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Effect of lymphovascular invasion (LVI) on local recurrence after wide local excision (WLE) and after mastectomy (Mx)

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ONCOPOOL is a data set (n = 17,000) compiled from primary operable (⩽5 cm) breast cancers in women aged ⩽50 in 12 European Breast Units, treated by first line operable therapy and entered in 1990−99 inclusive.

Purpose of Investigation: LVI has been frequently quoted as a risk factor for Local Recurrence. This could be because LVI is related to other prognostic factors or because LVI is an independent variable.

Method: LVI was regularly measured by H&E staining in 4 units (n = 4193). 20% were LVI+.

Results:

1997 underwent Wide Local Excision (WLE) + postoperative RT

% LR rates, WLE + postoperative RT			
LVI−		LVI+	
n	% LR @10 yr	n	% LR @10 yr
1610	8±1	387	14±2

Cox Analysis with integrated standard prognostic factors by using Nottingham Prognostic Index (NPI) showed no significance to LVI; the small overall difference was therefore because more LVI+ cases lay in the poorer prognostic groups.

2196 underwent Mastectomy (Mx)

% LR rates, Mastectomy			
LVI−		LVI+	
n	% LR @10 yr	n	% LR @10 yr
1458	8±1	738	11±1

Cox analysis entering LVI and NPI did not show significance to LVI.

Conclusions:

- 'LR' within the breast tissue after WLE is largely made up of residual primary tumour which. LVI cannot influence.
- LR in skin flaps is metastatic, probably through lymphatic channels: LR of this type is rare after RT.
- The overall significances in relation of LR to LVI are explained by the relation of LVI to other prognostic factors.

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An effect of basal-like molecular subtype of breast cancer and BRCA1/2 mutations on patients' survival depending on age

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Background: Basal-like molecular subtype of breast cancer (BLBC) is defined by the absence of estrogen, progesterone and HER2 expression, express basal cytokeratins CK5/14 (CK5/6), have the poor prognosis and the lack of therapeutic options. To clarify clinicopathological similarities and differences between breast carcinomas (BC) depending on age, we compared clinicopathological characteristics between tumors of young and old women. In our study have investigated whether young age at diagnosis is associated with biologically more aggressive cancers and BRCA 1/2 mutations. However, a little studies have demonstrated prognosis of this type BC in young women and with BRCA mutations.

Material and Methods: 573 patients with BC are included in research: 254 − young (till 35 years), 319 − old (over 35 years). ER, PR, Her-2/neu, p53, p63, Ki67, CK5/14, p21, Bag1, Mcl1, pS2, VEGFR, Her-1 were analyzed in all cases by immunohistochemistry and 235 patients (126 − till 35 years and 109 − over 35 years) were tested for the BRCA1 founder mutations 185delAG and 5382insC and the BRCA2 founder mutation 6174delT by flow cytometry. Groups were comparable on TNM classification and morphological variants of BC.

Results: BLBC was detected in 13.6% cases and had a higher prevalence (21.6% versus 7.2%; P < 0.0001) in young patients compared with old. BLBC immunophenotype was characterised by high expression of p53 and Ki67, but Bag1, Mcl1, pS2, VEGFR, Her-1 were negative. Young patients with BLBC have increased Ki67, p53, p63, VEGFR, Her-1 (P < 0.01). BRCA1/2 mutations were detected in 7.2% women, prevalent in young patients than in old (11.1% versus 2.7%, P < 0.05). The higher prevalence of BRCA1/2 mutations was in young patients with BLBC (12.7% versus 4.3%; P < 0.05) than old. The overall 5-year survival rate in young women has made − 73.2%, with BLBC − 65.5% (P = 0.07), in old − 85.3%, with BLBC − 52.2% (P < 0.001).

Conclusions: Young patients had a higher prevalence BLBC with lower indicators of survival rate than old (P < 0.05). There was detected an interrelation between BLBC and BRCA1/2 mutations (P = 0.007), however the authentic data about influence of BRCA1/2 mutations on survival rate has not been received in the multifactorial analysis. BRCA mutations lead to decrease of survival rate (P = 0.002), but in young patients with BLBC this influence is not marked (P > 0.05).

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Three different antibodies for estrogen receptor analysis in breast cancer − implications for positive frequency, reproducibility and clinical outcome

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Background: Estrogen receptor is a predictive factor in breast cancer patients. Assessment with different antibodies might produce different results.

Material and Methods: 564 premenopausal women with stage two breast cancer were randomised to tamoxifen for two years vs no tamoxifen independent of estrogen and progesterone receptor status. Recurrence-free survival (RFS) was chosen as the primary outcome.

A tissue microarray was prepared from 500/564 primary tumors. Immunohistochemical staining (IHC) with three different antibodies for estrogen receptor were evaluated (ER1D5 (DAKO, Denmark), ERSP1 (Neomarker, CA, USA), 352 evaluable cases and DAKO kit (DAKO, Denmark), 347 evaluable cases) twice by a pathologist using a semiquantitative score of positive cells. Scores were grouped in order to evaluate numbers of positive and negative cases and reproducibility at the 10% cut off. Categorization into three groups, totally negative, <50% positive cells and ⩾50% positive cells, was also evaluated.

Results: With a 10% cut off, the number of positive cases in the first reading was 223 (63%), 252 (72%), and 211 (64%) with ER1D5, ERSP1 and DAKO kit, respectively. The overall agreement between evaluation one and two was 97%, 100% and 98%. When classifying cases as totally negative, <50% positive and ⩾50% positive cells, the frequencies in the first reading were for ER1D5 104 (30%), 54 (15%), 194 (55%), for ERSP1, 69 (20%), 52 (15%), and 231 (66%), and for the DAKO kit 105 (30%), 103 (30%), and 139 (40%), respectively. Overall agreement between evaluation one and two was 93%, 95% and 91%.

Combining the first readings of ER1D5 and ERSP1, with cut off 10%, a total of 222 cases were positive with both antibodies and 100 cases were negative with both. All the remaining 29 cases were positive with ERSP1 and negative with ER1D5. With a follow-up period of 5 years, the recurrence-free survival of the discordant group resembles that of the double negative group, logrank P = 0.77 compared to P = 0.06 when comparing it to the double positive group. However, for recurrence-free survival the first two years after diagnosis, a reverse pattern was observed.

Conclusion: The evaluated cut offs are fairly well reproducible with all three antibodies. Choice of antibody is important for recurrence free survival of estrogen receptor positive and negative patients.

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Positive HER2 status − Is it a discriminating factor for disease outcome in steroid receptor-positive early breast cancer patients treated with adjuvant endocrine therapy only?

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Background: Since HER2-positive status has been repeatedly reported as negative predictive factor for response to endocrine therapy, we investigated the influence of HER2 status on disease outcome in ER+ and/or PgR+ early breast cancer (BC) patients treated with adjuvant endocrine therapy only.

Patients and Methods: We analyzed 263 (148 premenopausal and 115 postmenopausal) stage 1/2 SR+ BC patients who underwent a radical