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"Patients non-clinical related factors associated with the use of breast conservative surgery in the treatment of primary breast cancer in Italy"

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Purpose: (1) to evaluate retrospectively trend of Breast Conservative Surgery (BCS), defined as lumphectomy or quadrantectomy with axillary dissection, in Italy over a 5 years period and (2) to identify non clinical factors associated with use of BCS.

Methods: data of 2,328 consecutive patients affected by primary breast cancer, surgically treated from 1992 to 1996, were selected fro the IGEO (Italian Group for the Evaluation of Outcomes in oncology) database. Patient age, level of education, time from diagnosis and place of residence were considered.

Results: The percentage of patients submitted to BCS among all patients surgically treated increased progressively from 1991 to 1996 (91:18.8%–>96:51.5%). Increase of BCS was different among North (20.2%–>58.0%), Center (17.9%–>48.9%) and South (15.8%–>41.3%) Italy.

BCS was employed in 32.5% of patients with primary school certificate (North: 34.0%, Center 33.6%, South 28.0%), in 40.0% of patients with secondary school certificate (North: 44.0%, Center 37.8%, South 32.4%) and 45.9% in patients with high school certificate and degree (North: 51.5%, Center: 42.7%, South 40.9%).

Women less than 40 years old were treated with BCS in 52.6% (North: 64.5%, Center: 44.9%, South: 44.8%), 40–50 years old in 45.0% (North: 50.0%, Center: 44.3%, South: 38.2%), 50–60 years old in 36.6% (North: 39.2%, Center: 37.7%, South: 31.2%), 60–70 years old in 29.0% (North: 27.7%, Center: 30.3%, South: 22.2%), >70 years old in 30.9% (North: 37.1%, Center: 25.3%, South: 22.2%).

Conclusions: (1) Non clinical variables as education level and age seem to influence the choice of BCS in surgical treatment of primary breast cancer and (2) significant difference can be detected in rate of patients submitted to BCS among different geographic region of the Italy. Surgeons knowledge, patients information as well as radiotherapy center availability can play a role in determining these geographic difference in percentage of BCS.

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Breast conserving surgery and radiotherapy for early breast cancer: Is optimal dose per fraction established?

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Guided by radiobiological advice, there has been a recent trend towards smaller "dose per fraction" for breast radiotherapy. This is particularly so in North America with doses of 1.8 or 2 Gy per fraction recommended and overall treatment times of 6 to 8 weeks. For many years we have employed larger fraction sizes and a shorter overall time and our results are presented.

Between 1989 and 1992, 2299 patients with early breast cancer were treated at the Christie Hospital by breast conserving surgery and radiotherapy. The target dose to the breast was 40 Gy in 2.66 Gy fractions over 3 weeks using a 4MV linear accelerator. No boost was given to the tumour bed and adjuvant chemotherapy or hormone therapy was given as appropriate. Median follow up is now 5.6 years, with a maximum of 9.5 years.

163 patients (7%) have developed histologically proven ipsilateral breast tumour recurrence. Of these, 92 (56%) were treated with further surgery, 85 having mastectomy. Of the 71 (44%) patients not treated surgically, 53 were found to have distant metastases at the time of local recurrence.

The cosmetic results were assessed retrospectively in a large subgroup of patients both by the patient and the treating clinician. In the majority of cases the result was assessed as good or very good.

We conclude that this radiotherapy regime is safe, practical and economic in the adjuvant setting, with good local control and cosmetic results. A large prospective UK study has recently been established to compare our approach with a "standard" tumour dose of 50 Gy in 2 Gy fractions.

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The effect of adjuvant clodronate on bone mineral density (BMD) in pre- and postmenopausal breast cancer patients. A randomized 5 yr. follow-up study

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Purpose: Adjuvant chemotherapy exposes premenopausal patients to early menopause and rapid bone loss, while antiestrogens prevent bone loss. We evaluated the effect of adjuvant clodronate on BMD.

Methods: 79 pre- and 70 postmenopausal women with primary breast cancer were randomized to adjuvant clodronate 1.6 g daily 3 yr. Premenopausal patients were treated with CMF chemotherapy and postmenopausal patients with tamoxifen or toremifene for 3 yr. Lumbar spine BMD (LS) and fernoral neck BMD (FN) were measured before the treatment and after 1, 2, 3 and 5 yr.

Results: In premenopausal patients with menstruation LS and FN decreased 2.13% and 1.19% in the control and 0.54% and 0.43% in the clodronate gr ($p = 0.001$ and 0.21); in patients with amenorrhea LS and FN decreased 11.58% and 5.69% in the control and 8.48% and 2.80% in the clodronate gr ($p = 0.02$ and 0.60, respectively). In postmenopausal patients the decrease in LS and FN were 2.82% and 5.07% in the control and 0.77% and 0.35% in the clodronate gr ($p = 0.04$ and 0.004).

Conclusion: Adjuvant 3-yr clodronate treatment reduces bone loss in premenopausal CMF-treated patients and even prevents the bone loss in antiestrogen treated postmenopausal patients. The beneficial effect of clodronate on BMD persists at least 2 yr after finishing the treatment.

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Prognostic value of cytokeratin (CK)-positive bone marrow micrometastsaes (BMM) detected in high-risk breast cancer patients after adjuvant chemotherapy

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Purpose: At present, there is no validated marker available to predict patients' outcome after adjuvant chemotherapy unless retrospectively from the recurrence of disease. This study was designed to evaluate whether monitoring of tumor cells in BM can predict the response to systemic chemotherapy in breast cancer.

Methods: In a prospectivly planned study, we analyzed BM aspirates from 59 newly diagnosed breast cancer patients with either inflammatory (n = 23) or advanced (>4 nodes involved) disease (n = 36). BM aspirates were taken before and after chemotherapy with taxanes and anthracyclins. We applied the monoclonal antibody A45-B/B3 directed against CK to detect tumor cells. The median follow-up time of 48 evaluable cancer patients was 18 months (range, 6–39).

Results: In 59 patients, 29 (49%) and 26 (44%) presented with CK^+ tumor cells in BM before and after chemotherapy, respectively. After chemotherapy, less than half of the previously CK^+ patients (14 of 29; 48%) had a CK BM finding, and 11 (37%) of 30 previously CK^- patients had a CK^+ BM finding. Univariate Kaplan-Meier analysis revealed a significantly reduced OS ($P = 0.02$; log-rank tes) if CK^+ cells were detected after chemotherapy. In Cox multiple regression analysis, the CK-positivity of BM after chemotherapy was an independent predictor for reduced OS ($P = 0.03$); the relative risk for cancer-related death was 6.4.

Conclusion: In spite of wide-spread acclaim, cytotoxic agents currently applied for chemotherapy in high-risk breast cancer patients lead to an only incomplete elimination of hematogenously disseminated tumor cells. The presence of these tumor cells after chemotherapy is associated with poor prognosis. Thus, the presented validated assay for BM monitoring might be a suitable tool to predict response to cytotoxic chemotherapy.