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Diagnosing and managing colorectal cancer

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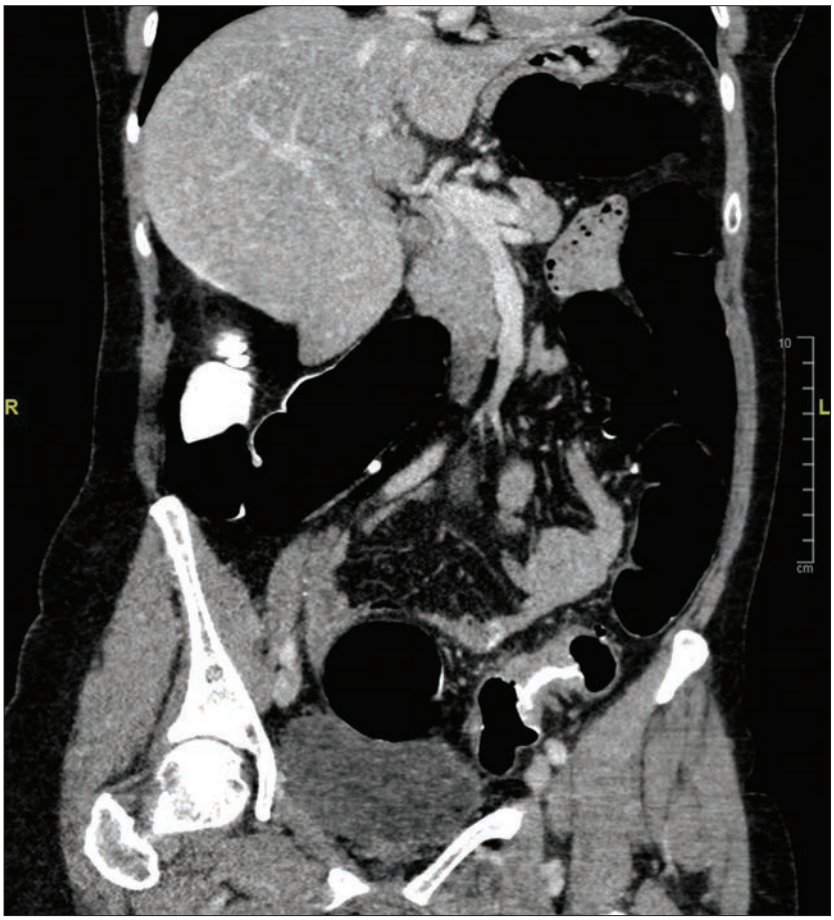

FIGURE 1
CT colonography showing a stenosing sigmoid colon cancer

When should colorectal cancer be suspected?

Which patients are at increased risk?

How is diagnosis confirmed?

COLORECTAL CANCER IS THE FOURTH MOST COMMON CANCER IN THE UK POPULATION. Approximately 42,000 new colorectal cancers are diagnosed every year, and it is the second most common cause of cancer death in the UK.[1] The incidence of colorectal cancer increases with age and it is diagnosed most often in the seventh and eighth decades.[1] It is thought to develop from colonic adenomas. The prompt detection of colorectal cancer is vital as there is good evidence that survival is significantly improved by early diagnosis and intervention.[2,3]

PRESENTATION

Colorectal cancer presents differently according to its location. More than 50% of cancers are located in the rectum and left colon.[1] Right-sided cancers most often present with anaemia. As the diameter of the caecum is large and the bowel contents at this stage liquid, it is uncommon for right-sided cancers to present with obstructive symptoms.[4] Cancers arising from the descending colon typically present with a change in bowel habit, blood in the stool or colicky abdominal pain. Rectal cancers can present with fresh red bleeding however, large tumours can cause tenesmus (the intense and frequent desire to defecate, with little or no stool passed). In both right- and left-sided cancers occasionally the patient may notice an abdominal mass or weight loss.

REFERRAL

The NICE guideline on referral of patients with suspected cancer (NG12) recommends that the following patients should be referred for an urgent appointment with a specialist within two weeks via the suspected cancer pathway referral route:[5]

- Aged 40 and over with unexplained weight loss and abdominal pain
- Aged 50 and over with unexplained rectal bleeding
- Aged under 50 with rectal bleeding and unexplained abdominal pain or change in bowel habit or weight loss or iron deficiency anaemia
- Aged 60 and over with iron-deficiency anaemia or changes in bowel habit
- Any patient with a positive faecal occult blood test (FOBT)
- Any patient with a rectal or abdominal mass

RISK FACTORS FOR COLORECTAL CANCER

Genetic risk factors

There are two well characterised genetic conditions Lynch syndrome (formerly known as hereditary non-polyposis colorectal cancer) and familial »

Table 1

Summary of common surgical procedures

Operative procedure	Location of tumour	Segments of bowel removed	Stoma
Right hemicolectomy	Caecum/ascending colon	Terminal ileum, caecum, ascending colon, hepatic flexure	Only if not fit to join
Extended right hemicolectomy	Transverse colon/splenic flexure	Terminal ileum, caecum, ascending colon, part of transverse colon	Only if not fit to join
Left hemicolectomy	Splenic flexure/descending colon	Part of transverse colon, descending colon, part of sigmoid colon	None
Sigmoid colectomy	Sigmoid	Sigmoid colon	None
Hartmann's procedure	Sigmoid	Sigmoid colon	Colostomy - may be temporary
Anterior resection	Rectal	Sigmoid colon, part of rectum	Temporary ileostomy in some patients
Abdomino-perineal resection	Low rectal tumours not suitable for anastomosis	Sigmoid colon, rectum, anus	Permanent colostomy
Subtotal colectomy	Synchronous tumours, in emergency situations	Caecum, ascending colon, transverse colon, descending colon, sigmoid colon	Ileostomy - may be temporary
Panproctocolectomy	Synchronous tumours, familial adenomatous polyposis	Entire colon, rectum and anus	Permanent ileostomy

adenomatous polyposis (FAP).[6]

Lynch syndrome is an autosomal dominant condition that accounts for 3% of colorectal cancers.[6] It presents with early colorectal cancer typically diagnosed in the fifth decade and is associated with a number of other cancers including endometrial, stomach, small bowel, urothelial (renal pelvis, ureter, bladder) and ovarian cancer.[6]

Recent NICE guidance (DG27) recommends that all patients diagnosed with colorectal cancer should have immunohistochemical testing of their cancer for evidence of Lynch syndrome.[7] If positive the patient and their family can be offered genetic counselling and screening. The Amsterdam II criteria (see box 1, below) can aid in identification of patients at risk of Lynch syndrome based on family history alone who can subsequently be referred for genetic testing.

Box 1

The Amsterdam II criteria

- A minimum of three relatives with a Lynch syndrome associated cancer, one of whom should be a first-degree relative of the other two
- At least two successive generations affected
- At least one cancer diagnosed before age 50
- Familial adenomatous polyposis should be excluded

FAP is inherited in an autosomal dominant fashion due to a mutation in the adenomatous polyposis coli (APC) tumour suppressor gene on chromosome 5q although 20% of cases are caused by new mutations. FAP accounts for < 1% of colorectal cancers.[8] The condition presents with hundreds of adenomatous polyps of the colon in the second and third decades of life. Those affected also develop duodenal adenomas along with well characterised extra-colonic manifestations of the disease.

Dietary and lifestyle risk factors

There is strong evidence that high consumption of red meat (beef, pork and lamb) and processed meat increases the risk of developing colorectal cancers.[9] There is also an increased risk in those with a high fat diet. In contrast diets rich in wholegrains, dietary fibre and dairy products are considered to be protective.[9]

Being physically active is associated with a reduction in the risk of colorectal cancer, whereas being overweight or obese is associated with an increased risk.[9] A large meta-analysis found the risk to be increased by 5% for every 5 kg/m^2 the patient is above normal BMI.[7] Smoking is associated with an increased risk of developing colorectal cancer[7] as is high alcohol consumption (more than 30 g per day).[9]

Predisposing conditions

Inflammatory bowel disease (Crohn's disease and ulcerative colitis) is associated with an increase in the risk of developing colorectal cancer. The risk to these patients remains the same as the general population in the first few years following their diagnosis but rises to 2% at ten years.[10] All colitis patients should be offered surveillance colonoscopy ten years after the onset of symptoms.[10,11] The frequency of subsequent surveillance is determined by initial surveillance colonoscopy findings.[10,11]

CONFIRMING DIAGNOSIS

Endoscopy

Colonoscopy is the gold standard investigation for suspected colorectal cancer.[12] It visualises the entire large bowel, is very sensitive for colorectal cancer and allows for both tissue diagnoses and polypectomy.[13] A complete colonoscopy, whereby the caecum is intubated, is reliant on

Table 2

Five-year relative survival rates of patients diagnosed with colorectal cancer based on stage at diagnosis[1,13]

Dukes stage	TNM	Frequency at diagnosis	Histological features	Five-year survival rate Men	Five-year survival rate Women
Dukes A	T1 or T2, N0, M0	11%	Invasive carcinoma not breaching the muscularis propria	95%	100%
Dukes B	T3 or T4, N0, M0	35%	Invasive carcinoma breaching the muscularis propria but not involving the regional lymph nodes	84%	86%
Dukes C	Any T, N1 or N2, M0	26%	Invasive carcinoma involving regional lymph nodes	63%	63%
Dukes D	Any T, Any N, M1	28%	Distant metastasis present	7%	8%

adequate bowel preparation, patient tolerance and technical skill.[14] Colonoscopy is an invasive test which carries a risk of bleeding, perforation and complications as a consequence of sedative medication such as myocardial infarction and pneumonia.[14]

CT colonography

CT colonography or virtual colonoscopy (see figure 1, p17) is non-invasive, widely available and has replaced the use of barium enemas in most UK centres.[4,15] It is used as an alternative to endoscopy in patients who cannot tolerate bowel preparation e.g. the frail and elderly, as it is able to detect polypoid lesions as small as 6 mm.[4]

STAGING

Once a diagnosis of cancer has been made the patient will undergo staging with a CT of the chest, abdomen and pelvis with intravenous contrast.[12] This allows for assessment of local invasion, lymph node spread and distant metastasis (most commonly in the liver and lungs). For rectal cancers, the patient will also have an MRI of the pelvis to determine the necessity for preoperative radiotherapy or chemotherapy in the hope of reducing local recurrence rates.[12,15]

A baseline blood test for the colorectal tumour marker carcinoembryonic antigen (CEA) is also taken.

All cases of colorectal cancer should be discussed at a specialist colorectal multidisciplinary team (MDT) meeting to determine the optimum treatment plan.

TREATMENT

Surgery

Surgery is the only potentially curative treatment for colorectal adenocarcinoma. Around two-thirds of patients diagnosed with bowel cancer are offered surgical management.[3] The aim of surgery is to optimise the oncological outcome while maintaining as normal bowel function as possible.

The exact procedure performed depends on the location of the tumour and depth of invasion (see table 1, p18). Increasingly laparoscopic surgery is being used, with more than half of major resections in 2014-2015 completed laparoscopically.[3] NICE recommends laparoscopic surgery in patients who are felt to be suitable for either laparoscopic or open procedures.[12]

Stomas

A defunctioning (or loop) stoma is formed from a bowel segment upstream from the area of anastomosis, which diverts stool to protect the patient from bowel content leakage while the anastomosis heals. These types of stomas are frequently seen following rectal surgery as the rectum has a poor blood supply and heals more slowly compared with the rest of the colon. These stomas do not have to be permanent and discussions can be had with the surgeon at a later stage to consider restoration of bowel continuity.

A permanent end colostomy or ileostomy may be formed as part of surgical treatment.

Surgical management of metastases

Patients with liver and lung metastases can be considered for resection, in situ ablation or oncological treatments.[15] If the liver disease is considered resectable it can be performed as a single- or two-stage procedure combined with the bowel resection depending on the patient's fitness and specialist MDT input.

Chemotherapy/radiotherapy

Patients with Dukes B and C disease may be offered adjuvant chemotherapy to reduce risk of recurrence (see table 2, above).[12,15] There is evidence of improved survival rates even in Dukes D patients treated with chemotherapy.[12,15]

Rectal cancers can be downsized or the risk of local recurrence reduced with preoperative chemotherapy or radiotherapy.[15]

Decisions on appropriate treatment should be made at MDT meetings in conjunction with discussions with the patient.

Palliative management

Palliative management may involve best supportive care only, palliative chemotherapy/radiotherapy or palliative stenting in obstructing tumours. Palliative stenting cannot be performed in rectal cancers as it causes intractable tensesmus.[12]

Emergency management

In patients presenting as an emergency with obstruction treatment options include: emergency surgery, colonic stenting as a bridge to elective »

key points

SELECTED BY

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Colorectal cancer is the fourth most common cancer in the UK. Approximately 42,000 new colorectal cancers are diagnosed every year, and it is the second most common cause of cancer deaths in the UK. Most cancers are thought to develop from colonic adenomas and incidence is strongly related to age.

The majority of cancers are left sided and typically present with a change in bowel habit, blood in the stool or colicky abdominal pain. Rectal cancers can present with fresh red bleeding and large tumours can cause tenesmus (the intense and frequent desire to defecate, with little or no stool passed). Right-sided cancers most often present with anaemia. As the diameter of the caecum is large and the bowel contents at this stage liquid, it is uncommon for right-sided cancers to present with obstructive symptoms. In both right- and left-sided cancers occasionally the patient may notice an abdominal mass or inexplicable weight loss.

Lynch syndrome is an autosomal dominant condition that accounts for 3% of colorectal cancers. It presents with early colorectal cancer typically diagnosed in the fifth decade and is associated with a number of other cancers including endometrial, stomach, small bowel, urothelial (renal pelvis, ureter, bladder) and ovarian cancer. Familial adenomatous polyposis is also inherited in an autosomal dominant fashion and accounts for < 1% of colorectal cancers. Lifestyle risk factors include high consumption of red or processed meat, low fibre intake, sedentary lifestyle, obesity, smoking and high alcohol consumption. Patients with IBD are also at increased risk and all colitis patients should be offered surveillance colonoscopy starting ten years after onset of symptoms.

Colonoscopy is the gold standard investigation for suspected colorectal cancer. CT colonography is used as an alternative to endoscopy in patients who cannot tolerate bowel preparation e.g. the frail and elderly. Once a diagnosis of cancer has been made the patient will undergo staging with a contrast-enhanced CT of the chest, abdomen and pelvis. This allows for assessment of local invasion, lymph node spread and distant metastasis (most commonly in the liver and lungs). For rectal cancers, the patient will also have an MRI of the pelvis to determine the necessity for preoperative radiotherapy or chemotherapy in the hope of reducing local recurrence rates.

Surgery is the only potentially curative treatment for colorectal adenocarcinoma and is offered to around two-thirds of patients. Increasingly, laparoscopic surgery is used. Defunctioning stomas are frequently created following rectal surgery as the rectum has a poor blood supply and heals more slowly compared with the rest of the colon. Patients with Dukes B and C disease should be considered for adjuvant chemotherapy to reduce the risk of recurrence. All patients who undergo resection for colorectal cancer should have formal specialist follow-up.

resection or as a palliative procedure and a defunctioning stoma as a palliative procedure.

OUTCOMES

The overall five-year survival rate for patients diagnosed with colorectal cancer is 59%.[1] The survival rates can be further stratified according to histological features. There are several commonly used staging systems including Dukes staging and TNM (see table 2, p19).

A large Europe-wide population-based study found the average five-year survival rate for colon cancer in the European Union to be 57% for both women and men.[17] The best survival rate was in Germany, with 62.2% of patients surviving five years post diagnosis.[17] In comparison the same study found that the five-year survival rate in the UK was 51.8%.[17] The five-year survival rates when broken down by region show better survival rates in Northern Ireland (55%) and the worst survival rates in Wales (49.9%).[17] No conclusive evidence to account for this difference has yet been presented. Five-year relative survival rates of patients diagnosed with colorectal cancer based on stage at diagnosis are shown in table 2, p19.[2]

SCREENING

In England, Northern Ireland and Wales patients are offered screening by FOBT every two years from the age of 60 to 75. In Scotland this is now offered from the age of 50. There is strong evidence that screening in this way significantly reduces mortality from colorectal cancer by 15-33% as demonstrated in three large randomised controlled trials.[18,19,20]

There is a move towards abandoning FOBT in favour of faecal immunochemical testing. This has already happened in Scotland, and is based on evidence of improved detection sensitivity and better patient uptake of the single sample test compared with the FOBT which involves multiple samples.[21,22]

In addition to faecal testing, the Bowel Scope programme which offers a single flexible sigmoidoscopy to all men and women aged 55 in England is being rolled out. This has recently been shown to confer 30% improvement in mortality over a 17-year follow-up period.[23]

MONITORING AND FOLLOW-UP

All patients who undergo resection for colorectal cancer should have formal specialist follow-up. There is evidence that the main benefit of follow-up is earlier detection of metastatic disease.[15] There is no conclusive evidence as to what is the optimal follow-up regimen.[15] Most notably the FACS randomised clinical trial looked at intensive six monthly CEA, CT and combined CEA/CT follow-up and concluded that compared with minimal follow-up (a single CT scan at 12-18 months) there was earlier detection of recurrence and a higher rate of surgical treatment with curative intent, but overall no survival benefit.[24]

NICE recommends six monthly CEA measurement for the first three years and a minimum of two CT scans in the same period.[12] Patients are also offered colonoscopy at one and five years to aid detection of further adenomatous polyps.[12] The exact follow-up regimen may vary according to local guidance. Patients should be reinvestigated at any point if there is clinical, radiological or biochemical evidence of disease recurrence.[12]

LATE EFFECTS

The late effects of colorectal cancer and its subsequent treatment include radiation proctitis, change in bowel and bladder control, sexual dysfunction and anterior resection syndrome.[25] The management of these problems requires a specialist approach and involvement of the MDT.

Competing interests: None

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Useful information

Cancer Research UK
www.cancerresearchuk.org/about-cancer/bowel-cancer

Bowel Cancer UK
www.bowelcanceruk.org.uk

Macmillan Cancer Support
www.macmillan.org.uk

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