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Tumor size and vascular invasion predict distant metastasis in stage I breast cancer. Grade distinguishes early and late metastasis

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Background: In a recent Dutch guideline, adjuvant systemic therapy (AST) is offered to women with high grade stage I breast carcinoma $\geqslant 1$ cm. High grade is defined as Bloom and Richardson grade 3 (B&R3), Nottingham modification, or a mitotic activity (MAI) $\geqslant 10/1.59$ mm^2. We felt that corroborative studies were needed with respect to the selection of these histological prognostic factors and the exclusion of others that are mentioned in the literature.

Materials and Methods: We used a case-control study design in which fifty cases with stage I breast carcinoma that developed distant metastases were selected from the regional cancer registry (IKR). They were matched for time of diagnosis to fifty controls without distant metastasis. None of the patients received AST. All H&E slides were revised by one pathologist for several histological prognostic factors.

Results: Compared to controls, cases more often had tumors $\geqslant 1$ cm (47 vs. 40, p=0.019), B&R3 tumors (20 vs. 12, p=0.059), grade 3 nuclei (28 vs. 15, p=0.005), and vascular invasion (10 vs. 1, p=0.007). No differences were found for MAI $\geqslant 10$ (14 vs. 11, p=0.46). In a multivariate analysis, the only statistically significant variables were vascular invasion and tumor size (odds ratios 8.21 and 5.35 respectively). In a separate analysis, the 50 cases were divided in 25 patients with early distant metastasis (before the median time to metastasis of 3.7 years) and 25 patients with late distant metastasis (after 3.7 years). Compared to those with late metastasis, those with early metastasis more often had B&R3 tumors (15 vs. 5, p=0.009) and grade 3 nuclei (19 vs. 9, p=0.006). No differences were found for tumors $\geqslant 1$ cm (25 vs. 22), vessel invasion (6 vs. 4) or MAI $\geqslant 10$ (10 vs. 4). Under the present Dutch guideline for AST, based on B&R3, 20 cases and 11 controls would have received AST. Based on MAI $\geqslant 10$, 14 cases and 11 controls would have received AST.

Conclusions: The present study shows that tumor size and vessel invasion are the best prognostic factors for disease free survival in patients with stage I breast cancer. It also demonstrates that the Dutch selection criteria for adjuvant systemic therapy for these patients need to be improved. In addition we show that some prognostic factors are time-dependent which makes the use of these factors as selection criteria for adjuvant systemic therapy more complicated.

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Results of surgical treatment of patients with breast sarcoma in relation to tumor size

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Aims: Breast sarcoma is a rare and heterogenous disease. Surgical resection is a primary treatment. However, due to rarity of the disease the further details of best treatment option are unknown. The aim of this study was to assess the results of surgical treatment of breast sarcoma patients in relation to tumor size.

Methods: Survival data of all 29 women treated between 1977 and 2001 were collected from hospital records. Twenty eight had mastectomy; in one case wide local excision was performed. No residual microscopic disease and no metastases in regional lymph nodes were found. Median size of the tumor was 10 cm (range: 3–30 cm). The diameter of breast tumor was bigger than 5 cm in 22/29 cases (76%). Cystosarcoma phyllodes was the most common histopathological type (48%). Mean and median disease-free survival times were calculated by the product-limit estimate method. Disease-free and overall survival probabilities were calculated according to Kaplan-Meier method for estimation of survival functions.

Results: The disease relapsed in 11 patients (38%); 8 of them died during follow-up (28%). The probability of disease free survival was 0.55 at 5 years and 0.44 at 10 years. The median length of disease free survival was 119 months. The overall survival probability was 0.69 at 5 years and 0.61 at 10 years, with a median length of overall survival of 137 months. Most of the patients whose disease recurred (10/11; 91%) and all who died had tumors larger than 5 cm. The majority of relapses were observed within two years after surgery. For patients with tumors not bigger than 5 cm the five-year overall survival probability was 1.00, the ten-year overall survival probability was 1.00. Survival estimates could not be computed for these patients since all observations were censored. For patients with tumors bigger than 5 cm the five-year overall survival probability was 0.60, the ten-year overall survival probability was 0.52; the median overall survival was 129.0 months (mean, 118.7 months).

Conclusion: The high probability of disease relapse in patients with large-sized breast sarcomas treated surgically is high, and warrants the search for more aggressive methods of treatment.

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Breast cancer characteristics and clinical outcome in geriatric patients

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Background: Breast cancer is a major source of morbidity and mortality in elderly women. Despite this, today there is no unique breast cancer treatment approach in elderly patients.

Methods: Retrospectively were followed: breast cancer biology, type of surgical treatment and overall survival rate using Kaplan-Meier analysis in period 1990–1995 years. Patients were divided in to study ($\geqslant 65$ years) and control group (<65 years).

Results: The study involved 1098 women (431 study group and 667 control group). The study group mean age was 71.3 years, and control group mean age was 50.7 years. Ductal carcinoma was the most frequently observed histological type-early stage (study group 70.3% vs. 61.92% control group). Modified radical mastectomy was the most used surgical procedure (71.46% vs. 76.46%). Kaplan-Meier analysis showed no significant statistic difference for overall survival among groups (p=0.961).

Conclusions: Breast cancer management is mostly inadequate in elderly patients. This study showed similar surgical treatment type, and no significant statistic difference for overall survival among examined groups.

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Age specific variation of oestrogen and progesterone receptor expression in 1340 primary operable breast cancers

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Background: In invasive breast carcinoma (IBC), the combined analysis of estrogen (ER) and progesterone receptor (PR) is more reliable than analysis of ER only in predicting response to endocrine therapy and prognosis. We analysed whether age at diagnosis affects differences in the combined expression of ER/PR by tumor cells.

Patients and Methods: Charts from 1340 consecutive female patients diagnosed with primary operable IBC (Jan. 2000 and March 2003) were reviewed, excluding those who received neoadjuvant therapy. Patients were divided in 5 age categories: $\leqslant 40$ y, 41–50 y, 51–60 y, 61–70 y and >70 y. IHC stains for ER (6F11/2) and PR (312) were categorised using the H-score as follows: $\leqslant 50$ (-); 51–100 (+); 101–200 (++) and 201–300 (+++). Each case was grouped according to the combined ER/PR expression (16 combinations). 233 IBCs were ER-ve/PR-ve (estrogen independent IBC). In 375 of 1107 cases with an estrogen dependent IBC (ER+ve and/or PR+ve) ER and PR belonged to the same category whereas ER and PR belonged to a different category in the remaining 732 cases. These patients were grouped as follows: ER<PR (n=20; ER<50); ER>PR (n=242; PR<50); ER<PR (n=164; ER>50); ER>PR (n=306; PR>50).

Results: 17.4% of all IBCs were ER-ve/PR-ve. The incidence of such estrogen independent IBC decreased significantly after the age of 40 (32.4% <40 y vs. 16.1% >40 y; p<0.001). Of all estrogen dependent IBC (n=1107), 1.8% were ER-ve/PR+ve, 21.8% were ER+ve/PR-ve and 76.4% were ER+ve/PR+ve. ER+ve/PR-ve tumors were significantly more frequent after the age of 50 (9.9% before 50 y vs. 23.1% after 50 y; p<0.001). In the group of ER+ve/PR+ve IBCs, those with PR expression exceeding ER expression were more numerous before than after age 50 y. This is due to the high proportion of PR+ve IBCs before age 50. After 50, there is an age dependent increase in ER expression but not in PR expression.

ER/PR by age group Total numbers	$\leqslant 40$ 108	41–50 323	51–60 371	61–70 328	>70 210	Total 1340
ER-ve/PR-ve	32.4%	16.7%	18%	13.4%	15.7%	233
ER-ve/PR+ve	4.7%	1.5%	1.9%	0.6%	0.5%	20
ER+ve/PR-ve	10.1%	7.7%	19.4%	26.2%	22.8%	242
ER+ve/PR+ve						
ER=PR	23.2%	31.2%	25.3%	30.1%	26.6%	375
ER>PR	14.8%	17.7%	25.2%	24.0%	30.2%	306
ER<PR	14.8%	25.4%	10.2%	5.7%	4.2%	164

Discussion: Estrogen dependent IBC show stronger PR positivity before than after age 50, when ER expression becomes increasingly dominant,