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Extra-capsular Extension of Axillary Nodal Metastases in Breast Cancer: a Single Centre Experience of 209 Patients

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Background: Axillary nodal metastasis is the most important prognostic factor in breast cancer and extra-capsular extension (ECE) is an established poor prognostic factor in node positive disease. There is paucity of literature on ECE in patients with lymph node-positive breast cancer. The aim of this study was to evaluate the factors affecting ECE and survival & relapse rate of node-positive patients with ECE.

Materials and Methods: We performed a retrospective analysis of the prospectively maintained database of the patients of breast cancer operated in our department between January 1993 and December 2005. All patients had undergone axillary lymph node dissection (ALND) and all those with >3 +ve nodes or ECE received axillary irradiation. Adjuvant chemotherapy and chest wall/ supraclavicular fossa radiotherapy and hormonal therapy were administered according to institutional protocol.

Results: The median age was 45 years (range: 20–83 years). Mean pathological tumor size was 4.4 cm. Extra-capsular extension was present in 29.6% of node positive patients (209 out of 705 node positive patients). Of the patients with ECE, 51 (24.4%) had less than 4 +ve nodes, 70 (33.5%) with 4 to 9 +ve nodes and 88 (42.1%) with >9 +ve nodes in axilla.

Multivariate analysis of association of different co-variables with ECE was done, which showed statistically significant incidence of ECE with central quadrant tumors ($p < 0.0001$), presence of skin changes ($p < 0.0001$), increasing tumor size ($p < 0.0001$), number of positive nodes ($p < 0.0001$).

After a median follow-up of 36 months (range: 24 to 189 months), a total of 92 (44%) patients relapsed, of which 74 (78.7%) had only systemic relapse, 7 (7.4%) each had local & systemic and regional & systemic relapse, 3 (3.1%) had loco-regional with systemic relapse and 1 (1%) had local relapse. None of the patients had isolated relapse regionally or loco-regionally. Sites of local failure were chest wall in 11 patients; sites of distant failure were bone (42 patients), lungs (30 patients), liver (29 patients) and brain (15 patients).

Conclusion: The rate of ECE is still high in developing countries due to advanced stage at presentation. Tumors in central quadrant, increasing tumor size, presence of skin changes and number of positive nodes are associated with increased risk of ECE. Most of them fail mainly systemically. Most of the patients who fail at local or regional sites also fail systemically. As per our experience we did not experience any isolated axillary nodal failure after a median follow-up of 36 months in lymph node-positive patients with ECE, who have undergone ALND and irradiation of axilla.

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Vascular Endothelial Growth Factor as Prognostic Factor in Patients with Breast Cancer. a Multicentric Long-term Follow up Study

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Background: In breast cancer (BC) patients, accurate evaluation of any potential prognostic factor can lead to a reduction of morbidity and mortality, as well as early detection of relapse. Because undetected metastases can contribute to the failure of primary treatment, their early identification has a substantial impact on adequate therapy and prognosis. In this setting, a number of hematological and tissue-extracting prognostic factors have been tested, and it has been shown that high microvessel density, an indirect measure of angiogenesis, correlates with increased tumor size, lymph node involvement, and distant metastases. Thus, angiogenesis represents one of the most important factors in cancer development and growing, inducing especially an increase in vascular permeability, and ultimately poor outcome of the disease. Many angiogenic factors have been identified, including fibroblast growth factor, platelet-derived endothelial cell growth factor, and angiogenic cytokines, such as vascular endothelial growth factor (VEGF), which is one of the most important angiogenic growth

factors measurable in the blood. The aim of this study was to evaluate the relationship between VEGF, cancer-free interval (CFI) and overall survival (OS) at ≥ 60 months follow-up in patients with BC.

Patients and Methods: Sixty-one women (median age 60 years, range 32–79) with confirmed ductal carcinoma *in situ* (N=9, 14.8%) or infiltrating ductal (N=52, 85.2%) breast carcinoma, were approached for this study. The following parameters have been recorded and analyzed: age of the patients, greatest diameter (size) of the tumor (pT), axillary node status (pN), VEGF, MIB-1, estrogen (ER) and progesterone (PR) receptor positivity, CFI, and OS. Serum VEGF was measured using a specific enzyme-linked immunosorbent assay commercial kit. Correlation between parameters was evaluated with the Pearson's correlation coefficient, and a p -value < 0.01 was considered statistically significant.

Results: As expected, both age and size were inversely related to CFI ($R = -0.33$, $p = 0.009$; $R = -0.38$, $p = 0.003$, respectively) and OS ($R = -0.37$, $p = 0.004$; $R = -0.38$, $p = 0.003$, respectively). No correlation ($p = NS$) was found between OS and ER, PR, and MIB-1. VEGF significantly inversely correlated with CFI ($R = -0.33$, $p = 0.009$), OS ($R = -0.36$, $p = 0.005$), and size ($R = 0.37$, $p = 0.004$), while it was independent of age ($R = 0.10$, $p = 0.44$), ER ($R = -0.12$, $p = 0.37$), and PR ($R = -0.16$, $p = 0.22$).

Conclusions: VEGF is an important angiogenic growth factors, and has prognostic significance in patients with BC. Our study showed that, at long-term follow-up, a high VEGF serum level was significantly associated with poor survival, and that VEGF was more sensitive than other prognostic factors, such as ER, PR, and MIB-1.

References

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Invasive Lobular Vs. Ductal Breast Cancer – Patterns of Recurrences Are Dependent On Estrogen Receptor Status

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Introduction: Invasive lobular breast cancer (ILC) is less common than invasive ductal breast cancer (IDC) and appears to have a distinct biology. Literature is inconsistent regarding disease free survival; most studies found no differences or a better survival for ILC. Studies concerning the patterns of recurrence in patients with breast cancer usually ignore the impact of histology.

This study aimed to compare risks and patterns of locoregional recurrences (LRR) and distant metastases (DM) between patients with ILC and IDC.

Methods: All surgically treated women diagnosed in 2003–2004 with ILC or IDC, without DM or second primary breast cancer were selected from the Netherlands Cancer Registry. Risk of LRR or DM 5-years after diagnosis was assessed using Cox regression analysis, hazard rates for 5 years follow-up were determined.

Results: Of 15,960 women identified, 13% had ILC and 87% IDC. Compared to IDC, ILC was significantly ($p < 0.001$) more likely to occur in older patients, to be larger, of lower grade, multifocal and estrogen receptor (ER) and progesterone receptor (PR) positive. ILC was more likely to metastasize to digestive organs (peritoneum), bones and genital organs (ovaries).

Multivariable analysis (adjusting for other risk factors) showed no significant differences for the risk of both LRR and DM between IDC and ILC. However, the hazard rate pattern for IDC showed a peak within 2 years after diagnosis for LRR and DM. For ILC, the recurrence pattern revealed an almost constant level for LRR and DM within 2 years after diagnosis. Subset analysis for ER– patients only, revealed a similar peak for both ILC and IDC within 2 years after diagnosis. For ER+ patients the risk was highest at 1.5 years after diagnosis, which stayed at this level until 5 years after diagnosis. The highest observed risk for ER+ was much lower than for ER– patients.

Conclusion: No significant difference for recurrence risk was observed between ILC and IDC after 5 years. The differences in recurrence pattern between ILC and IDC was related to the ER receptor status, with ILC reflecting the recurrence pattern of ER+ patients. The stable pattern of recurrence for ER+ patients and the peak seen in ER– patients could be taken into account for the frequency and duration of follow-up visits.