395 PUBLICATION

Mode of presentation is a prognostic factor in breast cancer

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Background: Controversy exists concerning the survival benefit of screening for breast cancer. Our study set out to see if the mode of presentation had any bearing on the outcome of patients with breast cancer.
Methods: All women aged 50–65 treated for breast cancer between October 1995 and September 1997 in two regional centres were studied. These patients were followed up for five years, and had data collected prospectively including mode of presentation, treatment, and relapse. Patients with in-situ disease were excluded from our study.
Results: A total of 369 women were diagnosed and treated for invasive breast cancer over the 24 month period, of which 270 were screen-detected and 99 were symptomatic. We found, as expected, commonly-accepted prognostic factors correlate with outcome – nodal status, size and grade. Multi-variate analysis (Kaplan-Meier survival curves, 95%CI, logrank test for statistical significance) also revealed that in our cohort, mode of presentation is a prognostic factor. Symptomatic breast cancer was associated with greater chance of death ($P = 0.004$) and recurrence ($P = 0.02$).
Conclusions: Our results support the theory that symptomatic patients have a worse prognosis than screen-detected patients, and screening does have a survival benefit. Mode of presentation should also be borne in mind in deciding appropriate adjuvant therapy.

396 PUBLICATION

Postoperative radiotherapy in male breast cancer

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Background: To evaluate the outcomes of radiation therapy treatment of male patients with breast cancer in our single institutional cohort and discover possible adverse prognostic factors.
Methods: We retrospectively evaluated 42 male patients (median age 55; range 33–77 years) with breast cancer treated between July 1994 and August 2001 at Hacettepe University Radiation Oncology Department. All patients were irradiated postoperatively in 2 Gy/fraction/day to chest wall $\pm$ lymphatics to a total median dose of 50 Gy (range, 46–60 Gy). Prescription of chemotherapy varied as neoadjuvant or adjuvant due to initial tumor burden and referral centers. Possible prognostic factors used in this retrospective analysis were as follows: tumor size ($\leqslant$5 cm vs. >5cm), number of metastatic nodal involvement (0 vs. 1–3 vs.> 4 LN), percent positive nodal involvement (metastatic nodes $\times$ 100/total nodes; 0% vs. $\leqslant$25% vs. 26–50% vs. >50%), AJCC 2002 staging, type of surgery (biopsy, excision, mastectomy), surgical margin status (negative vs. positive), neoadjuvant chemotherapy (present vs. absent), adjuvant chemotherapy (present vs. absent), and grade (grade I vs. grade II vs. grade III/IV). Calculations were based on the date of initiation of radiotherapy. Actuarial survival analyses were performed using the Kaplan-Meier method. A chi-square test was used to assess differences in patient distribution between groups. Outcome for overall survival (OS), disease-free survival (DFS), loco-regional relapse free survival (LRRFS), and distant metastasis-free survival (DMFS) in this cohort was compared with our institutional results of 1033 female breast cancer patients.
Results: Median follow-up was 39 months (range, 4.5–118 months). Initial surgery was as follows: excisional biopsy, 2; simple mastectomy, 1; modified radical mastectomy, 29; radical mastectomy, 10 patients. TNM staging was recorded as stage I, 1 (2.4%); stage IIA, 10 (23.8%); stage IIB, 7 (16.7%); stage IIIA, 6 (14.3%); stage IIIB, 7 (16.7%); stage IIIC, 11 (26.1%) patients. Eleven patients had neoadjuvant and 36 patients had adjuvant Adriamycin based chemotherapy. Eighteen (43%) patients were disease free, while 9 (21%) had local, 2 (5%) had distant and 1 (2.5%) had both local and distant disease at the time of analysis. Only one patient died without disease, but 2 (5%) with local, 6 (14%) with distant and 3 (5%) with local + distant disease. The actuarial 5-year OS was 77%, whereas the actuarial 5-year DFS, LRRFS, and DMFS rates were 45%, 69%, and 66%, respectively. Univariate analysis of variables including patient characteristics, treatment modalities and factors, and tumor characteristics failed to show an association with OS, DFS, LRRFS, and DMFS. Only LRRFS was found to be significantly worse in this cohort in comparison to female patients (Hazard Ratio for female patients: 0.34).
Conclusion: The outcome of male patients with breast cancer in this cohort is in accordance with the previous literature while our analysis for prognostic factors was limited due to the relatively small number of patients. However, it seems that male patients have a worse outcome in regard to LRRFS in comparison with our female patients.

397 PUBLICATION

Outcome of node-negative mucinous, medullary and tubular breast carcinoma

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Backgroud: Among breast cancer, invasive carcinoma(NOS) is the most common histologic subtype of invasive breast cancer. The less common subtype-mucinous, medullary, and tubular cancer has known good histologic subtype, especially node negative tumor. The purpose is to evalulate tumor characteristics and outcome of the mucinous, medullary, and tubular carcinoma.
Materials and methods: Twenty-six node negative medullary carcinoma, 14 with tubular carcinoma, 65 with mucinous carcinoma and 3129 with invasive carcinoma(NOS) were identified. The database was used to evaluate patient's tumor characteristics, and outcome. Survival curves and predictors of survival were analyzed.
Results: Disease free survival and overall survival of mucinous, tubular and medullary carcinoma is statistically significant between four histologic subtypes within the first 10year after treatment. Disease free survival-invasive (DFS) – mucinous, medullary, tubular – is 81%, 94%, 100%, 100% respectively($p = 0.02$). Overall survival (OS) is 87%, 96%, 100%, 100% respectively($p = 0.06$). Between size group, there are no significant difference of outcome. DFS and OS of invasive carcinoma with 1.0 cm or less is 92% and 89%.
Conclusions: Difference in prognosis by histologic type-invasive ductal, mucinous medullary, tubular carcinoma were identified. Node negative minor type carcinoma has better prognosis than those of invasive carcinoma(NOS). Especially, IDC with 1 cm or less in size (DFS: 92% OS: 89%) is comparable with other type without association with size. SO, we recommend that is needed that adjuvant therapy – chemotherapy – is reconcerned about good prognostic histologic type.

398 PUBLICATION

A comparison between adjuvant and numeracy; two freely available, web-based prognostic models for early breast cancer

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Introduction: Adjuvant! and Numeracy, are two freely available, web-based programs that determine for patients with early breast cancer the 10-year risk of recurrence and/or death without adjuvant therapy, and with different popular adjuvant therapies.
Methods: We have compared the prognostic and predictive estimates made by Adjuvant! and Numeracy in a population-based cohort of 434 breast cancer patients. In this cohort, we have also compared estimated outcomes with observed outcome.
Results: Baseline 10-year recurrence rates estimated with Adjuvant! and Numeracy correlated well. But, independent of prognosis, baseline Numeracy recurrence rate estimates were slightly lower than baseline Adjuvant! recurrence rate estimates. Estimates of the benefit of adjuvant systemic therapy were also lower with Numeracy than with Adjuvant!. Average Adjuvant! disease free interval estimates, but not average Numeracy disease free interval estimates corresponded well with observed disease free interval percentages.
Conclusion: In our opinion Adjuvant! is the preferable prognostic mode l.

399 PUBLICATION

Dose finding study of sequential administration of biweekly docetaxel followed by epirubicin and cyclophosphamide in high-risk breast cancer patients

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Background: Biweekly schedule of docetaxel (Doc) shows a high efficacy and decreases the hematologic toxicities in comparison with normal schedule. Therefore, biweekly Doc facilitates outpatient administration and maintains QOL. We planned the clinical study of sequential administration of biweekly Doc followed by EC (epirubicin / cyclophosphamide) combination chemotherapy. The purpose of this study was to establish a maximum-tolerated dose (MTD) of biweekly Doc and recommend a phase II Doc dose.
Patients and methods: Doc was administrated over 1 hour once every 14 days in postoperative breast cancer patients with axillary lymph node

positive or high-risk (T ⩾ 2 cm). Following the completion of 6 cycles Doc chemotherapy, all patients received 4 cycles Epirubicin 80 mg/m^2 and Cyclophosphamide 600 mg/m^2 every 3 weeks. The starting dose of Doc was 45 mg/m^2, and dose was escalated in increments of 5 mg/m^2 until MTD was reached. Patients were treated in cohorts of three to six per group by using a standard phase I study design. If none of three patients had dose limiting toxicity (DLT) during cycle 1 to 3, Doc dose was escalated to next level. If one or two of three patients had DLT during cycle 1 to 3, then three additional patients were treated at the same dose level. The MTD was considered dose level of three of three patients or more than three of six patients had DLT during cycle 1 to 3. Toxicity was evaluated by NCI-CTC ver2. DLT was defined as febrile neutropenia (fever ⩾ 38^{0}C and grade 3 to 4 neutropenia), grade 4 neutropenia, grade 3 to 4 thrombocytopenia, grade 3 to 4 nonhematologic toxicity (except nausea, vomiting, fatigue, and anorexia), or administration interval more than 3 weeks.

Results: DLT was not reached until Doc 65 mg/m^2 level. However, three DLTs were observed to five patients on 70 mg/m^2 level, and MTD of biweekly Doc was 65 mg/m^2.

Conclusions: Doc 65 mg/m^2 was selected as the phase II recommended dose. We plan a phase II clinical study of sequential administration of biweekly Doc followed by EC chemotherapy as preoperative chemotherapy in high-risk breast cancer patients.

400 PUBLICATION

Sentinel node biopsy and axillary node sampling in women with breast cancer undergoing breast conserving surgery. Preliminary results of a prospective study

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Background: Axillary dissection still represents the most accurate means of determining axillary lymph node status in patients with breast cancer (BC), but at the expense of significant morbidity. However, sentinel node biopsy (SNB) technique does not reach 100% sensitivity in detecting (or excluding) axillary node metastases, especially in the presence of unsuspected micrometastases. The aim of this study was to asses the accuracy of axillary node sampling (ALNS) in addition to SNB in patients with BC undergoing curative surgery.

Patients and methods: Sixty-seven consecutive women (median age 54 years, range 28–68 years) with pT1 primary BC undergoing breast conserving surgery were enrolled in the study. Patients were prospectively randomizes to undergo SNB alone (Group A, 35 patients) or ALNS in addition to SNB (Group B, 32 patients), followed by level I-II axillary dissection. In all cases, a combined method using radioisotope and blue dye was used for SNB. Patients with positive SNB were excluded.

Results: The age of the patients (54.8±8.2 vs. 54.1±9.2, p = 0.74) and the number of the removed nodes (median 19, range 16–25 in each Group) did not differ significantly (p = NS) between Groups. A median of 7 lymph nodes (range 6–9) was removed in Group B patients. In all patients intraoperative frozen section examination did not show positive nodes, whilst final histopathology showed micometastases in six (8.9%) patients. The sensitivity of SNB technique alone (false-negative rate: 14.3%) and SNB in addition to ALNS (false-negative rate: 3.1%) was 85.7% and 96.9%, respectively.

Conclusions: SNB alone in inaccurate in detecting axillary node micrometastases, and ALNS should be performed in all patients with macroscopically suspicious nodes and negative SNB.

401 PUBLICATION

Concomitant weekly tumour bed boost with whole breast irradiation in patients with locally advanced breast cancer undergoing breast conservation therapy: a prospective study

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Aim: To evaluate prospectively the feasibility of concomitant weekly tumour bed electron boost along with whole breast radiotherapy following breast-conserving therapy (BCT) in patients with locally advanced breast cancer (LABC) with the aim of reducing treatment duration by 1week.

Methods: Thirty patients with LABC suitable for BCT following neoadjuvant chemotherapy were eligible for the study. Conventional bilateral tangential photon fields to the whole breast and a direct supraclavicular field was delivered every day from Monday to Friday for 25 fractions to a dose of 50 Gy. In addition, an electron boost to the tumour bed was delivered every Saturday, delivering 5 such weekly fractions to a boost dose of 12.5 Gy. During radiotherapy (RT), patients were evaluated every week and skin reactions recorded as per CTC criteria. Cosmesis was recorded as per 4 point EORTC breast cosmetic score by two clinicians independently blinded to each other before RT and at 6 month follow up. This prospective cohort of 30 patients (Concomitant Boost [CB group]) was compared to a similar cohort of 32 patients treated conventionally with tumour bed boost of 15 Gy/6# given after the completion of whole breast irradiation (Conventional Radiotherapy [CRT group]).

Results: Chemotherapy achieved a complete clinical response in 25 (40%) patients, partial response in 33 (53%) patients and pathological complete response in 12 (19%) patients. Median interval between lumpectomy and the start of RT was 87 days (range, 31 to 163 days). All patients completed RT as planned. No patient in either group developed Grade IV skin toxicity. At conclusion of RT, in the CB group, one patient (3.3%) developed confluent moist desquamation (Grade III) in the tumour bed region and 3 (10%) developed this outside the tumour bed region. In the CRT group, 2 and 4 patients (6.3%) developed moist desquamation in and outside the tumour bed region respectively. The median duration of radiation was 35 days (range, 32–40 days) in CB group patients and 45 days (range, 41–55 days) in CRT group patients. Although the cosmetic outcome was significantly worse at 6 month post RT as compared to baseline pre RT evaluation in some domains (skin colour, p = 0.001, location and shape of nipple, p = 0.004), it was not significantly different in the two groups.

Conclusion: Concomitant tumour bed boost along with whole breast RT appears to be safe and feasible in a select group of patients. Moreover it can be completed earlier by a median of 10 days than conventional practice, which can have favourable human and machine resource implications.

402 PUBLICATION

Toremifen is a more desirable component of standard treatment of breast cancer than Tamoxifen

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Background: Estrogens are acknowledged as an important pathogenetic element of the development of breast cancer. Blocking of estrogen receptors results in an improvement of the prognosis and reduction of breast cancer mortality. Toremifen and Tamoxifen are the common agents blocking estrogen receptors. However, Tamoxifen, unlike Toremifene, has genotoxic and oncogenic effects, which are due not merely to hydrooxidation of Tamoxifen.

Material and methods: We have studied the effects of Toremifen and Tamoxifen on the hormonal homeostasis of 52 patients with stage 2 breast cancer by using RIA with 'Immunotech' kits in order to determine the serum levels of follicle-stimulating hormone (FSH), luteinising hormone (LH), estrogen and progesterone in 3 and 6 months following the beginning of administration of Toremifen or Tamoxifen. Estrogen and progesterone receptors were determined by using standard enzyme-linked immune assays.

Results: Toremifen effects have been shown to be more favourable on the pathogenetic level: estrogen levels havetripled by month 6 of treatment with Tamoxifen, whereas estrogen levels have only doubled by month 6 of treatment with Toremifen. FSH levels were lowering upon administration of either of the studied drugs, however, upon administration of Tamoxifen, FSH levels were reduced by 1/3, whereas upon administration of Toremifene – by 4 times, which testified to Toremifen superiority on the pathogenetic level. Five-year follow-up of 21 patients taken the mentioned drugs have shown positive results of administration of Toremifene in both receptor-negative and receptor-positive patients.

Conclusions: Accounting for the aforementioned facts and the general oncogenicity of Tamoxifen, we suggest Toremifen to be a more suitable component of the standard treatment of breast cancer.

Poster presentations (Mon, 31 Oct)
Breast cancer – advanced disease

403 POSTER

The amino-terminal propeptide (PINP) of type I collagen is a clinically valid indicator of bone turnover in osseous metastatic breast cancer while osteocalcin and CTX show inferior monitoring performance

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Background: Efficacy control of any treatment of metastatic spread to the bone in breast cancer is difficult and usually initiated later than restaging of visceral – or soft tissue metastases. The amino-terminal propeptide (PINP)