MR Imaging of Pathological Complete Response Following Neoadjuvant Chemotherapy

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Purpose

Neoadjuvant chemotherapy (NAC) is becoming an important part of treatment and management for breast cancer. Current chemo-regimens can not only allow down-staging of cancers to render them operable and/or to facilitate breast conservation surgeries but can also reach the goal of pathological complete response (pCR). pCR is agreed to be the most relevant prognostic factor in patients receiving NAC. pCR is associated with fewer local and distant recurrences as well as improved survival. At our institution we have an active on-going NAC protocol. Patients receive 2-4 cycles AC treatment (anthracycline such as doxorubicin, and cyclophosphamide) then followed by Taxane regimen, including Paclitaxel(T) or Nab-paclitaxel(Ab) with Carboplatin(Ca), with trastuzumab(Herceptin-H) for HER-2-positive patients or bevacizumab (Avastin-Av) for HER-2-negative patients. The initial study results have indicated that this protocol for HER-2-positive cancer can achieve a high pCR, and although not as high, a much improved pCR rate in HER-2-negative arm. Using MRI, patients undergoing NAC regimen present a unique opportunity to observe the change in tumor during and after treatment to assess treatment efficacy. The accuracy of MRI in diagnosing pCR after finish an aggressive chemotherapy has not been reported. The accurate diagnosis of pCR may help the oncologist to decide when to stop, and it may help select the type of surgery after chemotherapy toward more conservative procedures. This study is aimed to compare the final MRI findings with the pathology in chemotherapy patients to determine the accuracy of MRI is in diagnosing pCR. We also intended to evaluate whether HER-2 status or different chemo-regimens will affect the performance of MRI in predicting pCR.

Methods

Fifty one breast cancer patients, including 25 HER-2 positive and 26 HER-2 negative, receiving NAC were included in this study. All patients had a baseline MRI before chemotherapy, several follow-up studies during treatment, and a final MRI before surgery. The study was performed at 1.5T. Spin echo T1W sagittal and axial pre-contrast images and axial 3D SPGR dynamic contrast-enhanced images were acquired. The last MRI after finishing all chemotherapy was studied and correlated with the pathological findings after final surgery. All MR images were read by a radiologist and an imaging scientist with substantial experience reading breast MRI, reaching consensus decision. Figure 1 shows several examples. The clinical complete response (CCR) was defined as without any residual enhancement from the previous lesion site. When minimal enhancement shadow was found at the previous lesion site, which was comparable or less than the enhancement of other normal glandular tissue in the same breast, it was defined as probable CCR. Other two categories included partial response (PR) and non-response (NR). pCR was defined as no residual malignancy or with residual DCIS but without invasive cancer in the final pathological examination according to the guideline of MD Anderson. When invasive cancer cells were identified, regardless of the foci size, it was defined as non-pCR.

Results

The results are summarized in Table 1. Of the 25 HER-2 positive patients, 17 had TCaH, 7 had AbCaH and 1 had TCaH plus AbCaAv as the second regimen. Of the 26 HER-2 negative patients, 20 had TCa and 6 had AbCaAv as the second regimen. Complete clinical response on MRI (MR-CR) was identified in a total of 34 patients (35/51, 69%), including 28 patients without any enhanced lesion (CCR) and 7 patients with shadow or very mild enhancement as probable CCR. Overall, pCR was achieved in 27 patients (27/51, 53%), including 22 patients without any malignant cells and 5 patients with DCIS but without invasive component. Of the 7 probable CCR, 5 were proved to have pCR (5/7, 71%) and two had residual invasive cancer. MRI correctly diagnosed 26 pCR (26/35, 74%) but failed to detect small IDC foci in 8 patients (false negative rate 8/35, 23%). One pCR in HER-2 negative group was wrongly diagnosed as with residual disease. When comparing different study groups, 19 of 25 HER-2 positive patients (76%) and 16 of 26 HER-2 negative patients (62%) had MR-CR determined by MRI; and 18 of 25 HER-2 positive patients (72%) and 9 of 26 HER-2 negative patients (35%) reached pCR. MRI accurately diagnosed 18 of 19 pCR (95%) in HER-2 positive group and 8 of 16 pCR (50%) in HER-2 negative group. Considering chemo agents in the HER-2 positive group, five of seven with AbCaH achieved MR-CR and pCR; and 14 of 17 in TCaH group showed MR-CR and 13 of them achieved pCR. While in HER-2 negative group, MRI diagnosed 4 MR-CR in 6 patients receiving AbCaAv, and 12 MR-CR in the 20 TCa group. MRI correctly predicted one pCR (1/4, 25%) in AbCaAv which is lower than that of the TCa group (7/12, 58%). The MR prediction accuracy in different drug groups are summarized in Table 2.

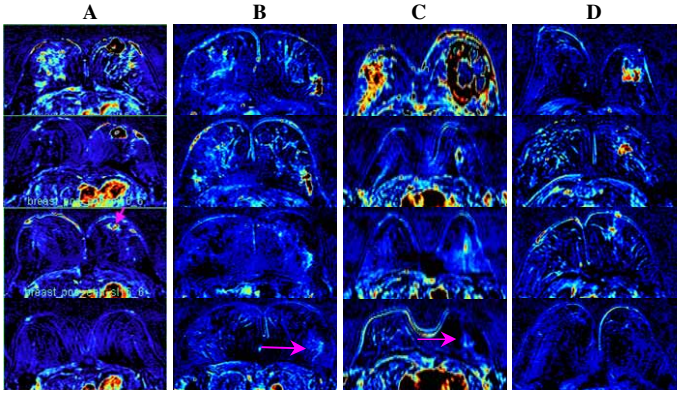

Fig. 1: Cases demonstration of MR diagnosis related to final pathologies.
A: CCR-pCR; B: Probable CCR-pCR; C: Probable CCR-pCR; D: CCR-non-pCR

Table 1. Tumor Responses Determined on MRI and pCR in HER2 +/- Patients

	CCR	Probable CCR	pCR	MR accuracy for pCR
HER2 + (N= 25)	15	4	18 (72%)	18/19 (95%)
HER2 – (N= 26)	13	3	9 (35%)	8/16 (50%)
All patients (N= 51)	28	7	27 (53%)	26/35 (74%)

Table 2. MR Prediction of Accuracy in Different Drug Groups

	MR-CR	pCR Accuracy
TCaH (N=17)	14	13/14 (93%)
AbCaH (N=7)	5	5/5 (100%)
TCa (N=20)	12	7/12 (58%)
AbCaAv (N=6)	4	1/4 (25%)

Discussions

After NAC, MR-CR rate determined on MRI was higher in HER-2 positive patients than in HER-2 negative group (76% vs. 62%). Final pathological also found HER-2 positive group had much higher pCR rate (72% vs. 35%). When minimal shadow of enhancement (probable CCR) was found in final follow-up MRI before surgery, it most probably represents pCR (5/7, 71%). MRI is an excellent imaging modality in predicting pCR (74%) especially with a high accuracy in HER-2 positive patients when compared with the HER-2 negative counterpart (95% vs. 50%). Our results showed that MRI is a reliable imaging technique in the evaluation of pCR especially for HER-2 positive patients. This might help determining the breast conservation surgery. In patients receiving avastin (AbCaAv), MRI predicted pCR less well compared to the TCa group (1/4, 25% vs. 7/12 58%). This was probably due to the reduced tumor vascularity and decreased enhancement of residual cancer with Avastin treatment. MRI was equally effective in predicting pCR for patients with AbCaH or TCaH in HER-2 positive group (5/5, 100% vs. 13/14, 93%).

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