

Comparison of Clinico-pathological and Radiological Parameters of Response to Neoadjuvant Chemotherapy in Breast Cancer

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ABSTRACT

Complete histological response following neo-adjuvant chemotherapy (NACT) for breast cancer has great prognostic value. This study would assess rates of complete clinical, radiological and pathological response in patients of breast cancer treated with neo-adjuvant chemotherapy.

To Assess Rates of Complete Clinical, radiological And Pathological Response in Patients of Breast Carcinoma Being Treated with NACT.

Keywords: Neo adjuvant chemotherapy(NACT), locally advanced breast cancer. (LABC)

INTRODUCTION

Complete histological response following neo-adjuvant chemotherapy (NACT) for breast cancer has great prognostic value. [1],[2]. The significance of a lesser degree of histological response in terms of prognosis is also colossal as a major percentage of patients fall under the category of partial responders. [3],[4],[5],[6],[7]

In spite of the differences in the criteria adopted to measure and report the pathological findings after primary noninvasive treatment, most groups have shown a similar correlation between residual disease found at surgery and patient outcome. [7] Till date, no parameter/s has/have been validated to assess clinical or pathological response of breast cancer to NACT.

The change in clinical dimensions of tumor, as assessed during serial clinical breast examination, is used to evaluate the response to therapy in accordance with RECIST criteria. [8] Radiological measurements (by ultrasonogram [USG], mammography, CT scan or MRI)

have also been used for response assessment as a logical extension to (more accurately) measure the tumor size in certain centers. Radiological imaging is resource intensive and the additional expenses involved limit the utility of this option in developing countries.

The primary aim of this study was to correlate and compare the clinical, radiological, and the gold standard pathological parameters in assessing the tumor response to NACT. The secondary aim was to assess rates of complete clinical and pathological response in patients of breast carcinoma being treated with NACT. Thus the present study was aimed at correlating and comparing the conventional methods of assessment to pathological parameters of response.

PATIENTS AND METHOD

Prospective study was conducted. Total duration of study is 11 months (January 2016 to November 2016). Data collection period will be approximately 9 months (February 2016 to August 2016). Patient having breast lump and consulting outdoor department of surgery of SSG Hospital. Convenient sampling is done for which 55 patients are taken in this study. Diagnosis is confirmed by tru-cut biopsy

Those patients who had undergone previous biopsy are again examined at the end of three months. Data entry will be done in MS Excel 2013.

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Patients with histopathologically proven case of carcinoma breast size more than 2 cm with or without lymph node were included. Patients with Age more than 18 Years were part of this study Patient Previously treated for Breast cancer were excluded. Also patients having distant metastatic lesions. Male breast cancer patients were not part of this study.

STATISTICAL METHOD

Paired T Test was applied and The P value less than 0.05 was considered to be statistically significant.

RESULTS

A prospective study was carried out in the Department of General Surgery, during the period from January 2016 to November 2016 in 55 patients having Carcinoma Breast. full details of the patients were recorded in the Performa.

Amongst 55 patient age distribution range was 28-75 year with mean age 52.7 year, among those patient 17 were premenopausal and 38 were postmenopausal, all received Anthracyclin based chemotherapy.

Among 55 patients, all patients had complain of lump of variable duration, with 7 patients is having associated pain and 10 pt is having associated complaint of discharge.

By comparing breast lump on clinical examination, at pre-chemotherapy as well as post-chemotherapy time, size of breast lump in cm of is as follow

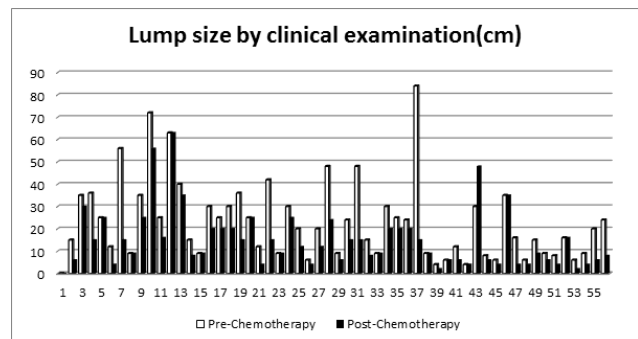
Here 29 pt had Right sided carcinoma of breast, while 26 patients were having left carcinoma of breast. And 31 patient had upper outer quadrant lump, 12 had upper inner quadrant lump, 8 had lower outer quadrant lump while 4 pt has upper inner as well as outer quadrant lumps.

By examining clinically all patients pre-chemotherapy and post-chemotherapy by different examiner, size of lump is measured.

By clinical examination, average mean decrease in breast lump is 8.34 cm² which is 36% of original breast lump size.

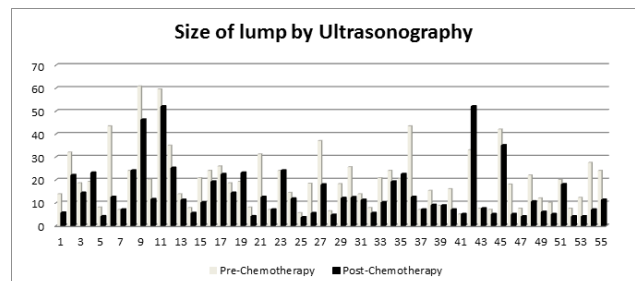
Bar diagram of the same is as below,

CHART 1



While looking at pre chemotherapy and post chemotherapy **ultrasonography** , results are as shown below,

CHART 2



Mean decrease in size of lump by ultrasonographic measures is 6.18 cm² (31%) as compared to 8.34 mean decreased observed by clinical examination

Histopathologically almost all patients were having invasive ductal carcinoma of breast. Axillary lymph nodes were palpable in 13 patients in clinical examination and seven patients were having small ulcer over skin which healed in all patients in post-chemotherapy examination,

By applying paired T-test to clinical examination findings and comparing pre and post chemotherapy results, SD for pre-chemotherapy shows value of 23.47±17.56 and SD for post chemotherapy shows value of 15.13±12.99 _with P value <0.0001, shows statistically significant decrease in size by neoadjuvant chemotherapy.

Similaraly, by applying paired T-test to ultrasonographic examination findings and comparing pre and post chemotherapy results, SD for pre-chemotherapy shows value of 20.00± 12.81 and SD for post chemotherapy shows value of 13.82±12.99 with P value <0.0001, shows statistically significant decrease in size by neoadjuvant chemotherapy.

While comparing the efficacy of clinical and radiological parameters in assessing response of neoadjuvant chemotherapy, results of each parameters are compared by single T-test.

TABLE 1

	Clinical Parameters	Radiological Parameters
Arithmetic Mean	8.34	6.17
Standard Deviation	12.44	8.07
P value is 0.28		

DISCUSSION

The current rationale for NACT is based on its usefulness in quickly evaluating the likely benefit of new approaches to treatment the biological characteristics of the individual tumor. [3],[5].

This approach has the advantage of enabling *in vivo* assessment of tumor sensitivity to chemotherapy. The complete clinical and pathological response of a primary breast cancer to NACT has been shown to be important prognostic factor in survival of these patients. [2],[

A critical component of this strategy is to use improved methods for monitoring tumor response to treatment. Patients who do not demonstrate an initial response, or who cease to respond to therapy, would have the option to change to other available agents to maximize response or can choose straight to go for surgery. Evidence is emerging that pathological response after NACT can be used as a surrogate endpoint for survival. [5],[7].

In spite of the differences in the criteria adopted to measure and report the pathological findings after primary noninvasive treatment, most groups have shown a similar correlation between residual disease found at surgery and patient outcome. [2] Using current standard chemotherapy regimens, approximately 70-90% of patients demonstrate at least a 50% reduction in tumor size clinically. However, only 10-20% patients demonstrate a complete pathological response in all literature. [3],[4],[5],[6],[7]

We found a 36% decrease in lump size by clinical examination and 31% decrease in lump size by

radiological measure in our study.

Physical examination is often considered unsatisfactory for assessment of the response of locally advanced breast cancer to primary medical treatment. Feldman *et al.* reported that 45% of complete clinical responders had macroscopic tumor at histological examination; inversely, 60% of patients without any histological gross residual tumor had an incomplete clinical response. [1] In the series of 49 patients studied by Cocconi *et al.*, physical examination overestimated tumor regression in 23% of cases and underestimated the response in 9%.

Several studies in the past have attempted to study the accuracy of CT scan or ultrasound to measure the tumor response but the results have been controversial. Operator dependence has been one of the factors quoted to be responsible for interfering with the accuracy. Modification of tumoral echogenicity induced by chemotherapy has been also quoted as one of the factors.

This density diminution may interfere and cause misrepresentation of measurements because of the decreased contrast ratio between tumoral and normal tissue. Balu-Maestro found ultrasound to be poorly reliable in evaluating the size of residual tumor after chemotherapy, correlating in only 43% of cases. In other series ultrasound was found to be superior to physical examination and mammography especially when the tumor was hypoechoic. Akashi-Tanaka *et al.* compared the results in 42 cases of clinical examination, mammography, ultrasound, and presurgical CT after four courses of chemotherapy with the results of histopathology.

There are several flaws to this study:

One, it is a prospective observational study with a small sample size and not designed with a statistical power to it;

two, there were several missing values for radiological assessment of response; and

three, clinical and radiological measurements were done by different clinicians each time.

In spite of the inherent flaws, our observations show that serial clinical assessment was better of the two methods to predict extent of histopathological response

However, it is important to note that both methods of assessment of response (clinical and radiological) suffer from poor sensitivity rates, and although radiological assessment seemed to have a 100% specificity rate, the low observed complete responses on radiological assessment render this value open to question. A larger sample size may provide more conclusive evidence regarding superiority of one method over another by providing adequate power to it. There are a number of recent studies which have evaluated the role of various other imaging modalities (PET, MRI, Doppler USG, optical tomography, etc.) in assessing the response to neo-adjuvant chemotherapy in carcinoma breast.

Of these Magnetic resonance imaging (MRI) holds promise in future, as it not only provides accurate information about the degree of response but also the pattern of response. Although it is still not widely available and is costly, but in future with increased experience of its use in this setting, it will prove to be very useful.

SUMMARY

A prospective study was carried out in the Department of General Surgery, during the period from January 2016 to November 2016 in 55 patients having Carcinoma Breast. All having tumour size more than 2 cm have been underwent neoadjuvant chemotherapy after biopsy confirmation.

All patients were assessed clinically and radiologically before and after chemotherapy. Post-operative breast specimens were sent to histopathology for final pathological diagnosis.

By clinical examination, average decrease noted is 36% of original breast lump and average decrease in size noted by ultrasonography is 31% of original lump, both are statistically significant decrease. While comparing clinical, radiological and pathological parameters in assessing response of neoadjuvant therapy, superiority of clinical examination could not be proved clearly (P value=0.28)

CONCLUSION

It is shown in the present study that clinical assessment of response to NACT, shows a higher sensitivity compared to radiological assessment. However the overall low sensitivity and specificity rates

of clinical assessment mandate a search for a better method of evaluation.

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Conflict of Interest : Nil

Ethical Clearance: Taken From Institutional Ethics Committee.

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