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Local recurrence (LR) after breast-conserving therapy (BCT) in node-negative premenopausal patients: Influence of perioperative chemotherapy (PeCT)

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Purpose: PeCT decreases the LR rate after BCT. This study was intended to identify premenopausal patients who benefit most of this adjuvant therapy.

Methods: 361 T1-3 NO premenopausal patients treated with BCT were drawn from a prospectively randomized adjuvant trial (EORTC 10854; POP trial) comparing surgery followed by one course of chemotherapy (fluorouracil, doxorubicin and cyclophosphamide) versus surgery alone. Histology slides were reviewed. Immunohistochemical staining was performed for the following proteins: bcl-2, CD31, cyclin D1, E-cadherin, EGF receptor, ER, PR, Ki-67, c-erbB2/neu, and p53.

Results: In the multivariate analysis young age (<43 years), negative ER and positive p53 are risk factors for developing a LR. All subgroups showed a benefit from PeCT; patients with high vascular count and high mitotic count benefit most from this effect.

Conclusion: Age is an important independent risk factor for LR. PeCT decreases the LR risk in all patients, however no clinical useful subgroups can be identified.

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The occurrence of deletions and point mutations in the estrogen receptor gene in breast cancer specimens

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Purpose: Oestrogen receptor status has been recognised as a useful guide to the likely therapeutic response to Tamoxifen. However it is recognised that not all patients who are ER positive respond well and equally some ER negative patients do respond. One explanation for this would be alterations in the ER gene.

Methods: In order to address this question we have screened 118 breast cancer specimens for large deletions in the estrogen receptor gene by carrying out RT-PCR reactions using standard sets of primers and looking for PCR products of reduced size by agarose gel electrophoresis. Only two out of the 118 specimens yielded smaller than normal PCR products. One of these was a homogeneous deletion of exons 2–5 in the mRNA by alternative splicing. The other specimen was very heterogeneous containing many variants of estrogen receptor mRNA. The individual variants from this specimen were cloned and the deletions characterised.

Conclusion: Automated DNA sequencing of RT-PCR products of estrogen receptor mRNA from breast cancer specimens showed that in this group of specimens there was only a low incidence of point mutations suggesting that simple mutation and deletion is not a major cause of Tamoxifen resistance.

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Tenascin-C expression in invasion border of early breast cancer – A predictor of local and distant recurrence

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Purpose: Tenascin-C (Tn-C) is an extracellular matrix glycoprotein expressed transiently in areas of epithelial-mesenchymal interaction during embryogenesis and neoplasia. Our previous work showed an association between metastasis and Tn-C expressed in invasion border of axillary node-negative breast carcinomas. Our aim was to relate this Tn-C expression with several histopathological and biological variables and to compare their usefulness to predict recurrences.

Methods: The original patient group consisted of 143 women with axillary node-negative breast cancer (one bilateral) treated with breast conserving surgery and postoperative radiotherapy and followed for a median of 8 years. Due to the small number of recurrences an additional group of 15 similarly treated women with a recurrent breast cancer was also studied. The size of the tumour, its histology including a possible intraductal component, and grade were re-evaluated. The expression of erbB-2, p53, Ki-67, and Tn-C was evaluated by immunohistochemistry. Ploidy and S-phase fraction (SPF) were assessed by flow cytometry.

Results: The only statistically significant prognostic factor for local recurrence was Tn-C expression in the invasion border. For metastasis Ki-67 positivity, tumour size, and Tn-C expression in the invasion border were statistically significant, but Ki-67 was the only independent prognostic factor.

Conclusions: Tn-C expression in the invasion border was associated with a higher proliferation rate measured by Ki-67 and SPF, which is consistent with the suggested growth promoting activity of Tn-C. Tn-C may be a useful marker in selecting patients for adjuvant therapies to reduce the rate of both local and distant cancer recurrences.

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Age the limiting factor for breast conservative treatment in T1 breast cancer?

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Between January 1984 and December 1995, 1071 patients with breast cancer were treated with breast conservative treatment, limited surgery and radiation therapy. From the 1071 patients 860 (69%) were pT1 and 203 (28.5%) pT2.

This is an analysis of the 860 pT1 patients. The follow-up ranged from 3–159 months with a mean of 60 and a median of 55 months. The age ranged from 27–89 years with a median of 56 years.

The familiar history was recorded as no, 1 or > = 2 first degree relatives (F.D.R.) and was for the 860 pT1 patients 78, 15 and 3% respectively. The pN was 642 (74.5%) pN0 and 207 (24%) pN1. Of the 207 pN1 patients 165 had 1–3 and 42 >3 positive nodes.

The histology was 74% ductal, 10% lobular and 4.5% tubulair carcinoma. With 71 (8%) we had histologicaly positive margins of the lumpectomy and 25% showed also DCIS in the lumpectomy. From the 205 pN1 patients 82% (168) had adjuvant chemo or hormonal therapy depending on the menopausal status.

Results: The local recurrence rate was 3.4% (29/860). Looking at the influence of the familiar history in F.D.R., the pN status, number of positive nodes, positive margins and DCIS on the local recurrence rate, we show for no, 1 or > = 2 F.D.R. respectively 25 (3.6%), 3 (2.4%) and 0 local recurrences. The pN0 21 (3.3%) and pN1 8 (4%) local recurrences. Looking to the number of positive nodes we had 3.6% with 1–3 and 4.7% with >3 positive nodes. Positive margins had 3 (4.2%) local recurrences and DCIS 9 (4.2%). These factors were not significant.

Patients were subdivided according to age in three groups, = <40 (67/860), 41–50 (216/860) and >50 (577/860) years. The local recurrence rate was 12 (8/67), 5 (11/216) and 1.7% (10/577) respectively (p = 0.000).

The distant metastasis rate was 11.8% (101/860) and for the three age groups 29.8%, 13% and 9.2% respectively (p = 0.000). In the age group = <40 4/8 (50%) patients had local recurrences and metastasis, of which only 2 patients had local recurrence and metastasis at the same time

Conclusion: Looking to the local recurrence rata age seems to be a limiting factor for breast conservative treatment in T1 breast cancer.

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Platelet-derived endothelial cell growth factor/thymidine phosphorylase expression in macrophages correlates with tumor angiogenesis and prognosis in breast cancer

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Purpose: We evaluated the correlation of platelet-derived endothelial cell growth factor/thymidine phosphorylase (PD-ECGF/TP) expression with tumor angiogenesis and prognosis in patients with invasive breast carcinoma (IBC).