Original Research Article

Dynamic contrast-enhanced MRI; A predictive assessor in triple negative breast cancer

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Abstract

Aim and Objective: The aim of the present study is to investigate the association of Magnetic Resonance Imaging (MRI) features of triple-negative breast cancer (TNBC) compared to non-triple negative breast cancer (nTNBC). **Materials and Methods:** Patients recruited for this study are diagnosed with Breast cancer (BC) and core-needle biopsy was taken from the patient and performed immune histochemical analysis. The morphological features and kinetic features were studied by using MRI. **Results:** Among the recruited group of 120, it was found that 35 cases were found to be TNBC positive and rest were negative. It was also found that, there was greater mean lesion size and signalling intensity on T2 weighed images in comparison with nTNBC group. It was significant that TNBC group exhibited low Epeak values and high SER values in comparison with nTNBC group. **Conclusion:** Our study results found that, up on kinetic and morphological analysis it is understood that dynamic contrast enhanced MRI might be useful in pre-treatment risk assessment in patients with TNBC and also stands as a support for evidence based clinical decision.

Key Word: breast cancer, magnetic resonance imaging, triple negative breast cancer, immunohistochemistry

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Received Date: 25/02/2019 Revised Date: 02/04/2019 Accepted Date: 15/06/2019
DOI: https://doi.org/10.26611/10131038

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 26 June 2019

INTRODUCTION

Cancer has drawn the health of an individual into major risk. India being a developing country accounts for 14 lakh cancer patients in 2016 according to Indian Council of Medical Research (ICMR) reports. Upon differentiation, the government of India has identified four major cancers *viz* breast cancer, oral cancer, cervical cancer and lung cancer which together constitute 41 percent.[1]. Among which breast cancer is the leading cancers in women causing mortality. Triple negative breast cancer is a subtype of breast cancer which does not comprises three major receptors namely, human epithelial growth factor receptor type, progesterone receptor and estrogen receptor. This heterogeneous nature of cancer implicate complications to both patients and physicians. Among the different subtypes of Breast cancer 13-20% are screened as triple negative breast cancers (TNBC). The immune histochemical subtypes of TNBC have a variant entity with respect to other BC types with huge histological grade, poor prognosis and increased recurrence.[2,3]. Patients with triple negative breast cancer are reported to have distinct metastatic disease andless mean time compared to non-triple negative breast cancers. These patients were also diagnosed with increased incidence of early brain metastases.[4,5]. Since, this type of cancer patients are unresponsive to usual endocrine therapies, it results in low survival rates. Additionally, women reported with BRCA1 mutation are found to have breast cancer at an early stage with high prevalence of triple negative breast cancer.[6,7]. The metabolic and hormonal arrangements rely on tumour prognosis and also angiogenesis which together implicate significant role in prognosis. These can be investigated by Magnetic resonance imaging (MRI) of breast considering

How to cite this article: Anant Madhukarrao Bhuibhar, Challa Anil Kumar, Lalwani Shyam Tekchand. Dynamic contrast-enhanced MRI; A predictive assessor in triple negative breast cancer. *MedPulse International Journal of Radiology.* June 2019; 10(3): 46-49.
http://www.medpulse.in/Radio%20Diagnosis/

the variant patterns of enhancement closely related to hyper vascularity.[8] However, there are limited literature available on MR imaging of triple negative breast cancer features. The study hypothesised on comparison of MRI features of triple and non-triple negative breast cancers. This could yield additional information in treatment planning and prognosis assessment as well as to know the biologic behaviour of the disease. The aim of this study is to screen morphological and kinetic MRI features of triple negative breast cancer subtypes and breast can subtypes

MATERIALS AND METHODS

Patients: The study was conducted in Department of Radiology, Great Eastern Medical School and Hospital, Srikakulam from May 2017 to October 2018 the patients recruited for the study are undergone breast MRI for suspected breast lesion and diagnosed with BC. The enrolled patients were total 120, classified into two groups with histological diagnosis of TNBC (60) and non-TNBC (60). The age group of the patient was from 31 to 60 and the size of the cancer ranged from 0.3 to 11.0 cm.

Magnetic Resonance Imaging protocol: MRI was performed by using a 1.5 Tesla magnet accompanied with dual coil mainly dedicated to the study. The patients were undergone MRI breast in the 7-14 day period of their correct menstrual cycle inorder to avoid artifacts that reduce the diagnostic sensitive. The protocol involved precontrast sequences; T2 short-tau inversion recovery in the axial plane with weighted sequencies, time 5310/ echo time 57 ms; field of view read 300; slice thickness 3.2 mm without any gap; 3D Flash non-fat saturated T1 sequences in the axial plane with weighted sequences repetition time of 7.02/TE 4.56ms; Flip angle 25, Field of view read 320; Field of phase 100; thickness 1mm. 3D gradient Recalled Echo (GRE) T1-weighted sequences were used as like postcontrast sequences in the sagittal and axial planes with single precontrast scan and rest of the consecutive scans after the contrast medium is injected. The parameters used for acquiring GRE dynamic MR images were TE/TR , 4.3/8.5, Flip angel 24; FOV 300, FOV phase 100; thickness 1mm with no gap between sections. The total time required for acquisition of 3- dimensional T1 weighed GRE dynamic sequence was 360 seconds. Contrast medium was injected by using automatic injector with the administration of gadobutrolo at a dose of 0.1mmol/kg of body weight with injection rate of 2ml/s in combination of 10ml of saline bolus.

The analysis of MR images: The obtained MR images were reported by the radiologist having 25 years of experience in breast MRI. The morphological and kinetic parameters of lesions obtained in MR images will be evaluated according to the protocol of Breast Imaging Reporting and Data System lexicon. Morphological features evaluated were; lesion size, enhancement type, necrosis presence, lymph node involvement, background parenchymal enhancement and rim enhancement. Kinetic features were peak enhancement and its signal at maximum peek, peek enhancement time, percentage of peek enhancement corresponding to Epeak obtained from the signal intensity of peak enhancement and intensity of precontrast signal by using the formula; Epeak=100x Speak–S0/S0. As washout measure signal enhancement ration was calculated by using the following formula SER= S1-S0/ S2-S0, These signals S1 and S2 represent the intensity of precontrast signal in first and second minute of contrast enhancement[9,10].

Histological data: The patients recruited were undergone a breast core-needle biopsy by using a semi-automated biopsy gun. A minimum of 4 tissue samples were obtained from each biopsy. The immunohistochemistry/ fluorescence in-situ hybridization data revealed 4 different subtypes of breast tumours with different status of ER and PgR, HER-2 and Ki67 cell proliferation rate. The positive HER-2 cases were screened by immunohistochemistry by performing in triplicates. The identified subtypes were Luminal A and Luminal B (expression of ER and PgR and Ki67 rate), TNBC (absence of hormonal receptors and HER-2) and HER2+ characterized by its positive expression and absence of hormonal receptors. [11.] The patients recruited in the study were undergone breast surgery and the characteristics of the tumour is confirmed by resection specimens.

Statistical analysis: Data obtained was tested for statistical significance by performing mean and standard deviation for qualitative as well as quantitative variables. Statistical analysis was performed by SPSS 20 for windows and $p < 0.05$ is considered as a statistically significant.

RESULTS

Among the selected patients 35 patients were included in TNBC group and 75 patients in n-TNBC group. In TNBC group, a mean lesion of 5.8 cm which was significantly higher in size than n-TNBC group was noticed in MRI scan. TNBC group exhibited low E Peak values (p=0.002) and high SER values (p=0.02). Even though the increased tumour size of TNBC group could be accounted for more SER, it was noticed that there was no significant association between TNBC group lesion size and SER values. Additionally, we could not observe any significant co-relation in between time peak and specific breast cancer subtypes. In addition to this, two groups were stratified kinetically according to tumour grade. The

60% of the patients in TNBC group presented increased tumour grade with respect to those of nTNBC group.

DISCUSSION

The results obtained from the current study suggest that the imaging and the characteristic features of triple negative breast cancer will help in pre-treatment options. There are limited reports available on dynamic imaging findings in TNBC, it generally considered as most severe subgroup representing a small number.[12]. Many reports suggest that MRI features of TNBC are differently significant from other BC immune types which may correlate with prognostic markers.[13]. Present investigation revealed that TNBC type exhibited lower BPE grade in co-ordination with n-TNBC, however in similar previous reports, it was demonstrated that TNBCs are associated with higher T2 signal intensity and enhancement of rim in comparison with n-TNBC[14]. However, in accordance with this, our results are in coordination with high intra tumoral signal intensity on T2 weighed images in TNBC as a sign of necrosis intra tumorally. The study conducted by Schmitz *et al*. found enhancement of rim in TNBC patients by MR findings was in association with increased histologic grade and triple negative cancer subtype.[15] Another study conducted by Uematsu *et al* found a hyperintensity T2 weighted images in high percentage as common findings. This is due to more cytoplasm, edematous necrosis and stroma that can be a prognostic factor in invasive BC.[16].In accordance with that, our study esults suggest high intratumoral signal intensity on T2-weighted images in TNBC as a good sign of necrosis. The difference between our study and other studies is that, they demonstrate the association of TNBCs with higher T2 signal intensity and unifocality. In our study, we documented potential correlation between TNBC and unifocal mass like enhancement. Most of the triple negative breast cancers are diagnosed to have rim enhancement which was associated with smooth margins. The study conducted by Teifke *et al* documented that rim enhancement might be the well implemented MR imaging finding for screening triple-negative breast cancer. The limitations of the present study are less sample size, hence statistical significance may not be sufficient. Therefore validation is required with large sample size. We have focussed only on semiquantitative analysis, with high resolution of breast parenchyma cells than a high temporal resolution.

CONCLUSION

We conclude from the study that contrast enhanced breast MRI with kinetic and morphological analysis may be useful in identifying histological subtype of Triple Negative Breast Cancer. Eventhough, triple negative breast cancer reduce lesions with benign morphology, early recognition of triple-negative breast cancer by using MR imaging might assist in prognosis as well as pre treatment and also to understand the behaviour of the disease biologically.

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Source of Support: None Declared
Conflict of Interest: None Declared