Assessment of early therapeutic response in locally advanced breast cancer using ADC, volume and diameter

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OBJECTIVE

To evaluate the potential of apparent diffusion coefficient (ADC), volume and diameter to predict the early therapeutic response of locally advanced breast cancer (LABC) patients undergoing neo-adjuvant chemotherapy (NACT).

INTRODUCTION

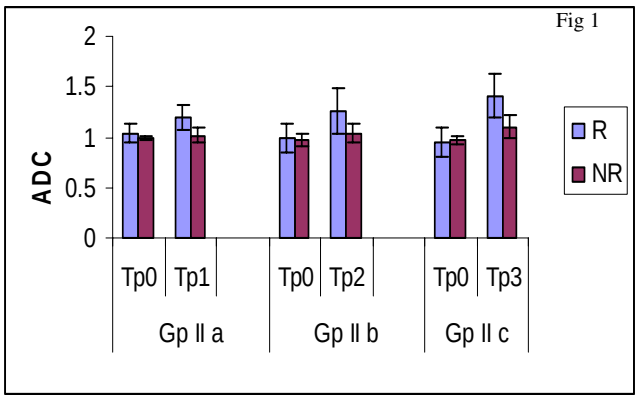
Early assessment of therapeutic response of tumor in patients with LABC undergoing NACT aids in identifying the non-responders (NR), saves them from toxicity of ineffective therapy, provides the options of initiation of second line therapy and early surgery. The ADC measured through diffusion-weighted imaging (DWI) has been recently recognized as a potential MR parameter for monitoring the treatment response of breast tumors (1-4). A relatively low sensitivity of ADC in predicting the early response of breast cancer patients to NACT compared to T2 relaxation time and water-to-fat ratio after the second cycle of chemotherapy has been reported (1). However, the same group has demonstrated that diffusion changes preceded tumor size reduction and that changes in ADC could be observed after the first cycle of NACT (2). A systematic investigation to evaluate the use of a specific parameter or combination of functional and structural parameters to detect the response as early as first cycle of NACT in clinical setting is essential. Therefore, in the present investigation we carried out sequential measurements of MR parameters like ADC, volume and longest diameter pre-therapy (Tp0) and after I (Tp1), II (Tp2) and III (Tp3) cycles of NACT in a large cohort of patients. A retrospective analysis of the percentage change in ADC, volume and diameter was also carried out in predicting the early tumor response.

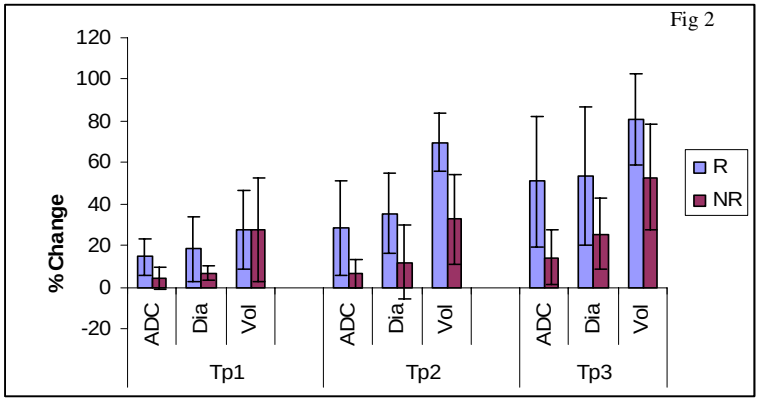
MATERIAL AND METHODS

A total of 71 women including 15 normal volunteers (Group I, mean age 31.2 ± 6.5, range 24 - 44 yrs) were studied. Fifty six patients with cytologically proven infiltrating ductal carcinoma (mean age 48.5 ± 10.6, range 25 - 75 yrs) who were scheduled to undergo NACT formed Group II. Written informed consent obtained and Institutional ethical committee approved the study. Tumor size was measured using Vernier calipers. MR investigations were performed using circularly polarized double breast array coil at 1.5 T (Sonata/Avanto, Siemens, Germany) within two weeks of NACT. Fat saturated T2- weighted images were obtained in three planes to estimate the extent and boundary of the tumor. DW images were acquired in transverse plane covering both the breasts using an EPI sequence with the diffusion gradients applied along orthogonal direction concurrently to reduce motion artifacts. The parameters used were b = 0, 500 and 1000 s/mm^2; TR = 5000 ms; TE= 87 ms; NS = 1, EPI factor =128 and acquisition matrix = 128 x 128; and slice thickness = 5 mm. To study the sequential changes in MR parameters, the patients of Group II were pooled; Group IIa: 11 patients monitored at Tp0 followed by Tp1, Group IIb: 24 patients monitored at Tp0 followed by Tp2 and Group IIc: 29 patients scanned at Tp0 followed by Tp3. A retrospective analysis of comparison of ADC value and structural parameters was carried out between clinical responders (R) and NR. Paired student t test was used to compare the pre- and post-therapy mean ADC between R and NR. A p-value < 0.05 was considered as significant. All statistical analyses were carried out using statistical software SPSS 11.5.

RESULTS

Pre-therapy mean tumor ADC was statistically lower ($p<0.001$) compared to normal breast tissue of controls. The pre-therapy ADC value showed progressive significant increase following I, II and III, NACT in clinical R compared to NR (Fig. 1). A comparison of the percentage change in ADC, volume and diameter following I, II and III NACT between R and NR showed that among the Group IIa patients, the mean percentage increase of ADC in clinical R was 14.5 ± 8.8% which was significantly higher ($p = 0.03$) compared to that observed for NR (4.3 ± 5.3%) (Fig. 2). However, the mean percentage decrease of tumor volume and diameter was statistically not significant between R and NR. In patients of Group IIb and IIc, post-therapy changes in ADC, volume and diameter were statistically significantly higher in R compared to NR (Fig. 2). The sensitivity to detect R was similar for volume and diameter (89%) with a specificity of 50% for volume and 70% for diameter after III NACT. ADC showed a sensitivity of 68% with 100% specificity. The sensitivity, specificity and accuracy, when all the three parameters were combined (taken together) was 84%, 60% and 76%, respectively.





DISCUSSION

Early prediction of tumor response is essential in treatment planning. In this study we measured both the structural parameters (tumor volume and diameter) and the functional parameter (ADC) in LABC patients. Our results indicate that pre-therapy ADC of malignant tissue was significantly lower compared to the normal breast tissue of controls which is attributed to the high cellularity present in the malignant tissue. A significant increase in ADC of tumor after I NACT compared to pre-therapy value was observed and the change was statistically significant in clinical R compared to NR. However, the mean percentage decrease after I NACT in volume and diameter was not statistically different between R and NR. Therapy induced changes in structural parameters; diameter and volume were evident only after II NACT. The specificity of differentiating R from NR after III NACT was found to be 100% for ADC compared to volume and diameter. This suggests the ability of ADC in differentiating NR from R at an early stage of therapy and the potential of DWI to become an important tool in clinical imaging to predict therapeutic response. Pickels et al have also reported similar observation (2). The progressive increase of ADC and the reduction of tumor volume in R are in agreement with the changes in the tumor physiology and morphology in response to therapy.

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