Article published online: 2022-05-23

Original article

Role of Scintimammography in Assessing the Response of Neoadjuvant Chemotherapy in Locally Advanced Breast Cancer

Romeeta Trehan, Rajeev K. Seam[1], Manoj K. Gupta[1], Ashwani Sood[2], Kislay Dimri, Rohit Mahajan

Department of Radiotherapy, Government Medical College and Hospital, [2]Department of Nuclear Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, [1]Department of Radiotherapy, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India

Abstract

Locally advanced breast cancer (LABC) is a common cancer in the developing countries. Neoadjuvant chemotherapy (NACT) is a very important step in the treatment of such tumors and hence that the disease can be down staged and made amenable for surgery. All the tumors do not respond to the therapy equally. Hence, it becomes very important to predict the response of chemotherapy in such cases. This study evaluated the role of scintimammography in assessing the response to NACT in 23 patients with LABC. Histologically proven 23 patients of LABC were recruited in this study. Prechemotherapy tumor size was measured clinically in all patients and technitium (Tc)-99m sestamibi test was performed before NACT for each patient. Early (10 min) and delayed (2 h) image of the breast were acquired in anterior and lateral views after Tc-99m sestamibi intravenous injections and wash out rate (WOR) was computed. After 3-4 cycles of chemotherapy, surgery in the form of modified radical mastectomy was performed in 20 out of 23 patients (3 patients lost to follow-up) with pathologic evaluation of the residual tumor size. The pretherapy Tc-99m sestamibi WOR ranged from 8.3% to 68% with mean ± SD of 34.5% ±16.5%. The prechemotherapy Tc-99m sestamibi study predicted chemoresistance (WOR >45%) in 6 out of 20 patients and no chemoresistance (WOR <45%) in 14 out of 20 patients. When the WOR cut-off was set at >45%, the predictivity of the test was indicated by sensitivity of 91.7%, specificity of 62.5%, positive predictive value of 78.6%, and negative predictive value of 82.3% with a likelihood ratio of 0.1. Tc-99m sestamibi WOR is a reliable test for predicting tumor response to NACT. WOR >45% is highly predictive of chemoresistance with likelihood ratio of 0.1 than WOR <45% being predictive of chemoresponsiveness.

Keywords: Breast cancer, neoadjuvant chemotherapy, response assessment, scintimammography

Introduction

Breast cancer is one of the most common cancers affecting females. It is not only associated with considerable morbidity and mortality, but is also a psychological trauma to females.[1] In India, like in other developing countries, approximately 25-30% of breast cancer presents as locally advanced, which are associated with high relapse rates and increased chances of metastasis.[2] Breast cancer is considered as a systemic disease, as micrometastasis is already present at the time of diagnosis. Neoadjuvant chemotherapy (NACT) is the treatment of choice for patients with locally advanced breast cancer (LABC) which provides better local disease control, improved breast conservation and increased survival rate. In addition, it also has the advantage of *in vivo* assessment of tumor sensitivity to chemotherapy so that nonresponders can be switched over to other drugs.[3] Treatment failure due to multidrug resistance (MDR) is the major obstacle in breast cancer. Hence, accurate assessment of tumor response is important and challenging. Clinical and radiological evaluation of response of the tumor is not reliable, as it cannot differentiate between fibrosis and actual

Access this article online

Quick Response Code:

Website: www.wjnm.org

DOI: 10.4103/1450-1147.144816

Address for correspondence:
Dr. Romeeta Trehan, Department of Radiotherapy, Level II, B Block, Government Medical College and Hospital, Sector 32, Chandigarh - 160 030, India. E-mail: trehanromeeta@gmail.com

residual disease. Hence, some metabolic method is required. P-glycoprotein is an energy dependent efflux transporter, which is encoded by the MDR gene. It is seen that technitium (Tc) sestamibi is transport substance for P-glycoprotein. Breast scintigraphy with Tc sestamibi is a noninvasive tool which provides information on tumor cell viability. Tc sestamibi is single photon tracer with high uptake in breast cancer as compared with normal breast. It has proven valuable for assessing activity of lesion and used as general probe for functional imaging of MDR pumps. Chemoresistance is a multifactorial phenomenon and MDR is commonly used to indicate an overexpression of transmembrane glycoprotein, which allows outward transport of the antineoplastic drugs like anthracyclins. This study evaluated the role of Tc-99m sestamibi scintimammography in predicting the response of NACT in LABC.

Materials and Methods

Patients

A prospective study, reviewed and approved by institutional ethics committee was carried out, in which histological proven 23 patients with LABC with no previous history of surgery and chemotherapy for breast cancer were recruited. LABC was defined as malignant tumors that were >5 cm in dimension (T3), invaded the chest wall or skin (T4), had fixed lymph node metastasis (N2/N3) or involved a significant fraction of a small breast. Clinical evaluation was performed in all patients before chemotherapy was started. Metastatic disease was ruled out by chest X-ray, abdominal ultrasonography and bone scan. A cardiac evaluation with an echocardiogram was carried out in all patients to assess their suitability for anthracycline based chemotherapy. Patients with LABC who consented to undergo scintimammography at baseline and post NACT, and with a pretreatment hemoglobin >10 gm%, total leucocytic count >4000/cmm, normal liver function test and kidney function test, karnofsky performance status >50, age <70 years were included in this study. All patients received 3-4 cycles of FAC regime (5-flourouracil-500 mg/m^2 intravenous [i.v], adriamycin-50mg/m^2i.v,cyclophosphamide-500mg/m^2i.v), which was repeated every 21 days. Clinical evaluation was carried out after each cycle of NACT and before surgery. Pathological status was obtained after surgery in all patients.

Technitium-99m sestamibi breast scintigraphy

Technitium-99m sestamibi was done twice in the same patient. First imaging was done just prior to chemotherapy, which was aimed at predicting the tumor response to NACT. This study was repeated after three or four cycles of chemotherapy just before surgery, which investigated the effect of just completed chemotherapy and was aimed at assessing actual tumor mass and at confirming the pretherapy study prediction. Patients were injected intravenously with 20 mCi (740 MBq) of Tc-99m sestamibi in the arm contralateral to the side of lesion in the breast. A scintimammopad with specially designed lead cut outs was used to allow the breast to be fully dependent. Images were acquired in the anterior view in the supine position and lateral views with the patient in the prone position with the help of scintimammopad. The axilla of the affected breast was also included in the field of view. The same imaging sequence was used in all patients. Dual time imaging was done with initial imaging at 10 min (early imaging) followed by second imaging done at 2 h (delayed imaging) post Tc-99m sestamibi injection.

Imaging reading and processing

Multiplexed ion beam imaging (MIBI) images were analyzed both qualitatively and quantitatively, using the tumor to normal breast (T: N) MIBI uptake ratio. The regions of interest were drawn on the lateral views around lesion and nearby normal breast tissues in the image obtained at 10 min and then were translated to images obtained at 2 h. The tumor to normal breast ratio (T: N) was calculated from early and delayed images. The uptake index was calculated both for early and delayed images by the ratio of the tumor to background mean count, with decay correction for delayed images. Washout of Tc-99m MIBI from the tumor (wash out rate [WOR]) was computed as follows:

$$\text{Wash out rate} = \frac{\text{Early T:N} - \text{Late T:N} \times 100}{\text{Early T:N}}$$

Tumor uptake was interpreted by two nuclear medicine physicians independently. To control for inter-observer bias, an average of the WOR measurements made by the two nuclear physicians was taken as the final WOR reading if the difference was ≤5%, If the difference in the readings of the two observers were >5%, then third reading was taken and average of the two closest readings was taken as the final WOR measurement.

Response evaluation

Clinical response evaluation

Tumor size was measured clinically with the help of caliper and surface area of the primary tumor was determined by measuring the two longest perpendicular diameters. After completion of 3-4 cycles of chemotherapy and prior to surgery, tumor size was again measured with the same caliper and surface area of the tumor was determined by the same method. An objectively determined reduction in the dimensions of the

tumor (i.e., reduction in the product of the two largest perpendicular diameters of the postchemotherapy clinical residual tumor size versus the baseline clinical tumor size) was considered the criterion for the clinical response. Response was evaluated according to WHO criteria.[4] Response was defined as complete response, on complete disappearance of all target lesions without any residual lesion; partial response, on 50% or more decrease in target lesions, without a 25% increase in any one target lesion; stable disease, on neither partial response or progressive disease criteria met; and progressive disease, on 25% or more increase in the size of measurable lesion or appearance of new lesions. Patients were labeled as clinically responders, on complete regression of the tumor or on more than 50% regression of the tumor. Conversely, patients were labeled as clinically nonresponders, on less than 50% regression of the tumor or on the increase in the tumor size.

Pathological response evaluation

The patients were subjected to surgery after three to four cycles of chemotherapy. Tumor size was again measured grossly on cut section of the pathologic specimen and surface area was calculated by measuring the two largest perpendicular diameters. An objectively determined reduction in the dimensions of the tumor (i.e. reduction in the product of the two largest perpendicular diameters of the pathologic residual tumor size versus the baseline clinical tumor size) was considered the criterion for the pathologic response. Response was evaluated according to WHO criteria in the same way as clinical response. The pathologic response was classified as no response to chemotherapy (pathological nonresponder), if there was less than 50% regression of the tumor or there was an increase in the tumor size. The pathological outcome was conversely classified as a positive response to chemotherapy (pathological responders), if there was complete regression of the tumor or there was more than 50% regression of the tumor.

Scintigraphy test evaluation

Prediction of the tumor response to NACT was based on the results of the pretherapy Tc-99m sestmibi WOR. Cut-off value for WOR was taken as 45% by likelihood ratio for best results. Accordingly, the test identified the positive response (responders), if there was WOR <45% and negative response (nonresponder), if WOR ≥45%.

Statistical analysis

Data were analyzed using Epi Info software (epi info software 3.51 version) for windows. Study population variables were described in terms of numbers and percentages. The results of Tc-99m sestamibi test were cross tabulated with pathological response to treatment and sensitivity (%), specificity (%), positive predictive value (PPV) (%), negative predictive value (NPV) (%), positive likelihood ratio, and negative likelihood ratio were calculated. The proportions were compared by Fisher's exact test where relevant. Correlations between WOR and pathologic reduction in tumor size were done and correlation coefficient was obtained. The level of agreement between clinical measurement of response and pathological response was also evaluated by kappa coefficient. $P \leq 0.05$ was considered as statistically significant.

Results

Table 1 lists the results of clinical, pathological, and scintigraphic response.

Patient and tumor characteristics

A total of 23 patients were included in the study. All patients were females with a mean age 47 years (range: 31-60 years). Eleven patients were premenopausal and 12 were postmenopausal. Left breast was involved in 12 patients, while right breast was involved in 11 patients. 65% of the tumors were in upper outer quadrant of the breast. All the patients had Stage III tumor at presentation.

Treatment

All patients received chemotherapy consisting of 5-fluorouracil, doxorubicin, and cyclophosphamide administered on a 3-weekly basis. Three to four cycles were given based on the level of response to treatment, after which patient was sent for surgery.

Response

Response was assessed both clinically and pathologically. Thirteen out of 23 patients (56.5%) were judged to have clinical response to therapy. Of 13 responders, 6 patients showed more than 75% of regression in the tumor size. Remaining 10 patients (43.5%) did not show response to chemotherapy on clinical examination. Pathological response was evaluated in 20 out of 23 patients. Two patients did not undergo surgery and lost to follow-up. One patient developed metastatic disease so did not undergo surgery. Of 20 patients, 12 patients (60%) responded to chemotherapy, while 8 (40%) patients did not respond to chemotherapy.

Sestamibi imaging results

All patients underwent two MIBI scans over the course of therapy. One MIBI scan was done prechemotherapy and the other one after 3-4 cycles of chemotherapy. WOR cut value was set at >45% by likelihood ratio of 2.44. The pretherapy Tc-99m sestamibi WOR ranged from 8.3% to 68% with mean ± standard deviation (SD) (34.49% ± 16.52%). Mean of WOR among responders and nonresponders were 32.3% (SD ± 11.2%) and 41.6% (SD ± 16.3%), respectively.

Table 1: Clinical, pathological and scintigraphic results

Patient no.	Prechemoclinical Tm size (cm^2)	Clinical response R or NR	Postchemopathological Tm cm^2	Pathological response R or NR	WOR (%)	MIBI response R=WOR≤45% or NR=WOR>45%
1	24.75	R	12	R	20.0	R
2	20.00	NR*	30	NR*	8.30	R
3	24.00	R	-	-	16.0	R
4	27.50	R	3.3	R	23.0	R
5	39.00	R	6.0	R	14.0	R
6	33.00	NR	3.9	R	27.0	R
7	24.75	R	12	R	36.0	R
8	10.50	R	8.7	NR	51.0	NR
9	10.50	R	-	-	68.0	NR
10	16.00	NR	09	NR	31.0	R
11	52.50	NR	30	NR	53.0	NR
12	45.00	NR	37	NR	58.0	NR
13	22.50	R	-	-	37.0	R
14	225.0	R	40	R	35.0	R
15	30.00	R	06	R	11.0	R
16	180.0	R	18	R	36.0	R
17	35.75	R	05	R	30.0	R
18	30.00	NR	05	R	37.5	R
19	42.00	R	06	R	54.5	NR
20	09.00	NR	06	NR	45.5	NR
21	49.00	NR	27	NR	52.0	NR
22	100.0	NR	42	R	42.0	R
23	144.0	NR	96	NR	09.0	R

*Progressive disease. R: Responder; NR: Nonresponder; WOR: Wash out rate; MIBI: Methoxyisobutylisonitrile

Accordingly, patient were defined as responder in 16 (69.5%), who had WOR ≤45% and nonresponder in 7 (30.4%), who had WOR >45%.

Clinical response was compared with scintigraphic prediction in 23 patients. It was observed that WOR correctly identified 10 patients as responders [Figures 1 and 2-case no. 17] and falsely identified 6 patients as responders when compared with clinical response. WOR correctly identified 4 patients as nonresponders out of 7 patients [Figures 3 and 4-case no. 21]. Pathological response was measured in 20 patients and was compared with scintigraphic prediction. It was observed that WOR correctly identified 11 patients as responders and falsely identified 3 patients as responders when compared with pathological response. WOR correctly identified 5 patients as nonresponders out of 6 patients. When clinical response was compared with pathological response, it was observed that, out of 20 patients, 9 clinical responders and 7 clinical nonresponders were correctly identified pathologically. Total 16 out of 20 patients matched clinically and pathologically. When level of agreement between clinical response and pathological response was seen, the findings were statistically different ($P = 0.009$). The level of agreement as seen by kappa coefficient was moderate. So, likelihood ratios are more relevant for pathological response that to the clinical response.

When WOR prediction is compared with pathological response, it is observed that, WOR rate has sensitivity of 91.7%, specificity of 62.5%, PPV of 78.6%, NPV of 83.3%, positive likelihood ratio of 2.4 and negative likelihood ratio of 0.1 [Table 2]. It is observed that WOR is more sensitive in predicting whether patients will respond to chemotherapy, but is less specific. NPV of test is more important than PPV in predicting that patients will not respond to chemotherapy. When WOR prediction is compared with clinical response, it is observed that, WOR rate has sensitivity of 76.9%, specificity of 40%, PPV of 62.5%, NPV of 57.1%, positive likelihood ratio of 1.3 and negative likelihood ratio of 0.6 [Table 3].

On correlating WOR with reduction in tumor size at histological examination, it was observed that with an increase in WOR, reduction in tumor size decreased. Out of responders, 8 (80%) patients had 80-90% regression in tumor size [Chart 1].

Discussion

Breast cancer is the most common site specific cancer in women and is the leading cause of death from cancer in women aged 40 to 45 years.[5] The affluent societies carry the greatest risk, with an incidence rate of >80/100,000 populations/year.[6,7] Despite improvements in early breast cancer detection due to awareness in self-breast

Table 2: Predictiveness of test to chemotherapy (WOR vs. pathological response)

WOR (%)	Pathological response (*n*=20)		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive likelihood ratio	Negative likelihood ratio
	Responded	Not responded						
≤45	11	3	91.7	62.5	78.6	83.3	2.4	0.1
>45	1	5						

WOR: Wash out rate; PPV: Positive predictive value; NPV: Negative predictive value

Table 3: Predictiveness of test to chemotherapy (WOR vs. clinical response)

WOR (%)	Clinical response (*n*=23)		Sensitivity (%)	Specificity (%)	PVV (%)	NPV (%)	Positive likelihood ratio	Negative likelihood ratio
	Responded	Not responded						
≤45	10	6	76.9	40	62.5	57.1	1.3	0.6
>45	3	4						

WOR: Wash out rate; PPV: Positive predictive value; NPV: Negative predictive value

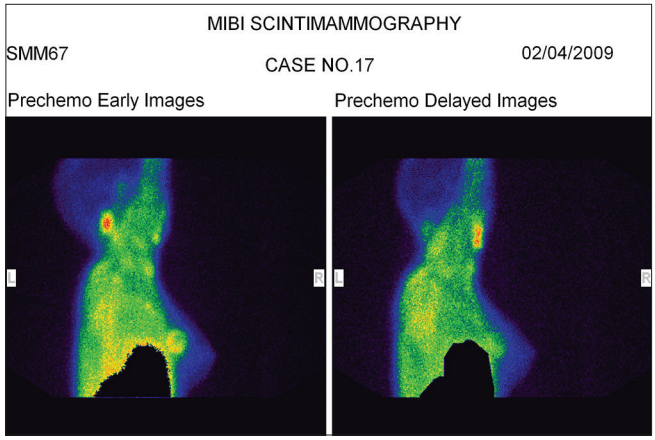

Figure 1: Patient no. 17 (responder case) - shows early and delayed images of scintigraphy studies of breast, who showed good response to chemotherapy on pathological examination. It evidenced intense tracer uptake in tumor in early image and low wash out rate in delayed image predicting good response to chemotherapy

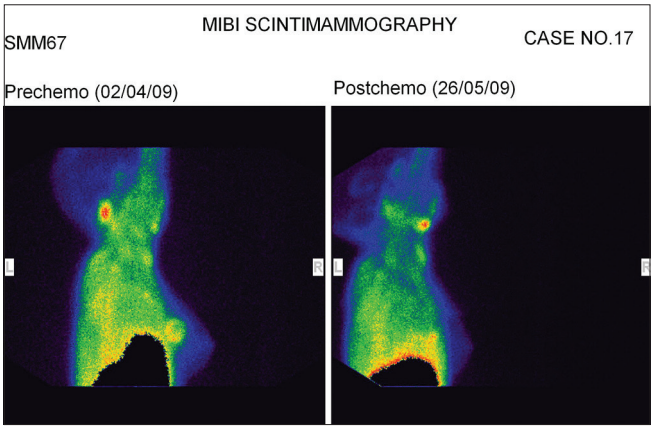

Figure 2: Patient no. 17 (responder case) - shows comparison of early pretherapy image with early posttherapy image, which confirmed positive response to chemotherapy, showing small area of residual tracer uptake in tumoral region

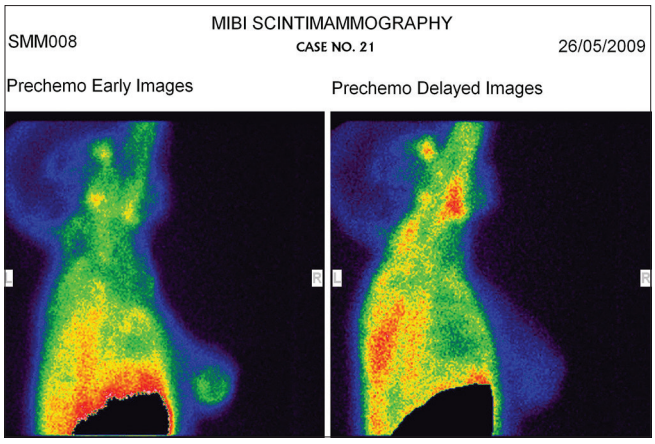

Figure 3: Patient no. 21 (nonresponder case) - shows early image and delayed image of scintigraphy studies, who showed no response to chemotherapy on pathological examination. It evidenced intense tracer uptake in tumor in early image and high wash out rate in delayed image predicting poor response to chemotherapy

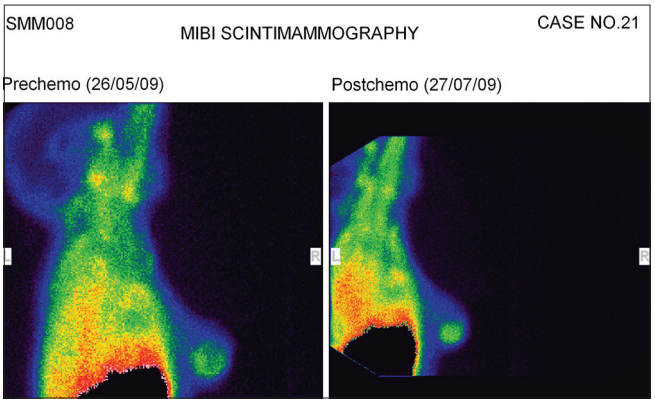

Figure 4: Patient no. 21 (nonresponder case) - shows comparison of early pretherapy image with early posttherapy image, which confirmed no response to chemotherapy, showing same volume of residual disease as evidenced by same tracer uptake in tumor region

examination and greater utilization of screening mammography, up to 28% patients still present with LABC and it continues to be a significant problem and a common breast cancer presentation in the developing country like, India.[7]

Chemotherapy has come a long way as systemic therapy in breast cancer. Initially chemotherapy was given after

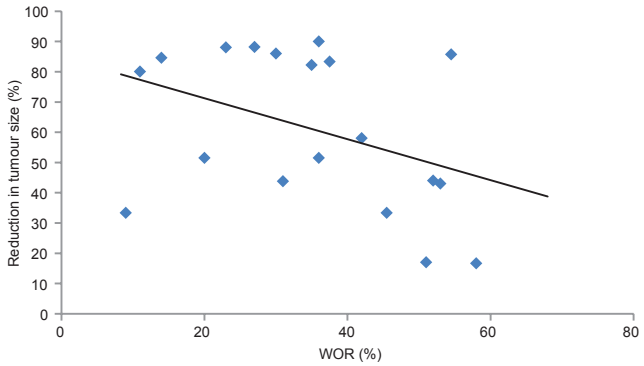

Chart 1: Correlation between wash out rate (WOR) and reduction in tumour size at pathological examination ($n = 19$; $R = -0.4$; $P = 0.149$). Percentage of reduction in tumor size (dependent variable) is plotted on y axis and WOR (independent variable) is plotted on x axis

the operation with the intent of eliminating tumor cells that had been systemically disseminated during surgery. Later, the rationale for the use of chemotherapy shifted with the aim to destroy micro-metastasis that was already present at the time of surgery.

Neoadjuvant chemotherapy was started with intent to reduce the primary breast tumor size and to take care of distant micrometastasis early in the course of the disease. In addition, it also provides an *in vivo* indication of tumor chemosensitivity in the patient who will require postsurgical adjuvant chemotherapy. All patients do not respond to NACT equally. So, sometimes change in chemotherapeautic regimen is beneficial. Treatment failure due to the development of MDR is a major obstacle. In fact, as intrinsic chemo-resistance is present in 18-50% of the untreated cancer, whereas resistance is acquired later during the treatment in up to 75% of patients.[8,9] Unfortunately, clinical examination as well as mammography and ultrasonography are inadequate to assess the response to treatment and also are not able to distinguish fibrosis from residual disease.[10-12] Pathological examination is the only way to see the extent of tumor response after chemotherapy which is an invasive procedure. Therefore, noninvasive imaging with Tc-99m MIBI is a topic that raises interest.[13-15] Tc-99m MIBI tumor uptake reflects metabolic status, and is directly related to blood flow of tumor. Retention of Tc-99m MIBI appeared to correlate with chemosensitvity to anthracyclins.[16]

It has been shown by different studies that Tc-99m sestamibi scintimammography is an attractive imaging modality to see early assessment of NACT response. It guides the management of patients by assuring continuation of therapy in those who respond and instituting alternative therapy who do not respond.

A study on this topic has been reported previously, which evaluated Tc-99m MIBI efflux kinetics by clearance analysis in 39 patients with LABC and concluded that this functional approach may identify patients at high risk of treatment failure. However, this method was too complex and time consuming with high rate of false negative results.[17]

In the current study, response of the tumor to chemotherapy was predicted on the basis of WOR of Tc-99m MIBI in the tumor, which is a simple, reproducible and reliable method. This method performed well in predicting chemoresistance with almost comparable results as reported by Sciuto *et al*.[18] Sciuto reported sensitivity of 100% and specificity of 80%. In our study, there is sensitivity of 91.7%, which is quite similar but specificity is slightly less which is 62.5%. We observed sensitivity significantly higher than that previously reported by Ciarmiello *et al*. (91.7% vs. 65%).[19] The difference was likely caused due to different criteria used to set the cut-off value.

In this study, NPV was 83.3% and PPV was 78.6% as compared to 100% and 83% in the study by Sciuto *et al*.[18] In this study, WOR was >45% which is highly predictive of chemoresistance with a likelihood ratio of 0.1 than WOR <45% being a predictor of chemoresponsiveness.

Similar study is also done recently, which has almost similar results with PPV and NPV of 41.9% and 72.7%, respectively in differentiating responders from nonresponders.[20]

A false positive test was observed in three patients. In one case, surgery was delayed for 1 month after chemotherapy, which may be the reason for nonresponse of the tumor at pathological examination, as disease may have progressed in that time. In other cases, patient may have acquired chemoresistance during therapy, as it is well-mentioned in the literature that 70% of patients acquire chemo-resistance during chemotherapy.[21] In our study, one patient was observed to have false negative test. In this case, WOR was high, thereby meaning nonresponder, but patient responded to chemotherapy with a positive response pathologically. However, patient was found to have progressive disease immediately after completion of the treatment. At the first follow-up, patient presented with metastasis in the liver and was put on second line chemotherapy.

Recently positron emission tomography-computed tomography (PET-CT) imaging has also been proposed as an alternative for the rapid assessment of tumor response to chemotherapy. A reduction in ^{18}F-fluorodeoxyglucose uptake has been postulated to predict the eventual clinical or pathological response. PET scanning requires expensive equipment and a supply of short lived isotopes. PET-CT imaging is very costly equipment

and is not readily available in all the centers. Very few centers have PET-CT imaging facility in the developing countries like India. Due to financial constraints, all the patients cannot get the advantage of PET-CT imaging for predicting and assessing response to NACT. Hence, in such circumstances, scintimammography is an ideal and cheaper substitute for the patients to get the same benefit as with PET-CT imaging.

This study validated Tc-99m sestamibi WOR, as a test for predicting tumor response to NACT, is a reliable, simple, noninvasive, reproducible, and effective.

Conclusion

This study has demonstrated a strong correlation between the WORs and response to chemotherapy. Lesser WOR meaning prolonged stay of tracer in the tumor is associated with good response to chemotherapy. Higher WOR, meaning shorter stay of tracer in the tumor is associated with poorer response to chemotherapy. The nonresponder group thereby required change in the chemotherapy regimen. The clinical role of the test is quite important, because a negative test (WOR ≤45%) rules out chemoresistance, ensuring the effectiveness of NACT. Conversely, a positive test (WOR >45%) indicates a high probability of chemoresistance and chemorevertant or chemomodulator agents should be used. This study showed that Tc-99m sestamibi WOR, as a test for predicting tumor response to NACT, is reliable, simple, noninvasive, reproducible, and effective. Though further studies with more number of patients are required to say conclusively, this simple and noninvasive technique can be used to predict responder from nonresponder. The relative inexpensiveness of MIBI imaging in comparison with PET and MRI and its wide availability makes it attractive clinical tool in evaluating breast cancer response to NACT.

References

1. Saxena S, Rekhi B, Bansal A, Bagga A, Chintamani, Murthy NS. Clinico-morphological patterns of breast cancer including family history in a New Delhi hospital, India-A cross-sectional study. World J Surg Oncol 2005;3:67.
2. Jussawalla DJ, Yeole BB, Natekar MV, Narayan RA. Epidemiology of breast cancer in India. Indian J Cancer 1975;12:231-42.
3. Goldstein LJ. MDR1 gene expression in solid tumours. Eur J Cancer 1996;32A: 1039-50.
4. Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting results of cancer treatment. Cancer 1981;47:207-14.
5. Harris JR, Morrow M, Bonadonna G. Cancer of the breast. In: Devita VT, Hellman S Jr, Rosenberg SA, editors. Cancer Principles and Practice of Oncology. 4th ed. Philadelphia: JB Lippincott Company; 1993. p. 1264-332.
6. Guinee VF. Epidemiology of breast cancer. In: Bland KI, Copeland EM, editors. The Breast: The Comprehensive Management of Benign and Malignant Diseases. 3rd ed. Philadelphia: WB Saunders; 1998. p. 339.
7. Jemal A, Murray T, Samuels A, Ghafoor A, Ward E, Thun MJ. Cancer statistics, 2003. CA Cancer J Clin 2003;53:5-26.
8. Goldstein LJ, Galski H, Fojo A, Willingham M, Lai SL, Gazdar A, *et al*. Expression of a multidrug resistance gene in human cancers. J Natl Cancer Inst 1989;81:116-24.
9. Keith WN, Stallard S, Brown R. Expression of mdr1 and gst-pi in human breast tumours: Comparison to *in vitro* chemosensitivity. Br J Cancer 1990;61:712-6.
10. El-Didi MH, Moneer MM, Khaled HM, Makarem S. Pathological assessment of the response of locally advanced breast cancer to neoadjuvant chemotherapy and its implications for surgical management. Surg Today 2000;30:249-54.
11. Chagpar AB, Middleton LP, Sahin AA, Dempsey P, Buzdar AU, Mirza AN, *et al*. Accuracy of physical examination, ultrasonography, and mammography in predicting residual pathologic tumor size in patients treated with neoadjuvant chemotherapy. Ann Surg 2006;243:257-64.
12. Peintinger F, Kuerer HM, Anderson K, Boughey JC, Meric-Bernstam F, Singletary SE, *et al*. Accuracy of the combination of mammography and sonography in predicting tumor response in breast cancer patients after neoadjuvant chemotherapy. Ann Surg Oncol 2006;13:1443-9.
13. Schomäcker K, Schicha H. Use of myocardial imaging agents for tumour diagnosis-A success story? Eur J Nucl Med 2000;27:1845-63.
14. Piwnica-Worms D, Chiu ML, Budding M, Kronauge JF, Kramer RA, Croop JM. Functional imaging of multidrug-resistant P-glycoprotein with an organotechnetium complex. Cancer Res 1993;53:977-84.
15. Hendrikse NH, Franssen EJ, van der Graaf WT, Vaalburg W, de Vries EG. Visualization of multidrug resistance *in vivo*. Eur J Nucl Med 1999;26:283-93.
16. Fujii H, Nakamura K, Kubo A, Enomoto K, Ikeda T, Kubota T, *et al*. 99mTc-MIBI scintigraphy as an indicator of the chemosensitivity of anthracyclines in patients with breast cancer. Anticancer Res 1998;18:4601-5.
17. Maini CL, Tofani A, Sciuto R, Semprebene A, Cavaliere R, Mottolese M, *et al*. Technetium-99m-MIBI scintigraphy in the assessment of neoadjuvant chemotherapy in breast carcinoma. J Nucl Med 1997;38:1546-51.
18. Sciuto R, Pasqualoni R, Bergomi S, Petrilli G, Vici P, Belli F, *et al*. Prognostic value of (99m) Tc-sestamibi washout in predicting response of locally advanced breast cancer to neoadjuvant chemotherapy. J Nucl Med 2002;43:745-51.
19. Ciarmiello A, Del Vecchio S, Silvestro P, Potena MI, Carriero MV, Thomas R, *et al*. Tumor clearance of technetium 99m-sestamibi as a predictor of response to neoadjuvant chemotherapy for locally advanced breast cancer. J Clin Oncol 1998;16:1677-83.
20. Mittal BR, Singh RK, Kumari S, Manohar K, Bhattacharya A, Singh G. Role of Tc99m-Sestamibi scintimammography in assessing response to neoadjuvant chemotherapy in patients with locally advanced breast cancer. Indian J Nucl Med 2012;27:221-5.
21. Sarkadi B, Müller M. Search for specific inhibitors of multidrug resistance in cancer. Semin Cancer Biol 1997;8:171-82.

How to cite this article: Trehan R, Seam RK, Gupta MK, Sood A, Dimri K, Mahajan R. Role of scintimammography in assessing the response of neoadjuvant chemotherapy in locally advanced breast cancer. World J Nucl Med 2014;13:163-9.

Source of Support: Nil, **Conflict of Interest:** None declared