The MRI features of the complete pathological response of locally advanced rectal cancer to neoadjuvant chemotherapy

Poster No.: C-2086
Congress: ECR 2011
Type: Scientific Paper
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Keywords: Oncology, Pelvis, MR, Diagnostic procedure
DOI: 10.1594/ecr2011/C-2086

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Purpose

Locally advanced rectal carcinoma is frequently treated with neoadjuvant chemoradiotherapy, and 10-30% have a complete pathological response (ypT0) at resection post treatment. There is clinical interest in the non-surgical management of patients with locally advanced rectal cancer who have a complete response to CRT, but no established criteria for determining a complete response on imaging.

MRI is the standard imaging technique used for the local assessment of rectal cancer before and after CRT. After chemoradiotherapy, there may be no visible abnormality at MRI: a complete radiological response (ymrT0).

The purpose of this study is to describe the pre- and post-chemoradiotherapy MRI features of ypT0 rectal tumours, and the sensitivity of ymrT0 for ypT0.

Methods and Materials

This was a retrospective study at a single institution. Between January 2005 and December 2009 all patients at our institution with locally advanced rectal cancer, who received long-course chemoradiotherapy (CRT) prior to surgical resection were identified on the histopathological archive. Twenty seven patients had a complete pathological response after CRT. One patient was excluded due to the presence of a synchronous ovarian malignancy and six patients were excluded due to incomplete MRI imaging data. 20 patients met study criteria and were included.

Terminology

As suggested by Moran et al the terms mrT, ymrT, ypT were used to mean T staging by pre-CRT MRI, post-CRT MRI and by post-CRT histopathology respectively. Complete pathological response was therefore ypT0 and complete radiological response by MRI was ymrT0.

Neoadjuvant therapy

Neoadjuvant treatment consisted of either radiation therapy alone or radiation therapy with concomitant chemotherapy. A total dose of 45Gy was delivered over 6 weeks. Chemotherapy consisted of either continuous infusion of 5-fluorouracil or a combination of fluorouracil and leucovorin calcium in radiation therapy weeks 1 and 5 or two oral
applications of capecitabine on every 1st day of the week on which radiation therapy was administered.

**MRI Imaging**

The post-treatment MRI was performed 4-6 weeks after completion of CRT. The median time between the post-CRT MRI and surgery was 49 days (range 21-154 days). MRI was performed with a 1.5T system (Signa Echospeed or Signa HDX Twinspeed, GE Medical Systems, Milwaukee, Wis., USA) with a pelvic phased-array surface coil. As part of the standardised rectal staging protocol, high spatial resolution T2-weighted fast spin-echo (SE) images were acquired (repetition time, TR = ms; echo time, TE = ms, echo train length, ETL = 16; slice thickness = 3mm; field of view, FOV = 20cm; 256x256 matrix; number of excitations, NEx = 3) in the oblique axial and oblique coronal planes, oriented perpendicular and parallel to the long axis of the segment of rectum containing the tumour.

**MRI Image Assessment**

An imaging assessment protocol was designed based on morphological criteria used by Beets-Tan and colleagues and RECIST guidelines for the assessment of primary tumour size (see Appendix 1).

Images were assessed independently by two Consultant Radiologists with 12 and 6 years experience reporting rectal MRI, respectively. Anonymized pre- and post-CRT MRI images were presented separately to each assessor in a random order. Assessors were blinded to the original MRI report and to each others’ assessment. Completed proformas were collated and discrepancies were resolved by a second review and consensus agreement.

**Response Definitions and Data Analysis (Figures 2, 3 and 4)**

Assessors were asked to measure the maximum dimensions and lateral extent of the tumour before and after CRT. They were asked to make binary decisions about whether the muscularis propria was intact and if there was extramural extension post-CRT. On the post-CRT images they were asked to estimate the percentage size reduction of any residual abnormality compared to the baseline MRI and also estimate the percentage of the residual abnormality replaced by very low T2 signal - assumed to be fibrosis at histology. Estimated tumour volume reduction was calculated as (1-(percentage fibrosis x percentage size reduction)) x 100. Maximum dimension was the greatest dimension in any plane, measured using electronic calipers. ymrT0 was defined as the absence of any detectable abnormality on post-CRT MRI. ymrT0+ was defined as the either the presence of ymrT0 or complete replacement of tumour with low T2 signal fibrosis.
Results are expressed as frequencies at which the features occurred. These are also expressed as a percentage (sensitivity). On the basis that larger tumours were a priori less likely to achieve ymrT0, subgroups based on tumour maximum length (<4cm, 4-6cm, <6cm, ≥6cm) were compared for the frequency of ymrT0. Fisher exact tests were used for subgroup comparisons, with $p<0.05$ (two-tailed) taken to be significant.

Images for this section:
APPENDIX 1: PROTOCOL FOR THE ASSESSMENT OF RECTAL CARCINOMA BY MRI AFTER NEOADJUVANT CHEMORADIOThERAPY

Rectal Cancer ypT0 Study Patient___ Assessing Radiologist:

ASSESSMENT OF PRE CRT SCAN

T-stage _____ N-stage _____

Length of primary tumour (cm)_______

Maximum lateral extension of primary tumour (mm) _____

Mucinous/non-mucinous (delete as appropriate)

ASSESSMENT OF POST CRT SCAN

Comparison made with staging MRI. Tick all boxes that apply. Circle responses as appropriate.

Definitions: 'Low T2 signal' = T2 signal equivalent to T2 muscle signal

MRI Characteristics Assessment

No visible abnormality

Tumour replaced by region of _____% uniform low T2 signal.

No extramural extension

Muscularis propria visible and not interrupted.

Any extramural extension but without surrounding distortion

Any extramural extension with surrounding distortion / retraction

Extramural extension. Indicate extension below.

Extension ______ mm beyond muscularis propria

Decrease in tumour size. Indicate approximate reduction _____%

Other descriptive features not covered above:

1.

2.

3.  

Continue overleaf as required
Fig. 1: Appendix 1: Protocol for the assessment of rectal carcinoma by MRI after neoadjuvant chemoradiotherapy

Fig. 2: T2-weighted axial MRI before and after neoadjuvant chemoradiotherapy demonstrating a mid-rectal tumour which has responded completely to treatment (y mrT0)
Fig. 3: T2-weighted axial MRI before and after neoadjuvant chemoradiotherapy demonstrating a mid-rectal tumour which has responded to treatment and has become completely fibrotic (arrow) (ymrT0+)
Fig. 4: T2-weighted coronal MRI before and after neoadjuvant chemoradiotherapy demonstrating a mid-rectal tumour which has responded to treatment but has residual regions of high signal (arrow) within the rectal wall, in keeping with residual disease. This patient had no evidence of residual tumour at histological assessment (ypT0).
Results

Patient characteristics and pre-treatment tumour characteristics

There were 20 patients included in the study, 9 female and 11 male. Median age was 67 years (range 40-84 years). There were 4 proximal rectal tumours and 7 distal rectal tumours, of which 3 involved the anorectal junction. The remaining tumours were mid-rectal. There were 2 T2 tumours, 17 T3 tumours and 1 T4 tumour. The average pre-treatment tumour length was 5.6cm. The average pre-CRT extramural extension (T3/4 tumours only) was 6mm (95% CI 3.2-12.5).

ymrT0 (Figure 1)

Seven of 20 (35%, 95% CI 18.0-56.8%) tumours were ymrT0. There was a trend for smaller ypT0 tumours to achieve ymrT0 more frequently than larger tumours: 47% (7/15, 95% CI 24.8-69.9%) tumours <6cm in maximum dimension achieved ymrT0 compared with 0% (0/5, 95% CI 0-48.9%) of tumours ≥6cm (p=0.113, FET).

Fibrotic change, size and estimated tumour volume reduction

All tumours had a good response to CRT on MRI, with at least 50% size reduction. 17/20 (85%, 95% CI 63.1-95.6%) had decreased in size by ≥75%, of which 10 (50%, 95% CI 29.9-70.1%) had decreased in size by ≥90%.

13 tumours did not achieve ymrT0 appearances. All demonstrated a degree of very low T2 signal in keeping with fibrosis. Tumour was completely replaced by a residual abnormality of very low T2 signal in 3 (15%) patients.

Muscularis propria and extramural extension

The muscularis propria was intact with no extramural extension in 14/20 (70%, 95% CI 47.9-85.7%) patients. In 6 patients there was abnormality extending extramurally to an average depth of 6mm.

Images for this section:
Fig. 1: Percentage of rectal tumours achieving ymrT0 appearances by pretreatment size
Conclusion

A proportion of rectal cancers have a complete pathological response to neoadjuvant chemoradiotherapy. MRI may be useful in identifying patients with a complete response to chemoradiotherapy, who may be amenable to non-operative management.

This study indicates that, although tumours which are ypT0 at resection show a good radiological response to chemoradiotherapy, the MRI appearances of the complete pathological response are heterogeneous. Conventional MRI complete response criteria (ymrT0) will detect ypT0 with a sensitivity of only 35%.

The heterogeneous appearances and the modest sensitivity of ymrT0 found in this study are consistent with other studies that have investigated re-staging of LARC after CRT, which have included subsets of patients achieving ypT0 have reported an accuracy of re-staging MRI of only 37-52%

It is uncertain whether rectal MRI can reliably detect patients with a complete pathological response to CRT. A prospective study to evaluate the diagnostic performance for ypT0 of the MRI features described in this study is required to establish the value of MRI tool in this setting.

References


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