*Papers and Originals***RESULTS OF TREATMENT OF CARCINOMA OF COLON AND RECTUM**

BY

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A personal series of cases of carcinoma of the colon and rectum has been reviewed to provide current information on three problems: (1) post-operative mortality accompanying resection of carcinoma of the large bowel; (2) five-year-survival rate; and (3) association of carcinoma in the large bowel with primary carcinoma in other organs.

Present Series

The series reviewed, treated consecutively during 1947-62, comprises 1,015 cases (Table I). The age incidence (Fig. 1) and sex incidence (Fig. 2) do not depart from the

TABLE I.—*Distribution of Carcinoma of Colon and Rectum in 1,015 Cases*

Site	No.
Right colon	117
Caecum	46
Ascending colon	32
Hepatic flexure	24
Proximal transverse colon	15
Upper left colon	70
Distal transverse colon	14
Splenic flexure	19
Descending colon	37
Sigmoid colon	113
Total	300
Rectum	688
Anal canal and anus	27

FIG. 1.—Age incidence for carcinoma of large bowel. Right colon shows a slight preponderance of older people.

FIG. 2.—Sex incidence of carcinoma of large bowel. Steady increase in incidence in males from right to left colon is shown.

usual order. Carcinoma in the right colon occurs in a slightly older age-group. Carcinoma of the colon is more common in females, but this is reversed in the rectum.

Nearly all cases have come from South-East Australia. A small number treated on international visits have been included. Private and public cases (Royal Melbourne Hospital) have been grouped together.

Follow-up.—There has been a complete follow-up on all cases. This has been the responsibility of a follow-up secretary (Mrs. E. Debney). The invaluable assistance provided by medical colleagues is gratefully acknowledged. General practitioners have taken considerable trouble to obtain vital information. The introduction of the Cancer Follow-Up Clinic at the Royal Melbourne Hospital proved important for this work. Sister T. E. Williams, of that clinic, and Miss M. E. Flood, cancer records clerk of the Royal Melbourne Hospital, and the Central Cancer Registry have provided many missing links. In most instances the cause of death is known. However, a necropsy was not always carried out on patients dying in hospital soon after operation, and although pulmonary embolism, coronary thrombosis, or peritonitis was suspected there was some uncertainty. With patients dying in the remote post-operative period exact information such as this was less important, but a great deal of trouble was taken to ascertain the presence and site of secondary spread from the original tumour.

Non-resectable Cases

All cases, resectable and non-resectable, have been included in the total of 1,015 cases. The incidence of non-resectable cases is shown in Table II. The most common reason for non-resectability was spread of the tumour. Only a small number were rejected because of age, frailty, or refusal. Although the non-resectable group is important, with considerable therapeutic implications, it is not considered further in this review.

TABLE II.—*Incidence of Non-resectable Cases in Carcinoma of Colon and Rectum*

Site	No.	Not Resected
Right colon	117	15 (13%)
Upper left colon	70	6 (9%)
Sigmoid colon	113	19 (17%)
Total	300	40 (13%)
Rectum	688	64 (9.3%)

Resectable Cases**Mortality Associated with Resection**

Deaths within four weeks of operation have been classified under "operative," regardless of the cause. The mortality accompanying resections of carcinoma of the colon and rectum is shown in Table III.

The mortality was greater when resection was performed as a palliative procedure. The resection was classified as palliative when the tumour had spread beyond the range

of resection or when a patient was in a weakened condition and did not appear able to tolerate the optimal resection (Table IV).

TABLE III.—*Operative Mortality After Resection of Carcinoma of Colon and Rectum*

Site	No.	Post-operative Deaths
Right colon	102	5 (4.9%)
Upper left colon	64	4 (6.3%)
Sigmoid colon	94	5 (5.3%)
Total	260	14 (5.4%)
Rectum	625	34 (5.4%)

TABLE IV.—*Post-operative Mortality After Palliative and Curative Resections*

	Palliative		Curative	
	No.	Post-operative Deaths	No.	Post-operative Deaths
Colon	98	6 (6.1%)	162	8 (4.9%)
Rectum	218	20 (9.2%)	407	14 (3.4%)

The post-operative mortality rose in the older age-groups (Table V). The older persons progressed well through the operation, and failure was often unexpected.

TABLE V.—*Post-operative Mortality in Three Main Age-groups*

	Under 60		60-69		70 and Over	
	No.	No. Dead	No.	No. Dead	No.	No. Dead
Colon	108	2 (1.9%)	77	5 (6.5%)	75	7 (9.3%)
Rectum	272	5 (1.9%)	198	10 (5.1%)	155	19 (12.3%)

In 7 of the 14 deaths occurring after excision of a carcinoma of the colon coronary occlusion or pulmonary embolism was responsible for an unexpected abrupt end. Two patients were in a senile state and a palliative Paul-Mikulicz type of operation was performed; in neither case was death related apparently to operation. Two patients died of peritonitis (one not proved), and a third had a severe haemorrhage into the rectum which disrupted the anastomosis. One patient died of proved bronchopneumonia; another had a ruptured aortic aneurysm.

In 17 of the 34 deaths after excision of the rectum either pulmonary embolism or coronary occlusion seemed to be responsible for a sudden end. The incidence for this mode of death was the same as that occurring after excision of a carcinoma of the colon (Table VI). In eight patients the cause of death was peritonitis or was strongly suspected as such. This occurred after low intrapelvic anastomosis or after the early types of pull-through anastomosis (Table VII). With the pull-through operation of the type advocated by Bacon (1960) and Turnbull and Cuthbertson (1961) death from peritonitis has been eliminated in a consecutive series of 36 cases.

TABLE VI.—*Incidence of Sudden Post-operative Deaths After Excision of Carcinoma of Colon or Rectum*

	No. of Cases	Sudden Deaths
Colon	260	7 (2.7%)
Rectum	625	17 (2.7%)

TABLE VII.—*Effect of Anastomosis and Preservation of Anal Sphincters on Mortality After Operation*

Type of Operation	No. of Cases	Deaths
Excision of rectum with terminal colostomy anastomosis	391	18 (4.6%)
Miscellaneous (local excision and Hartmann's operation)	220	14 (6.4%)
Miscellaneous (local excision and Hartmann's operation)	14	2 (14.3%)

Five-year-survival Rate

In this series 143 patients with carcinoma of the colon were treated five years or more ago and 63 (44.1%) survived. Of 347 cases with carcinoma of the rectum treated five years or more ago, 134 (38.6%) survived. These percentage figures give the absolute five-year-survival rate (Table VIII).

TABLE VIII.—*Five-year Survivors After Treatment of Carcinoma of Colon and Rectum*

Site of Tumour	No. of Cases	No. Alive After Five Years
Right colon	57	25 (43.9%)
Upper left colon	27	6 (22.2%)
Sigmoid colon	59	32 (54.2%)
Total	143	63 (44.1%)
Rectum	347	134 (38.6%)

If curative excisions only are analysed the five-year-survival rate for carcinoma of the colon is 78.8%, and for carcinoma of the rectum 64.8% (Table IX).

TABLE IX.—*Five-year Survivors After Curative Excision of Carcinoma of Colon and Rectum*

Site of Tumour	No. of Cases	No. Alive After Five Years
Right colon	33	25 (75.8%)
Upper left colon	10	6 (60.0%)
Sigmoid colon	37	32 (86.5%)
Total	80	63 (78.8%)
Rectum	199	129 (64.8%)

Of the 17 patients subjected to curative excision of carcinoma of the colon and who did not survive five years the cause of failure is shown in Table X. So far three patients have died from recurrence of carcinoma after the five-year period. One of these exhibited secondary deposits in the liver eight years after removal of a carcinoma of the sigmoid colon. The second died with a secondary mass in the left lobe of the liver 6 years and 11 months after resection of a carcinoma of the right colon. The third died with secondary deposits in the peritoneal cavity five years and one month after resection of a carcinoma of the sigmoid colon and of the rectum.

TABLE X.—*Cause of Failure in 17 Patients who Died Within Five Years of Curative Excision of Carcinoma of Colon*

Cause of Failure	No.
Post-operative deaths	4
Peritoneal recurrence (7)	9
Liver metastases (1)	1
Local recurrence (1)	1
Lung metastases	2
Carcinoma elsewhere	1
Coronary occlusion	1

There were 70 patients subjected to curative excision of the rectum who failed to survive five years (Table XI). In 18 patients the tumour recurred after the five-year period had expired. In all but two the recurrence was "systemic"

TABLE XI.—*Cause of Failure in 70 Patients who Died Within Five Years of Curative Excision of Carcinoma of Rectum*

Cause of Failure	No.
Post-operative deaths	8
Peritoneal recurrence	30
Liver metastases	2
Local recurrence	12
Systemic recurrence { Lung	2
Bone	2
Brain	2
Coronary occlusion	8
Cerebrovascular accident	2
Suicide	1
Bronchopneumonia	1
Uncertain	4

outside the portal or "regional" field. The site and timing of the recurrence are shown in Fig. 3.

FIG. 3.—Diagram showing incidence of late systemic metastases.

These results reveal an important difference between rectal and colonic carcinoma. In the former there is a special tendency to develop systemic metastases.

Development of Additional Second Primary Carcinoma

In the series of 1,015 cases of carcinoma of the large bowel 54 have so far had more than one primary tumour. In 27 the second tumour was observed at the same time as the first. In 18 of these 27 the second focus was in the bowel close to the first and the problem was not complicated. In seven the second tumour was more remotely situated in the large bowel (Fig. 4). In two the second tumour was present on the skin (lip, forehead) at the time of the resection.

In nine patients a carcinoma developed in the colon or rectum some time after removal of a tumour from the large bowel. The time interval in this series varied from 30 to 2 years (Fig. 5).

In eight cases there was an association between carcinoma of the breast and carcinoma of the large bowel. In seven the breast tumour developed first, and in seven instances the large-bowel tumour occurred in the rectum (Fig. 6).

In one case a carcinoma of the stomach developed five years after removal of a carcinoma of the caecum (and prior to this a carcinoma had been removed from the rectum). In another case carcinoma of the prostate occurred three years after removing a carcinoma of the ascending colon. In one woman a carcinoma of the anal

canal was removed and three months afterwards she developed symptoms found to be caused by a post-cricoid tumour. A woman had a carcinoma of the cervix and 14 years later developed a carcinoma of the rectum. Two patients had a carcinoma of the skin after receiving treatment for a carcinoma of the rectum. Another developed a carcinoma of the rectum four years after removal of a primary tumour in the lung. New bladder carcinomas appeared in two patients. One patient had a carcinoma of the vulva and 14 years later a primary tumour in the rectum.

Discussion

This series has been a continuous, personal one, free of some of the disadvantages of collective series from one or more institutions. The follow-up studies have been complete, although the exact cause of death was not always known. In the early stages the follow-up of these cases was difficult because it introduced a procedure to which many people, medical and lay alike, were not accustomed. General practitioners have been quick to realize the importance of such studies and have been most helpful. In public hospitals there is a tendency for patients to get "lost," and in the activities connected with teaching and research it has proved unfortunately common for patients to enter hospital, even into adjoining wards, and for one not to learn about it for some time. The study of human cancer extends over a long period of time—this series represents 15 years' work—and it is impossible for one individual to watch all patients from start to finish. This calls for the closest team-work between practitioner and specialist, an association which must continue when patients drift away from one or the other. The importance of follow-up investigations cannot be overemphasized. The fate of patients must be known if methods of treatment are to be evaluated.

Most tumours have been resected, although only about half the patients have prospects of permanent cure. An occasional patient has a long survival after palliative excision, but this is exceptional. The term "curative" resection has been used to designate procedures carried out with the intention of cure. They are not all "radical"—that is, some procedures have entailed fulguration of a superficial carcinoma in the lowest part of the rectum. On the other hand, it is sometimes necessary to be quite radical to obtain palliation. One of the reasons it has been difficult to compare results of treatment has been the various use of, and the different meanings attached to, terms such as "curative" and "radical."

FIG. 4

FIG. 5

FIG. 6

FIG. 4.—Seven cases with a second carcinoma situated in a remote segment of bowel and occurring simultaneously with the first. FIG. 5.—Nine cases with a second carcinoma situated in a remote segment of bowel and occurring subsequent to the first. FIG. 6.—Eight cases of carcinoma of breast and carcinoma of large bowel.

The incidence of curative excisions in this series (54% for the colon and 59% for the rectum) is much less than the 67% for carcinoma of the rectum reported from St. Mark's Hospital and 75% and 68.3% respectively reported for colon and rectum from the Presbyterian Hospital, New York, but my better five-year results indicate that different criteria are used to decide curability. The absolute five-year survival figures are better in my series, but the St. Mark's Hospital and Presbyterian Hospital figures include cases treated two and even three decades before the first in my own series.

The operative mortality has been just over 5% for both colon and rectal resections (Table XII); and in both half the deaths have been sudden and unexpected in the early post-operative period. It has not always been possible to decide whether coronary thrombosis or pulmonary embolism has been responsible. Most fatalities in the present series were in patients of over 70 who had a history of heart disease, and the operation more often than

TABLE XII.—Mortality After Excision of Rectum

Author	No. of Cases	Type of Operation	% Mortality
Bacon (1960) ..	439	Miles's excision of rectum	2.9
Mayo <i>et al.</i> (1951) ..	689	" " " "	4.1
Colcock and Jarpa (1958) ..	300	" " " "	4.1
Bacon (1960) ..	673	Pull-through excision of rectum	4.3
Hughes (present series)	391	Excision of rectum—various methods	4.6
Abel (1957) ..	200	Miles's excision of rectum	5.3
Hughes (present series)	220	Excision of rectum and anastomosis	6.4
Lloyd-Davies (1957)	1,090	Synchronous combined excision of rectum	8.6
Goligher (1961) ..	350	All types	9.0
Gabriel (1957) ..	1,223	Perineo-abdominal excision of rectum	9.2

not was palliative because of the advanced state of the malignancy. It is of interest to observe that in 11 of the 14 deaths after 300 abdomino-perineal excisions reported by Colcock and Jarpa (1958) cardiovascular and pulmonary factors were responsible. Gilchrist (1961) has called attention to the importance of myocardial infarction in surgical patients. He reports 37 patients who sustained acute post-operative myocardial infarction, 24 (65%) of whom had pre-existing evidence of cardiac disease. The infarct occurred during operation or on the first post-operative day in about one-third of the cases, during the next three days in another third, and by the end of the tenth day in the remainder. Chest pain was recorded in only 10 of the 37 cases. He quotes the work of Driscoll, Hobika, Etsten, and Proger (1960), who performed electrocardiography 24 hours after operation in 271 patients aged over 50 years and found acute myocardial infarcts in 12 (4.5%). Ten had clinical coronary disease, but fewer than half the patients complained of pain. Schweizer and Howland (1961) reviewed the results of electrocardiography performed in the first 24 hours after operation at the Memorial Hospital, New York. Acute myocardial infarction was found in 11 cases; in only five of them was there a history of cardiovascular disease.

As might be expected, the commonest type of failure in treatment of carcinoma of the large bowel is incomplete excision. Many cases classified as curative excisions have large or active tumours, and although excision was performed hopefully it was recognized that there was little prospect of cure. In about half the failures after curative excision for carcinoma of the colon and for carcinoma of the rectum the recurrence has been "regional" in nature—that is, in the surrounding tissues, in the peritoneal cavity, or in the liver. The most notable difference between the two groups has been in the number of systemic recurrences which have appeared after excision of a carcinoma of the

rectum. These have been most uncommon after treating carcinoma of the colon. The apparent cause is the dual venous drainage of the rectum, and it is possible that early ligation of the inferior mesenteric vein in the course of dissection of these tumours is partly responsible. Once this vein has been ligated most of the blood is temporarily diverted into the systemic circulation via the middle and inferior haemorrhoidal veins. This aspect of large-bowel carcinoma recurrence has attracted little attention, but has proved a notable feature in this series.

Studies of survival beyond the conventional five-year period have shown that while carcinoma of the colon does not often recur after this interval it is not uncommon for carcinoma of the rectum to do so, and nearly always in the systemic system. Later recurrence in the spine, in the brain, and especially in the lung is not uncommon.

An interesting feature in this series, also emphasized by Garlock, Lerman, Klein, Lyons, and Kirschner (1962), has been a tendency for a primary tumour to develop elsewhere at the same or at a different time. This second tumour is most often in the immediate neighbourhood of the first, in the large bowel. A second tumour may originate in another segment of the large bowel, or in such distant organs as the breast, lungs, stomach, etc. This should be kept in mind when these patients report for follow-up examination. A very complete regular review of the patient is necessary, and this should include sigmoidoscopy (even for right-sided carcinoma of the colon) and radiological examination of the chest. The appearance of a mass should not be automatically considered to represent metastases.

Summary

A personal series of 1,015 cases of large-bowel carcinoma has been reviewed. There has been a complete follow-up of all cases.

In 13% of colon carcinomas and 9.3% of rectal carcinomas the tumour was not resectable.

The operative mortality following resection of cancer of the colon was 5.4% and after resection of the rectum 5.4%. In half of both groups the cause of death was sudden, unexpected, and classifiable as pulmonary embolism or coronary occlusion. The mortality rose with age and was higher when the operation was palliative.

The absolute five-year survival rate for carcinoma of the colon was 44.1% and for carcinoma of the rectum 38.6%. The five-year survival rate after curative excision of the colon was 78.8% and of the rectum 64.8%. A notable difference in recurrence was the strong and persistent tendency for carcinoma of the rectum to produce systemic metastases.

The current incidence of a second primary carcinoma in this series was approximately 5%. Most frequently the second tumour was in the large bowel. The breast was a second site, and in nearly all instances the tumour in the breast preceded the tumour in the large bowel (mostly situated in the rectum).

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