

446

POSTER

# **Familial history in breast conservative treatment of breast cancer a good prognostic factor?**

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In the Twente-Achterhoek region we do breast conservative treatment since 1984 for patients with T1 and T2  $\leq$  3 cm breast carcinoma. Since 1990 we register and follow-up consequently our known and new breast cancer patients with a breast conservative treatment. Until now we have treated more than 1350 patients with breast conservative treatment, all according to the same protocol.

The family history of breast cancer is registered as none, 1 first degree relative (F.D.R.) or  $\geq$  2 F.D.R. This is an analysis of 1071 patients treated up to and including 1995. 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 age of 56 years. According to the TNM classification we had 644 T1N0, 205 T1N1, 103 T2N0 and 97 T2N1 patients.

The familial history of breast cancer showed 15% (161 pat.) with one F.D.R and 2.7% (29 pat.) with  $\geq$  2 F.D.R.

We looked at the influence of the family history on the pathological T and N stage, the incidence of local recurrence, metastasis and on the survival.

There was no difference in pT between the patients with none, one or  $\geq$  2 F.D.R. There was less pN1 in 1 or more F.D.R., 30 vs. 24.5 vs. 21%.

Local recurrence was comparable for none and 1 F.D.R. 3.9 and 4.4%, but no local recurrence for  $\geq$  2 F.D.R. Also for distant metastasis there was a striking difference 14 and 12.5% vs. 3.5%.

Looking at the corrected, for intercurrent dead, survival 9% of the patients with none or 1 F.D.R. died of tumour. No patients with  $\geq$  2 F.D.R. died of tumour ( $p = 0.002$ ).

Considering the patients with  $\geq$  2 F.D.R. as the most important group with an almost certain hereditary breast cancer, we were surprised to see no local recurrences and only one patients with metastasis. The corrected survival for those patients was 100%. Taking together all patients with F.D.R., we still see a significant better survival for this group ( $p = 0.004$ ).

**Conclusion:** Patients with F.D.R. seem to have a better prognosis.

447

POSTER

# **Differential impact of high steroid hormone receptor concentrations on overall survival (OS) in primary breast cancer subgroups**

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**Purpose:** Occasional reports have suggested an unfavorable effect of high estrogen receptor (ER) concentrations in primary breast cancer. In a population-based study we identified a subgroup explicitly exhibiting this seemingly paradoxical effect. We excluded a similar phenomenon for the progesterone receptor (PgR).

**Methods:** ER and PgR were prospectively measured in a single laboratory by multiple point DCC assay. The relative risk of death in relation to the concentration of the interval-scaled variables ER and PgR was continually estimated by serial Cox-Regression analyses. Thus, we circumvented loss of information due to primary categorization and avoided assumptions about relations between factor and risk.

**Results:** Based on 2035 consecutively accrued primary breast cancer cases (median follow-up 56 months) we identified node-negative patients up to 60 years of age as the relevant subpopulation. High ( $\geq 300$  fmol/mg protein) ER concentrations exhibited an even more unfavorable impact ( $p < 0.02$ ) on OS than ER concentrations below 10 fmol/mg protein. The well-known association of age and ER concentration was definitely excluded as underlying biological cause for the increased risk. Differences in the distribution of other prognostic factors (HER-2/neu, Ki-67, DNA ploidy) were also excluded. As we observed a preponderance of pT2 tumors in the high ER group, we repeated the analysis, selectively focusing on pT2 tumors in the relevant subgroup, but the effect remained unchanged. In contrast, node-positive patients adjusted for age significantly ( $p = 0.02$ ) profited from high ER concentrations as compared to the ER negative group. We excluded a comparable phenomenon for age-matched node-negative patients regarding PgR.

**Conclusions:** As the phenomenon did not occur in node-positive patients receptor defects in the high ER group seem unlikely. Contrarily, we suspect that ER overexpressing tumor cells are hypersensitive to even low levels

of estrogens. Once they have sneaked past local barriers prior to primary surgery they may cause early death in the absence of appropriate adjuvant endocrine therapy.

448

POSTER

# **Analysis of variables associated with recurrence/metastasis in breast cancer tumor of $\leq 1$ cm**

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**Purpose:** To individualize variables predicting recurrence/metastasis in small breast cancer tumor.

**Methods:** A group of 344 patients with breast invasive tumor of  $\leq 1$  cm amongst a cohort of 3198 patients (T0 T1 T2  $> 3$  cm) seen consecutively between 1975 et 1996, operable and treated with primary surgery and axillary nodal dissection.

**Results:** The univariate analysis showed that vascular invasion ( $p = 0.009$ ) and ER ( $p = 0.02$ ) were significant factors for recurrence, whereas axillary nodal invasion ( $p = 0.08$ ) and modified SBR ( $p = 0.07$ ) were of marginal significance.

Multivariate analyses selected only modified SBR as the independent factor for overall survival (OS); modified SBR and negative ER for metastasis free survival (MFS); and vascular invasion and negative ER for disease free survival (DFS).

With a median follow-up of 77 months, ten year DFS is 85.4% for the whole cohort of 344 patients. One hundred and sixty three patients, who were all node negative, with mSBR 1, no vascular invasion and positive ER had a 10 year DFS of 97.5%.

**Conclusion:** In small ( $\leq 1$  cm) primary tumors, histobiological factors appear to be more potent prognostic indicators than axillary nodal involvement. The prognosis for tumors measuring  $\leq 1$  cm is excellent and women in this category (about half the group) should not be considered as candidates for systemic adjuvant therapy.

449

POSTER

# **Does prior pregnancy influence breast cancer outcome in young women?**

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**Purpose:** To determine the impact of prior pregnancy on breast cancer outcome in young women.

**Methods:** Tumor and patients characteristics and outcome were compared according to prior pregnancy in 577 young women (less than or equal to 35 years) with breast cancer treated between 1963 and 1990. 163 patients (28%) had no prior pregnancy, 21 patients (4%) had concurrent pregnancy. Last delivery had occurred between 0 and 12 months before diagnosis of breast cancer in 75 patients (13%), between 13 and 24 months in 43 patients (7%) or from more than 24 months in 275 patients (48%).

**Results:** Median follow-up was 12 years. Tumor stage (T, N, pN) was significantly higher in patients with concurrent pregnancy or interval from delivery  $\leq 2$  years. Survival was shorter in these two groups than in other patients. When adjusted to tumor stage as well as to age or clinical and biological factors, relative risks of metastasis and death were 1.5 times higher when last delivery occurred  $\leq 2$  years before breast cancer ( $p = 0.01$ ). These findings persisted after adjusting for systemic treatment.

**Conclusion:** This study, limited to patients less than or equal to 35 years, shows that pregnancy influences clinical characteristics of breast cancer up to 2 years following delivery. These patients did worse than patients with interval less than or equal to 2 years from last delivery or than patients who had no prior pregnancy. The interval between last delivery and diagnosis of breast cancer should therefore be taken into account when defining treatment strategies in young women with breast cancer.

450

POSTER

# **Expression of the apoptosis-related genes *c-myc*, *p53* and *bcl2* in breast carcinomas from operable patients. Only *bcl2* expression is associated with a lower risk of death**

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**Purpose:** To investigate the prognostic value of the expression of apopto-