

Original Research Article

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Correlation between magnetic resonance imaging-based radiological response after 8 weeks of neoadjuvant chemoradiotherapy and postoperative histopathological response in rectal adenocarcinoma

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ABSTRACT

Background: Neoadjuvant chemoradiotherapy (NACRT) is the standard of care for locally advanced rectal adenocarcinoma, facilitating tumor downstaging and improving surgical outcomes. Magnetic resonance imaging (MRI) is widely used to assess treatment response after NACRT; however, its ability to accurately predict histopathological tumor regression remains variable. Reliable radiological prediction is essential for individualized treatment planning and consideration of organ-preserving strategies.

Methods: This prospective observational study included 47 patients with mid or low rectal adenocarcinoma (≤ 12 cm from the anal verge) who received long-course NACRT followed by total mesorectal excision. Pelvic MRI performed 8 weeks post-NACRT assessed tumor response using the MRI tumor regression grade (mrTRG). Histopathological response was evaluated using the Rödel tumor regression grade (TRG) system. Correlation between mrTRG and pathological TRG was analyzed using Spearman's correlation, and the diagnostic accuracy of MRI in predicting pathological complete response (pCR) was calculated.

Results: MRI demonstrated mrTRG 1–2 in 22 patients (46.8%), mrTRG 3 in 16 (34.0%), and mrTRG 4–5 in 9 (19.1%). Histopathology revealed pCR (TRG 0) in 11 patients (23.4%). MRI correctly identified 8 of 11 pCR cases. MRI prediction of pCR showed a sensitivity of 72.7%, specificity of 85.3%, positive predictive value of 61.5%, and negative predictive value of 90.3%. A significant correlation was observed between mrTRG and pathological TRG (Spearman's $r=0.64$, $p<0.001$).

Conclusions: MRI-based assessment at 8 weeks post-NACRT demonstrates a significant correlation with histopathological response and provides reliable exclusion of complete response. Integration with clinical assessment is recommended for optimal treatment decision-making.

Keywords: Rectal cancer, Neoadjuvant chemoradiotherapy, Magnetic resonance imaging, Tumor regression grade, Pathological complete response, Radiological-histopathological correlation

INTRODUCTION

Locally advanced rectal adenocarcinoma (LARC) is commonly treated using a multimodal approach that includes neoadjuvant chemoradiotherapy followed by curative surgical resection. The rationale for administering

neoadjuvant chemoradiotherapy (NACRT) includes improving local control, enabling sphincter preservation, and achieving pathological tumor regression.^{1,2} Despite its efficacy, tumor response to NACRT varies widely. Pathological complete response (pCR), defined as the absence of viable tumor cells in the resected specimen, is

observed in 15–30% of patients and is associated with improved disease-free and overall survival.^{3,4} Magnetic resonance imaging (MRI) is considered the gold standard for local staging of rectal cancer. After NACRT, MRI is also utilized to assess treatment response. However, distinguishing residual tumor from fibrosis or mucinous changes can be challenging. The MERCURY group introduced the MRI tumor regression grade (mrTRG), which attempts to replicate histological tumor regression grading using radiological features such as signal intensity, fibrosis, and residual mass.⁵

Accurate prediction of histopathological response using MRI is essential for implementing organ-preservation strategies such as the “watch-and-wait” approach in patients showing a complete clinical response.

This study evaluates the concordance between MRI-based assessments performed 8 weeks after completion of NACRT and the final histopathological tumor regression in patients undergoing surgical resection.

METHODS

Study design and population

This prospective observational study was conducted for a period of 24 months from January, 2020 to December, 2022. The study was conducted in Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow. Following all the required approval from the Institutional Ethical Committee (IEC) of Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow.

Inclusion criteria include patients diagnosed with mid or low rectal adenocarcinoma (≤ 12 cm from anal verge) who received standardized NACRT followed by total mesorectal excision.

Sample size was calculated based on correlation analysis, assuming a moderate expected correlation coefficient ($r=0.5$) between MRI-based tumor regression grade and histopathological tumor regression grade. With a two-sided alpha of 0.05 and 80% power, the minimum required sample size was 29 patients. Accounting for possible dropouts and incomplete data, a final sample size of approximately 40-50 patients was considered adequate for the study.

MRI was performed 8 weeks after completion of chemoradiotherapy.

Exclusion criteria included prior pelvic irradiation, distant metastases, or mucinous adenocarcinoma.

Neoadjuvant treatment protocol

All patients received long-course NACRT consisting of 50.4 Gy in 28 fractions with concurrent capecitabine-based

chemotherapy. Surgery was scheduled 8–10 weeks post-NACRT.

Radiological assessment

High-resolution pelvic MRI was conducted using T2-weighted and diffusion-weighted imaging (DWI) sequences. Tumor response was evaluated using the MRI-based tumor regression grade (mrTRG), ranging from grade 1 (complete response) to grade 5 (no response). Radiological assessments were performed by two experienced radiologists blinded to pathological findings.

Histopathological evaluation

Surgical specimens were assessed by gastrointestinal pathologists using the Rödel tumor regression grade (TRG) system. TRG 0 indicated complete response (pCR), while TRG 1–3 indicated varying degrees of partial response, and TRG 4 reflected minimal or no response.

Statistical analysis

Data were analyzed using chi-square tests for categorical variables and Spearman’s correlation to evaluate the strength of association between mrTRG and pathological TRG. Sensitivity, specificity, and predictive values of MRI in detecting pCR were calculated. A $p<0.05$ was considered statistically significant.

RESULTS

Patient demographics

A total of 47 patients were included in the study. The median age was 48 years (range 32–69), with a male-to-female ratio of 2.1:1. All patients completed NACRT and underwent MRI and curative surgery.

Radiological and histopathological findings

MRI at 8 weeks showed: mrTRG 1 in 9 patients (19.1%), mrTRG 2 in 13 patients (27.7%), mrTRG 3 in 16 patients (34.0%), and mrTRG 4–5 in 9 patients (19.1%).

Histopathology showed: TRG 0 (complete response) in 11 patients (23.4%), TRG 1–2 (good response) in 19 patients (40.4%) and TRG 3–4 (poor response) in 17 patients (36.2%).

Correlation and predictive accuracy

Among the 11 patients with TRG 0, 8 were correctly identified as mrTRG 1 or 2. MRI predicted pCR with sensitivity: 72.7%, specificity: 85.3%, positive predictive value (PPV): 61.5% and negative predictive value (NPV): 90.3%.

A statistically significant correlation was observed between mrTRG and pathological TRG (Spearman’s

$r=0.64$, $p<0.001$), indicating moderate-to-strong agreement.

DISCUSSION

The accurate prediction of pathological response using post-NACRT MRI is essential for planning treatment in rectal cancer. In this study, MRI-based tumor regression grading performed 8 weeks after NACRT showed moderate to strong correlation with histopathological findings, suggesting its reliability in clinical practice.

These results align with previous studies, such as the MERCURY II trial, which demonstrated that mrTRG could reliably identify complete or near-complete responders.⁶ The high NPV observed in our study indicates that MRI is particularly effective in ruling out complete response, reducing the risk of undertreatment in surgical candidates.

However, false positives remain a limitation. In our cohort, 3 patients graded as mrTRG 1 showed residual tumor on histopathology, reflecting challenges in distinguishing fibrosis from viable tumor cells. Advanced imaging techniques such as diffusion-weighted imaging (DWI) and dynamic contrast-enhanced (DCE) MRI may improve specificity but are not universally available.

Our findings support the integration of radiological and clinical assessments, such as digital rectal examination, endoscopy, and serum markers, for more precise response evaluation. Multimodal response prediction may offer better patient selection for organ-preserving approaches, minimizing unnecessary surgical morbidity.

The timing of MRI after NACRT also influences response assessment. Performing MRI at 8 weeks, as in our protocol, allows sufficient interval for tumor regression and fibrotic maturation while remaining within the optimal window for surgery.

Limitations

Limitations of the study include a relatively small sample size and the absence of volumetric or radiomic analysis. Larger multicenter trials incorporating radiogenomic markers could further refine predictive accuracy.

CONCLUSION

This study demonstrates a significant correlation between MRI-based radiological assessment after 8 weeks of neoadjuvant chemoradiotherapy and histopathological tumor response in rectal adenocarcinoma. MRI shows good sensitivity and negative predictive value for detecting complete response, making it a valuable non-invasive tool for treatment planning. However, limitations in specificity underscore the need for integrated clinical decision-making. Future research should explore enhanced imaging modalities and composite predictive models to

improve response assessment and enable organ-preserving strategies.

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