

00–04 ($p < 0.0001$); 2) the frequency of T1 also augmented gradually from 26.1% in 90–94, to 33.3% in 95–99, and to 44.8% in 00–04 ($p < 0.0001$).

Conclusions: Our results show that, during the last 15 years, the diagnosis of breast cancer has had a clear improvement in our community.

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PUBLICATION

Skin-sparing mastectomy with conservation of nipple-areola complex and immediate reconstruction is a safe procedure

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Background: Skin-sparing mastectomy (SSM) with immediate reconstruction has become popular with patients undergoing total mastectomy. Previous studies showed this procedure is safe and better aesthetic result. Recently preservation of nipple-areola complex (NAC) was tried and the risk of tumor involvement of NAC and local recurrence are issued.

Materials and methods: We reviewed clinicopathologic characteristics and complications of 79 cases of planned SSM with conservation of NAC and immediate reconstruction between July 1999 and January 2004 retrospectively.

Results: The median age was 37.4 years (22–57), mean tumor size was 2.2 cm (0.1–8.0) and mean distance from nipple to tumor was 2.1 cm (0–6.0). According to AJCC staging, 18 cases (22.8%) was stage 0; 27 cases (34.2%), stage I; 27 cases (34.2%), stage II; 5 cases (6.3%), stage III and 2 cases (6.3%) was malignant phyllodes tumor. According to reconstruction methods, 51 cases (64.6%) was TRAM; 24 cases (30.4%), direct implant; 4 cases (5.1%), tissue expander. All cases were performed intraoperative frozen section biopsy for NAC involvement of tumor and NAC was resected in 12 cases (15.2%) due to DCIS involvement. Only 1 case (1.5%) of preserved NAC, permanent pathologic report showed DCIS in resected margin of NAC. Partial necrosis of NAC was occurred in 11 cases (13.9%) and mean time of spontaneous recovery was 8.9 weeks (3–12). Asymptomatic pulmonary thromboembolism was occurred in 4 cases (6.0%). Postoperative implant infection was occurred in 2 cases (3.0%) and finally tissue expander was removed. During a mean follow-up of 15.0 months (4.1–71.0), no local and systemic recurrence were detected.

Conclusion: In patients who are candidates for total mastectomy and immediate reconstruction, SSM with intraoperative frozen section biopsy of the NAC offers the opportunity of NAC conservation. We conclude this procedure is safe and achievable satisfactory aesthetic result.

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PUBLICATION

Relationship between hormone receptor rate, CEA, CA 15–3 and MIB-1 in patients with breast cancer recurrence

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Background: Several tumor markers and risk factors have been investigated in patient with breast cancer (BC) for predicting recurrence and monitoring patients. The aim of this study was to analyze the correlation between estrogen (ER) and progesterone receptor (PgR) rate, serum tumor markers CEA and CA 15–3, MIB-1 proliferation index, and risk of BC relapse.

Patients and methods: Data regarding a series of 363 consecutive women with pT1–2 BC who underwent curative surgery and were followed-up for 24–120 months were reviewed. The following parameters were recorded: age (years), greatest diameter of the tumor (size, mm), ER and PgR rate, MIB-1 index (%), CEA (ng/mL) and CA 15–3 (U/L) serum levels. Two Groups of patients were considered: 1) Group A cases ($N = 62$, 17.1%, median age 55 years, range 35–83 years) with local or distant relapse, and 2) Group B controls ($N = 301$, 82.9%, median age 61 years, range 28–88 years) without relapse.

Results: In univariate analysis CEA, CA 15–3, MIB-1 index, and PgR values did not differ ($p = NS$) between Groups, whilst ER rate (65.7 ± 12.2 vs. 58.8 ± 17.1 ; $p = 0.003$) and size (24.3 ± 7.1 vs. 20.7 ± 10.2 mm; $p = 0.009$) were significantly different.

Overall, a linear relationship between CEA and CA 15–3 (Group A: $R = 0.43$, $p = 0.001$; Group B: $R = 0.21$, $p = 0.003$), and between ER and PgR (Group A: $R = 0.38$, $p = 0.002$; Group B: $R = 0.54$, $p < 0.001$) was found. In Group A patients there was a significant correlation between age and both CEA ($R = -0.47$, $p = 0.0003$) and CA 15–3 ($R = -0.46$, $p = 0.0007$), and between MIB-1 index and size ($R = 0.43$, $p = 0.0005$), age ($R = 0.36$, $p = 0.004$) and CEA ($R = -0.36$, $p = 0.004$). In Group B patients there was a

week correlation between size and both age ($R = 0.18$, $p = 0.001$) and PgR ($R = 0.20$, $p = 0.0004$).

Conclusions: Preoperative serum tumor markers CEA and CA 15–3, ER and PgR rate, and MIB-1 index are not useful in predicting the clinical outcome of patients with BC who underwent surgery.

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PUBLICATION

DCIS in core needle biopsy – an indication for sentinel node biopsy?

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Background: Ductal carcinoma in situ (DCIS) is nowadays a common finding in patients with screen detected breast cancer. There are no axillary metastases in DCIS, by definition. When DCIS is suspected in mammography, core needle biopsy (CNB) is recommendable to evaluate possible invasion. However, invasion remains undetected in 10–20% of the patients in CNB, because it represents only a minor proportion of the tumour. Tumour characteristics like high-grade histology, palpable mass, radiographic mass, suspicion of microinvasion, visibility in ultrasonography and extensive disease are found to have an elevated risk for invasion. We aimed to study the role of sentinel node biopsy (SNB) in the treatment of these patients.

Patients and methods: Between June 2001 and November 2004, screen detected DCIS lesions were detected in 79 female patients. The CNB-samples were reviewed by an expert breast pathologist and data were collected concerning the treatment of these patients. 67 of these had sufficient data and definite DCIS in CNB. SNB was performed to 27 (40%) of these.

Results: Surgical excision specimens revealed 47 (70%) pure DCIS lesions, 8 (12%) lesions with microinvasion and 12 (18%) invasive tumours. Axillary node metastases were found in 2 patients (4%) with pure DCIS, in one (13%) with microinvasive cancer and in two patients (17%) with invasive cancer. Of these metastases, only one was a macrometastasis, two were micrometastases and one was an isolated tumour cell-finding. Only visibility in ultrasonography was found to be a significant ($p = 0.006$) “high risk” factor; 13 (50%) of the 26 US-visualized tumours had invasive histology in the breast resection or mastectomy specimen. Comedo-type histology was found in CNB in 28 tumours and 12 (43%) of these turn out as invasive in ($p = 0.062$).

Conclusions: A substantial (18%) proportion of tumours diagnosed as DCIS by CNB have turn out as invasive cancers. In this study, only visibility of the tumour in ultrasonography was regarded as a “high risk” factor for invasiveness. These tumours are associated with an only small number of axillary metastases and SNB could therefore be helpful in the staging and treatment of such patients.

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PUBLICATION

Re-irradiation and hyperthermia after macroscopic complete resection for locoregional recurrent breast cancer in previously irradiated area

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Background: Subsequent local control after salvage treatment for locoregional recurrent breast cancer in previously irradiated area is generally poor. The cohort of 51 patients treated with macroscopically complete excision, re-irradiation and hyperthermia (RT/HT) in the Academic Medical Center from 1990–1998 was analysed.

Patients and methods: All 51 patients were previously irradiated to ≥ 50 Gy, and the majority had one or more lines of systemic therapy. The recurrence at stake was the first recurrence in 62% of patients. Time interval was < 2 years in 12% and < 5 years in 55% of patients. Recurrences were single in 42%, multiple in 25%, diffuse in 24% and ulcerating in 9% of patients. At start of RT/HT there was no macroscopically detectable tumour. This was achieved by minor surgery in 49%, by major surgery in 47% and by chemotherapy in 4% of patients. RT/HT consisted of 32 Gy/8 fractions/4 weeks, twice a week, and normally 4 (3–6) sessions of superficial hyperthermia with 434 Hz microwave antennas.

Results: Median survival of the entire group was 24 months. Fourteen patients (27%) suffered a subsequent locoregional recurrence, 5 of which only outfield. Actuarial local control stabilized at 20 months at 71%. Time interval to the current locoregional recurrence and original TNM classification were significantly predictive for subsequent local control. Severe late toxicity consisted of radiation ulcer (4) brachial plexopathy (3) and ribnecrosis (3).

Discussion: Interpretation of these results is difficult due to the heterogeneity of this group. Yet, despite the poor prognosis in these patients, many of whom already had multiple lines of treatment for their recurrent breast cancer, the combination of removal of macroscopic tumour, re-irradiation and hyperthermia appears to achieve a good locoregional control, at the cost of some severe toxicity.

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PUBLICATION

Potential health economic benefits of adjuvant (A) trastuzumab (H) therapy of node-positive (N+) her-2+breast cancer (BC)

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Background: H, an established, effective therapy for patients (pts) with HER-2+metastatic (M) BC, has been reported to reduce the rate of relapse for pts with early stage BC (ESBC) by approximately 50% when combined with adjuvant (A) chemotherapy (CT) (NSABP and INT, HERA: ASCO 2005). There is a perception that AH might have serious negative health economic consequences. We attempted to analyse the potential cost implications of AH, in the context of current use of H in MBC (MH), and of predicted reduction in the risk of relapse.

Material and methods: We conducted a retrospective analysis of the mean per pt cost of AH and MH in St. Vincent's Hospital. All AH pts were treated on BCIRG 006, and received a mean of 27 cycles of AH over one year (12–18 weeks of weekly schedule, with three-weekly to completion of year). Based on published/presented data (BCIRG 001), we assumed a 35% risk for relapse at five years for pts with HER-2+, node+ BC receiving conventional ACT, and a 50% risk reduction (RR) for AH (ASCO 2005 data), providing an absolute benefit of 17.5%. We also costed the following drugs administered in standard A regimens: docetaxel (D-BCIRG 001), paclitaxel (P-CALGB 9344) and, filgrastim (G-CALGB 9741, dose-dense), and noted the following published absolute relapse reductions for these regimens: D-7%, P-5% and G-4%.

Results: We identified 50 and 63 pts who received AH/MH respectively. The following are the mean cost/per pt. for the listed agents in standard A regimens (Euro): AH -34 k, AD-8.8 k, AP-7.4 k, G-9.3 k. The mean cost per pt. for MH was 47 k. The following costs per relapse prevented (CRP) were calculated: AH-194 k (i.e. 3.4 m/17.5%); P-(148 k); G-(231 k); D-126 k. In addition, in the absence of retreatment with MH, the incremental cost of AH for 100+ pts. is 1.8 m (100% × 34k = 3.4 M for AH, minus 35% × 47 k = 1.6 M) or 18 k/pt. Under this "no-re-treatment with MH" assumption, the cost per relapse prevented (CRP) for AH would equal 102 k.

Conclusions: 1) AH appears to be a relatively cost-efficient means of reducing relapses. 2) The optimal schedule of AH must be determined. 3) The efficacy of MH following prior AH must be determined. 4) It is possible that the impact and cost-efficiency of H will be greater in patients selected for HER-2+ by FISH.

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PUBLICATION

Tumor characteristic and clinical outcome of elderly women with breast cancer

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Background: Breast cancer is major health problem in elderly women. Although the number of elderly patients with breast cancer is increasing, knowledge about possible differences in the biology and clinical outcomes of breast cancer according to age is limited.

Methods: Retrospectively were followed: tumor characteristic and clinical outcome of breast cancer treated women at the Surgical Clinic in Nis between 1990–1995. Patients were divided in two groups: study (≥ 65 years) and control group (< 65 years).

Results: The study involved 619 women (262 study group; 357 control group). The mean age was 74.3 years, study group, and 49.7 years control group. Ductal carcinoma was the most frequently observed histological type in (70.3% vs. 61.92%). The majority of our patients presented with early-stage disease (69.02% vs. 60.20%). Estrogen receptor positive tumors occurred in 67.88% of elderly patients versus 28.42% of young cases, and negative axillary lymph nodes were observed in 45.78% and 34.40% of patients in the elderly and young group, respectively. Modified radical mastectomy was the treatment of choice for both groups. There is no significant difference in disease-specific survival by age.

Conclusion: In our population the presentation, surgical treatment, and survival from breast cancer is similar in older and younger women.

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PUBLICATION

Suggestions for follow-up (FU) strategies according to the risk of recurrence in patients with T1N0M0 breast cancer (BC): a single-institution experience

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Background: The risk of recurrence for early stage (T1N0M0) BC after multimodal therapies is not well defined and the FU strategies are still controversial.

Materials and methods: We retrospectively evaluated 214 T1N0M0 BC patients (pts) diagnosed at Istituto Clinico Humanitas/Cliniche Gavazzeni during April 1999–June 2003. Fifty-eight pts (27%) had T1a-b and 156 pts (73%) T1c BC. Pts characteristics (T1a-b/T1c, respectively): premenopausal 26/36%; invasive ductal 71/79%, invasive lobular 4/11%, other histology 25/10%; G1–2 90/80%, G3 10/12%; ER+ 93/88%, PgR+ 86/82%. Most pts were treated with conservative surgery (91/90%) followed by radiotherapy. In T1a-b group 4 pts (7%) received adjuvant chemotherapy vs 63 pts (40%) in T1c. Pts with ER+ and/or PgR+ received adjuvant tamoxifen (TAM) ± LHRH-analogues according to menopausal status; 8 (14%) T1a-b and 43 (26%) T1c pts received or switched to aromatase inhibitors due to contraindications or intolerance to TAM.

Results: At a median FU time of 34.7 mos (range 8.6–64.6) we observed 3 recurrences (5%) in T1a-b group: 2 relapses in homolateral breast and 1 in chest wall with lung metastasis. In T1c group there were 7 recurrences (4%): 2 local relapses (1%) and 5 (3%) metastatic diffusions in bone (2pts), liver (1pt), supraclavicular lymphnodes (1pt) or other site (1pt). Second tumours in contralateral breast were observed in 1 (2%) T1a-b pt and 6 (4%) T1c pts. All the bone recurrences were diagnosed after bone scan for pain; lymphnode recurrence by ultrasonography (US) and fine needle agobiopsy (FNA) after clinical evidence of lymphadenopathy; liver recurrence by routine US and confirmed by FNA; lung recurrence by routine chest X-ray. All the homolateral relapse and contralateral BC were detected by routine mammography (Mx).

Conclusions: Our data show that T1N0M0 BC has a very low risk of early recurrence after multimodal therapies. At a median FU time of about 3 yrs, no differences in the recurrence rate were found between T1a-b and T1c BC, with a trend (not statistically significant) for higher incidence of distant metastases in T1c group. These observations suggest that in this group of pts early FU strategies should be targeted to detect local relapses more than distant metastases. Medical interview, physical examination, Mx and breast US are strongly recommended but there is not enough evidence to support the routine use of other diagnostic exams without specific clinical indications.

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PUBLICATION

The implications of delaying the start of aromatase inhibitor (AI) therapy

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Background: The introduction of AIs has transformed adjuvant hormonal therapy for postmenopausal women with early breast cancer (EBC). However, debate continues as to the optimal AI administration strategy.

Methods: Initial adjuvant trials randomise patients (pts) about to begin adjuvant therapy to tamoxifen (T) or an AI for 5 years. Switching trials randomise pts partway through a 5-year course of adjuvant therapy and compare the relative efficacy of continuing with T or switching to an AI. Extended adjuvant trials enrol pts after completion of 5 years' T and evaluate the efficacy of additional therapy with an AI versus placebo or no treatment. Switching and extended adjuvant trials select pts who have already responded to 2–3 years' or 5 years' T, therefore, pts with an early recurrence will be excluded from such trials. Results from trials using an AI initially versus sequencing will not be available for several years.

Results: Modelling indicates that the risk of recurrence and especially the years of life lost to recurrence are always lower over the first 10 years of follow-up when an AI is initiated first. Switching to an AI will reduce the risk of recurrence, compared with continuing on T, but even after 10 years recurrences are more likely than in those who received an AI from the outset. This is particularly apparent in the progesterone receptor (PgR)-negative subgroup, but the results are model dependent for the PgR-positive subgroup. The ATAC trial, a double-blind randomised trial, compared anastrozole with T as initial adjuvant therapy in 6241 postmenopausal women with EBC. Risk: benefit data from ATAC (68 months' median follow-up) show that, compared with T, anastrozole