 'Asian', 22 (5.4%) were 'Black' and 28 (6.9%) were 'Other'. Median age was 60 (23−92) and 285 patients' procedures were done as day-cases with 121 patients remaining in hospital for one or more nights. On univariate analysis, the relationship to length of stay was found to be significant with age ($p = 0.007$), procedure ($p < 0.001$) and histology ($p = 0.01$) and was not found to be significant with ethnicity ($p = 0.972$) or Index of Multiple Deprivation score ($p = 0.621$).

Conclusion: In this study age, procedure and tissue diagnosis affected length of hospital stay but ethnicity and socio-economic deprivation did not. This suggests that patients undergoing surgery for breast cancer may be suitable for day-case surgery regardless of their ethnicity or socio-economic background.

327 Poster

The Serum HER-2 Reflects the Tumor Burden of Breast Cancer

Y. Yasuda[1], H. Furusawa[1], Y. Maeda[1], K. Komaki[1]. [1]*Breastopia Namba Hospital, Breast Surgical Oncology, Miyazaki, Japan*

Background: Human epidermal growth factor receptor-type2(HER-2) has been recognized as the prognostic and the predictive factor of breast cancer. That is HER-2 over expression breast cancer grows rapidly and is sensitive to trastuzumab and lapatinib. On the other hand, most of all breast cancer cells have HER-2 in some degree. However it is said that there is a correlation between the tissue HER-2 and the serum HER-2 (sHER-2) which is a shed extracellular domain(ECD) of HER-2 protein, HER-2 expression of breast cancer cells are divided into four degrees in the immunochemical stein. Even if in case of lower level HER-2 expression (HER-2; IHC 1+), sHER-2 ought to increase to the tumor burden.

Purpose: To investigate whether sHER-2 reflects the tumor burden or not. And then to inspect that sHER-2 can be used as the tumor marker of breast cancer recurrence.

Patients and Methods: Retrospective study. Measurement and comparison sHER-2(ng/ml) (1) by clinical staging excluding DCIS, the neoadjuvant drug therapyand the far advanced cases (n = 167). (2) before and after surgery (n = 167).(3) to the tumor area (mm^3) (n = 65). (4) to the tumor volume (ml) (n = 336). (5) between the recurrent and the non-recurrent cases(n = 36 and 92). sHER-2 was measured by the ADVIA Centaur(Siemens Healthcare Diagnostics Co.Ltd.). Mann-Whitney U-test and Spearman's rank correlation coefficient were used in the statistical analysis and test.

Results: (1) There was a significance between Stage I and Stage IIIC($p < 0.05$) or Stage II and Stage IIIC ($p < 0.05$). The change rate of sHER-2(Δ) was Δ-8.1% in Stage I, Δ-12.9% in Stage IIA, Δ-22.7% in Stage IIB, Δ-30.5% in Stage IIIA. (2) Δ-8.5% in IHC;0, Δ-10.5% in IHC;1+, Δ-14.5% in IHC;2+, Δ-24.5% in IHC;3+. (3) There was a correlation to the tumor area ($p = 0.0002$). (4) There was a correlation to the tumor volume ($p = 0.02$). (5) There was a significance between the recurrent and non-recurrent cases ($p < 0.001$).

Conclusions: The sHER-2 reflects the tumor burden of breast cancer. The sHER-2 can be used as the tumor marker in HER-2 over expression breast cancer.

328 Poster

Prognostic and Predictive Factors in Breast Cancer Relapse. Long-term Retrospective Study in a Cohort of Patients with Invasive Ductal Carcinoma

F. Lumachi[1], F. Marino[2], R. Tozzoli[3], D.A. Santeufemia[4], G.B. Chiara[5], S.M.M. Basso[5]. [1]*University of Padova School of Medicine, Department of Surgical & Gastroenterological Sciences, Padova, Italy;* [2]*University of Padova School of Medicine, Department of Pathology, Padova, Italy;* [3]*S. Maria Degli Angeli Hospital, Department of Clinical Pathology, Pordenone, Italy;* [4]*S. Maria Degli Angeli Hospital, Oncology, Pordenone, Italy;* [5]*S. Maria degli Angeli Hospital, Chirurgia 1, Pordenone, Italy*

Background: Serum tumor markers (STM) are still widely used in cancer patients, either in monitoring the response to therapy or in predicting recurrence of the disease. However, only in selected cases they are useful for screening purposes, due to their limited sensitivity. In patients with breast cancer (BC) the most common STM used are carcinoembryogenic antigen (CEA) and cancer antigen 15−3 (CA 15−3). Other useful prognostic markers are estrogen (ER) and progesterone (PR) receptors rate, monoclonal antibody MIB1 against the Ki-67 proliferating antigen, epidermal growth factor receptor 2 (HER2) status and the expression of p53. The aim of this study was to evaluate the relationship between the main prognostic markers in BC women with and without cancer relapse.

Patients and Methods: Overall, data from 348 medical charts of women with stage I or IIA (pT1−2, pN0, and M0 at the time of surgery) primary BC (invasive ductal carcinoma in all cases) not requiring adjuvant chemotherapy, who had undergone curative surgery, were retrospectively reviewed. Two groups were considered: Group A (cases), 54 (15.5%) patients with cancer relapse, and Group B (controls), 294 (84.5%) cancer-free patients at $\geqslant$60-month follow-up. The following parameters were analyzed: age of the patients, size of the tumor (pT), CEA and CA 15−3 baseline serum levels, MIB-1, ER, and PR rate. Student's *t*-test, and Spearman's correlation coefficient (R) calculation were used to test the results. $P < 0.05$ was considered statistically significant.

Results: As expected, there was a significant difference between groups (A *vs*. B) in age (56.9±12.0 *vs*. 61.2±12.9, $p = 0.023$), size (20.3±7.3 *vs*. 16.7±10.2, $p = 0.014$), and ER rate (66.0±12.3 *vs*. 58.8±17.1, $p = 0.003$), while PR (56.6±19.5 *vs*. 54.4±17.3, $p = 0.40$) and MIB-1 (22.6±10.6 *vs*. 21.6±13.3, $p = 0.58$) rates, as well as baseline CEA (6.1±5.8 *vs*. 6.3±5.0, $p = 0.79$) and CA 15−3 (27.7±13.6 *vs*. 26.1±12.4, $p = 0.39$) serum levels did not differ (p = NS). In both groups (A; B) a correlation between CEA and CA 15−3 ($R = 0.43$, $p = 0.002$; $R = 0.29$, $p = 0.0008$), and between ER and PR ($R = 0.37$, $p = 0.003$; $R = 0.52$, $p < 0.0001$) was observed. There was no correlation between size and CA 15−3 ($R = 0.18$, $p = 00.19$; $R = 0.10$, $p = 0.07$) or CEA ($R = -0.11$, $p = 0.33$; $R = -0.006$, $p = 0.92$), while MIB 1 correlated with age ($R = 0.37$, $p = 0.003$), size ($R = 0.44$, $p = 0.0004$) and CEA ($R = -0.37$, $p = 0.003$) only in patients with cancer recurrence (Group

A). No correlation (p = NS) was found between hormone receptors and CEA, CA 15−3, and MIB-1 in both groups.

Conclusions: Our results suggests that (1) baseline STM CEA and CA 15−3 are not useful for prognostic purposes, (2) age, size, and ER are week isolated prognostic factors, and (3) the cumulative risk of relapse increases in the presence of multiple factors such younger age associated with highest levels of STMs and MIB-1, and low ER rate, together.

References

Lumachi *et al*. Anticancer Res 2010; 30: 2331–2334.

329 Poster

Expression of MMTV-homologous Sequences in the Patients with Breast Hyperplasia and Ductal Carcinoma in Situ

E.G. Zenit-Zhuravleva[1], A.A. Lushnikova[1], L.N. Lyubchenko[2], E.B. Polevaya[2]. [1]*N.N.Blokhin Cancer Research Center, Carcinogenesis Institute, Moscow, Russian Federation;* [2]*N.N.Blokhin Cancer Research Center, Clinical Oncology Institute, Moscow, Russian Federation*

Background: Earlier, mouse mammary tumor virus (MMTV)-related sequences were revealed in significant proportion of human breast cancer (BC) tissues and blood sera samples. Mammary hyperplasia (MH) and ductal carcinoma in situ (DCS) are considered as a first steps for BC progression. A relationship between expression of MMTV-related provirus (hMTV) genome sequences and BC initiation/ progression is mostly unclear.

Material and Methods: 25 DCS and 10MH fresh or fixed archival tissues and blood samples from 35 primary patients (age is 21−56 years old) were studied by PCR and one-tube RT PCR after DNAase treatment to avoid pseudo positive results. Tumor histology was verified by routine staining of BC or normal tissue sections. Specific PCR products were sequenced and compared by BLAST and/or CLUSTAL programs.

Results: DNA sequences with 92%-95% homology to the *env* MMTV gene and 89−97% homology to 3′LTR MMTV were revealed in 11/25 (44%) DCS and 3/10 (30%) MH tissue samples, as well as in 17/25 (68%), 5/10 (50%) blood samples, correspondingly, *vs* 0/7 normal mammary tissue control samples. All hMTV-positive patients, except five ones, had pathological immune system status: rheumatoid arthritis, chronic lung infections, dental or nosofaringeal diseases. The hMTV sequence expression was found in 9/25 DCS and 3/10 H tissue samples. The sequences integration sites were studied by RACE method and were sporadic, without any predominant genome localization. An analysis of more number of malignant mammary tissue samples would clear provirus integration pattern and its possible localization near cell oncogenes.

Conclusions: a preliminary data suppose a role of hMTV sequences expression as a risk factor for genome instability and MH or DCS development. Cloning and sequencing of *env, gag*, Sag and HRE-coding hMTV sequences revealed in DCS and MH samples and its prognostic evaluation is in process.

330 Poster

Leptin and VEGFR Expression in Sporadic Breast Cancer Patients

D.N. Kravchenko[1], E.V. Peredereeva[2], A.A. Lushnikova[2]. [1]*N.N.Blokhin Cancer Research Center, Clinical Oncology Institute, Moscow, Russian Federation;* [2]*N.N.Blokhin Cancer Research Center, Carcinogenesis Institute, Moscow, Russian Federation*

Background: Hormone leptin (Lep) is produced by adipose tissue and regulates cell metabolism and growth through signal transduction by interaction with leptin receptor (LepR). It is found that LepR-dependent signal pathways have common points with VEGF-dependent ones. Lep signaling regulates VEGF activity mainly through HIF-1α and NFkappaB. The effects of Lep/LepR expression on mammary cell proliferation and proteins associated with Lep /LepR signaling are important for understanding of breast cancer (BC) induction and progression, especially in BC patients suffered with obesity and other metabolic diseases.

Material and Methods: Expression of Lep/LepR and VEGFR-2 was studied in tumor tissues samples obtained from 15 sporadic BC patients (4 − obesity, 3 − high body mass, 8 − normal body mass, 24−45 yo, mean age 32$\pm$6.4 yo) using immunohistochemistry and RT PCR. Tumor and normal mammary tissue images (100–150 per sample) obtained by using monoclonal antibodies anti-LepR, anti-VEGFR-2 (Dako) and immunohistochemical staining (EnVision system, Dako) were analysed by MatLab 7.0 program. The data were compared with RT PCR results obtained by using total tumor RNA as a matrix and specific primers for *Lep, LepR* long isoform and *VEGFR-2* gene regions.

Results: Mean density of stained anti-LepR granules was significantly higher in tumor mammary tissues than in normal tissue: LepR − 37.4$\pm$3.6 *vs* 8.2$\pm$2.3, $p < 0.002$; mean density of anti-VEGFR-2 granules per length unit of vascular endothelium was 1.78$\pm$0.62 *vs* 0.82$\pm$0.34, $p < 0.05$. RT PCR results confirms that Lep, LepR and VEGFR-2 expression levels in BC tumors under study were significantly higher in tumor mammary tissue than in normal mammary tissue of sporadic BC patients. Moreover, LepR expression correlated with Lep and VEGFR-2 expression. There were no any relationships between body mass index and Lep/LepR/VEGFR-2 expression levels, probably, because of small patient number.

Conclusions: The results confirm high expression level of Lep/LepR/VEGFR-2 in mammary tumor cells in sporadic BC patients. A concordance between high LepR − Lep and LepR/Lep − VEGFR-2 expression levels in BC tissues in spite of patient body mass was also revealed. The data supports an involvement of Lep/LepR signalling into mammary tumor carcinogenesis; it is indicative of Lep regulation of VEGF/VEGFR expression. Continued study of prognostic value for Lep/LepR expression using results of immunohistochemistry, ELISA and RT PCR is in process.

331 Poster

What is the Influence of Early Loco-regional Recurrence in Triple-negative Breast Cancer Patients on Disease Outcome?

V. Posarac[1], S. Susnjar[2], M. Milovic-Kovacevic[2], A. Karaferic[2], J. Aleksic[3], M. Jevric[1]. [1]*Institute for Oncology and Radiology of Serbia, Department of Surgical Oncology, Belgrade, Serbia;* [2]*Institute for Oncology and Radiology of Serbia, Department of Medical Oncology, Belgrade, Serbia;* [3]*Health Center Dr Ristic, Belgrade, Serbia*

Introduction: Triple negative breast cancer (TNBC) is a biologically heterogeneous group of breast tumors with generally poor prognosis. The aim of this analysis was to investigate how early occurrence of loco-regional relapse (LRR) influenced the outcome of these patients (pts).

Patients and Methods: From June 2006 to the end of 2009 a total of 243 stage I-IIIB TNBC pts were diagnosed at the Institute for Oncology and Radiology of Serbia. Since 21 pts were lost to follow up, 222 pts were analyzed. TN status was defined as IHC ER0−3/PR0−3/HER2:0−1 or IHC HER2:2+/CISH−. The majority of them had radical surgery +/− postoperative radiotherapy (RT) and adjuvant chemotherapy (CHT) as per protocol. The main end points were disease-free survival (DFS) defined as the time between surgery and BC relapse or death without BC relapse, and overall survival (OS) defined as the time from BC diagnosis to death from any reason. Statistics included Pearson Chi-squared test and Log-rank test.

Results: During the median follow up period of 25 months (range 3−58) LRR occurred in 15/222 (7%) pts, 5 of whom developed synchronous distant metastases. At the same time 28/222 (13%) pts were diagnosed with distant relapse only. Significantly higher proportion of LRR pts are older than 65 years (60%) and had positive nodal status (67%) compared to pts without LRR (27% and 36%, respectively) (c_1^2 test, p = 0.019 and c_1^2 test, p = 0.006, respectively). We looked separately at a group of pts with LRR only (10/222) and compared their disease outcome with pts who developed distant metastases. There was no significant difference in DFS [15 ms (95% CI 4.2–25.8 vs. 13 ms (95% CI 7.8–18.2)] and OS [39 ms (95% CI 10.0–67.9) vs. 40 ms (95% CI 33.6–46.4)] between LRR only and distant metastasis groups of pts (Log rank test, p > 0.05 for both).

Conclusion: Our results seem to point out that early relapse in TNBC pts means decreased survival irrespective of the first relapse site (loco-regional only vs. distant metastases).

332 Poster

Evaluation of Molecular Parameters and Risk Factors of Breast Cancer in Therapeutic Decisions

R. Soares[1], Y. Shvets[1], N. Afonso[1], H. Rodrigues[1]. [1]*Instituto Portugues de Oncologia, oncology, Oporto, Portugal*

Introduction: Biological characteristics of breast cancer (BC) are of increased importance in treatment decision. Molecular parameters (MP) considered of prognostic importance can be positively correlated with more traditional risk factors (RF) or might change an initial prognosis based on these RF. We purposed to review our clinical practice using data of patients admitted in our institution with BC from 1.Jan.2007 until 31.Dec.2007 and identify the association between MP and RF and how this affected treatment decision and survival.

Methods: Demographic and clinical characteristics of patients were reviewed using clinical records. As RF considered in treatment options we considered: age (<35 years old and >35 years old) and TNM stage. The MP investigated were: grade (G), hormonal receptors (HR), HER2. An indication for chemotherapy was used as surrogate of clinical consideration of worse prognosis. Statistical package SPSSv.17 was used for statistic analysis and categorical variables were compared using x^2 test and continuous variables using Mann-Whitney U test. A p value <0.005 was considered of statistically significance. A multivariate analysis using