40   Poster

The role of duct cytology in patients presenting with nipple discharge

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Background: Nipple discharge accounts for up to 5% of referrals to breast surgical services. With the vast majority of breast carcinomas originating in the ductal system, symptomatic dysfunction of the ductal system often raises disproportionately elevated clinical concern. Pathologic nipple discharge has traditionally caused somewhat of a diagnostic dilemma, with benign and malignant causes of pathological nipple discharge being difficult to distinguish clinically, radiologically and histologically. The aim of our study was, firstly, to evaluate the clinical importance of nipple discharge as an indicator of underlying malignancy and, secondly, to assess the diagnostic application of duct cytology in patients presenting with nipple discharge.

Methods: We performed a retrospective analysis of all patients presenting with nipple discharge as their primary symptom to the symptomatic breast unit at Mater Misericordiae University Hospital over a 30-month period (n = 313). The Hospital Inpatient Enquiry (HIPE) System and BreastHealth database were used to identify our study cohort. The medical records, radiologic imaging and cytologic reports of all patients were analysed. Parameters evaluated included patient demographics, presenting complaint, clinical evaluation, radiological assessment (including mammography, ultrasound and magnetic resonance imaging) and cytological analysis.

Results: Of the 313 patients presenting with nipple discharge as their primary complaint, 0.32% (1/313) were male and 99.68% (312/313) female. The discharge was bloody in 43.8% (137/313) of cases, serous in 41.5% (130/313) of cases, milky in 8.6% (27/313) of cases and green in 6.1% (19/313) of cases. 23.6% (74/313) of all cases presenting with nipple discharge had nipple aspiration performed and duct cytology analysed, of which 6.8% (5/74) had an underlying diagnosis of breast carcinoma. Duct cytology was diagnostic of the underlying breast carcinoma in 3/5 cases. Of our cohort of 313 patients presenting with nipple discharge, invasive breast carcinoma was identified in 4.2% (13/313) of patients.

Conclusion: Nipple discharge can be an alarming symptom for a patient, however it is a poor indicator of an underlying malignancy. With a systematic approach to patients with pathologic nipple discharge, involving clinical, radiological and histological evaluation, the risk of underlying carcinoma can be accurately defined. Nipple aspiration and duct cytology for the assessment of nipple discharge is of limited diagnostic benefit.

41   Poster

Neoadjuvant chemotherapy in breast cancer – prediction of pathological response by FDG PET

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Background: Neoadjuvant chemotherapy (NACT) is used with increasing frequency for operable breast cancer (BC): it allows to increase breast conservation surgery and to evaluate chemosensitivity of the tumor. An important goal of NACT is pathological complete remission, that correlates with a higher relapse-free and overall survival rate. Anyway the correlation between clinical and pathological complete response is quite poor (about 50%). In this study (Arianna 01 Project) we investigate if PET can improve this correlation and if it is able to identify early predictive signs of response in pts treated with neoadjuvant anthracycline- and taxane-based chemotherapy for BC.

Materials and Methods: we included in the present study T2−4 N0−3 M0 hystologically confirmed BC pts and M1 olygometastatic pts, if the therapeutic program included breast surgery after chemotherapy. Pts were evaluated with PET scan at baseline, every 2 courses and at the end of NACT. Metabolic therapy response was quantitatively measured by SUVmax within the primary lesion and by relative (%) SUVmax decrease. Pathological response was evaluated according to Miller and Payne classification, that ranges from grade 1 (no response) to grade 4−5 (only small clusters or individual cells residual, or no malignant cells at all).

Results: Up to now 33 pts have been enrolled and 8 of them are still on NACT. The present analysis is focused on the first 25 pts. Median age 49 (range 31−72), median KPS 100%; stage II: 12 pts; stage III: 10 pts; stage IV (olygometastatic): 3 pts. After 6−8 courses of NACT we observed 12 (48%) grade 4−5 pathological remissions (36% and 12% respectively). All pts had pathological baseline PET (focal lesion with SUVmax > 2,

median 10, range 2.5−23) at primary tumor level; a complete normalization (SUVmax ≤ 2) was observed in 17/25 cases (68%) at the end of NACT. The overall concordance between PET and pathological evaluation was 72% (18/25), while PET overestimated pathological response in 6/25 cases (24%). The positive and negative predictive values were 88% and 65%, respectively. After the second course of NACT the cut-off value of SUVmax reduction according to ROC curves analysis was 65%: 10/12 pts (83%) with grade 4−5 pathological response and 4/13 pts (31%) with grade 1−2-3 pathological response had a SUVmax decrease >65% (p < 0.002).

Conclusions: the concordance between PET at the end of NACT and pathological remission is 72%; a decrease of SUVmax > 65% after 2 courses of NACT is significantly more frequent in pts with optimal pathological remission (83% vs 31%). Therefore in the absence of PET response after 2 courses of NACT the probability of pathological response is low and a different therapeutic approach could be considered in these pts.

42   Poster

Potential impact of preoperative MRI on breast-conserving surgery of invasive breast cancer

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Objective: The aim of this retrospective cohort study was to assess whether differences in completeness of tumor excision exist between women who underwent preoperative contrast-enhanced (ce-) MRI (the MRI-group) and those who did not (the non-MRI-group).

Methods: A cohort of 527 women eligible for breast-conserving therapy (BCT) between November 2000 and June 2004 was evaluated. Eligibility for BCT was established by conventional breast imaging and clinical examination. Five-hundred-and-thirty-five breast tumors were found. The mean age of the women was 57.2 years (range 28−89). Two-hundred-and-sixteen patients (41%) underwent a preoperative MRI in addition to conventional imaging. Patient and tumor characteristics, and differences in surgical outcome were evaluated. In addition, the impact of the preoperative MRI on the treatment strategy was assessed.

Results: In 31 women (14.4%) more extensive disease was detected with MRI, which led to treatment change (mastectomy (12%) or wider excision (2.3%)). MRI also depicted six contra-lateral tumors (2.8%). The rate of incompletely excised infiltrating ductal carcinoma (IDC) was 16/245 (6.5%) in the non-MRI group and 3/153 (2.0%) in the MRI group (p = 0.03). No significant difference was found in the rate of incompletely excised infiltrating lobular carcinoma: 9/31 in the non-MRI group vs 6/21 in the MRI-group (both 29%).

Conclusion: Preoperative ce MRI may lead to a lower rate of incompletely excised IDC in breast-conserving surgery compared to the rate after conventional mammography, ultrasonography and palpation only.

43   Poster

"Artery and Vein together" synonymous of benignity in mammary nodules?

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Introduction: Stravros in 1995 described the ultrasound characteristics of the benign nodules in the breast. In some probable benign or indeterminate nodules, Doppler color visualizes an artery accompanied by his vein in the periphery of the lesion. We might suppose that this constitutes an anatomical normal condition, contrasting with new disordered vessels product of tumor angiogenesis in malignant lesions. Might it be consider a new sign of benignity?

Aims: Evaluate the frequency of the sign "artery and vein together" in the Doppler color in our series of Core-biopsies. Determine his association with benign, pre-malignant and malignant lesions and precise the value for benignity.

Material and Method: Between 2002 and 2007 we biopsy 1058 consecutive nodules under Ultrasound (ultrasound scanners Philips HDI5000, IU22, transducers: 5−17 MHz, pistol Bard, needles 14G). They were evaluated with Doppler Color before the biopsy. The ultrasound characteristics of Doppler color of every nodule and the histological results were registered in a database (FileMarker Pro8.5). For the sign "artery and vein together" we calculated sensibility, specificity, predictive positive value (PPV), predictive negative value (PNV) and diagnostic accuracy. We exclude 297 cases with no record of the histology.

Results: We find 113 nodules (113/761 = 14.8%) presenting the sign "artery and vein together" in 105 patients (average age: 44.35 years, range: 20−94). They were classified BI-RADS 3 (n = 28) and BI-RADS 4 (n = 85).

Size: between 5 and 41 m (mediate: 13.2 mm).

Histological distribution: benign 109 (96.5%), pre-malignant 3 (2.6%) and malignant 1 (0.9%).

Sensibility: 98.1%, specificity: 19.9%, VPN: 96.5%, VPP: 32.4%, diagnostic accuracy: 41.9%.

The sign was present in 18.3% of the probably benign nodules, BI-RADS 3 of the series (28/153) and all (100%) turned out to be benign in the histology.

Conclusions: The sign "artery and vein together" has low association with pre-malignant and malignant injuries, which explains the excellent VPN (96.5%) for malignancy. The presence of this sign in probable benign BI-RADS 3 nodules allows choosing follow-up ultrasound instead of biopsy.

44   Poster

Value of core needle biopsy, as the first diagnostic procedure, in palpable breast mass

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Background: Breast core needle biopsy (CNB) provides enough tissue for histopathologic diagnosis and is considered a reliable method for establishing preoperative tissue diagnosis, omitting the need for open biopsy. The purpose of this study is to evaluate CNB as the first diagnostic step instead of excisional biopsy in palpable breast mass.

Methods: In this follow-up study, patients with palpable breast mass who underwent CNB were enrolled. Based on pathology report, patients with malignant lesions revealed by CNB were immediately candidated for surgery and those who had benign lesions were followed up to 3 years.

Results: 112 females with palpable breast mass were enrolled in the study. In 103 (91.9%) of cases first attempt CNB provided adequate sample tissue. While nine (8.1%) patients needed a 2nd CNB due to inadequate sample. CNB detected malignant lesion in seventy eight (70%) patients. All (100%) malignant CNB reports were reconfirmed at surgery specimen pathology. In 34 (30%) patients CNB revealed benign lesion. At the end of 3 year-follow up period, 25 (73%) of these patients underwent open biopsy leading to the detection of 1 (3%) malignant tumor. Overall, according to the gold standard defined as positive surgical biopsy or positive follow-up, sensitivity of CNB was calculated as 98.7% (95% CI, 94.1–100%) and its accuracy was 99.1% (95% CI, 97.4–100%). The specificity of the CNB procedure was 100%.

Conclusion: These findings suggest that the malignancy detection power provided by CNB may be weighed equal to that of open biopsy. Therefore, we propose CNB as the first choice in diagnostic evaluation of palpable breast mass especially for those in accessible sites and in experienced hands. However, benign lesions diagnosed by CNB must be followed up.

45   Poster

Agreement between computer-assisted quantitative measurement of mammographic breast density (MBD) and clinicians' assessment

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Background: Women with increased mammographic density have been shown to have an increased risk of developing breast cancer. MBD is generally classified according to various density scales by radiologists.

Aim: The purpose of this preliminary work is to evaluate a new computer-assisted method to quantify MBD and to compare its results with the semi quantitative assessment by clinicians.

Material and Methods: Craniocaudal (CC) and mediolateral oblique (MLO) mammograms of patients were digitized and analyzed using new software developed by Agfa and based upon Computed Radiology (CR?) Technology. The software computes a quantitative measurement of the breast density for each individual image, based only on the raw image information and expressed as a percentage value per image. Thereafter, the resulting percentages of different views are combined to compute one representative breast density percentage for each patient. These were classified according to the Boyd classification (in 6 categories). In this pilot study we used data of 58 consecutive patients who came for a mammography screening (after having excluded male patients, patients with prostheses, and breast cancer patients). The mammographic density was also classified according to Boyd by 3 independent readers. Agreement (A) was measured by kappa (K) and weighted kappa (WK),

where Kappa only considers exact matches between categories and weighted Kappa accounts for how far apart two readers are. Confidence intervals are given (CI).

Results: See the table.

Kappa (K) (95% CI) and Weighted Kappa (WK)	Reader 1	Reader 2	Software
Reader 1			K = 0.441 (0.270−0.612) *Moderate A* KW = 0.596 *Moderate A*
Reader 2	K = 0.568 (0.395−0.741) *Moderate A* WK = 0.714 *Good A*		K = 0.387 (0.212−0.562) *Fair A* KW = 0.557 *Moderate A*
Reader 3	K = 0.308 (0.136−0.480) *Fair A* WK = 0.553 *Moderate A*	K = 0.362 (0.186−0.538) *Fair A* WK = 0567 *Moderate A*	K = 0.236 (0.064−0.407) *Fair A* KW = 0.472 *Moderate A*

Conclusion: These first results are encouraging for the development of a systematic use of new computer-assisted method to quantify MBD. Further work will consist in evaluating its limits and on how to ameliorate it.

46   Poster

The clinical breast exam during the pregnancy conducted by three different professionals

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Background: The clinical breast exam (CBE) is an essential component of breast cancer diagnosis; when used in combination with mammography, CBE contributes significantly to the sensitivity of screening, reducing the frequency of false-negative results. The National Institute of Cancer in Brazil, recommends the CBE, once a year, in all women above 30 years old, accomplished by to physician or to nurse.

Actually, the age group of pregnant women pregnant in Brazil is increasing. This fact contributes to the association between pregnancy and some diseases that affect older women, like breast cancer. Contributing with this situation, two Brazilian studies showed that the age group of women diagnosed with breast cancer is reducing.

This current study evaluates the CBE performed by three different professionals during the pregnancy, inside to University Hospital.

Material and Methods: We recruited two hundred patients in the São Francisco University Hospital, admitted at the Obstetric Ward, post-partum.

The patients were submitted to a simple questionnaire, by medical students. We did five questions: the EBC was conducted without blouse and bust bodice, the patient was lying, the axillary lymph nodes were examined, the supraclavicular lymph nodes were examined and if the professional examined the two breasts. The CBE was performed properly, if 3 answers were positives.

Results: Between the 200 patients, 50% (100 patients) were submitted to the CBE at least once. Between these patients, 45% (45 patients) considered the CBE properly.

Evaluating the professional who held the ECB, 54.45% of physicians, 60% of nurses and 55.2% of medical students, conducted inadequately exam.

Between the patients examined by the professional, 74% received orientations of the breast self exam.

Conclusion: Despite being integrant part of the women care, the EBC don't receive the importance by the professional during the prenatal. This study shows that medical students realize the same as their teachers, no matter if is incorrect. More important than realize CBE, is realize adequately.

Breast cancer associated with pregnancy is a neoplasia with bad prognosis. There is no difference when comparing pregnant patients with non-pregnant patients in the same age range. The advanced clinical staging at the moment of diagnosis being the determinant factor for survival. Because CBE, when combined with mammography, increases the sensitivity of breast cancer screening, requirements for regular training on CBE should be started for clinical practitioners on prenatal.