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Case Study

Surgical resection for rectal cancer: a gold standard or a last resort?

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Key Learning Points

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In recent times, the management of rectal cancer has evolved and a multimodal approach utilising selective combinations of chemotherapy, radiotherapy and surgery are employed. Surgery may be local excision or proctectomy which in turn can be open, laparoscopic or robotic. Improvement in neoadjuvant treatment has demonstrated that some patients ultimately do not need to undergo surgery or may only require local excision of their tumour. However, this is a complex field where many treatment options exist and selecting the correct approach is reliant on accurate pre-operative staging and then tailoring treatments to each individual patient.

It is imperative that patients are informed of the advantages and disadvantages of each approach allowing them to make an informed decision based on the evidence. It is also crucial that in treating rectal cancer, the surgical team has all these tools in their armamentarium in order to treat all stages of the disease. In the present case, the patient underwent maximal neoadjuvant treatment with chemotherapy and chemoradiotherapy and ultimately required pelvic exenteration. The decision making in this process is truly multidisciplinary and requires many specialties and allied health teams to support the patient through this process.

Introduction

Colorectal cancer is the third most common cancer and the second leading cause of cancer death worldwide, with one-third of these cases being attributed to rectal cancer[1]. Surgical resection currently stands as the gold-standard treatment approach[1], but this paradigm has been challenged in recent times, in light of evidence which suggests that radical surgical intervention may not always be needed if a complete response can be achieved with neoadjuvant chemotherapy or chemoradiotherapy alone[2].

The following case report describes a patient who is diagnosed with a large, locally advanced rectal cancer at the age of 54. This patient is exposed to the full armamentarium of rectal cancer treatment, undergoing chemotherapy and chemoradiotherapy before finally undergoing a complex curative surgical resection procedure involving surgeons from multiple disciplines.

Case History

RJ is a 54 year-old male who first started to experience a change in bowel habit in the summer of 2018, noticing that he was unusually constipated. At this time, he was on a trekking holiday with his family and became conscious of his reduced stamina during long walks. Thereafter, RJ experienced pain on straining and would frequently find blood on wiping after passing stool. Even sitting down became an uncomfortable task. Despite taking laxative medications, his symptoms did not improve. In March 2019, RJ presented to his GP with complaints of these ongoing bowel symptoms and was referred to the Lower GI team for an endoscopy on the two-week wait pathway for suspected bowel cancer.

RJ's only significant past medical history is a childhood diagnosis of asthma, for which he uses a salbutamol inhaler as required. He has no family history of cancer and is a non-smoker with an insignificant alcohol intake history.

The endoscopic examination could not be done to its full intended extent due to obstruction imposed by a malignant-looking mass in the rectum. Rectal biopsies taken during the endoscopy found that large intestinal mucosa tissue had been infiltrated by a moderately differentiated invasive adenocarcinoma. Upon digital rectal examination, this circumferential rectal tumour was palpable.

A pelvic MRI scan showed an 8cm anorectal tumour at stage T3d i.e. the tumour had grown into the muscle layer of the bowel wall with a depth of mesorectal extension >15mm, and was abutting the prostate and seminal vesicle. The nodal status was N2 i.e. the cancer had spread to four or more mesorectal lymph nodes. Furthermore, the tumour classified as M1, as a small (<5mm) lesion was present in the otherwise healthy liver. The tumour showed no extramural vascular invasion, but the circumferential resection margin was found to be involved. A contrast CT of the thorax, abdomen and pelvis further illustrated the presence of the bulky, circumferential tumour at the distal rectum which was likely crossing the dentate line to extend into the anal

canal.

In May 2019, it was explained to RJ that he had been diagnosed with a large, locally advanced rectal cancer. At the recommendation of the Colorectal Multidisciplinary Team (MDT), RJ started a three-month regimen of neoadjuvant chemotherapy consisting of four cycles of IV Oxaliplatin and Capecitabine oral tablets. During chemotherapy, RJ experienced diarrhoea and some episodes of pyrexia but mostly tolerated the treatment well, continuing to work from home between cycles of chemotherapy. However, when RJ was rescanned at the end of the chemotherapy treatment, the MRI showed progressive disease, with the large anorectal tumour and continuous extramural mass having increased in size since the scan done three months previously. The tumour was invading the prostate and shown to be in contact with the prostatic urethra. The tiny liver lesion remained unchanged, and there were no other organ abnormalities.

The rectal tumour was continuing to progress despite chemotherapy, and RJ's symptoms of frequent loose stools and diarrhoea suggested that he was becoming obstructed. Though it had initially been proposed that chemotherapy would be followed by chemoradiotherapy (CRT) treatment, the Lower GI team now expressed concerns that CRT would cause further swelling of the tumour and cause more obstruction during treatment. It was proposed that RJ should have a defunctioning stoma formed prior to CRT. Though RJ was initially very resistant to stoma formation, at the time of his flexible sigmoidoscopy in early October, his symptoms of diarrhoea and concerns for obstruction where such that a defunctioning stoma would be required in order to complete CRT. In October 2019, RJ underwent laparoscopically assisted formation of a defunctioning loop colostomy. Having made a rapid post-operative recovery, RJ started CRT in late October, completing the course of treatment in early December.

In January 2020, MRI and CT images showed that the extramural tumour component had reduced in size but continued to invade the levator bilaterally and infiltrate the prostate. RJ had undergone chemotherapy and radiotherapy but the anorectal tumour persisted. With no medical treatment options left, the Lower GI team proposed the next option: surgical exenteration – complete removal of the cancer requiring en bloc removal of the bladder, prostate and rectum. The surgery would involve extended resection of the perineum and levators, leaving a pelvic defect that would be reconstructed with a flap of muscle, fat and skin taken from either the buttocks or abdominal wall. To redirect urine from the bladder post-exenteration, a colonic conduit would be formed, enabling the urine to exit the body by flowing from the kidneys, through the ureters which are anastomosed to a segment of colon that is matured at the abdominal wall.

RJ was overwhelmed by the magnitude of the proposed pelvic exenteration surgery, which he was told carried risks of <5% mortality and a significant morbidity rate of 40-50%, as well as post-operative loss of his ability to achieve erections and ejaculation.

In February 2020, ten months after his cancer diagnosis, RJ underwent pelvic exenteration surgery, a complex 13-hour procedure involving the collaborative effort of colorectal, urology and plastic surgeons. The defunctioning loop colostomy was taken down, the bladder, prostate and rectum were resected, and a colonic conduit was constructed and spouted at the site of the original loop colostomy. An end colostomy was sited superior to the colonic conduit. A VRAM myocutaneous flap was harvested to fill the pelvic defect.

RJ made a good post-operative recovery with no complications. By day 9 after surgery, his colostomy output was becoming more formed and he was eating and drinking well. On day 18, RJ was discharged and sent home with a 5-day course of prophylactic antibiotics and a 28-day course of dalteparin. He will be followed up routinely by the Colorectal Team.

High-resonance imaging plays a central role in guiding treatment approaches

Over the past decade, high-resolution imaging has played an increasingly central role in guiding treatment approaches for rectal cancer. The 2006 MERCURY Trial was pivotal in demonstrating the specificity of MRI for prediction of circumferential resection margin status, a strong indicator of whether or not tumour resection is likely to be curative[3]. Preoperative MRI reports were found to correctly predicted a clear circumferential resection margin in 92% of cases[3]. MRI now forms an integral role in the local staging of rectal cancer (Figure 1).

Tumour-Node-Metastasis (TNM) Staging System

Tumour-node-metastasis (TNM) staging is traditionally used to guide decisions about whether a colorectal cancer patient is likely to benefit from

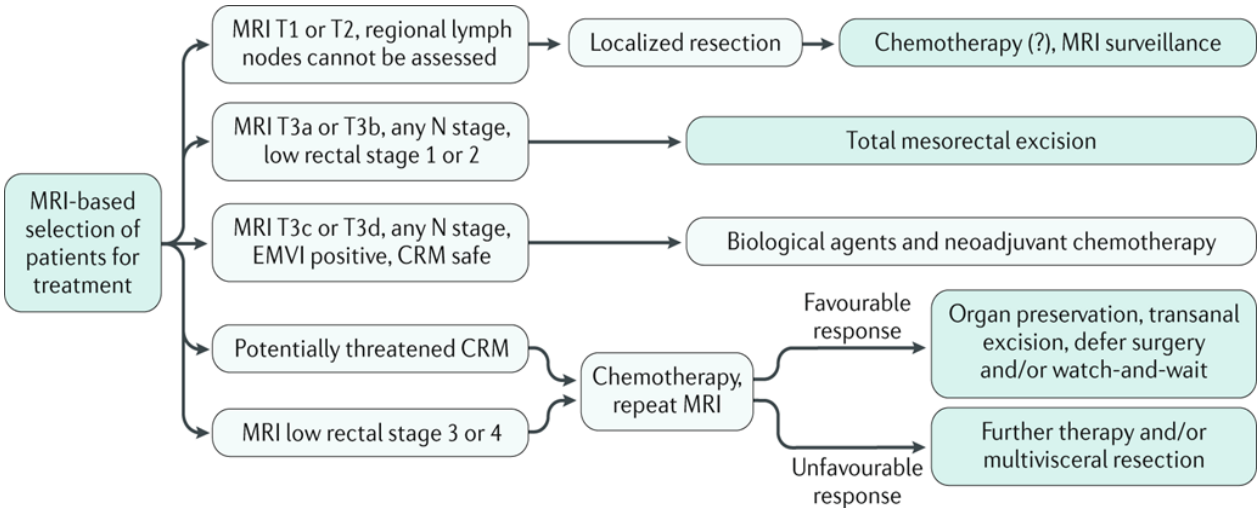

Figure 1: Example flowchart to guide multidisciplinary team treatment decisions for rectal cancer based on MRI findings. CRM = Circumferential Resection Margin. EMVI = Extramural Venous Invasion. Image from[1]

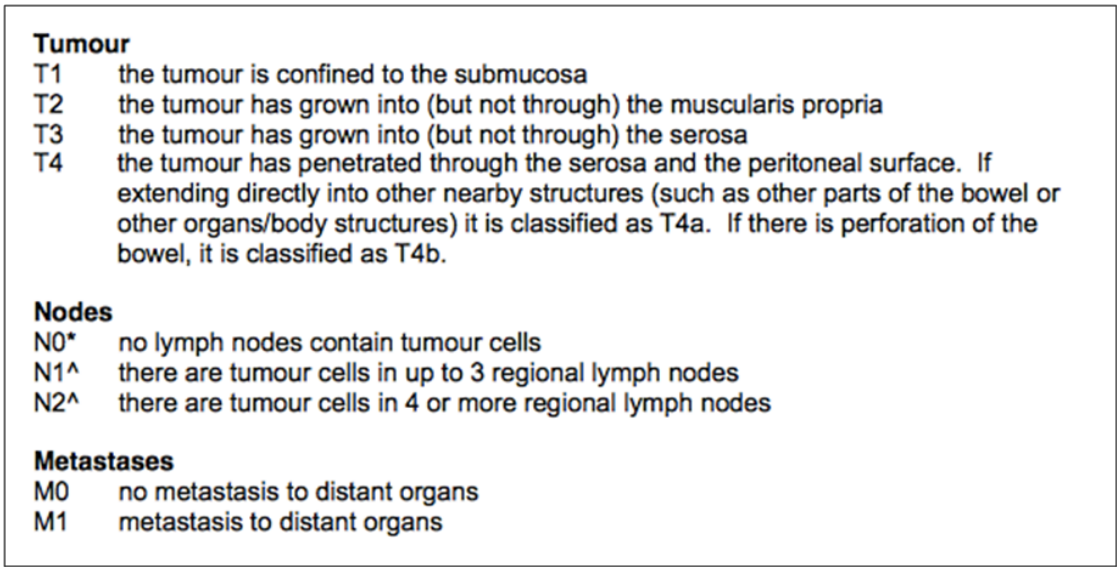

Figure 2: Summary of the TNM staging system for colorectal cancer[2]

neoadjuvant chemo/radiotherapy and/or adjuvant chemotherapy. T describes the relationship of the primary tumour to the bowel wall and whether it is invading surrounding tissues, N describes whether and how many local lymph nodes are involved, and M describes whether or not distant metastases are present (Figure 2).

T3 substaging

The T3 substage of T staging defines the extent of tumour penetration into the mesorectum. Prognosis varies depending on T3 substage, with 5-year survival rates being significantly worse among patients with further advanced T3 substage rectal cancer compared to those with less advanced T3 cancer i.e. less penetration into the mesorectum[4]. NICE guidelines therefore state that T3a/b tumours (<5mm penetration beyond the muscularis propria) are likely to have a good prognosis and do not require chemoradiotherapy in the absence of other risk factors, whilst T3c/d tumours (5-15mm or >15mm beyond muscularis propria, respectively) are prognostically poor and should be treated with chemoradiotherapy[5].

Circumferential resection margin

Tumours situated within 1mm of the mesorectal fascia (i.e. the outermost boundary of the mesorectum) are associated with a significantly greater risk of local recurrence[6]. This can be detected on a T2-weighted MRI and is termed a 'threatened circumferential resection margin (CRM)'. CRM status is the most important factor in predicting the need for neoadjuvant treatment and risk of local recurrence[1]. In a longitudinal study of 686 rectal cancer patients undergoing total mesorectal excision, the overall local recurrence rate was far greater among patients with CRM involvement (22%) compared to those with no CRM involvement (5%)[6]. 40% of CRM-positive patients went on to develop distant metastasis over the 29-month follow-up period, compared to 12% of CRM-negative patients[6].

Extramural venous invasion

Tumour invasion into surrounding blood vessels can be accurately detected using T2-weighted MRI. It is now well-established that extramural venous invasion – the presence of primary malignant tumour cells within blood vessels beyond the muscularis propria – is an indicator of poor disease-free survival outcomes and heightened risk of local recurrence[1]. This was demonstrated in a retrospective study by Smith et al. involving review of pre-operative MRI images from 133 patients who had undergone surgical resection of a primary colorectal cancer[7]. A pre-operative MRI-Extramural Vascular Invasion (MRI-EMVI) score from 0 to 4 was assigned depending on the extent of extramural vascular invasion, with 0 denoting no vessels located adjacent to areas of tumour penetration and 4 denoting distortion of vessel shape due to tumour invasion. Univariate analysis found that patients with an MRI-EMVI score of 3-4 had a significantly lower relapse-free survival rate (35%) proportion compared to patients scoring 0-2 (74%)[7].

Nodal disease

Tumour involvement of local lymph nodes is associated with risk of disease recurrence, however it has been argued that this risk is often overstated and not as important as historically thought for guiding treatment options[8]. The MRC-CR07 trial demonstrated that the apparent impact of nodal status on local recurrence is likely a reflection of poor surgical technique[9]. Surgical specimens of excised rectal tumours from 1156 patients were assessed by pathologists and the quality was classified as either 'poor', 'moderate' or 'good', according to the plane of dissection and CRM status. In patients with a 'poor' quality specimen, the 3-year local recurrence rate was up to 20% in those who were node-positive. Meanwhile, patients with a comparable nodal status who underwent total mesorectal excision (i.e. had a 'good' quality specimen) had 3-year local recurrence rates of only 6%. The optimal method of assessing lymph node metastasis is by histopathological examination of the surgical specimen which can only be obtained post-operatively[8]. Preoperative measurement of lymph nodes using MRI may be an inadequate means of determining malignancy risk, as demonstrated by a histological survey of >12,000 rectal cancer lymph nodes showing substantial overlap in the size of normal, inflammatory and metastatic nodes[10].

Surgical resection of rectal cancer is often preceded by neoadjuvant therapy

NICE guidelines state that surgery is the gold standard treatment for rectal cancer patients if the tumour is resectable[5]. For non-metastatic rectal cancers staged at T1-T2/N1-N2 or at T3-T4 with any nodal status, several

randomised controlled trials show that the delivery of radiotherapy or chemoradiotherapy prior to surgery results in lower incidence of local recurrence and better overall and disease-free survival compared to patients undergoing surgery alone[5,11].

These preoperative treatments, termed 'neoadjuvant' therapies, aim to reduce the extent of cancer prior to radical surgical intervention. There are three main approaches taken for neoadjuvant treatment of rectal cancer, with no convincing evidence so far suggesting that they confer significantly different clinical outcomes:

a) Long-course chemoradiotherapy
b) Induction chemotherapy followed by long-course chemoradiotherapy
c) Short-course radiotherapy

Traditionally, it was thought that an interval of 8-12 weeks between neoadjuvant therapy and surgery was optimal for a complete clinical response[1]. However, it is now recognised that a lengthy interval results in radiation-associated fibrosis which complicates surgical resection and worsens post-operative outcomes[1]. In a trial involving 265 rectal cancer patients due to undergo neoadjuvant therapy prior to surgical resection, patients were randomised to undergo surgery either 7 weeks or 11 weeks after completing neoadjuvant radiotherapy treatment[12]. Although there was no difference in the rate of complete pathological response (i.e. absence of tumour cells or lymph node involvement in the post-operative specimen) between groups, the 11-week group showed worse quality of mesorectal resection, longer operative times and an increased rate of medical complications[12].

There is no unanimous consensus on the ideal interval period between neoadjuvant therapy and surgery, with current evidence suggesting that surgery should occur any time from 5 to 12 weeks after chemoradiotherapy[1]. Overall path CR rate increases with a longer time from CRT.

There are several surgical approaches for excision of rectal tumours

Rectal cancer surgery aims to completely excise the tumour and surrounding mesorectum with a tumour-free margin. The current gold standard for curative resection is Total Mesorectal Excision (TME)[1,13], an operation in which the plane of dissection is formed by the mesorectal fascia which encloses the fatty mesorectum that surrounds the rectum[14]. A seminal study by Heald et al. demonstrated the superiority of the TME surgical method, which yielded local and overall recurrence rates of 5% and 22% respectively, as compared to conventional surgery combined with either radiation therapy (25% and 62.7%) or chemoradiotherapy (13.5% and 41.5%)[13].

TME is the gold standard surgical technique for proctectomy. However, if the sphincter complex is involved with tumour or the tumour is so close to the pelvic floor that an adequate distal resection margin cannot be achieved, the patient may require a permanent stoma. An abdominoperineal resection is when the anus, rectum and part of the sigmoid colon are removed. The proximal sigmoid colon is used to form a permanent colostomy on the abdominal wall.

There are several possible surgical approaches for rectal tumour resection, including open, laparoscopic, hand-assisted, robotic and transanal. In a trial by Stevenson et al. in which 475 rectal cancer patients were randomised to rectal resection either by open laparotomy or laparoscopy, the laparoscopic-operated patients showed significantly lower rates of a CRM-negative specimens and of TME completeness[15]. However, this trial also showed that there was no difference between groups in rates of successful resection or of a clear distal margin[15]. Long-term reports have identified no significant differences in oncological outcomes between laparoscopic and open surgery – patients undergoing surgery with either approach show comparable rates of local and regional cancer recurrence and disease-free survival[16].

Robot-assisted surgery can improve upon the technical and visual limitations of laparoscopic surgery but trials have suggested the oncological outcomes are similar to traditional laparoscopy. However, with greater uptake and availability of surgical robots combined with the advances in technology such as image guided surgery and augmented reality, it is possible that benefits will in time become apparent.

Local transanal excision of tumours is a viable option for patients presenting with small (<3cm), moderately-to-well differentiated T1 tumours with no nodal involvement. This approach is minimally invasive and can substantially reduce post-operative morbidity, and is therefore a favourable option for suitable patients with early-stage rectal cancer[1].

The watch-and-wait strategy – to operate or not to operate?

Chemotherapy and radiotherapy treatment for rectal cancer have proven so effective that complete tumour eradication can be achieved using these medical approaches alone. The role of surgery has therefore been brought into question, given that it may be unnecessary and even harmful.

A 4.5-year longitudinal study tracked patients with resectable stage 0 rectal cancer, all of whom achieved a complete clinical response after neoadjuvant chemoradiation[2]. Oncological outcomes were compared between patients subsequently underwent surgical resection (n=194) versus those who did not (n=71), revealing that there was no overall or disease-free survival advantage of having surgery[2].

The so-called 'watch-and-wait' approach, in which patients showing a complete clinical response are offered no immediate surgery and monitored carefully over two years, has yielded impressive outcomes in many patients, with a disease-free survival rate of 81% in 100 patients over a 3.5-year follow-up period[17].

Van der Valk et al. compiled an international registry on rectal cancer patients undergoing a watch-and-wait treatment strategy, having achieved a complete clinical response to neoadjuvant treatment[18] . The information gained from following the 1009 patients across 47 institutes has added valuable insight into the effectiveness of the watch-and-wait treatment strategy, demonstrating that local regrowth of cancer is most likely to occur within the first two years post-neoadjuvant therapy[18]. It is therefore vital to maintain careful endoscopic surveillance during this period to ensure that deferred surgical resection remains a viable option.

Whilst definitive surgery remains the gold standard for rectal cancer, the 'watch and wait' approach may be considered for suitable patients, as long as they are fully aware and accepting of the potential risks of deferring surgery.

Concluding Remarks

In the context of early-stage rectal cancer, there is evidence to suggest that surgical resection may be avoided

with chemoradiotherapy and a 'Watch and Wait' approach. This approach may avoid the need for potentially complex surgery and the possibility of needing a permanent colostomy. However, at present surgery does still remain the gold standard.

With regards to the particular case of patient RJ, the anorectal tumour was found to be large and locally advanced by the time it was diagnosed, and was therefore not amenable to non-operative intervention. Patient RJ underwent pelvic exenteration surgery, a radical procedure which carries a considerable rate of morbidity and long-term impact on quality of life.

In the UK, bowel cancer screening is currently offered on a biennial basis to men and women aged 60 to 74, as well as an additional one-off test for men and women in their 56th year. Given the growing evidence base demonstrating the efficacy of non-surgical treatment options in early rectal cancer, there is clearly a strong rationale for earlier routine screening programmes such that these tumours can be detected and treated at an earlier stage, avoiding the need for extended surgical resection.

Conflicts of interest
None.

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Consent
The patient has consented to the publication of this case study.

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