COLORECTAL NEOPLASIA—III: TREATMENT AND PREVENTION

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Principles of treatment of large bowel cancer

	Cure	Palliation	Recurrence
Resection	+++	+++	+
Radiotherapy	+	+	++
Chemotherapy	—	±	±

The mainstay of treatment for large bowel cancer is still surgery with wide excision, including the appropriate lymph drainage areas. For most patients the appropriate excision would be a right or left hemicolectomy, but in some patients with several adenomas and young patients with cancer some surgeons advocate a total colectomy and ileorectal anastomosis. Radiotherapy has as yet played little part in the treatment of carcinoma of the colon.

Right colonic cancer

Bowel removal by right hemicolectomy. A is anastomosed to B.

Cancer of the right colon with or without obstruction is treated by right hemicolectomy with primary anastomosis. Resection is indicated even in the presence of hepatic metastases because this gives the best palliation. In patients with manifest obstruction the operation has to be carried out as an emergency. Occasionally resection is not possible and the surgeon has to bypass the tumour by anastomosing the ileum to the transverse colon.

Left colonic cancer

Procedure for left hemicolectomy. A is anastomosed to B.

In the absence of intestinal obstruction the treatment of choice for cancer of the left colon is a wide excision by left hemicolectomy or sigmoid colectomy with primary anastomosis. Resection is carried out even in the presence of secondary tumours of the liver because this gives the best palliation. Colostomy alone is never justified in the absence of obstruction because it has little palliative value.

In cases of left colonic obstruction the traditional method was to use a three stage procedure: stage 1, colostomy alone; stage 2, resection with anastomosis; stage 3, closure of colostomy. In recent years there has been a tendency towards resection as the primary procedure. Usually no anastomosis is attempted at the emergency operation. The upper residual colon is exteriorised as a colostomy and the lower colon is either exteriorised (by producing a mucus fistula) or closed (by Hartmann's procedure). A second operation can be carried out when the patient is fully recovered and intestinal continuity restored.

Some groups of surgeons have gone further and not only have they resected the tumour but they have carried out primary anastomosis. This has been helped by on table lavage of the colon, which clears faeces and reduces the disproportion in size between bowel above and below the resected carcinoma. A further option is to perform a subtotal colectomy and anastomose the small bowel to the distal residual colon or rectum.

Carcinoma of the rectum

Procedure for anterior resection. A is anastomosed to B, restoring continuity.

Procedure for abdominoperineal resection. A is exteriorised as an end colostomy.

Operable carcinoma of the upper half of the rectum can be adequately excised and anastomosis effected. This procedure is called anterior resection of the rectum. The anastomosis may be carried out by hand suture, but the advent of circular stapling devices has made it technically easier to carry out some low anterior resections.

The treatment options for cancers in the lower rectum are more varied. The standard treatment for tumours less than 6 cm from the anal margin is still abdominoperineal excision of the rectum with an end colostomy. Other treatment options have to be considered. Some tumours at 5-6 cm diameter can be managed by rectal excision and coloanal anastomosis. In small tumours less than 3-4 cm in diameter without obvious extrarectal spread local treatment may be effective; with careful selection the results can be excellent. Satisfactory methods are local excision, diathermy destruction, and local radiotherapy.

Operative mortality and morbidity

Complications of large bowel resection

Immediate

Cardiorespiratory
Anastomotic leak
Wound infection
Urinary retention
Impotence

Late

Recurrence:
Systemic
Local

In most centres the operative mortality for surgery in large bowel cancer is less than 5% and in some centres it is less than 2%. The operative mortality is higher if surgery is carried out for obstruction or perforation. The principal causes of death are coincident cardiorespiratory problems in elderly patients and leakage from an intestinal anastomosis. Anastomotic leakage varies in severity from a minor self limiting problem to a major life threatening one. Though there is a slight risk of leakage from any colonic anastomosis, the risk is greater in low colorectal anastomosis. The surgeon and the technique are the other associated factors in the incidence of anastomotic leakage.

Other non-fatal complications are wound infection and genitourinary dysfunction. Both the incidence and the severity of wound infection have been reduced by using perioperative antibiotics as prophylaxis against both aerobic and anaerobic organisms. Genitourinary dysfunction may manifest as either postoperative retention or later impotence. The principal cause of both of these is damage to the autonomic nerves within the pelvis.

Follow up programmes

Follow up investigations

- Clinical review
- Measurement of carcinoembryonic antigen
- Colonoscopy
- Ultrasonography or computed tomography

The aim of any follow up programme should be to identify treatable recurrent disease as early as possible and to detect secondary metachronous carcinoma of the bowel. Regular clinical review is largely ineffective. For this reason attempts to detect asymptomatic recurrence or metachronous tumours are being assessed. Possible useful investigations may be endoscopy, assessment of tumour markers by blood sampling, and regular imaging by ultrasonography or computed tomography. Colonoscopy may lead to early detection of metachronous or recurrent tumours in asymptomatic patients. Regular blood tests for tumour products may be used. Measurement of carcinoembryonic antigen concentration is the most usual test and if it becomes raised then intensive investigation with the potential of a "second look" laparotomy is considered. Unfortunately it is unusual to pick up recurrence amenable to curative resection.

Another approach is to do regular imaging. Ultrasonography of the liver and computed tomography of the liver or pelvis have been suggested. It is uncertain whether such a costly regimen is justified and it has not won general acceptance in the United Kingdom.

Recurrence

Survival three years after treatment of carcinoma of the rectum

Age corrected survival of survivors of curative resection	82% (99/121)
Age corrected survival after curative resection	77% (99/128)
Crude survival after curative resection	70% (89/128)
Crude tumour free survival after curative resection	63% (81/128)
Crude survival	47% (89/189)
Crude tumour free survival of referred patients	43% (81/189)
Age corrected survival of survivors of curative resection	90% (93/104)
Age corrected survival after curative resection	86% (93/110)
Crude survival after curative resection	76% (84/110)

Different ways of reporting survival in a group of 189 patients with rectal cancer. Survival at three years varies from 43% to 90% depending on the criteria adopted.

Most tumour recurrence becomes manifest in the first three years after surgery, though there is still a risk of recurrence after this time. Distant recurrence is most commonly seen in the liver. This may possibly be lessened by hepatic perfusion with cytotoxic agents at operation, and this method is under investigation. A solitary secondary deposit in the liver or lung may be the only evidence of recurrence. In this circumstance radical excision by partial hepatectomy or lobectomy is surprisingly effective. Local recurrence due to implantation of viable tumour cells at the anastomosis is rare. Local recurrence is usually due to growth from extraluminal tumour deposits, which subsequently involve the bowel from without. For this reason a curative resection at "second look" laparotomy is rarely possible. Local recurrence is commoner when the primary tumour was bulky, of high grade malignancy, or had associated lymph nodes, or if it was in the lower rectum.

Improving the results of surgery

Types of recurrence

- Local
- Distant
 - Liver only
 - Lung only
 - Diffuse

The rate of local recurrence after rectal resection varies in different series from less than 5% to greater than 30%. This rate is related to the surgeon and the extent of local spread. Even radical resection may be incomplete because lymphatic chains extend beyond the limits of resection. Rectal cancer may recur in the lymphatic tissue of the lateral pelvic wall.

A margin of 2 cm distal to the tumour is considered adequate to remove radically all intramural tumour, but the mesorectum requires special attention. Inadequate removal of the mesorectum leaves potentially affected lymph nodes. Careful meticulous attention to dissection of the mesorectum is believed to reduce local recurrence rates.

Radiotherapy

Local recurrence free survival in those receiving surgery only and in those receiving preoperative radiotherapy in a randomised controlled trial.

Radiotherapy given either before or after the operation decreases the rate of local recurrence of rectal cancers. If given before the operation the tumour is easily targeted and it does not increase the risks of subsequent surgery. A minority of patients will be found to have early disease; radiotherapy does not confer any additional benefit for these patients. Patients can be selected for postoperative radiotherapy on the basis of the operative and pathological findings, but small bowel may be in the radiotherapy field and is at risk of significant radiation injury. While radiotherapy reduces the rate of local recurrence it does not seem to prolong survival as patients die of distant metastases outside the radiotherapy field.

Chemotherapy

The role of adjuvant chemotherapy is not established. In the United States it is advised for some cancers but is not yet accepted in the United Kingdom

Adjuvant therapy

At present there is no clear indication for routine adjuvant chemotherapy outside of clinical trials. Although individual studies show no benefit, meta-analysis of published randomised trials has shown a slight survival advantage for patients treated with 5-fluorouracil. A recent study has suggested some improved survival for patients given a combination of 5-fluorouracil and levamisole. Some authorities advocate that this treatment should be considered for patients with lymph node metastases. Adjuvant intraportal 5-fluorouracil given through a catheter introduced at laparotomy is currently under investigation in the United Kingdom in the AXIS trial (Adjuvant X-ray and Infusion Study).

For patients with advanced disease 5-fluorouracil is the drug of choice

Advanced disease

5-Fluorouracil is also the best drug for patients with advanced disease, but the response rate is poor and toxicity of treatment may impair the quality of life. Hepatic artery infusion of 5-fluorouracil with or without chemoembolisation with degradable starch microspheres may reduce systemic toxicity and is under evaluation. An inflammatory infiltrate in colorectal cancer is a favourable prognostic sign. Immunotherapy with the lymphokines interleukin 2 and interferon alfa to augment any antitumour immune response has caused subjective improvements, but the toxicity is high and significant objective responses have not emerged.

Prognosis

Bad prognostic features

- Clinical
 - Local fixity
 - Distant metastases
- Pathological
 - Depth of invasion
 - Lymph node metastases
 - Absent lymphocytic infiltration

The life expectancy of a patient with large bowel cancer depends on the degree of spread at presentation. Factors which adversely affect the prognosis are distant metastases, local spread causing fixation to irremovable structures, high histological grade malignancy, and spread to regional lymph nodes. For all patients the outcome in terms of survival is about 25%, but in patients thought to have a curable resection at operation it is better than 50%, and if the tumour has not penetrated the full thickness of the colonic wall there is almost normal life expectancy.

Prevention

Haemoccult test card. A sample of faeces is smeared on the test card. Hydrogen peroxide is added in the laboratory. A blue colour change indicates the presence of blood.

Causes of positive result on testing for faecal occult blood

- Hiatus hernia
- Peptic ulcer
- Piles and other minor anal disease
- Colonic adenoma
- Carcinoma of the colon

High risk groups

- People with a family history of familial polyposis
- People with a strong family history of large bowel cancer
- People with longstanding ulcerative colitis
- People who have undergone resection of colonic carcinoma or a polyp

Population screening

Studies in the United States, Germany, and the United Kingdom have suggested that the screening of large groups may help in either the prevention or the early diagnosis of large bowel cancer. The method is to test for blood in the faeces and to investigate subjects with positive test results. There are several simple tests, usually based on guaiac impregnated strips which change colour in the presence of blood (Haemoccult, Faecotest). One dilemma of occult blood testing is that if the test is very sensitive it yields huge numbers of false positive results, whereas if it is of low sensitivity false negative results occur.

All studies have had difficulty in getting good patient acceptance of screening procedures. Investigation of patients with positive test results should include clinical examination and colonoscopy. Most studies have shown a good yield of minor colonic disturbances but only a modest number of carcinomas. In some studies the cancers diagnosed appear to be at an earlier pathological stage. Other groups have thrown doubt on the usefulness of screening because both false positive and false negative results occur. Some hold that the yield of serious, asymptomatic colonic disease is so small that the cost of population screening is not justified.

Group screening

There has been some advocacy for routine regular examination of the large bowel as part of health checks in people aged over 50. As large bowel tumours are common this is superficially attractive, but, as yet, there is little evidence to support its usefulness.

Individual screening

Some people are known to have a high risk of developing large bowel cancer. Screening of people from families with a history of cancer, polyposis, and inflammatory bowel disease is now generally accepted. Any adenomas detected are removed and patients with multiple adenomas are treated by prophylactic excisional surgery.

The photograph was produced by the department of medical illustration, Salford Health Authority.

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