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Review Article

How Do MRI Findings Influence Rectal Cancer Management?

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Abstract

Treatment of rectal cancer is currently guided by the need to reduce local recurrence, improve survival, reduce treatment-related toxicity, and improve the patient's quality of life (QoL). Magnetic resonance imaging (MRI) scan is now the imaging modality of choice for rectal cancer. However, the role of MRI in rectal cancer has transformed beyond describing the local stage of cancer to becoming a tool to predict the prognosis of a patient by its ability to detect features associated with a high risk of recurrence and poor survival. This greatly helps the multidisciplinary team (MDT) responsible for treating patients with rectal cancer to stratify them based on the potential for recurrence and decide on the need for and type of preoperative treatment to be offered. MRI also has the ability to assess the response to such treatments, based on which the MDT can tailor the subsequent treatment. This has the potential to spare the patient from unnecessary treatment, thus improving the QoL. MRI provides a roadmap to the surgeon while planning the surgery. In this review, we give a brief overview of the current management strategies for rectal cancer and highlight the role of MRI in the decision-making process.

Keywords

- magnetic resonance imaging
- rectal cancer
- multidisciplinary team
- neoadjuvant treatment

Introduction

Colorectal cancers are the third most common cancer and the second leading cause of cancer-related deaths worldwide.[1] The management of rectal cancer has evolved over the years from only surgery to a multimodal treatment comprising surgery, radiation, and chemotherapy, central to which is the role of the multidisciplinary team (MDT) comprising surgeons, oncologists, and radiologists besides other ancillary specialists. Implementing an MDT approach to rectal cancer management has led to improved decision-making and better delivery of evidence-based care, thus reducing local recurrence and improving overall survival (OS).[2,3] A high-resolution magnetic resonance imaging (MRI) scan of the pelvis is currently the recommended imaging modality for local staging of rectal cancer, while an endorectal ultrasound may be considered in early superficial lesions considered for local excision where it may score over MRI or when an MRI is contraindicated.[4–6] The role of MRI in rectal cancer is not limited to assessing the local invasion of tumors into surrounding structures, but it also helps determine the presence of risk factors associated with recurrence, and in restaging after neoadjuvant treatment, all of which help the MDT to determine the treatment strategy.[4–6] The radiologist reporting rectal cancer MRI, therefore, needs to be familiar with the requirements and expectations of the MDT. In this review, we describe the current treatment strategies for treating rectal cancer, MRI-based risk stratification of rectal cancer, integrating the MRI-derived information into management algorithms, and the importance of a structured reporting of MRI in rectal cancer.

Management of Rectal Cancer

The evolution of treatment for rectal cancer has been shaped not only by the need to reduce locoregional recurrence (LRR)

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and distant metastasis, thereby improving the survival, but also, more lately, by patient preference for organ preservation, the need to reduce treatment-related toxicity, and improve the quality of life of the patient. The introduction of total mesorectal excision (TME) surgery and the use of postoperative (adjuvant) or preoperative (neoadjuvant) pelvic radiation with or without chemotherapy has resulted in excellent local control rates of 90 to 95%.[7–16] The standard of care for most patients with locally advanced rectal cancer (clinical T3–T4 and/or node positive) in the first decade of the millennium was neoadjuvant long course chemoradiation (LCRT) or short course radiation (SCRT) followed by TME and adjuvant chemotherapy. The second decade of the millennium, however, saw a shift in the management of rectal cancer from a stage-wise to a risk-adapted approach especially in Europe.[4] The MDT, aided by the findings on MRI, is now able to stratify patients into those at a high risk of recurrence who would benefit from neoadjuvant treatment including total neoadjuvant treatment (TNT) and those at a low risk of recurrence who may be treated with upfront surgery.[17–19]

The Role of MRI in Identifying Risk Factors in Rectal Cancer

There are many pathological factors that predict the oncological outcomes after treatment for rectal cancer for which a radiological counterpart exists. The various prognostic factors in rectal cancer, the ability to identify them on MRI, the prognostic value of identifying them on MRI, and the implications of identifying these factors on the treatment are described in the following sections.

Tumor Stage and Depth of Invasion Beyond Muscularis Propria

The depth of extramural extension (EME) of rectal cancer is an independent prognostic indicator[20,21] leading to heterogeneity in the survival among patients with T3 cancer. The 5-year survival rate of patients with pathological EME greater than 5 mm compared to $\leq$5 mm was 54 versus 85%, respectively, after upfront surgery and 47 versus 73% after neoadjuvant LCRT.[21,22] The magnetic resonance imaging and rectal cancer European equivalence (MERCURY) study demonstrated that MRI and histopathologic assessments of tumor spread were considered equivalent to within 0.5 mm, thereby validating MRI as a method of accurate preoperative prognostication using depth of extramural spread.[23] While a T3 tumor is generally considered an indication for neoadjuvant radiation, patients with MRI-predicted T3a/T3b tumors (<5 mm spread from the muscularis propria) and MRI-predicted safe circumferential resection margin (CRM) treated with surgery alone were shown to have a positive CRM rate of only 4.9%, LRR of 1.7%, and 5-year disease-free survival (DFS) of 81%, thereby successfully avoiding radiation in this group of patients.[24,25] Hence, T3 tumors can now be divided into low-risk (T3a/b and uninvolved mesorectal fascia [MRF] or high-risk (T3c/d and/or involved MRF) on the MRI, which will help the MDT to decide on the need for neoadjuvant treatment.

Mesorectal Nodal Stage

Patients with metastasis to $\leq$3 mesorectal nodes (N1) have a good prognosis after a TME surgery, while those with $\geq$4 nodes (N2) have a worse prognosis.[26] In addition, patients with N2 disease have other associated poor prognostic factors like extramural venous invasion (EMVI), and a higher T stage. While traditionally the accuracy of nodal staging using an MRI was low, with the use of high-resolution MRI and additional characteristics other than size, like the mixed signal intensity, shape, and irregular borders, the sensitivity and specificity of nodal staging has improved to 80 to 85%.[6,27–31]

Mesorectal Fascia Involvement

Pathological involvement of the CRM after a TME, defined as tumor $\leq$1 mm from the inked lateral resection margin, is one of the strongest predictors of LRR, metastasis, and poor survival.[32–35] The MRI can clearly delineate and predict the involvement of the MRF, which is the radiological counterpart to the potential pathological CRM, with a negative predictive value of 93 to 98% on baseline MRI and an accuracy of 94% on restaging MRI after LCRT.[36–39] The prognostic value of MRI-determined involvement of the MRF on LRR and survival has been shown by many studies including the MERCURY study in which the 5-year OS in patients with uninvolved versus involved MRF was 62.2 versus 42.2%, respectively, with a three- to fourfold increase in the LRR in the latter group.[40,41] Preoperative assessment of CRM status using high-resolution MRI is in fact superior to the American Joint Committee on Cancer TNM-based criteria for assessing risk of LRR, DFS, and OS.[40] One of the most important functions of the rectal cancer MDT is to prevent a positive CRM after surgery, and therefore, knowledge of the potential for CRM involvement can help the MDT to decide on the need for neoadjuvant radiotherapy,

Extramural Venous Invasion

Involvement of the veins beyond the muscularis propria is an independent risk factor for local and distant metastasis and poor survival.[42–44] MRI is an accurate and reproducible imaging modality for identifying EMVI in primary staging as well as restaging scans.[45–48] There is a moderate to strong correlation between MRI-identified EMVI (mrEMVI) and pathologic EMVI with mrEMVI scores of 3 to 4 in vessels $\geq$3 mm having a specificity of 88 to 94%.[46,49,50] Presence of mrEMVI is associated with worsened survival outcomes,[45,49–53] confers a four- to fivefold increased risk of synchronous or metachronous metastases[54] and supersedes clinical TNM staging in prognostic accuracy.[55] Moreover, the severity of mrEMVI score and the size of the involved vessels have been found to correlate with response to neoadjuvant LCRT and DFS.[50,53,56,57] Nearly 25 to 50% of patients with a baseline mrEMVI-positive status can be converted to mrEMVI-negative status after neoadjuvant LCRT[56–58] and MRI can be a useful imaging biomarker to assess the effectiveness of the neoadjuvant treatment. An improved 3-year DFS and lower recurrence rates have been observed in patients who, after neoadjuvant LCRT, show greater than

50% fibrosis in a previously detected EMVI compared to those with less than 50% fibrosis (88 vs. 46% and 9 vs. 44,% respectively).[57] Regression of mrEMVI post neoadjuvant CRT confers a similar low rate of distant metastasis as that of a baseline mrEMVI negative status while a persistent positive mrEMVI has a worse prognosis.[48,58] In light of its prognostic significance, EMVI identification in a primary staging MRI or its persistence after neoadjuvant radiation CRT may necessitate aggressive neoadjuvant treatment protocols.

Tumor Deposits

Extranodal tumor deposits (TD) are nodules of tumor cells within the mesorectum discontinuous from the primary tumor and its presence portend a poor prognosis with increasing size (>12 mm) and number (≥3) having the worst prognosis.[59] Seen in around 20% of patients with rectal cancer, the negative effects of TDs on survival are stronger than those of both lymph node metastasis (LNM) and EMVI.[59] MRI can reliably identify TDs, which are seen as nodules with irregular margins often located along the vessels.[60] Positive mrTD/mrEMVI has been shown to have a greater prognostic accuracy than the current clinical TNM staging in rectal cancer.[55] Patients with baseline mrTD-positive status who respond to neoadjuvant LCRT and become ymrTD negative have similar outcomes to baseline mrTD-negative patients.[55] This suggests that identifying TD in the primary staging MRI can help the MDT to decide on an aggressive neoadjuvant treatment protocol to induce regression of the TD and EMVI.

Lateral Pelvic Node

Metastasis to the lateral pelvic nodes (LPNs) can occur in 16 to 23% of T3–T4 low rectal cancer[61,62] and account for at least 50% of lateral local recurrences (LLRs), which are the most common form of LRR after surgery for rectal cancer.[63–65] Nearly 30 to 40% of patients with an LPN with short-axis diameter (SAD) greater than 10 mm on baseline MRI have an LLR within 5 years after neoadjuvant radiation and TME.[64,66] Internal iliac node enlargement is associated with an increased risk of LLR, whereas obturator nodes are associated with increased risk of distant metastasis and reduced survival.[66]

Clinically suspicious LPNs, defined as those located in the internal iliac or obturator compartment with SAD ≥7 mm on MRI, are seen in around 16% of patients with rectal cancer.[65,67,68] The Lateral Lymph Node Consortium study showed that in the presence of an LPN with ≥7 mm SAD on primary MRI, if after (chemo)radiotherapy a lateral pelvic node dissection (LPND) was performed along with TME, the LLR was 5.7% compared to 19.5% if the LPND was omitted.[65] This consortium later reported that following neoadjuvant (chemo)radiation. The 5-year LLR was 0, 53, and 8% in patients in whom the LPN had shrunk to ≤4 mm on restaging MRI and underwent TME alone, those with persistent LPN greater than 4 mm who underwent only TME, and those with persistent LPN greater than 4 mm but underwent TME with LPND, respectively.[69] This has been shown by others as well.[66] Hence, in patients with rectal cancer, the presence or absence of a clinically suspicious LPN should always be reported.[67] In low rectal cancers and a pretreatment MRI showing a clinically suspicious LPN, the MDT can decide on neoadjuvant (chemo)radiation. If these nodes respond by shrinking to ≤4 mm on the restaging MRI, LPND can be avoided but if they persist to greater than 4 mm in size especially in the internal iliac compartment or 6 mm in the obturator compartment, an LPND will be indicated.

Role of Restaging MRI

Restaging MRI, especially with diffusion weighted imaging (DWI), has proven to be valuable in assessing response to neoadjuvant treatment along with clinical examination.[70–72] A tumor regression grading system based on MRI reassessment (mrTRG) has been suggested to characterize the response to neoadjuvant treatment.[73] The 5-point mrTRG was shown to be an independent prognostic factor for oncological outcomes with a 5-year survival of 72 versus 27% for good versus poor mrTRG scores.[74] Combination of DWI patterns and T2 high-resolution MRI based MR-TRG can improve diagnostic performance of MRI for predicting complete pathological response.[75]

Restaging MRI can also be used not only to prognosticate patients but also to direct further therapy based on the response, as discussed in the following section. If a tumor with initial high-risk features on baseline MRI as discussed in the previous sections is downstaged to low risk on restaging MRI after neoadjuvant chemoradiotherapy, then the initial poor prognosis is altered to the prognosis of the final downstaged disease,[37,48,76] whereas if the high-risk features persist, the prognosis is poor and such patients may be candidates for a more intensive treatment like chemotherapy before surgery or a more radical surgery.

MRI-Guided Treatment Planning in Locally Advanced Rectal Cancer

MRI-determined risk factors have been enumerated in ►**Table 1**. In the absence of these risk factors on the MRI, patients with T3c/d could be offered neoadjuvant (chemo) radiation followed by TME, whereas those with T3a/b could be offered upfront surgery.[4,5,77] The presence of one or more of these risk factors on MRI is a strong indication for the MDT to

Table 1 Risk factors for recurrence in rectal cancer on the MRI

High risk of local recurrence	High risk of distant metastasis
Involvement of the MRF by either the primary tumor, EMVI, or tumor deposits	EMVI
T4b disease	Tumor deposits
Clinically suspicious lateral pelvic nodes	Any T4 disease
Low rectal cancers	N2 disease

Abbreviations: EMVI, extramural venous invasion; MRF, mesorectal fascia; MRI, magnetic resonance imaging.

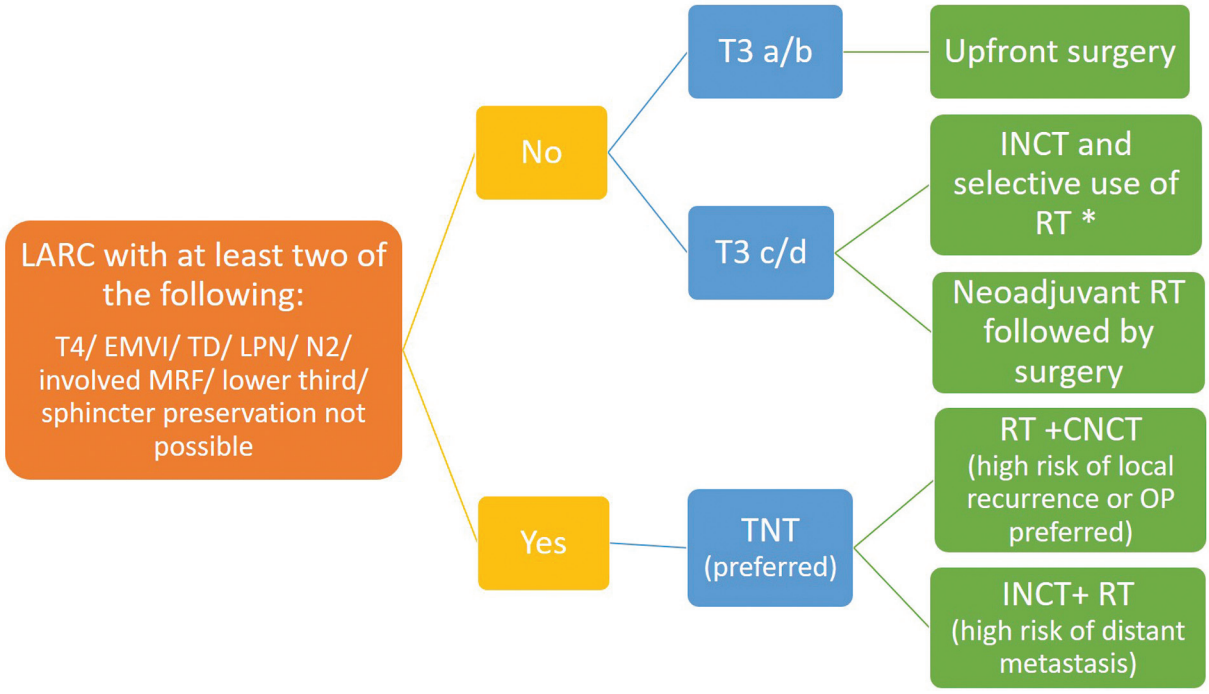

Fig. 1 Treatment algorithm for locally advanced rectal cancer based on MRI-assessed risk factors. CNCT, consolidation chemotherapy; EMVI, extramural venous invasion; INCT, induction chemotherapy; LARC, locally advanced rectal cancer; LPN, lateral pelvic node; MRF, mesorectal fascia; OP, organ preservation; RT, radiation therapy; TD, tumor deposit; TNT, total neoadjuvant treatment. *If response to chemotherapy is greater than 20%, then the patient can undergo surgery, but if the response is less than 20%, then the patient requires radiation therapy prior to surgery.

consider TNT (►**Fig. 1**). Radiation (LCRT or SCRT) followed by consolidation chemotherapy is preferred when risk factors for pelvic recurrence predominate or when organ preservation is to be attempted, whereas induction chemotherapy followed by LCRT or SCRT followed by consolidation chemotherapy is offered when there is a high risk for distant metastasis.

Further treatment can then be tailored based on one of three types of clinical response to the neoadjuvant treatment: poor response (ymrT3-4 or N+), a good response (ymrT1-2 and N0), or a complete clinical response (ymrT0N0; ►**Fig. 2**). Patients with a poor response are advised immediate TME surgery, whereas those with a good response may be candidates for an organ-sparing local excision.[5] The PROSPECT trial showed that following induction chemotherapy in patients with T2 node positive or any T3 tumor, if the primary tumor reduced in size by greater than 20%, the patients could proceed directly to surgery without the need for radiotherapy and without compromising the oncological outcomes.[78] Patients who achieve a complete clinical response after neoadjuvant therapy, especially after TNT, can now be offered an option of watch and wait where no surgery is performed and the patient is placed on intensive surveillance.[19,79,80] This approach has shown to be successful in preserving the rectum in up to 50% of patients with locally advanced rectal cancers with good long-term oncological and functional outcomes.[19,81,82]

Role of MRI in Guiding Surgical Strategy

Low rectal cancers are often a challenge to the surgeon as they are associated with a higher rate of local recurrence and reduced DFS compared to mid/upper third tumors.[83–85] The options of surgery in low rectal cancers include sphincter-preserving surgeries like low anterior resection or intersphincteric resection and sphincter resecting surgeries like a conventional or extralevator abdominoperineal excision (APE; ►**Fig. 3**). The choice of surgery for low rectal cancer depends on, besides other factors, the ability to achieve a negative CRM for which the surgeon must know the relation of the tumor to the levator ani, puborectalis, and the sphincter complex. MRI is an invaluable tool for the surgeon to plan surgery, especially in low rectal cancers.[86] Various MRI-based staging systems have been developed for low rectal cancers based on which the radiologist can clearly demonstrate tumor-free planes for surgical excision and the possibility of sphincter preservation.[87,88] In one such system, tumors at or below the puborectal sling are classified as stage 1 to 2 (tumor within the intersphincteric plane) where the intersphincteric plane is clear of tumor and a conventional APE can be performed safely or stage 3 4 (tumor extending into the intersphincteric plane and beyond) where the APE needs to be more radical to include the levator sling in the specimen (extralevator APE).[88]

The prospective MERCURY II trial successfully validated an MRI-determined low rectal cancer surgical resection plane (mrLRP) with a fivefold increase in the pathological CRM rate for an "unsafe" compared with "safe" preoperative mrLRP.[89] Involvement of the MRF on the immediate presurgical MRI should alert the surgeon to the need for a surgical approach going outside the conventional TME planes

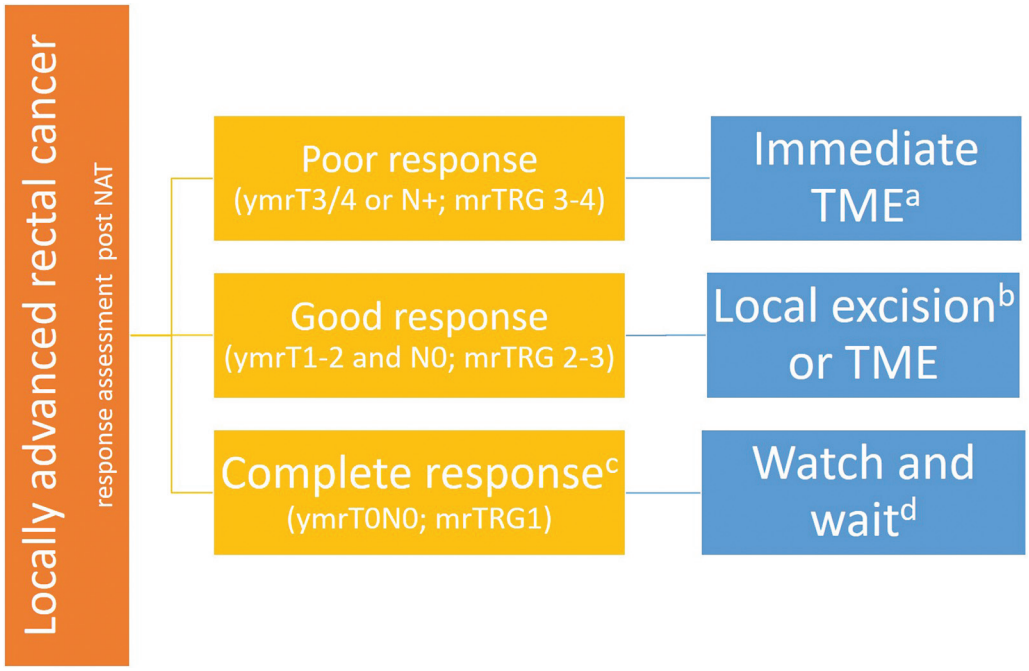

Fig. 2 Tailoring treatment after neoadjuvant therapy based on magnetic resonance imaging (MRI) assessed response to treatment. NAT, neoadjuvant therapy; TME, total mesorectal excision; TRG, tumor regression grade. [a]If the patient has not received TNT, there is an option of adding consolidation chemotherapy. [b]The residual scar/lesion should be less than 2 cm to perform local excision. [c]A complete clinical response also needs a finding of no palpable tumor on digital rectal examination and no visible residual tumor, nodule, or ulcer on white light endoscopy. [d]Based on patient preference to avoid surgery and willing to comply with an intensive surveillance schedule.

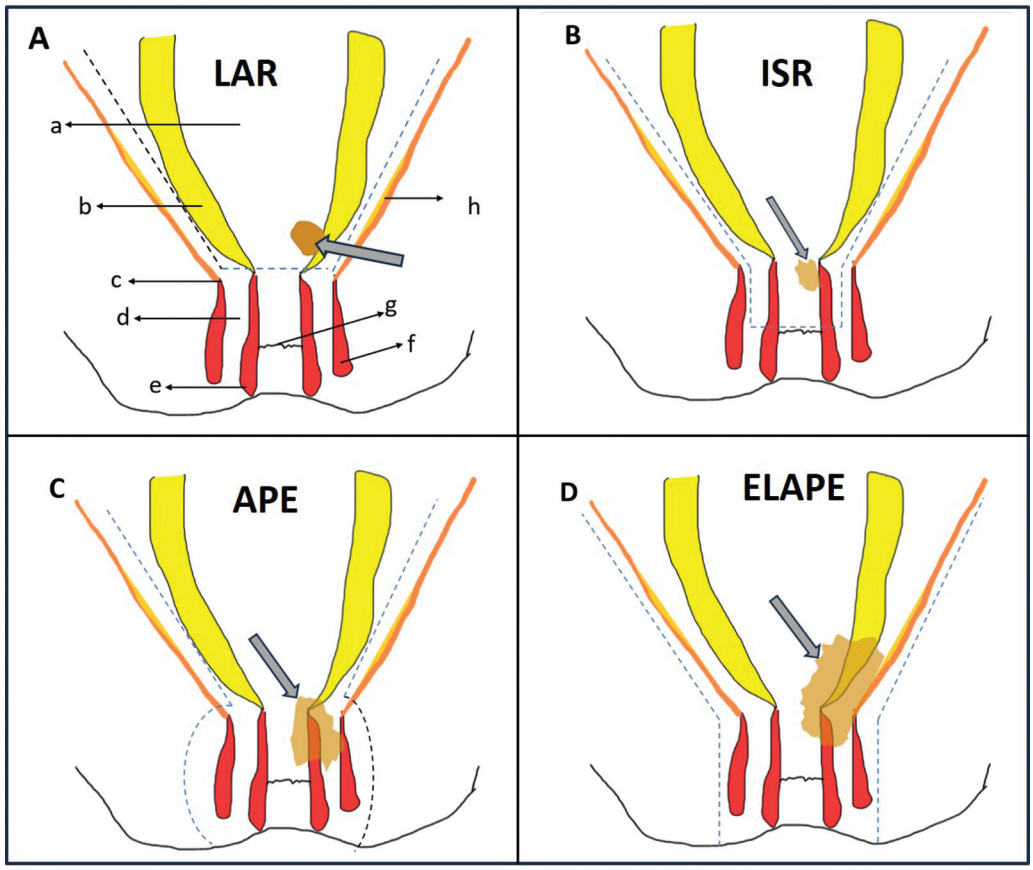

Fig. 3 Types of surgery for low rectal cancer. (**A**) Low anterior resection (LAR). (**B**) Intersphincteric resection (ISR). (**C**) Conventional abdominoperineal excision (APE). (**D**) Extralevator abdominoperineal excision (ELAPE). The *dotted line* indicates the plane of dissection for each type of surgery. a, rectum; b, mesorectum; c, puborectal sling; d, intersphincteric space; e, internal sphincter; f, external sphincter; g, dentate line; h, levator ani; *thick arrow* indicates the location of the tumor in the rectum.

(beyond TME approach) in order to achieve an R0 resection.[90] In patients with locally invasive primary or recurrent rectal cancers requiring pelvic exenteration, an MRI is the preferred imaging since it is able to predict involvement of the pelvic compartments with a high accuracy and also the risk of a positive resection margin and prognosis based on the compartment involved.[91,92] This knowledge can guide the surgeon in planning the surgical strategy to achieve an R0 resection, which is the most important predictive factor for survival following such surgeries.[93–95]

Structured Reporting

Reporting staging and restaging MRI of the rectum using proformas or in a structured or synoptic format significantly helps improve the quality and completeness of the reports.[96–98] In a comparative study, structured reports (SR) significantly improved the adequacy of information for surgical planning (94% in SRs vs. only 38% in free text) as well as definite clinical decision-making (surgery vs. neoadjuvant therapy; 96% of SRs vs. 60% of free text reports; $p < 0.001$).[97] Template report usage has been shown to significantly increase reporting of important prognostic indicators like EMVI status and CRM status compared to nontemplate reports.[99] Several reporting templates exist for primary as well as restaging MRI,[100–102] which incorporates all the essential elements required for the MDT to make appropriate treatment plans for patients with rectal cancer.

Conclusion

MRI is an invaluable tool for local staging of rectal cancer. It not only guides the surgeons in planning the surgical strategy but also has the potential to identify important prognostic features, which helps the MDT to plan appropriate risk-stratified treatment pathways and tailor the treatment based on its ability to assess the response to neoadjuvant treatment. Use of a structured reporting format ensures that all important information needed for planning treatment is available to the MDT.

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