70 population-based controls, matched for age, selected by random digit dialing telephone directory method were studied. To test our hypothesis that hyperinsulinaemia (insulin resistance) initiates a cascade of events that may lead to increase androgen production and oestrogen levels and modulate insulin growth factor (IGF) binding protein(BP), we measured fasting insulin levels(IN), free testosterone(FT), SHBG, estradiol as well as IGF-1 and IGFBP-3 from both cases and control. Results: The Odds Ratio (OR) for comparison of the second tertile with first tertile of FT levels was 7.4 with 95% CI of 1.9-28.1. The OR for the third tertile compared to the first was 14.5; 95% CI (3.1-67.9). This indicates a range of 7-14 fold risk increase of breast cancer, associated with plasma FT levels. For IN, the OR of the second and first tertile comparaison was 1.13 (p=0.81) and for the third tertile compared to the first 3.36 (1.15-9.85; p=0.03). No correlation was observed for IGF-1. Conclusion: The preliminary results of this study show that FT levels could be used as an interesting marker to predict the development of breast cancer among PM. Further studies are needed to correlate the possible association between insulin resistance syndrome and increased risk of breast cancer. Supported by the Jean H. Picard foundation

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The diagnostic value of ultrasonography as adjunct to mammography and clinical examination in breast cancer detection

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Purpose: To determine the diagnostic value of additional breast ultrasonography (US) next to mammography (MAM) and clinical examination (CE) in patients referred for mammography and to define subgroups of patients who benefit most from additional US examination.

Methods and Patients: Between October 1999 and August 2000 a prospective study was performed in which all consecutive patients referred for MAM underwent additional ultrasonographic examination. Results for CE, MAM and US were scored according to the BIRADS-lexicon and linked to pathology results after a minimum follow up period of 6 months.

The diagnostic value of additional US was determined by construction of ROC-curves and comparing the areas under the curves for US+MAM+CE with MAM+CE. Subgroups were defined according to reason of referral and ROC curves were studied.

Results: In total 3835 breasts were examined in 2020 patients. 131 Malignancies were detected in 128 patients leading to a prevalence of 6.3%.

The sensitivity and specificity of US+MAM+CE was 95% and 95% respectively.

Additional ultrasonography significantly improved the diagnostic value in this population (AUC: US+MAM+CE 0.977 versus MAM+CE 0.950, p=0.01).

Patients referred for palpable breast lumps and <50 years as well as patients referred from the National Breast Screening Program did benefit most from additional breast US (p=0.01 and p=0.05 respectively). Breast US had no additional diagnostic value in patients referred for follow up of a former breast malignancy (p=0:30) or benign pathology (p=n.a.). Finally no additional diagnostic value was found for US performance in patients referred for screening and in examination of the contralateral breast (p=0.78).

Conclusions: Systematic breast US in patients referred for MAM significantly improved the diagnostic value. Breast US has additional diagnostic value in patients with palpable breast lumps or an abnormal screening mammogram. There was no additional value for US performance in screening.

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Statistical design in published non-comparative prospective studies of chemotherapy in breast cancer

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Purpose: Several statistical designs for phase II studies have been proposed but their application is still jeopardized. The aim of this survey is to describe the rate of studies with identifiable statistical design in a series of phase II or prospective non-comparative studies of treatment against breast cancer.

Methods: Papers were selected by hand-searching from seven distinguished (impact factor constantly over 2) specialty journals, published between 1995 and 1999. Univariate contingency tables evaluated by the chi-square test and multivariate logistic regression were applied to determine factors predictive of statistical design presence.

Results: 145 studies were selected. A statistical study design was not identifiable in 94 (64.8%) studies. Referral to a previous phase I study, more recent year of trial start, private sponsorship, and multicenter study organization were predictive of the presence of a statistical design at univariate analysis. Multicenter organization was the only independent predictive factor (OR 3.22; 95% CI: 1.48-7.00) with 48.6% of the studies with statistical design as compared to 21.1% among single-center studies. The presence of the statistical design was correlated with higher impact factor and shorter time between study start and publication. Among the 51 studies with statistical design there was a notable heterogeneity in the type of design applied.

Conclusion: Only a minority of the phase II studies in breast cancer published between 1995 and 1999 in high quality journals had a proper statistical design. A wider application of statistical methodology in planning phase II trials is required.

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Primary male breast carcinoma: actually a worse prognosis compared to female?

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Purpose: Because of the rarity of breast cancer (BC) in males, current management is generally extrapolated from the treatment of female patients (pts). To investigate the relationship between treatment and disease outcome, an analysis of a series of male BC treated at our Institution over a 10-year period was performed.

Patients and methods: The records of 58 consecutive male BC pts were retrospectively reviewed and analyzed with respect to clinical presentation, treatment choice, significant prognostic factors and survival.

Results: The median age at presentation of 64 years (range 28-72); tumor diagnosis was most often by a self-detected lump (67%) or the appearance of nipple discharge (22%); only 7 cases (11%) were investigated with mammography. The most common site were central subareolar region (48%) and the upper outer quadrant (27%). Infiltrating ductal carcinoma was present in 72% of cases, lobular carcinoma in 14%; tumors were usually moderately differentiated (59% of 55 cases with grading information); node metastases were found in 57% of cases; receptor status was available in 52 cases, 34 of which (65%) were ER+ and 32 (59%) were PgR+. Primary treatment consisted of modified radical (84%) or simple (12%); only 2 pts were treated with lumpectomy alone. Forty pts received adjuvant post-operative treatment, including radiation, hormone therapy and chemotherapy, given alone or in combination. Median follow-up of 5.8 years, ranging from 18 to 152 months. The median 5-year disease-free and overall survival was 46% and 54%, respectively. Multiple regression analysis of prognostic factors showed that negative node status (p<0.001) and adjuvant treatment (p<0.003) had a positive impact on DFS; grading (p=0.001), node status (p<0.03) and adjuvant therapy (p<0.003) resulted the strongest parameters influencing survival. No significant difference in survival was found between radical and simple mastectomy, nor among the different adjuvant treatments.

Conclusions: With the limitations of a retrospective study on a small series, our experience showed that prognosis in male pts with BC did not significantly differ from that known in female, also suggesting a benefit from adjuvant treatment. Multiinstitutional prospective trials are needed in this area, specifically focused to identify molecular properties of male BC, particularly in relation to BRCA1 and BRCA2, to optimize treatment strategies in both the adjuvant setting and metastatic disease.