Radiotherapy and Oncology 193 (2024) 110124

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Magnetic resonance imaging for assessment of rectal cancer nodes after chemoradiotherapy: A single center experience

Brunella Barbaro [a,*], Maria Rachele PIa Carafa [b], Laura Maria Minordi [a], Priscilla Testa [b], Giulia Tatulli [b], Davide Carano [a], Claudio Fiorillo [c], Giuditta Chiloiro [a], Angela Romano [a], Vincenzo Valentini [b], Maria Antonietta Gambacorta [a]

[a] Department of Diagnostic Imaging, Oncological Radiotherapy, and Hematology. Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy
[b] Department of Diagnostic Imaging, Oncological Radiotherapy, and Hematology. Università Cattolica del Sacro Cuore, Rome, Italy
[c] Digestive Surgery Unit, Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Rome, Italy

ARTICLE INFO

Keywords:
Locally advanced rectal cancer
Mesorectum lymph nodes
Neoadjuvant chemoradiation therapy
MRI staging
MRI restaging

ABSTRACT

Background: Accurate nodal restaging is becoming clinically more important in patients with locally advanced rectal cancer (LARC) with the emergence of organ-preserving treatment after a good response to neoadjuvant chemoradiotherapy (nCRT).
Purpose: To evaluate the accuracy of MRI in identifying negative N status (ypN0 patients) in LARC after nCRT.
Material and Methods: 191 patients with LARC underwent MRI before and 6–8 weeks after nCRT and subsequent total mesorectal excision. Short-axis diameter of mesorectal lymph nodes was evaluated on the high resolution T2-weighted images to compare MRI restaging with histopathology.
Results: 146 and 45 patients had a negative N status (ypN0) and positive N status (ypN +), respectively. On restaging MRI, the 70 % reduction in size of the largest node was associated with an area under the curve (AUC) of 0.818 to predict ypN0 stage, with a sensitivity of 93.3 % and a negative predictive value (NPV) of 95.4 %. No nodes were observed in 38 pts (37 pts ypN0 and 1 patient ypN +), with sensitivity and NPV of nodes disappearance for ypN0 stage of 93.3 % and 92.5 % respectively. A 2.2 mm cut-off in short-axis diameter was associated with an AUC of 0.83 for the prediction of ypN0 nodal stage, with sensitivity and NPV of 79,5% and 91.1 % respectively.
Conclusion: A reduction in size of 70 % of the largest limph-node on MRI at rectal cancer restaging has high sensitivity and NPV for prediction of ypN0 stage after nCRT. The high NPV of node disappearance and of a $\leq$ 2.2 mm short-axis diameter is confirmed.

Introduction

Neoadjuvant chemoradiation therapy (nCRT) regimens were initially designed with the sole purpose of downsizing/downstaging tumors in order to increase the likelihood of an R0 resection and diminish the risk of local recurrence [1]. However, the 10 %-25 % pathologic complete response (pCR) rates have led clinicians to question the utility of radical surgery itself in such cases [2,3]. Moreover, organ-preserving treatment strategies (local excision or "watch-and-wait") have recently been introduced as a potential option for patients showing a (near-) complete response to CRT [4,5]. Current guidelines recommend routine MRI for restaging of rectal cancer after nCRT [6]; MRI - together with digital rectal examination and endoscopy - can play a role in selecting the right candidates [7]. These developments increase the need for accurate radiological assessment of response. The aim of this mono-institutional retrospective study was to evaluate MRI accuracy in identifying

Abbreviations: LARC, locally advanced rectal cancer; RT, radiotherapy; CRT, chemoradiotherapy; nCRT, neoadjuvant chemoradiotherapy; AUC, area under the curve; NPV, negative predictive value; pCR, pathologic complete response; DWI, diffusion-weighted imaging; CI, confidence interval.

* Corresponding author at: Department of Diagnostic Imaging, Oncological Radiotherapy, and Hematology. Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Largo A. Gemelli, 1 00168, Rome, Italy.
E-mail addresses: brunella.barbaro@unicatt.it (B. Barbaro), lauramaria.minordi@policlinicogemelli.it (L.M. Minordi), giulia.tatulli@outlook.it (G. Tatulli), giuditta.chiloiro@policlinicogemelli.it (G. Chiloiro), Vincenzo.Valentini@unicatt.it (V. Valentini), gambacorta@policlinicogemelli.it (M.A. Gambacorta).

https://doi.org/10.1016/j.radonc.2024.110124
Received 8 August 2023; Received in revised form 14 January 2024; Accepted 30 January 2024
Available online 2 February 2024
0167-8140/

negative N status (ypN0 patients) in locally advanced rectal cancer (LARC) after nCRT.

Materials and methods

Study design and patients

Between 2009 and 2015, 191 consecutive non-metastatic patients with LARC were considered in this retrospective study. The study was part of an imaging study, approved by the local institutional review board, for which all patients provided written informed consent.

Inclusion criteria consisted of (a) biopsy-proven rectal adenocarcinoma, (b) locally advanced disease, defined on primary staging T2-weighted MRI as a cT3 tumor stage and/or positive nodal stage, (c) treatment consisting of nCRT ± followed by total mesorectal excision, and (d) staging and restaging MRI performed in our Institution.

Exclusion criteria were (a) MRI several implant artifacts; (b) staging and/or restaging MRI images not available; (c) short course radiotherapy (RT) or nCRT; (d) watch and wait or local excision approach.

The RT treatment was performed with intensity modulated radiotherapy or volumetric modulated arc therapy techniques. The total RT dose on the mesorectum in toto and at lymphatic drainage stations, depending on the stage of the disease [8] was 45 Gy/1.8 Gy die. An overdose to the tumor and the corresponding mesorectum was prescribed at 50.4 Gy with a sequential boost of 5.4 Gy/day or at 55 Gy delivered with a concomitant boost of 2.2 Gy/day with a simultaneous integrated boost approach [9]. Concomitant chemotherapy consisted of the administration of oral capecitabine at a dose of 1650 mg/s or 5-fuorouracil 250 mg/mq for 1–5 days, with or without weekly administration of oxaliplatin (50 mg/mq for 1, 8, 21, 28 days). Different schedules were used depending on the clinical presentation [10,11]. Total mesorectal excision was performed at least 8 weeks after the end of nCRT and with a median interval after restaging MRI of 15 days (range 5–20 days).

MRI protocol

The MRI protocol consisted of standard two-dimensional high-resolution fast spin-echo T2-weighted sequences, as described in literature, after enema administration of a small amount of sonography transmission gel to distend the rectum [12]. Table 1 shows MRI acquisition parameters.

Image interpretation

Two readers independently analyzed the MR images: a senior and junior gastrointestinal radiologist with 20 and 6 years of expertise in reading pelvic MRI respectively. The readers were blinded to the surgical and pathological findings.

The following parameters were evaluated: 1) the total number of lymph nodes (both potentially benign and malignant) pre- and post-CRT, 2) the short-axis diameter of each lymph node pre- and post-CRT measured on the T2-weighted images, and 3) the change in size of each node post-CRT.

The nodes were drawn on an anatomical map to ensure accurate lesion-by-lesion matching between pre-CRT and post-CRT images and were considered in ascending order according to lymph node dimensions (the largest lymph node was considered lymph node number 1). If a node had disappeared on the post-CRT MRI, this was noted (Fig. 1) as well as if a node was changed in size (Fig. 2).

Histopathology analysis

Pathological examination was performed for each patient by a pathologist subspecialized in gastrointestinal pathology, according to standard methods described by Quirke et al. [13].

The total number of positive nodes and the percentage of positive nodes were always reported. Pathological complete response (pCR) was defined as the absence of viable tumor cells in the primary tumor and lymph nodes (ypT0ypN0). It was not possible to compare every lymph node found in the post-CRT MRI with the corresponding histopathological examination because not all pathological specimens were yet available at the time of the study.

Statistical analysis

Categorical variables were presented as numbers and percentages, while quantitative variables were presented as mean ± standard deviation or medians with their interquartile interval and compared by Student's *t*-test or by non-parametric tests according to their distribution.

The capacity of the MRI of studying lymph nodes status has been evaluated using the AUC-ROC curve methods.

The significance level was set at 0.05, two-sided. Variables significant at univariate analysis for AL onset were then entered into a logistic regression model to identify independent predictors. Results were

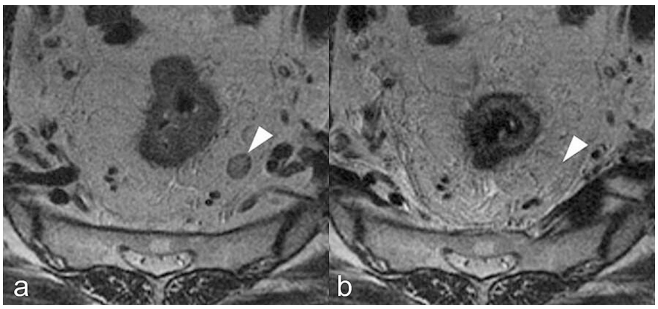

Fig. 1. 65-year-old-man with mid-rectal cancer. (**a**) HR axial T2-weighted MR image shows the largest lymph node (lymph node number 1) with 9 mm in short-axis diameter, inhomogeneous, located into the mesorectum, and indicating the potential N1 clinical stage (arrowhead). (**b**) Post-treatment axial T2-weighted MR image shows complete disappearance of the node (arrowhead). Histologic evaluation after total mesorectal excision reveals ypN0 stage.

Table 1
MRI acquisition parameters.

	Sagittal T2WI	Coronal T2WI	Axial T2WI	Axial DWI	Oblique HR T2WI
Sequence	FSE	FSE	FSE	EPI DWI	FSE
Matrix	256 × 256	256 × 256	256 × 256	128 × 128	256 × 256
TR (ms)/TE (ms)	2.500–5.000/100	2.500–5.000/100	2.500–5.000/100	> 8.000/minimum	2.500–5.000/100
ETL	16	16	16	–	16
Acquired signals	4	4	4	8	4
Field of view (cm)	24	24	30	30	18
Slice thickness (mm)	3	3	4	4	3
Intersection gap (mm)	0.3	0.3	0	0	0

Note. - Oblique axial and coronal T2 weighted images (WI) were oriented perpendicular and parallel to the rectal tumor axis respectively. TR = repetition time, TE = echo time, ETL = echo train length, FOV = field of view, FSE = fast spin echo, EPI = echo planar imaging, DWI = diffusion weighted imaging.

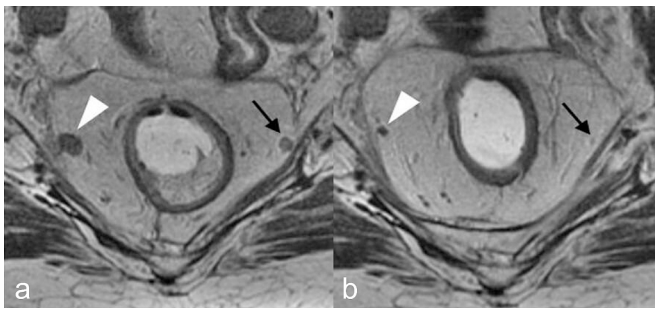

Fig. 2. 56-year-old-woman with low-rectal cancer. (**a**) HR axial T2-weighted MR image shows the largest lymph node (lymph node number 1) with 7 mm in short-axis diameter, inhomogeneous, ill-defined in the right mesorectum (arrowhead). The lymph node abuts the mesorectal fascia laterally, indicating the potential N1 clinical stage. Note a smaller lymph node with 5 mm in short-axis, in the left mesorectum (arrow). **(b)** Post-treatment axial T2-weighted MR image demonstrates that the largest node shows 71 % reduction in size, 2 mm in short-axis, and moves away from the mesorectal fascia (arrowhead). The other smaller lymph node in the left mesorectum shows 80 % reduction in size, and 1 mm in short axis (arrow). Histologic evaluation after total mesorectal excision reveals ypN0 stage.

expressed as odds ratio with a 95 % confidence interval (CI). All data were analyzed by SPSS v25® (IBM, IL, USA).

Results

The study population consisted of 191 patients, 123 (65 %) men and 68 (34 %) women. 146 patients had a ypN0 status, of whom 36 were ypT0, and 45 patients had a ypN +. Table 2 shows the distribution of patients with ypN among age, sex, different tumor pre-therapeutic cTN stage and response groups, yTN stage.

A total number of 532 positive nodes were identified at pre-CRT imaging, of which 353 (66.4 %) could be matched with the post-CRT MR images and 179 (33.6 %) were no longer visible (93.8 % ypN0 and 6.2 % ypN + patients, respectively). The total number of nodes per patient before and after CRT was significantly different ($p < 0.01$) between ypN0 patients (398 nodes before CRT, and 230 nodes after CRT) and ypN + patients (134 nodes before CRT, and 123 nodes after CRT), with a disappearance percentage of 42 % and 8 % respectively.

In 38 patients, no nodes were observed at MRI restaging, which was concordant with a ypN0 status at the histopathologic examination in 37 patients (1 patient was ypN1 status), thus sensitivity and negative predictive value (NPV) were 93.3 % and 92.5 % respectively.

Patients with ypN0 stage had a mean pre- and post-CRT size of 4.9 mm (±1.4, range 1–11 mm) and 1.58 mm (±1.83 range 0.9–3 mm) respectively; ΔLN size score 3.51 mm ($p < 0.01$).

Patients with ypN + stage had a mean pre- and post-CRT size of 5.86 mm (±1.83 mm, range 2.2–16 mm) and 3.21 mm (range 2.6—16 mm) respectively; ΔLN size score 2.27 mm ($p < 0.01$). Patients with positive nodal stage at histology (ypN +) had significantly larger lymph nodes, both before and after CRT, than patients with negative pathologic nodal stage (ypN0) ($p < 0.05$ before CRT and $p < 0.01$ after CRT).

After CRT, nodes size was associated with an AUC of 0.83 ($p < 0.01$) for prediction of ypN0 nodal stage, with optimal corresponding sensitivity and NPV of 79.5 % and 91.1 %, respectively, with a 2.2 mm cut-off in short-axis dameter (Fig. 3).

There was a significant difference ($p < 0.01$) of change in size on pre- and post-CRT MRI in ypN0 patients (69.01 % ±24.7) and ypN + patients (40.75 % ±17.13). The NPV and sensitivity of the decrease in size of at least 70 % for local LN MRI re-staging were 95.9 % and 93.3 % respectively. Comparing the mean size for the largest node for every patient, there was a significant difference ($p < 0.01$) between the ypN + group and the ypN0 group; a reduction in size of 70 % of the largest node was associated with an AUC of 0.818 ($p < 0.01$) for prediction of ypN0 stage with optimal corresponding sensitivity of 93.3 % and NPV of 95.4 %, respectively (Fig. 4).

Discussion

MR is currently the reference standard imaging modality in restaging neoadjuvant-treated rectal cancer, both for the primary tumor and the lymph nodes restaging [4,14–17]. MRI, endoscopic procedure, and rectal digital palpation are mandatory to confirm luminal complete response. Maas et al. [7] showed that when endoscopy, T2-weighted MR imaging and diffusion weighted imaging (DWI) all indicate that a tumor has responded completely, the chance for a true complete response was 98 %, but for lymph node restaging there is no other available modality proven better than MRI [18,19].

While in primary lymph node MRI staging, dimensional criteria are unreliable and the addition of morphologic criteria can increase accuracy [16,20], several studies [21,22] have demonstrated that the

Table 2
Distribution of patients with ypN among age, gender, different tumor pre-therapeutic cTN stage and response groups, yTN stage.

	All (n = 191)	ypN0 (n = 146)	ypN+ (n = 45)
Mean age/(range)	63 (26–83)	63 (26–81)	63 (28–83)
Male patients (%)	123 (65 %)	98 (67 %)	25 (56 %)
cT1	0	0	0
cT2	11	9	2
cT3	119	90	29
cT4	61	47	14
cN0	7	6	1
cN1	61	48	13
cN2	123	92	31
ypT0	38	36	2
ypT1	8	7	1
ypT2	60	51	9
ypT3	78	48	30
ypT4	7	4	3
ypN0	146	146	0
ypN1	37	0	37
ypN2	8	0	8

Note. cT = clinical T-stage; cN = clinical N-stage; ypT = pathologic T-stage; ypN = pathologic N-stage.

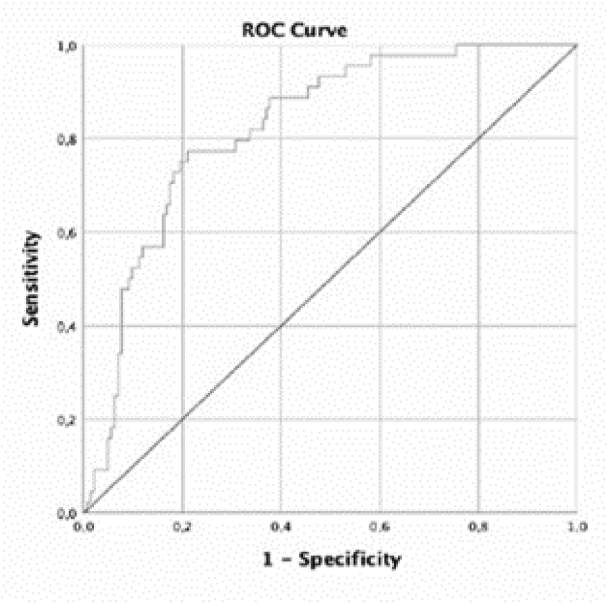

Fig. 3. AUC of 0.83 ($p < 0.01$) for prediction of ypN0 nodal stage with a 2.2 mm cut-off size.

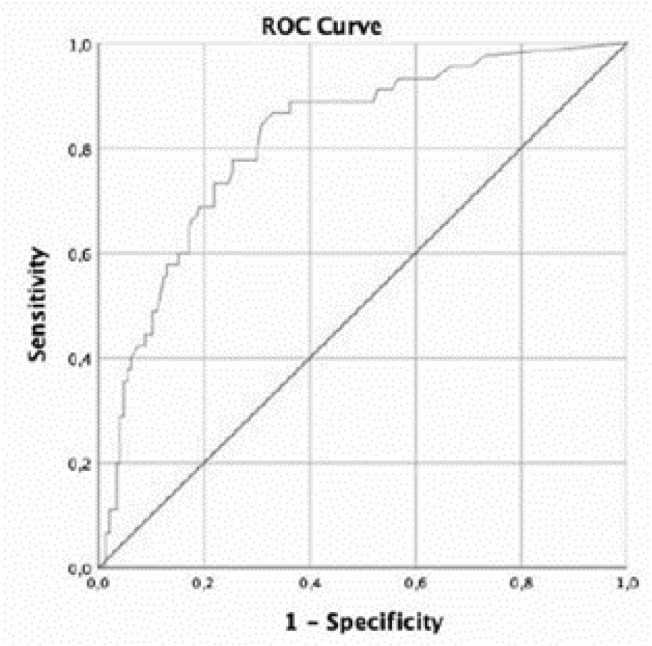

Fig. 4. AUC of 0.818 ($p < 0.01$) for prediction of ypN0 nodal stage with a percent change in size of 70 % of the largest node.

accuracy and mainly the sensitivity for the N staging, using the size criteria, increase in the N restaging due to the prevalence of the dramatical reduction of malignant nodes after CRT. A possible explanation for such better performance of size criteria after CRT is that the size and number of lymph nodes harvested after CRT are reduced [21], decreasing the potential for interpretation errors in the remaining small lymph nodes [22]. This increases confidence in predicting the yN stage setting compared to primary staging.

The use of DWI-MRI is not useful for the discrimination between benign and malignant nodes, but can be very useful to detect nodes [23]. An article by van Heeswijk et al. [24] showed that the absence of nodes on DWI after CRT is a sign of ypN0 (sensitivity and NPV of 100 % respectively), but this study was underpowered with only 10 patients (11 %) presenting with absence of nodes after CRT on DWI.

In our experience, in 38 patients no nodes were observed at T2-weighted MRI restaging, which was concordant with a ypN0 status at the histopathologic examination in 37 patients. Thus, our study showed that the sensitivity and NPV of nodes disappearance on T2-weighted MRI was high (93.3 % and 92.5 % respectively) as a sign of ypN0.

Given the small size of nodes after CRT, morphology can be difficult to evaluate and for practical purposes a consensus guideline from the European Society of Gastrointestinal and Abdominal Radiology [6] proposed to use a 5 mm short-axis diameter as the cut-off.

A crucial prognostic factor for rectal cancer is the involvement of lymph nodes [25,26]. The possibility of complete response on the primary tumor and persistence of lymph node disease, thus a yT0N + stage, should be emphasized. Disappearance in the local rectal neoplasm should not be interpreted as disappearance of disease, given the correlation between persistence of positive mesorectal lymph nodes and occurrence of distant metastases. In a retrospective study of 80 patients, Almlov et al. [27] showed indeed a significant correlation between mesorectal residual nodes with $\geq$ 5 mm in short-axis diameter after neoadjuvant therapy, and the appearance of metachronous metastases (87 % vs 65 %, $p = 0.02$). In our experience, we had two patients with complete T response (pT0) who still had a positive lymph node in the mesorectum (pN1), data taken into account for subsequent management of the patient.

Since 2007, Koh et al. [28] showed that thin-section (3-mm) high-spatial resolution T2-weighted MR images can be a useful tool for assessing nodal response to neoadjuvant treatment. In our experience, a short-axis of 2.2 mm cut-off diameter was associated with an AUC of 0.83 for prediction of ypN0 nodal stage, with optimal corresponding sensitivity and NPV of 79.5 % and 91.1 %, respectively, better than previous results reported by Heijnen et al. [29] in which a short-axis of 2.5 mm was associated with an AUC of 0.78 with corresponding sensitivity and specificity of 75 % and 64 %, respectively.

Pomerri et al. [30] found that using a cut-off value of a 70 % lymph node global size reduction rate, the sensitivity and NPV in the prediction of nodal status were 93 % (95 % CI, 70.2 %-98.8 %) and 97 % (95 % CI, 82.9 %-99.8 %) for observer 1 and 100 % (95 % CI, 79.6 %-100 %) and 100 % (95 % CI, 62.9 %-100 %) for observer 2. Thus, the authors suggested that the lymph node global size reduction rate value reduces the risk of undetected nodal metastases.

In our experience, the NPV and sensitivity of the decrease in size at least 70 % for local LN MRI restaging were 95.9 % and 93.3 % respectively.

Measuring the short-axis of all lymph nodes pre- and post-CRT can be time-consuming and non– reproducible but, as far as we know, we were the first to verify that a 70 % reduction in size of the largest lymph node was associated with an AUC of 0.818 for prediction of ypN0 stage, with optimal corresponding sensitivity (93.3 %) and NPV (95.4 %).

Our study had some limitations. First, it was a single-center retrospective study. Additionally, the lateral lymph nodes were not investigated because of the impossibility to verify the histology, however when involved there was an important influence on the long-term outcomes [31].

In conclusion, we found that a 70 % reduction in size of the largest node on MRI at rectal cancer restaging has high sensitivity and NPV for prediction of ypN0 stage after CRT. Furthermore, the study confirmed the high NPV of node disappearance as well as of a $\leq$ 2.2 mm in short-axis diameter.

CRediT authorship contribution statement

Brunella Barbaro: Conceptualization, Supervision, Writing – original draft, Writing – review & editing, Investigation, Methodology, Validation, Visualization. **Maria Rachele PIa Carafa:** Conceptualization, Writing – original draft. **Laura Maria Minordi:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Priscilla Testa:** Data curation, Writing – original draft, Writing – review & editing. **Giulia Tatulli:** Data curation, Writing – original draft, Writing – review & editing. **Davide Carano:** Data curation, Visualization, Writing – original draft, Writing – review & editing. **Claudio Fiorillo:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Giuditta Chiloiro:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Angela Romano:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Vincenzo Valentini:** Conceptualization, Supervision, Validation, Writing – original draft, Writing – review & editing. **Maria Antonietta Gambacorta:** Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Lambregts DMJ, Boellaard TN, Beets-Tan RGH. Response evaluation after neoadjuvant treatment for rectal cancer using modern MR imaging: a pictorial review. Insights Imaging 2019;10:15. https://doi.org/10.1186/s13244-019-0706-x.

[2] López-Campos F, Martín-Martín M, Fornell-Pérez R, García-Pérez JC, Die-Trill J, Fuentes-Mateos R, et al. Watch and wait approach in rectal cancer: Current controversies and future directions. World J Gastroenterol 2020;26:4218–39. https://doi.org/10.3748/wjg.v26.i29.4218.
[3] Macchia G, Gambacorta MA, Masciocchi C, Chiloiro G, Mantello G, di Benedetto M, et al. Time to surgery and pathologic complete response after neoadjuvant chemoradiation in rectal cancer: A population study on 2094 patients. Clin Transl Radiat Oncol 2017;4:8–14. https://doi.org/10.1016/j.ctro.2017.04.004.
[4] van der Valk MJM, Hilling DE, Bastiaannet E, Meershoek-Klein Kranenbarg E, Beets GL, Figueiredo NL, et al. Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study. Lancet (London, England) 2018;391:2537–45. https://doi.org/10.1016/S0140-6736(18)31078-X.
[5] Chiloiro G, Meldolesi E, Giraffa M, Capocchiano ND, Barbaro B, Coco C, et al. Could the conservative approach be considered safe in the treatment of locally advanced rectal cancer in case of a clinical near-complete or complete response? A retrospective analysis. Clin Transl Radiat Oncol 2021 Feb;25:1–9. https://doi.org/10.1016/j.ctro.2021.02.009.
[6] Beets-Tan RGH, Lambregts DMJ, Maas M, Bipat S, Barbaro B, Curvo-Semedo L, et al. Magnetic resonance imaging for clinical management of rectal cancer: Updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting. Eur Radiol 2018;28:1465–75. https://doi.org/10.1007/s00330-017-5026-2.
[7] Maas M, Lambregts DMJ, Nelemans PJ, Heijnen LA, Martens MH, Leijtens JWA, et al. Assessment of clinical complete response after chemoradiation for rectal cancer with digital rectal examination, endoscopy, and MRI: Selection for organ-saving treatment. Ann Surg Oncol 2015;22:3873–80. https://doi.org/10.1245/s10434-015-4687-9.
[8] Valentini V, Gambacorta MA, Barbaro B, Chiloiro G, Coco C, Das P, et al. International consensus guidelines on clinical target volume delineation in rectal cancer. Radiother Oncol 2016;120:195–201. https://doi.org/10.1016/j.radonc.2016.07.017.
[9] Caravatta L, Lupattelli M, Mantello G, Gambacorta MA, Chiloiro G, Tommaso DI, et al. Gastrointestinal Study Group of AIRO (Italian Association of Radiation Oncology and Clinical Oncology). Treatment volume, dose prescription and delivery techniques for dose-intensification in rectal cancer: A national survey. Anticancer Res 2021 Apr;41:1985–95. https://doi.org/10.21873/anticanres.14966.
[10] Rödel C, Graeven U, Fietkau R, Hohenberger W, Hothorn T, Arnold D, et al. German Rectal Cancer Study Group. Oxaliplatin added to fluorouracil-based preoperative chemoradiotherapy and postoperative chemotherapy of locally advanced rectal cancer (the German CAO/ARO/AIO-04 study): final results of the multicentre, open-label, randomised, phase 3 trial. Lancet Oncol 2015 Aug;16:979–89. https://doi.org/10.1016/S1470-2045(15)00159-X.
[11] Comella P. A review of the role of capecitabine in the treatment of colorectal cancer. Ther Clin Risk Manag. 2007 Jun;3:421-31. PMID: 18488072; PMCID: PMC2386354.
[12] Barbaro B, Vitale R, Leccisotti L, Vecchio FM, Santoro L, Valentini V, et al. Restaging locally advanced rectal cancer with MR imaging after chemoradiation therapy. Radiographics 2010 May;30:699–716. https://doi.org/10.1148/rg.303095085.
[13] Quirke P, Durdey P, Dixon MF, Williams NS. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumour spread and surgical excision. Lancet (London, England). 1986;2:996-99. doi:10.1016/s0140-6736(86)92612-7.
[14] Qureshi PAAA, Aleem J, Mushtaq N, Noor MA, Khalid Niazi I, Altaf MO. Role of diffusion-weighted imaging in the evaluation of post-treatment tumor response in rectal carcinoma. Cureus 2021;13:e17471.
[15] Moreno CC, Sullivan PS, Mittal PK. MRI Evaluation of Rectal Cancer: Staging and Restaging. Curr Probl Diagn Radiol 2017;46:234–41. https://doi.org/10.1067/j.cpradiol.2016.11.011.
[16] Kalisz KR, Enzerra MD, Paspulati RM. MRI Evaluation of the Response of Rectal Cancer to Neoadjuvant Chemoradiation Therapy. Radiogr a Rev Publ Radiol Soc North Am Inc. 2019;39:538-56. doi:10.1148/rg.2019180075.
[17] Lambregts DMJ, Vandecaveye V, Barbaro B, Bakers FCH, Lambrecht M, Maas M, et al. Diffusion-weighted MRI for selection of complete responders after chemoradiotherapy for locally advanced rectal cancer: a multicenter study. Ann Surg Oncol 2011;18:2224–31. https://doi.org/10.1245/s10434-011-1607-5.
[18] Maretto I, Pomerri F, Pucciarelli S, Mescoli C, Belluco E, Burzi S, et al. The potential of restaging in the prediction of pathologic response after preoperative chemoradiotherapy for rectal cancer. Ann Surg Oncol 2007;14:455–61. https://doi.org/10.1245/s10434-006-9269-4.
[19] Perez RO, Habr-Gama A, Gama-Rodrigues J, Proscurshim I, Julião GPS, Lynn P, et al. Accuracy of positron emission tomography/computed tomography and clinical assessment in the detection of complete rectal tumor regression after neoadjuvant chemoradiation: long-term results of a prospective trial (National Clinical Trial 00254683). Cancer 2012;118:3501–11. https://doi.org/10.1002/cncr.26644.
[20] Zhuang Z, Zhang Y, Wei M, Yang X, Wang Z. Magnetic resonance imaging evaluation of the accuracy of various lymph node staging criteria in rectal cancer: A systematic review and meta-analysis. Front Oncol 2021;11:709070. https://doi.org/10.3389/fonc.2021.709070.
[21] Engelen SME, Beets-Tan RGH, Lahaye MJ, Lammering G, Jansen RL, van Dam RM, et al. MRI after chemoradiotherapy of rectal cancer: a useful tool to select patients for local excision. Dis Colon Rectum 2010;53:979–86. https://doi.org/10.1007/DCR.0b013e3181dc64dc.
[22] Seo N, Kim H, Cho MS, Lim JS. Response assessment with MRI after chemoradiotherapy in rectal cancer: Current evidences. Korean J Radiol 2019;20:1003–18. https://doi.org/10.3348/kjr.2018.0611.
[23] Schurink NW, Lambregts DMJ, Beets-Tan RGH. Diffusion-weighted imaging in rectal cancer: current applications and future perspectives. Br J Radiol 2019;92:20180655. https://doi.org/10.1259/bjr.20180655.
[24] van Heeswijk MM, Lambregts DMJ, Palm WM, Hendriks BM, Maas M, Beets GL, et al. DWI for assessment of rectal cancer nodes after chemoradiotherapy: is the absence of nodes at DWI proof of a negative nodal status? AJR Am J Roentgenol 2017;208:W79–84. https://doi.org/10.2214/AJR.16.17117.
[25] Borgheresi A, De Muzio F, Agostini A, Ottaviani L, Bruno A, Granata V, et al. Lymph nodes evaluation in rectal cancer: Where do we stand and future perspective. J Clin Med 2022;11. https://doi.org/10.3390/jcm11092599.
[26] Gu C, Yang X, Zhang X, Zheng E, Deng X, Hu T, et al. The prognostic significance of MRI-detected extramural venous invasion, mesorectal extension, and lymph node status in clinical T3 mid-low rectal cancer. Sci Rep 2019;9:12523. https://doi.org/10.1038/s41598-019-47466-0.
[27] Almlöv K, Woisetschläger M, Loftås P, Hallböök O, Elander NO, Sandström P. MRI lymph node evaluation for prediction of metastases in rectal cancer. Anticancer Res 2020;40:2757–63. https://doi.org/10.21873/anticanres.14247.
[28] Koh DM, Chau I, Tait D, Wotherspoon A, Cunningham D, Brown G. Evaluating mesorectal lymph nodes in rectal cancer before and after neoadjuvant chemoradiation using thin-section T2-weighted magnetic resonance imaging. Int J Radiat Oncol Biol Phys 2008 Jun 1;71:456–61. https://doi.org/10.1016/j.ijrobp.2007.10.016. Epub 2007 Dec 31 PMID: 18164860.
[29] Heijnen LA, Maas M, Beets-Tan RG, Berkhof M, Lambregts DM, Nelemans PJ, et al. Nodal staging in rectal cancer: why is restaging after chemoradiation more accurate than primary nodal staging? Int J Colorectal Dis 2016;31:1157–62. https://doi.org/10.1007/s00384-016-2576-8.
[30] Pomerri F, Crimì F, Veronese N, Perin A, Lacognata C, Bergamo F, et al. Prediction of N0 irradiated rectal cancer comparing MRI before and after preoperative chemoradiotherapy. Dis Colon Rectum 2017;60:1184–91. https://doi.org/10.1097/DCR.0000000000000894.
[31] Ogawa S, Itabashi M, Inoue Y, Ohki T, Bamba Y, Koshino K, et al. Lateral pelvic lymph nodes for rectal cancer: A review of diagnosis and management. World J Gastrointest Oncol 2021;13:1412–24. https://doi.org/10.4251/wjgo.v13.i10.1412.