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Literature Review

Compiled by Dr. Chintamani

Half versus full vacuum suction drainage after modified radical mastectomy for breast cancer - a prospective randomized clinical trial [ISRCTN24484328]. *Chintamani*, Singhal V, Singh J, Bansal A, Saxena S. *BMC Cancer*. 2005;5(1):11

85 FNAC (fine needle aspiration cytology) proven cases of locally advanced breast cancer were randomized. (using randomly ordered sealed envelopes, which were opened immediately before the closure of the wound) in to 50 patients with full vacuum suction (pressure=700g/m²) and 35 cases in to half vacuum suction drainage (pressure=350g/m²) groups. The two groups were comparable in respect of age, weight, and technique of operation and extent of axillary dissection. Surgery was performed by the same surgical team comprising of five surgeons (two senior and three resident surgeons) using a standardized technique with electrocautery. External compression dressing was provided over the axilla for first 48hrs and following that patients were encouraged to do active and passive shoulder exercises. The outcomes measured were postoperative morbidity and the length of hospital stay. Statistical methods used were descriptive studies performed with SPSS version 10 and group characteristics were compared using student t-test.

Half vacuum suction drains were removed earlier than the full suction vacuum suction drains. There was no significant difference in the incidence of seroma formation in the two groups and there was a significant reduction in the total hospital stay in patients with half vacuum suction drainage systems as compared to the full suction drainage group (p<0.001) without any added morbidity. **CONCLUSIONS:** Half negative suction drains provide an effective compromise between no suction and full or high suction drainage after modified radical mastectomy by reducing the hospital stay and the post operative morbidity including post operative seromas.

Clinico-morphological patterns of breast cancer including family history in a New Delhi hospital, India—a cross-sectional study. Saxena S, Rekhi B, Bansal A, Bagga A, *Chintamani*, Murthy NS. *World J Surg Oncol*. 2005;13;3:67. sunita_saxena@yahoo.com

In an attempt to evaluate the clinico-morphological patterns of breast cancer patients, including their family history of breast and/or other cancers, a detailed analysis of 569 breast cancer cases diagnosed during the years 1989-2003 was carried out. Mean and standard deviation and Odds ratios along with 95% confidence intervals were estimated. Chi²/Fisher's exact test were employed to test for proportions. Mean age of the patient at presentation was 47.8 years, ranging from 13-82 years. Among the various histo-morphological types, Infiltrating duct carcinoma (IDC) was found to be commonest type i.e. in 502

cases (88.2%), followed by infiltrating lobular carcinoma (ILC) in 21 cases (3.7%) and other types forming 9(1%). Out of 369 cases where TNM staging was available, stage IIIB (35.2%) was the commonest. Lymph node positivity was observed in 296 cases (80.2%). Out of 226 cases evaluated for presence of family history, 47 cases (20.7%) revealed positive family history of cancer, among which breast or ovarian cancer were the commonest type (72.0%). Patients below 45 years of age had more frequent occurrence of family history as compared to above 45 years. Amongst familial cases, Infiltrating duct carcinoma was the commonest form accounting for 68.8% cases while ILC was found to be in a higher proportion (12.5%) as compared to non-familial cases (5.4%).

PMID: 16236180 [Pub Med]

Randomized trial comparing neo-adjuvant versus adjuvant chemotherapy in operable locally advanced breast cancer (T4b N0-2 M0). Deo SV, Bhutani M, Shukla NK, Raina V, Rath GK, Purkayasth J. *J Surg Oncol*. 2003;84(4):192-7. svsvdeo@yahoo.co.in

Locally advanced breast cancer (LABC) remains a major problem in developing countries. While trials utilizing neo-adjuvant chemotherapy demonstrate superior survival rates compared to historic controls, randomized studies evaluating the precise role of neo-adjuvant chemotherapy in LABC are lacking. In the present trial, neo-adjuvant chemotherapy was compared against adjuvant chemotherapy to assess survival advantage in operable T4b N0-2 M0 breast cancer.

A total of 101 women with operable LABC (T4b N0-2 M0) were randomized. In arm A, 50 patients received 3 cycles of CEF chemotherapy before and 3 cycles following surgery. In arm B, 51 patients had primary surgery followed by 6 cycles of CEF chemotherapy. In both arms, loco-regional radiotherapy was given after completion of CEF.

The response of primary tumor to neo-adjuvant chemotherapy was 66%, complete response (CR) 14% and partial response (PR) 52%. Clinical nodal response occurred in 95% of node positive patients. Only two (4%) patients had pathologic CR both in tumor and axilla. There was a significant (P = 0.02) increase in incidence of pathologically negative nodes in arm A. At a median follow up of 25 months, there was no significant difference in overall and disease free survival (DFS) in both arms (P = 0.42 and 0.18). Patients showing a response to neo-adjuvant chemotherapy had better DFS (P = 0.04) compared to those who had no response.

PMID: 14756429

delivered over 10 fractionated sessions, 6 hours apart over 5 days. Patient can take treatment as an outpatient and the balloon is deflated and removed after the last session of treatment without anaesthesia.

Intraoperative Radiotherapy An intraoperative radiation therapy technique (IORT) was developed by Veronesi et al⁶. A mobile linear accelerator using a robotic arm delivers electron beam energies from 3-9 Mega electron volts. Radiation is delivered using a perspex applicator directly into the lumpectomy cavity. An aluminum lead disk is placed between the breast and the pectorals muscle to protect the thoracic wall. A single fraction of 21 Gee has been estimated to be equivalent to 60 Gee over 30 fractions. Although the treatment was well accepted by patients, a large number of patients with a longer follow up mean follow up of 8 months) is yet to be reported to determine the efficacy and/or possible late side effects of such a large dose of radiation. The Target Trial is an international randomized controlled clinical trial comparing Single-Day Targeted Intraoperative Radiotherapy to Conventional Post operative Radiotherapy. This international study is designed to enroll 2,400 women, age 40 years or older with invasive breast cancer less than 3 cm in size.

External Beam Conformal radiation - Multiple CT-scan sections are obtained in the treatment position and a 3 dimensional plan is generated using advanced computer algorithms. The technique is best suited if the localization clips can be left in the lumpectomy cavity to determine the region of interest. It is possible to reduce the cardiac and lung dose while maintaining adequate tumour bed coverage with these techniques. Contralateral breast can also be spared the exit dose that is delivered by the lateral tangential field with conventional planning

Partial breast irradiation, accelerated partial breast irradiation may be an acceptable tool to augment breast preservation therapy in a resource limited country like India, however large randomized trial data in future will answer the question whether it should replace the conventional radiation.

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Literature Review

Role of p-glycoprotein expression in predicting response to neoadjuvant chemotherapy in breast cancer—a prospective clinical study. Chintamani, Singh JP, Mittal MK, Saxena S, Bansal A, Bhatia A, Kulshreshtha P. *World J Surg Oncol.* 2005. 14; 3: 61.

The expression of p-glycoprotein at initial presentation has been found to be associated with refractoriness to chemotherapy and a poor outcome. Against this background a prospective study was conducted using C219 mouse monoclonal antibody specific for p-glycoprotein to ascertain whether pretreatment detection of p-glycoprotein expression could be utilized as a reliable predictor of response to neoadjuvant chemotherapy in patients with breast cancer.

Fifty (50) cases of locally advanced breast cancer were subjected to trucut biopsy and the tissue samples were evaluated immunohistochemically for p-glycoprotein expression and ER, PR status. The response to neoadjuvant chemotherapy was assessed clinically and by using ultrasound after three cycles of FAC regime (cyclophosphamide 600 mg/m², Adriamycin 50 mg/m², 5-fluorouracil 600 mg/m² at an interval of three weeks).

A significant relationship was found between the pretreatment p-glycoprotein expression and clinical response. The positive p-glycoprotein expression was associated with poor clinical response rates. When the clinical response was correlated with p-glycoprotein expression, a statistically significant negative correlation was observed between the clinical response and p-glycoprotein expression ($p < 0.05$). There was another significant observation in terms of development of post NACT p-glycoprotein positivity. Before initiation of NACT, 26 patients (52%) were p-glycoprotein positive and after three cycles of NACT, the positivity increased to 73.5% patients. CONCLUSION: The study concluded that pretreatment p-glycoprotein expression predicts and indicates a poor clinical response to NACT. Patients with positive p-glycoprotein expression before initiation of NACT were found to be poor responders. Thus pretreatment detection of p-glycoprotein expression may be utilized, as a reliable predictor of response to NACT in patients

with breast cancer The chemotherapy induced p-glycoprotein positivity observed in the study could possibly explain the phenomenon of acquired chemoresistance and may also serve as an intermediate end point in evaluating drug response particularly if the adjuvant therapy is planned with the same regime.

PMID: 16164742 [PubMed]

Is drug-induced toxicity a good predictor of response to neo-adjuvant chemotherapy in patients with breast cancer?—a prospective clinical study. Chintamani, Singhal V, Singh JP, Lyall A, Saxena S, Bansal A. *BMC Cancer.* 2004; 4: 48.

The change in expression of apoptotic markers (Bcl-2 and Bax proteins) brought about by various chemotherapeutic regimens is being used to identify drug resistance in the tumor cells. A prospective clinical study was conducted to assess whether chemotherapy induced toxic effects could serve as reliable predictors of apoptosis or response to neo-adjuvant chemotherapy in patients with locally advanced breast cancer.

50 cases of locally advanced breast cancer after complete routine and metastatic work up were subjected to trucut biopsy and the tissue evaluated immunohistochemically for apoptotic markers (bcl-2/bax ratio). Three cycles of Neoadjuvant Chemotherapy using FAC regime (5-fluorouracil, adriamycin, cyclophosphamide) were given at three weekly intervals and patients assessed for clinical response as well as toxicity after each cycle. Modified radical mastectomy was performed in all patients three weeks after the last cycle and the specimen were re-evaluated for any change in the bcl-2/bax ratio.

There was a statistically significant correlation observed between clinical, immunohistochemical response (bcl-2/bax ratio) and the drug-induced toxicity. Responders also had significant toxicity while non-responders did not show significant toxicity following neoadjuvant chemotherapy. The chemotherapy-induced toxicity was observed to be a cost effective and reliable predictor of response to neo-adjuvant chemotherapy.

PMID: 15310398 [Pub Med - indexed for MEDLINE]