Colorectal cancer: management

Chris Cunningham
Ian Lindsey

Abstract
The last decade has seen a dramatic change in the management of colorectal cancer. This has been delivered through more thorough and informed preoperative assessment, widespread use of multimodal treatments, including neoadjuvant therapy, and the introduction of minimally invasive procedures and improvement in rectal cancer surgery. This contribution discusses current issues in the management of cancer of the colon and rectum. General principles can be applied to both sites, but rectal cancer is given particular attention because it has seen greater developments in surgery and neoadjuvant treatment.

Keywords abdominoperineal resection; chemotherapy; colorectal cancer; polypectomy; radiotherapy; transanal endoscopic microsurgery

What's new?

- Considerable advances have been made in minimally invasive surgery for colorectal cancer. This is now the accepted standard of care for elective resections as detailed in NICE gidelines
- Optimizing local control of rectal cancer continues to provide challenges, and techniques have evolved to improve resection of low rectal cancers requiring abdominoperineal resection
- In chemotherapy, new biological agents combined with cytotoxic drugs show promise in the treatment of advanced disease

Preoperative assessment of colorectal cancer patients

As recently as the 1990s, preoperative staging of colorectal cancer was given little attention because exploratory laparotomy was undertaken in all patients fit for general anaesthesia. Surgery was the only effective treatment, and staging methods lacked the sensitivity and specificity to influence clinical decisions. However, most surgeons now stage the disease in three areas (local disease, distant disease and synchronous colonic lesions), and the results are considered with patient factors (e.g. general health, comorbidity) to determine the optimum treatment. These final decisions are taken with the support of a multidisciplinary team.

Chris Cunningham ***FRCSEd*** *is Consultant Colorectal Surgeon at the John Radcliffe Hospital, Oxford, UK. He qualified from the University of Edinburgh Medical School, and trained in colorectal surgery in Edinburgh, Glasgow and Paris, France. His interests include the minimally invasive treatments for colorectal diseases, familial colorectal cancer syndromes and pelvic floor disorders. Competing interests: none declared.*

Ian Lindsey ***FRACS*** *is Consultant Colorectal Surgeon at the John Radcliffe Hospital, Oxford, UK. He qualified from the University of Melbourne, Australia, and trained in colorectal surgery at St Vincent's and Box Hill hospitals, Melbourne and the John Radcliffe Hospital, Oxford. His interests include minimally invasive treatments for colorectal diseases and pelvic floor disorders. Competing interests: none declared.*

Local disease in the colon is assessed by CT. Information on the presence of T4 disease (invasion through the bowel wall with or without direct invasion of adjacent structures; see pages 302–305) is helpful in operative planning. This may take the form of ureteric stent placement or *en bloc* resection of involved organs. In the rectum, assessment of tumour invasion (T stage) and local lymph node involvement (N stage) is improved by the use of MRI and transrectal ultrasonography. The latter is particularly helpful in the identification of early cancers (T1 and early T2), that may be amenable to local endoluminal excision.

Metastatic disease – the liver and lungs are routinely assessed for metastatic disease. Abdominal CT is usually undertaken, but ultrasonography of the liver is the minimum recommendation. Chest disease is assessed by plain radiography, though CT is used increasingly. Positron emission tomography (PET) and, particularly, PET-CT have an increasing role in the preoperative assessment of metastatic disease, particularly in identifying those patients where otherwise occult metastases would be a contraindication to extensive visceral resection. The presence of non-resectable metastases may prompt non-operative management or use of minimally invasive palliative treatments.

Synchronous disease – identification of a colorectal primary cancer should prompt complete assessment of the remainder of the colon. Synchronous cancers are present in 2–4% of patients and adenomas in about 20%. The optimum investigation is colonoscopy, during which polyps can be removed or the site tattooed allowing identification at the time of resection. The proximal bowel can be assessed by contrast enema in those with an obstructing cancer. More recently, CT colography has successfully replaced contrast studies.

Early disease

Cancer arising within polyps may be treated adequately by colonoscopic polypectomy alone. Advanced polypectomy techniques (e.g. endoscopic mucosal resection) have been developed to improve tumour clearance and reduce the incidence of colonic perforation. It is helpful to tattoo sites of 'advanced polypectomy' to enable precise endoscopic follow-up and easy identification at subsequent open resection, if required. Experienced and

meticulous pathological assessment is essential in determining the adequacy of local excision and risk of lymph node involvement. The latter is guided by Haggitt's staging of malignant polyps and Kikuchi's levels of submucosal invasion in sessile lesions. These classifications provide an informed estimate of the likelihood of lymph node involvement and may avoid the need for formal resectional surgery, depending on factors such as patient age, fitness and personal choice. Other histopathological factors which favour formal resection over local excision include poor tumour differentiation, vascular or lymphatic invasion and the involvement of a resection margin. International trials are under way examining chemoradiation combined with complete excision of T1 and some T2 cancers, but this is not standard practice in the UK.

The therapeutic possibilities are greater in the rectum. In addition to colonoscopic polypectomy, many lesions can be removed by per-anal excision. Transanal endoscopic microsurgery enables precise removal of benign and early malignant lesions under direct vision with sophisticated instrumentation permitting full-thickness excision of the rectal wall.[1]

The incidence of early-stage cancer is expected to increase with the planned introduction of national screening by faecal occult blood testing (FOBT) for those aged 60–69 years from 2006 in the UK.

Locally advanced disease

Principles of surgery in colorectal cancer

Surgical resection remains the most effective means of treating colorectal cancer; 5-year survival is 90% in Dukes' A cancer and 75% in Dukes' B. The aims of surgery are adequate tumour resection followed by safe anastomosis, ensuring well-vascularized bowel ends approximated under no tension. Surgical planning is helped by accurate preoperative staging. The primary tumour should be removed with associated lymphatic drainage. This should be resected as a complete anatomical unit; breaching of planes should be avoided, as this increases the likelihood of cancer involving the resection margin with an inevitable increase in local recurrence. If adjacent structures are involved, they should be removed *en bloc* with the primary cancer.

Anastomotic failure is a life-threatening complication, with an incidence as great as 10% in rectal cancer resection. A high index of suspicion aids early diagnosis, and prompt resuscitation and operative intervention reduces the risk of sepsis and multi-organ failure. In some cases, the anastomosis is protected by a proximal diverting ileostomy or colostomy. Alternatively, use of an anastomosis may be avoided by formation of an end-stoma, as in Hartmann's resection of sigmoid disease.

Surgery in rectal cancer management

Survival and local control in patients with rectal cancer have improved with developments in surgical technique, most notably the widespread adoption of total mesorectal excision (TME). In the technique of TME, the rectum is excised with its enveloping mesorectal package of blood vessels, fat and lymph nodes surrounded by an intact parietal fascia.[2] This precise anatomical dissection under direct vision is associated with local recurrence rates of less than 10% when performed by surgeons with appropriate training.

An appreciation that distal clearance of the cancer could be limited to 1–2 cm meant that many rectal cancer patients who would have previously been treated by abdominoperineal resection could undergo low colorectal anastomosis and avoid a permanent colostomy. Improved understanding of pelvic anatomy facilitated effective cancer surgery with preservation of pelvic autonomic nerve function and techniques have been developed to improve postoperative functional outcomes by incorporation of a colonic pouch or 'neorectum' (see pages 311–316).

Radiotherapy in rectal cancer management

Radiotherapy is employed in four main modalities in rectal cancer: preoperative short course, preoperative long course as neoadjuvant treatment, postoperative when directed by unfavourable pathology and palliative for symptom control.

Reports of the use of preoperative radiotherapy in rectal cancer have indicated a reduction in the local recurrence rate from more than 25% to less than 10%, and this was subsequently translated into a survival advantage.[3] There is little doubt that preoperative radiotherapy has been used to compensate for poor surgical technique. The use of short-course preoperative radiotherapy as a means of reducing pelvic recurrence in addition to best surgical practice is still debated. In a randomized study of TME with or without preoperative short-course radiotherapy, local recurrence was 8.2% in patients treated with surgery alone and 2.4% in those who received short-course preoperative radiotherapy (25 Gy over 5 days).[4] A weakness of this trial is that preoperative staging of rectal cancer was not standardized, and it may now be possible to identify the subgroup of patients most likely to benefit from preoperative radiotherapy. Similar results have been demonstrated in the preliminary report of CR07, a UK-based randomized trial examining the use of preoperative short course radiotherapy versus selective preoperative treatment with postoperative radiotherapy for those where pathology showed involved margins.[5]

MRI has had a major influence on determining the need for radiotherapy in rectal cancer treatment, enabling detailed assessment of the circumferential margin (Figure 1), though its accuracy is heavily dependent on skilled interpretation. Anterior resection without preoperative treatment can be considered when circumferential clearance of the tumour or involved lymph nodes of more than 1 mm is predicted; this may equate to 5 mm or less on MRI, depending on radiology expertise. When the circumferential margin is threatened or involved, preoperative radiotherapy is indicated; the authors' preference is chemoradiation using long-course radiotherapy (45 Gy over 5 weeks) combined with 5-fluorouracil (5-FU). This neoadjuvant treatment aims to 'downsize' the cancer and increase the potential for curative surgery. Most series show a complete pathological response in 10–15% of cases, with no persisting cancer in the resected specimen. This practice is also advocated in patients with anterior cancer close to the sphincter, where the clearance margin is limited, and in those whose body habitus is likely to render surgery difficult.

Postoperative radiotherapy is generally less efficacious than preoperative treatment. Furthermore, it is associated with deleterious effects on the functioning of the neorectum and damage to small bowel trapped in the pelvis as a result of surgical adhesions. It is used when the circumferential margin is found to be involved in the pathological specimen, if no preoperative treatment was given. This often represents a failure of accurate preoperative staging or surgical excision.