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Clinical Paper

Re-Staging Following Long-Course Chemoradiotherapy For Rectal Cancer: Does It Influence Management?

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ABSTRACT

Background: In patients with locally advanced or low rectal cancers, long-course chemoradiotherapy (LCCRT) is recommended prior to surgical management.[1] The need for restaging afterwards has been questioned as it may be difficult to interpret imaging due to local tissue effects of chemoradiotherapy. The purpose of this study was to determine if restaging affected the management of patients receiving long-course chemoradiotherapy for rectal cancer.

Methods: A retrospective review of patients with rectal cancer discussed at the South Eastern Health and Social Care Trust Lower Gastrointestinal Multi-Disciplinary Team Meeting (LGIMDT) in 2013 who had received long-course chemoradiotherapy was performed. Patients were identified from the Trust Audit Department, LGIMDT notes and patient records. Imaging results and outcomes from meetings were obtained through the Northern Ireland Picture Archiving and Communications System® (NIPACS) and Electronic Care Record® (ECR). Data including patient demographics, initial radiological staging and LGIMDT discussion, restaging modality and result, outcome from post-treatment LGIMDT discussion and recorded changes in management plans were documented using a proforma.

Results: Seventy-one patients with rectal cancer were identified as having LCCRT in 2013 (M:F 36:35; age range 31 - 85 years). Fifty-nine patients were restaged following long-course treatment with computed tomography (CT) and magnetic resonance imaging (MRI). Twelve patients did not undergo restaging. Data was not available for 6 patients, one patient underwent emergency surgery, two patients were not fit for treatment, one failed to attend for restaging and two patients died prior to completion of treatment. Of the 59 patients restaged, 19 patients (32%) had their management plan altered from that which had been proposed at the initial LGIMDT discussion. The most common change in plan was not to operate. Ten patients had a complete clinical and radiological response to treatment and have undergone intensive follow-up. Nine patients had disease progression, with 3 requiring palliative surgery and 6 referred for palliative care.

Conclusion: Of those patients who were restaged, 32% had their management plan altered from that recorded at the initial LGIMDT discussion. Seventeen per cent of patients in this group had a complete clinical and radiological response to treatment. Fifteen percent demonstrated disease progression. We recommend, therefore, that patients with rectal cancer be restaged with CT and MRI following long-course chemoradiotherapy as surgery may be avoided in up to 27% of cases.

INTRODUCTION

Rectal cancer is a tumour with its lower edge within 15cm of the anal verge. It remains the second most common cause of cancer death in the United Kingdom. 70-80% of patients will present with T3 or node positive disease.[2] Treatment has been modified in recent years with improved imaging techniques, neoadjuvant treatment strategies and the dawn of total mesorectal excision (TME). More recently, chemoradiotherapy has become a standard practice pre-operatively to downstage tumours to achieve sphincter preservation and reduce local recurrence rates.[3] When a tumour fails to respond, aggressive surgery or palliation may be indicated. Imaging is central to such decisions in a multidisciplinary setting. Recent literature has debated the role of re-staging following pre-operative long-course chemoradiotherapy (LCCRT), in particular, the ability to discriminate malignant from non-malignant tissue.[3-8] We performed a retrospective review of patients presented at the LGIMDT to determine the role of re-staging in patients who have received LCCRT for rectal cancer and its impact on their management.

METHODS

A retrospective review of patients discussed at the LGIMDT in 2013 was performed. All patients diagnosed with rectal cancer that received LCCRT and were re-staged prior to re-

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discussion at the LGIMDT were included. Local research ethic committee approval was obtained. Data were collected using a proforma which included patient demographics, primary radiological staging and initial LGIMDT plan, mode of neoadjuvant treatment, restaging modality and result, outcome of re-discussion at the LGIMDT and changes in the initial treatment plan. Imaging results were obtained through the Northern Ireland Picture Archiving and Communications System® (NIPACS). In accordance with Northern Ireland Cancer Network (NICaN) guidelines, the clinical, histological and radiological findings for each patient were discussed at the LGIMDT.[9] The treatment plan was recorded. For each patient who was deemed to have a potentially threatened or involved margin, pre-operative neoadjuvant therapy was commenced. Treatment options included long-course chemoradiotherapy, short-course radiotherapy, long-course radiotherapy or extensive radical surgery. Only patients receiving LCCRT were included in this study. Following re-staging, patients were again discussed at the LGIMDT and a treatment plan agreed. Options recommended included surgery, regular follow-up or palliative care referral.

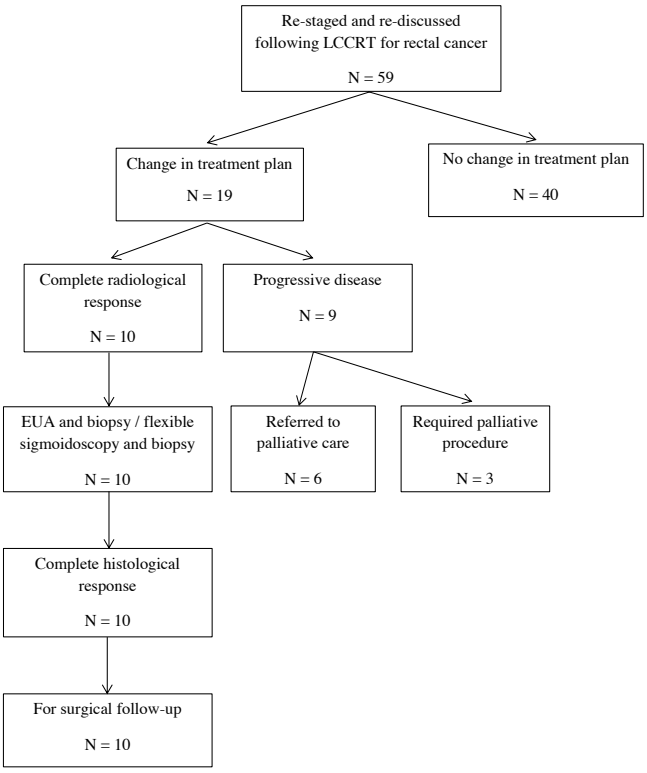

Fig 1.

RESULTS

We identified 71 patients with rectal cancer discussed in 2013 at the LGIMDT who had received LCCRT and were re-staged prior to re-discussion. Thirty-six males, 35 females with age range 31 to 85 years were included. Of these, 6 patients had incomplete data available, 2 patients had died, 1 patient declined further management, 2 patients were deemed not fit for further treatment due to multiple medical co-morbidities and 1 patient had an emergency resection. All of the 59 remaining patients had re-staging magnetic resonance imaging (MRI) of pelvis-rectum and computed tomography (CT) of the chest, abdomen and pelvis (Figure 1). Of the 59 patients re-staged, a change in the original treatment plan occurred in 19 patients (32%). Ten patients (17%) were found to have a complete radiological response to LCCRT. Of these 10 patients, all have remained under regular surveillance with three monthly examination under anaesthetic/flexible sigmoidoscopy and biopsy and 6 monthly MRI pelvis-rectum. One of the 10 patients had died at the time of writing with a synchronous primary lung tumour. The remaining patients were alive at an average of 3.5 years of follow-up. Nine patients were found to have disease progression (15%). Of these, 3 patients required a palliative procedure. The remaining 6 patients were considered for palliative chemotherapy and, where appropriate, referred for palliative care. In total, of the 59 patients included in the study, 16 patients (27%) avoided surgery following re-staging.

DISCUSSION

Chemotherapy and/or radiotherapy followed by total mesorectal excision (TME) is the gold standard treatment for locally advanced rectal cancer increasing the likelihood of sphincter preservation and reducing local recurrence rate. Tumour within 1mm of the circumferential resection margin (CRM) strongly predicts local recurrence and poor survival. Patients with CRM involvement have been reported to have at least 3 times the risk of local recurrence and twice the risk of death.[10] In these patients, pre-operative long course chemoradiotherapy (LCCRT) may facilitate successful TME with a reduction in tumour volume and greater likelihood of a sphincter-saving procedure.[10,11] It is thought that pre-operative treatment of well-oxygenated tissue increases sensitivity to radiotherapy as well as reducing the risk of small bowel radiation injury.[11]

Many authors advocate MRI to determine CRM status before and after LCCRT.[12-16] By contrast, clinical examination understages in approximately 47% of patients and is highly dependent on the examiner's appreciation of tumour mobility and fixation.[17] Endoanal ultrasound (EAUS) tends to overestimate tumour depth and is associated with difficulty in determining tumour from fibrosis/inflammation. There has been a growing interest in positron emission tomography (PET-CT), however, there is a need for standardisation of criteria used to measure response with this modality.[2] In addition, sensitivity and specificity of PET in predicting response to treatment varies from 45 – 100% and 59 – 96% respectively.[2] The MERCURY trial demonstrated that MRI assessment of the CRM is feasible and reproducible.[10] It has also been shown that multidisciplinary discussion of MRI results and implementation of a pre-operative treatment plan leads to significantly reduced positive CRM.[16]

If a complete clinical response occurs, a policy of careful observation may be adopted after discussion with the patient.

Complete response of the primary rectal tumour has been observed in up to 30% of patients after restaging.[18] After neoadjuvant treatment, accurate assessment of the tumour has proved difficult due to local response to LCCRT resulting in fibrosis.[3] Prediction of CRM involvement is reported to be 66-85% while determination of rectal wall invasion and nodal disease after LCCRT have been quoted to be as low as 50% (specificity 35%; sensitivity 100%) and 65% respectively.[7,8,19] The MERCURY group showed an overall accuracy of 91% for predicting CRM in patients going straight to surgery versus 77% in patients undergoing pre-operative LCCRT.[10] Fibrosis of the bowel wall from radiation can easily be misinterpreted as tumour. Furthermore, peri-tumour inflammation and infiltration and vascular proliferation can correlate with peri-lesional enhancement leading to overstaging.[11]

TABLE 1.

Complete responders: initial radiological staging and position of tumour within the rectum.

Initial Radiological Staging	Position of tumour
T3 N0	Lower
T4 N2	Upper
T2 N0	Middle
T3 N1	Upper
T3 N0	Middle
T4 N0	Lower
T2 N0	Lower
T3 N2	Middle
T4 N0	Upper
T2 N0	Middle

Understaging is usually explained by an inability to locate residual tumour encased in fibrotic tissue.[3] This has led to recent literature questioning the role of restaging patients who have had LCCRT and raising doubt as to its clinical and cost-effectiveness.[3,4,20,21] Some studies have concluded that none of the available imaging modalities can accurately determine whether or not there has been a complete pathological response.[5,22,23] We set out to challenge these hypotheses and determine whether there was a role for restaging in patients with rectal cancer treated with LCCRT.

All of our patients were re-discussed following restaging at the LGIMDT. This typically has consultant radiologists, oncologists, the colorectal surgical body and other healthcare professionals present. A colorectal surgeon leads the LGIMDT discussion. Outcomes from the meeting are based on group consensus amongst the specialists present and documented in an accessible online care pathway. Imaging, in particular, is actively discussed and independent second opinions sought where interpretation is difficult. In such cases, comparison of pre- and post-treatment images has proven useful. Re-imaging results are based on the agreement between two independent consultant radiologists who both attend the LGIMDT. Where a complete response was agreed, patients proceeded to timely clinical assessment.

The 10 patients in our group found to have a complete radiological response underwent examination under anaesthetic/flexible sigmoidoscopy and biopsy. None of these patients were found to have residual tumour present following histological analysis. Of these ten patients, 7 were found to have stage II or III disease on initial imaging (Table 1). No direct assessment of response rates between low and locally advanced disease was performed. Follow-up, under direction of the LGIMDT, encompassed re-assessment every 3 months with MRI pelvis-rectum every 6 months. If clinical concerns arose, patients were reviewed earlier and re-discussed. After approximately three and a half years of follow-up 1 patient had succumbed to a synchronous lung tumour and the remaining patients continue on regular surgical follow-up. 16 patients were able to avoid an unnecessary operation as a direct result of restaging. This included patients with disease progression who were able to avoid a major resection and whose care was directed towards symptom control and palliation.

There is recognition that improved imaging techniques will enable better interpretation and more accurate assessment of response. Comparison of pre- and post- treatment images, use of MR volumetry and perfusion MRI are just some approaches suggested.[8] Functional MRI techniques will enable greater understanding of tumour biology, microcirculation, vascular permeability, and tissue cellularity leading to more accurate interpretation and prognostication.[24] Such techniques may enable accurate noninvasive surveillance in a greater number of selected patients.[24]

This study demonstrates that restaging continues to play an important role in the management of patients with rectal cancer. Limitations include a small sample size, retrospective review, limited follow-up and reliance on electronic data. Although all patients were discussed at our local LGIMDT, time from end-of-treatment to re-staging was not standardised. In addition, there was no intention to assess the accuracy of imaging against resected histological specimens as this was not likely to add any further information to current knowledge. Our study does, however, emphasise the essential role of re-imaging in making treatment decisions for patients with rectal cancer.

CONCLUSION

While we acknowledge that restaging techniques require further improvement in order to accurately assess treatment response and assist in surgical planning, we have shown that restaging alters management and avoids surgery in a significant number of patients. Therefore, despite the

controversy, we recommend that all patients who receive pre-operative LCCRT for rectal cancer undergo restaging in a multidisciplinary setting.

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