Management of colorectal cancers

R Lewis, A Flynn, M E Dean, A Melville, A Eastwood, A Booth

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The management of colorectal cancers, published in a recent issue of *Effective Health Care*, is reviewed.

This article is based on a recent issue of *Effective Health Care* which focused on the research evidence for the management of colorectal cancers.¹

Colorectal (bowel) cancer is the second most common cancer in terms of both incidence and mortality in England and Wales. Over 30 000 new cases are diagnosed each year, of which about half will have colorectal cancer registered as the underlying cause of death.

There is evidence that the earlier colorectal cancer can be detected, the better the outcome for the patient. However, early detection is difficult as the most common presenting symptoms of colorectal cancer—change in bowel habit, rectal bleeding, abdominal pain and anaemia—are non-specific, occur relatively frequently in the population, and have a wide variety of causes.

Prognosis for patients depends on the spread of the cancer at diagnosis. Approximately 55% of patients in England and Wales present with advanced colorectal cancer (stage III or IV; Dukes C or D),² so even where surgical removal of the primary tumour is an option, accurate staging is essential for appropriate choice of treatment. Survival rates vary between English health authorities but the average is now around 45% at 5 years after diagnosis, and most of those who live this long are cured.³

This article is based on a series of systematic reviews carried out by the Centre for Reviews and Dissemination to inform the update of the 1997 service guidance for colorectal cancer published by the National Institute for Clinical Excellence (NICE),⁴ from whom full details are available.

ACCESS TO APPROPRIATE SERVICES

NHS referral guidance for colorectal cancer was introduced in July 2000, requiring patients who were suspected by their GP of having cancer to be seen by a specialist in secondary care within 2 weeks of being referred.⁵ The evidence examining the 2 week wait criteria is not extensive, but wide variations exist between services provided.^{6–9}

The CHI/Audit Commission report found that 18% of patients with colorectal cancer were referred as “not urgent” when adherence to national guidelines should have led to urgent referral.¹⁰ This study also found that at least half of those referred as urgent cases did not fit the criteria. Between 1.7% and 14% of patients

referred through fast track services described in the evidence review were found to have cancer.^{7–9 11–24}

Delays associated with inadequate assessment of iron deficiency anaemia are an issue because anaemia may be the only symptom of colon cancer. It appears that the majority of patients with anaemia of unknown cause are not referred for the relevant investigations.²⁵

Open access and one stop lower GI endoscopy services

The service available to patients in the UK is variable, with a wide range of clinic models and diagnostic algorithms in use.^{6–9 11–24 26–28}

Most open access clinics for patients with bowel symptoms offer flexible sigmoidoscopy. The yield of cancers and polyps detected varies widely between clinics.^{6–9 11–24 26–28} Establishment of these services produced other benefits: one report noted that the waiting time for routine outpatient clinics fell from 16 to 8 weeks²⁹ while another noted improvements in the stage of cancers diagnosed.¹⁴

A survey of 164 endoscopy units in the UK revealed that the median number of colonoscopies performed was 375 per 250 000 population per year.³⁰ A shortage of endoscopists and a lack of nursing support and theatre time prevented additional weekly endoscopy sessions.

Surgical specialisation and patient throughput

Six systematic reviews^{31–36} and a number of more recent primary studies were consistent in showing evidence that, for rectal cancer at least, higher patient volumes and greater specialisation among surgeons were associated with much better outcomes—lower surgical complication rates, decreased local recurrence, lower colostomy rates and improved survival.

DIAGNOSIS

In cases of suspected colorectal cancer there are two main types of investigation: endoscopy (flexible sigmoidoscopy or colonoscopy) and imaging (barium enema and CT colonography). Each method has specific advantages and disadvantages that make it more or less appropriate for particular patients. The choice of diagnostic method should depend on the patient's symptoms, age, family history, other risk factors such as colitis or Crohn's disease, as well as their general condition and ability to tolerate any preparation and the test itself. The local availability of facilities, equipment, and skilled staff will inevitably influence the choice of investigation used.

Endoscopic investigation has the advantage of permitting biopsy and histopathological

See end of article for authors' affiliations

Correspondence to:
A Booth, Centre for
Reviews and
Dissemination, University
of York, York YO10 5DD,
UK; ab42@york.ac.uk

assessment of any suspicious lesion and removal of polyps. A prospective study of 13 580 colonoscopies carried out by surgeons in the US found that complication rates were very low.³⁷ Diagnostic colonoscopy caused perforation in 0.02% of cases. Therapeutic colonoscopy (colonoscopy with polypectomy) caused bleeding in 0.19% of cases and perforation in 0.15%.

Flexible sigmoidoscopy is the most appropriate initial investigation for the majority of patients with symptoms that suggest possible lesions in the left (descending or distal) colon, sigmoid or rectum. There is evidence to suggest that, for patients who present with symptoms alone (usually rectal bleeding, changed bowel habit or pain), further investigation after a negative flexible sigmoidoscopy is rarely necessary.³⁸

Diagnostic colonoscopy is usually appropriate for patients with right sided symptoms, except for those with palpable masses for whom imaging (barium enema or CT) is likely to be more suitable. If a complete colonoscopy is not achieved and clinical doubt remains, imaging is necessary.

The reliable diagnosis of colon cancer by colonoscopy requires a skilled colonoscopist who can achieve a high rate of completion (when the whole of the colon is inspected, all the way to the caecum). Two research studies and a UK hospital audit found a clear correlation between completion rates and the number and frequency of examinations performed.^{37 39 40} The total number of colonoscopies carried out by endoscopists was also important. Improvement continues with experience up to a level of 200 cases.^{37 39}

Traditionally, endoscopy has been carried out by hospital doctors. However, there is accumulating evidence that both flexible sigmoidoscopy and diagnostic colonoscopy can be carried out safely by appropriately trained nurses and GPs.^{41–46}

Barium enema is well established in the NHS and staff are experienced in its use. A systematic review of studies of the accuracy of double contrast barium enema and colonoscopy found that colonoscopy is significantly more sensitive than barium enema for the detection of both colorectal cancer and polyps, but barium enema is associated with a much lower risk of complications.⁴⁷ A large retrospective study from a UK teaching hospital came to similar conclusions.⁴⁸

CT colonography (also known as “virtual colonoscopy”) is a relatively new diagnostic technology requiring expertise in its use.⁴⁹ A systematic review of studies comparing CT colonography with colonoscopy found that CT colonography was capable of correctly identifying most polyps over 10 mm in size.⁵⁰

PREOPERATIVE STAGING OF LIVER CANCER

A number of imaging techniques are available to identify liver metastases—ultrasound (US), CT scanning, and magnetic resonance imaging (MRI).

Studies of the diagnostic accuracy of preoperative liver imaging suggest that, overall, CT scanning is slightly better than US.^{51–53} However, there have been few direct comparisons between CT scanning and US in this situation, and the studies that were identified have serious methodological flaws. In general, where abdominal US identifies metastases, it is likely to be accurate, but up to half of patients with negative US scans do in fact have cancer in the liver.^{51–53}

One study (n = 73) reported sensitivity figures for contrast enhanced CT scanning of 94% with a specificity of 92%.⁵¹ However, a smaller study (n = 44) reported a much lower figure for the sensitivity of CT (37.5%) with a specificity of 97%.⁵⁴

LOCAL STAGING OF RECTAL CANCER

MRI appears to be better than CT scanning in locally staging primary rectal cancer.^{55–65} A systematic review found that MRI was superior to CT for the assessment of bowel wall

penetration and the identification of metastatic lymph nodes.⁵⁵ Of several primary studies not included in the systematic review, only one compared imaging techniques directly,⁵⁶ the others used histopathological findings alone as a reference standard.^{57–61 66–68} These studies found that MRI using a body coil^{60 61} or endorectal coil^{56 66–68} was superior to CT^{56–59} for correctly staging rectal cancer. For the assessment of metastatic lymph nodes, MRI using the body coil^{60 61} was found to be superior to CT.^{56–59}

Good quality comparative research studies are required, particularly as the technology used in these studies may now be considered out of date.

Rectal endosonography and endoscopic ultrasonography are used to demonstrate the extent of tumour invasion into the layers of the muscle wall. A systematic review found a sensitivity of 93% and specificity of 81% for rectal endosonography or endoscopic ultrasonography for differentiating benign tumours and early rectal cancers.⁵⁵ Other primary studies have reported levels of sensitivity varying from 0%^{65 69} to 100%,^{56 70–72} and specificity from 80% to 98%.^{56 65 69–72}

The systematic review also found that, compared with CT and MRI, rectal endosonography was the most accurate way of assessing tumour penetration.⁵⁵ However, CT and MRI provide more staging information and are more widely available.

SURGERY

Surgery with curative intent aims to remove the whole tumour; if it succeeds, the patient may be rendered free from cancer. Good surgery—particularly total mesorectal excision (TME) for patients with rectal cancer—is associated with reduced local recurrence and improved long term survival.^{73–76}

Colorectal stents may be used to provide temporary relief of acute intestinal obstruction so that emergency surgery can be avoided.^{77–85} The use of a stent can avoid the need for a stoma.^{77 78 85–88}

Expanding metal stents usually remain effective for more than a year and, in many cases, can provide good palliation until death.^{77–81 87 89–91}

The removal and identification of lymph nodes containing tumour is crucial both to reduce the risk of recurrence and to the decision making on adjuvant therapy.⁹² There is evidence that removing 10 or more nodes improves the accuracy of staging.^{93–95} Patients classed as node negative on the basis of fewer nodes have been shown to have significantly poorer recurrence and survival rates than those classed as node negative on more nodes.^{93 95–97} A study carried out using cancer registry data from 1988–1991 found that 14% of patients treated in the UK had 12 or more nodes examined.⁹⁸

RADIOTHERAPY IN PRIMARY DISEASE

Comparison between radiotherapy combined with blunt dissection surgery with surgery alone for rectal cancer shows that the addition of radiotherapy significantly reduces local recurrence rates.^{99–101} Preoperative radiotherapy at a biological equivalent dose (BED) of ≥ 30 Gy produces a greater proportional reduction in local recurrence when compared with no radiotherapy, than postoperative radiotherapy (57% and 37%, respectively).¹⁰⁰ Preoperative radiotherapy also leads to a significant reduction in mortality rates among patients who receive a BED of 30 Gy or more.¹⁰⁰

Modern treatment methods using megavoltage equipment with a planned volume technique to deliver radiotherapy to smaller volumes of tissue reduce the toxicity of treatment. However, even this form of radiotherapy is likely to cause long term problems with bowel function.¹⁰²

Radiotherapy given before TME reduces local recurrence from 8.2% to 2.4% ($p < 0.001$), but no reduction in mortality has been shown at a median of 2 years after surgery.¹⁰³ Two

randomised controlled trials currently in progress are expected to throw further light on the issue of whether radiotherapy is worthwhile for patients who undergo TME.^{104–105}

ANAL CANCER

Anal cancer is a rare disease and all patients should be referred to multidisciplinary anal cancer teams to optimise their outcomes.

Two large randomised controlled trials comparing radiotherapy (RT) alone with chemoradiotherapy (CRT) have shown a highly statistically significant reduction in local failure.^{106–107} Both saw improvements in colostomy-free survival and reduction in deaths from anal cancer with CRT. Neither showed any significant effect on overall survival. A third randomised controlled trial tested the benefit of adding mitomycin C to 5-fluorouracil (5FU) and radiotherapy.¹⁰⁸ This also demonstrated statistically significant improvements in colostomy-free and disease-free survival. Other forms of treatment, such as surgical excision, may be considered by anal cancer multidisciplinary teams but surgery is usually reserved for salvage.

The current National Cancer Research Network phase III randomised controlled trial (ACT2) is comparing two CRT schedules (mitomycin C, 5FU, and RT versus cisplatin, 5FU, and RT) and post-CRT adjuvant chemotherapy (cisplatin/5FU ×2 versus control).¹⁰⁹ The radiotherapy fields used in this trial are designed to improve outcomes and reduce acute toxicity.

FOLLOW UP

The results of two recently conducted systematic reviews showed that intensive follow up that includes liver imaging was associated with a decrease in mortality from any cause.^{110–111} However, it was not clear which elements of the intensive follow up programme were important. There is some evidence to suggest that CT scanning as part of a routine follow up programme may be useful.^{110–115} One randomised controlled trial found that follow up is efficient and cost effective if patients at higher risk are followed up more intensively than those at lower risk.¹¹⁶ Patients at greatest risk are those with more advanced tumours at the time of resection—particularly stage III cancers.

TREATMENT OF RECURRENT AND ADVANCED DISEASE

Two meta-analyses found significantly lower mortality rates with palliative chemotherapy for patients with metastatic colorectal cancer. In four studies, quality of life was found to be either similar or better in patients who received chemotherapy than in those who did not.^{117–118}

Chemotherapy given early in the course of metastatic disease produces better outcomes than chemotherapy given after symptoms have become severe, increasing survival by 3–6 months without increasing adverse effects on quality of life.^{117–118}

External radiotherapy used alone eases pain in a high proportion of patients with locally advanced rectal cancer. In some patients tumours have gone into complete remission or regressed sufficiently to permit curative surgery after prolonged fractionated radiotherapy of 45–50 Gy.^{99–101}

PALLIATIVE CARE

Most patients with advanced colorectal cancer are cared for at home by GPs and district nurses. Specialist pain control is particularly important for patients with locally recurrent rectal cancer in whom pain can be very severe and difficult to manage. However, a postal survey showed that some GPs were unwilling to define patients as needing palliative care, although an unambiguous diagnosis of incurable malignancy

Implications

The following key recommendations have been identified as priorities for the NHS with the aim of improving outcomes in colorectal cancer:

- Action should be taken to improve recognition of potential symptoms of colorectal cancer in primary care and in the community.
- There is an urgent need for substantial expansion of lower gastrointestinal (GI) endoscopy services.
- Cancer networks and trusts should review the composition and function of colorectal cancer multidisciplinary teams.
- Emergency patients (particularly those with intestinal obstruction) should be managed by colorectal cancer multidisciplinary teams.
- Patients with rectal cancer should be managed by teams trained in all aspects of total mesorectal excision (TME).
- All aspects of patient centred care should be re-assessed.

had been made.¹¹⁹ At the same time, the GPs expressed dissatisfaction with the promptness, clarity about treatment, future management, and the adequacy of information provided by the hospital.

Authors' affiliations

R Lewis, A Flynn, M E Dean, A Eastwood, A Booth, Centre for Reviews and Dissemination, University of York, York, UK
A Melville, Porthmadog, Gwynedd, UK

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