

# Site, Emergency, and Duration of Symptoms in the Prognosis of Colorectal Cancer\*

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Four prognostic factors, *i.e.*, site of the tumors, mode of presentation, duration of symptoms, and pathologic staging, were correlated to the results of surgical treatment, *i.e.*, curative resectability, postoperative complications and mortality, and five-year survival, in 161 patients operated upon for colorectal cancer.

Only 31 (19 per cent) of the growths were right-sided; 71 patients (44 per cent) had symptoms less than six months. Fifty-four of them had a localized cancer; a radical procedure was performed in 114 (71 per cent), and postoperative complications occurred in 42 cases (26 per cent). The overall crude five-year survival was 38 per cent (53 of the 140 followed-up patients).

The length of the clinical history did not correlate with the pathologic staging, which greatly influenced curability and survival.

A statistically significant poorer prognosis was observed in patients with left-sided tumors, with an emergency presentation and with a duration of symptoms shorter than six months.

A better prognosis can be achieved by means of a presymptomatic diagnosis. [Key words: Prognosis; colorectal cancer; site, symptom duration; postoperative complications; survival]

COLORECTAL CANCER is the leading malignancy in many Western countries, and its incidence is progressively increasing.<sup>1</sup> Approximately 12,000 people died from colorectal neoplasms in 1974 in Italy, and some 25,000 new cases are expected each year (Italian Institute of Statistics).

Among the factors influencing the outcome of surgery and survival are duration of symptoms, mode of presentation, and site of tumor. All have been described with controversial findings.<sup>2-6</sup>

This study investigates the correlations between these prognostic factors and the results of surgical treatment, expressed in terms of radical procedures, postoperative complications and mortality, and five-year survival in a group of patients operated upon for

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colorectal cancer in a general surgery department in Italy.

## Patients and Methods

A total of 161 patients with histologically proven colorectal cancer who were admitted to the Istituto di Clinica Chirurgica of the Catholic University of Rome between January 1967 and July 1975 forms the basis of this study.

No tumor was classified as carcinoma unless there was definite invasion of malignant cells through the muscularis mucosae. Clinical records were reviewed, the age and sex were recorded, and patients were divided into four groups according to duration of symptoms observed on admission to the hospital: less than three months, three to six months, six to 12 months, and more than 12 months. Operative details and pathologic findings were reviewed, and all patients were allocated to one of the following pathologic stages: Stage A, confined to the bowel wall; Stage B, penetration of the bowel wall by tumor; Stage C, involvement of regional lymph nodes; Stage D, involvement of peritoneum or remote metastases. Location of the tumor, mode of presentation, indications for emergency, type of operation performed, and percentage of radical operations were also con-

TABLE 1. Duration of Symptoms in 161 Patients: (Interval Between Onset of Symptoms and Hospitalization)

	Number of Patients	Per Cent
<3 mo.	45	28
3-6 mo.	26	16
6-12 mo.	56	35
>12 mo.	34	21

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TABLE 2. Correlation between Duration of Symptoms (in months) and Results of Surgical Treatment

	<3 Mo. (45 pts.)		3-6 Mo. (26 pts.)		6-12 Mo. (56 pts.)		>12 Mo. (34 pts.)		X <sup>2</sup>	P
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent		
Radical operations	25	56	19	73	43	77	27	79	83.72	<0.00005
Postoperative complications	12	26	5	19	15	27	13	38	14.43	<0.0005
Postoperative mortality	7	15	3	14	1	2	4	12	134.28	<0.00005
Five-year survival	15	36	4	22	23	49	11	34	23.20	<0.0001

TABLE 3. Correlation between Duration of Symptoms (in months) and Pathologic Staging

	<3 Mo.		3-6 Mo.		6-12 Mo.		>12 Mo.		X <sup>2</sup>	P
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent		
Stage A	3	7	0	0	2	35	3	9		
Stage B	14	31	6	23	19	34	7	21	43	67
Stage C	7	16	12	46	24	43	14	41		0.20
Stage D	21	46	8	31	11	19.5	10	29	45	55

sidered. Radical procedures were defined as operations in which all known growth was removed, and no evidence of residual local or metastatic disease was described.

The policy of the surgeons concerned was to attempt removal of the primary tumor even if this might not be curative.

Postoperative complications and deaths (*i.e.*, deaths occurring within the first 30 days after surgery) were also recorded. Follow-up data were available in 75 per cent of cases (121 patients) from the clinical records, from the survivors, or from the dead patients' relatives. In 19 patients (12 per cent), data on five-year survival rates were collected from the Registry of the Anagrafe of Rome. The remaining 13 per cent (21 patients all living outside of Rome) were lost to follow-up.

Multiple cancers and nonoperated patients were excluded from the study. Mechanical (laxatives, enemas) and antimicrobial (oral erythromycin or systemic ampicillin) preparations were used before elective surgery.

Most of the operations were performed by senior surgeons trained in general surgery.

As far as correlation between prognostic factors and results of surgery are concerned, the Chi-square test was used to determine the statistical significance of differences.

### Results

**Age and Sex:** Thirty-four per cent of our patients were aged 61 to 70; 26 per cent, 51 to 60; 19 per cent, 71 to 80; 11 per cent, 41 to 50; 9 per cent, 21 to 40, and 1 per cent over 80.

Eighty-six were men, with a male:female ratio of 1.14:1.

**Symptoms:** Rectal bleeding occurred in 95 of our patients (59 per cent), abdominal pain in 82 (51 per cent), constipation in 58 (36 per cent), weight loss (> 5 lb) in 50 (31 per cent) and diarrhea in 29 (18 per cent).

Duration of symptoms (interval between onset of symptoms and hospitalization) is represented in Table 1. Seventy-one patients (44 per cent) presented within six months of the onset of symptoms.

The relationship between duration of symptoms and results of surgical treatment is indicated in Table 2. The group of patients whose symptoms lasted more than six months before treatment showed a significantly higher rate of radical operations ( $P < 0.00005$ ), a lower postoperative mortality ( $P < 0.00005$ ), and a higher five-year survival ( $P < 0.0001$ ), but showed a higher frequency of postoperative complications ( $P < 0.0005$ ).

TABLE 4. Correlation between Site of Tumor and Results of Surgical Treatment

	C Number	A Number	HF Number	T Number	SF Number	D Number	S Number	R Number	Right Large Bowel		Left Large Bowel		X <sup>2</sup>	P
									Per Cent	Per Cent	Per Cent	Per Cent		
Radical operations	6	10	4	4	4	5	25	56	77	69	16.57	<0.0005		
Postoperative complications	2	3	1	0	4	2	8	16	19	23	1.75	n.s.		
Postoperative mortality	0	1	1	0	1	2	4	6	6	10	7.24	<0.05		
Five-year survival	3	4	3	1	1	2	13	20	44	28	18.58	<0.0005		

C = cecum; A = ascending colon; HF = hepatic flexure; T = transverse colon; SF = splenic flexure; D = descending colon; S = sigmoid; R = rectum.

TABLE 5. Correlation between Mode of Presentation and Results of Surgical Treatment

	Emergency		Effective		X <sup>2</sup>	P
	Number	Per Cent	Number	Per Cent		
Radical operations	7	54	106	72	59.10	<0.00005
Postoperative complications	9	69	55	37	244.25	<0.00005
Postoperative mortality	4	31	11	7	40.07	<0.00001
Five-year survival	5	38	48	38	1.05	n.s.

Patients whose symptoms lasted from six to 12 months had more radical operations, fewer postoperative deaths, and longer survival if compared with patients of the other group. All differences were statistically highly significant:  $P < 0.0001$  ( $X^2 = 25.13$ ),  $P < 0.00005$  ( $X^2 = 824.41$ ), and  $P < 0.00005$  ( $X^2 = 111.71$ ), respectively.

The group of patients with a shorter clinical history (less than three months) did not show any difference in their postoperative complications and five-year survival, whereas they showed a lower curative resectability rate ( $P < 0.00005$ ;  $X^2 = 111.45$ ) and a higher postoperative mortality ( $P < 0.00005$ ;  $X^2 = 96.94$ ).

No correlation was found between duration of symptoms and pathologic staging, as shown in Table 3.

**Site of Tumor:** Seventy-six tumors (47 per cent) were sited in the rectum (that means that the lower edge of the lesion was located not more than 15 cm from the anal verge at sigmoidoscopy or level with or below the sacral promontory at laparotomy), 42 (26 per cent) in the sigmoid, eight (5 per cent) in the descending colon, five (3 per cent) in the splenic flexure, five (3 per cent) in the transverse colon, five (3 per cent) in the hepatic flexure, 13 (8 per cent) in the ascending colon, and 8 (5 per cent) in the cecum. In nine of the 11 emergency cases, tumors were sited in the left large bowel, and 70 of the 130 patients with left-sided lesions were men (54 per cent).

The relationship between site of the tumor and outcome of surgical treatment is shown in Table 4. Two possible correlations were tested.

The difference in prognosis was not statistically significant when colonic cancer was compared with rectal cancer. However, patients with left large-bowel cancers showed a lower occurrence of radical operations ( $P < 0.0005$ ), a higher postoperative mortality ( $P < 0.05$ ), and a lower five-year survival ( $P < 0.0005$ ) when compared with those affected by a right large-bowel cancer.

**Mode of Presentation:** Thirteen of our patients had emergency operations: seven radical and two palliative primary resections, four palliative colostomies. Eleven of them were acutely obstructed; two had free colonic perforation.

Seven of the emergency patients' symptoms lasted less than three months. The influence of mode of presentation on the outcome of surgical treatment is shown in Table 5. Patients who were operated upon after an emergency presentation showed a lower number of radical procedures ( $P < 0.00005$ ) and a higher number of postoperative complications and deaths ( $P < 0.00005$ ). No statistically significant difference was observed between emergency and elective operations as far as five-year survival was concerned.

**Pathologic Staging:** Fifty-four of our patients (33 per cent) had a localized cancer (*i.e.*, Stage A and B) without any lymph node, peritoneal or distant metastases. Table 6 shows the correlation between pathologic staging and results of surgical treatment. Localized cancers led to a higher number of radical procedures and five-year survivors, with a shorter rate of postoperative complications and mortality ( $P < 0.000001$ ,  $< 0.0001$ ,  $< 0.001$  and  $< 0.0001$ , respectively).

**Radical Operations, Postoperative Complications, and Deaths—Survival Rate:** Seventy-nine patients (49 per cent) had abdominoperineal excision of the rectum; 32 patients (20 per cent) had right hemicolectomy; 27 patients (17 per cent) had left hemicolectomy; 26 patients (16 per cent) had anterior resection; eight patients (5 per cent) had subtotal colectomy; eight (5 per cent) had local excision; and three patients (2 per cent) had transverse resection. The total number of radical procedures was 114 (71 per cent). Forty-five patients (28 per cent) had complicated postoperative courses with 15 deaths (9 per cent) mainly due to peritonitis following anastomotic dehiscence.

cence and to heart failure. Postoperative complications and causes of death are listed in Table 7.

Overall crude five-year survival rate was 38 per cent (53 of the 140 followed-up patients).

**Discussion**

Most colorectal cancers occur in elderly people. Ninety per cent of our patients were between 40 and 80 years of age; almost the same figure is reported both from Western and Eastern authors.<sup>7,8</sup>

In our series, there were slightly more men than women (53 per cent of men and 47 per cent of women). The same finding is reported by Vajrabukka,<sup>8</sup> Alarcon and Greenwood,<sup>9</sup> and Mzabi *et al.*,<sup>10</sup> whereas a prevalence of women is described by Welch and Donaldson<sup>7</sup> and by Lockhart-Mummery *et al.*<sup>11</sup>

Duration of symptoms is somewhat diverse in the different series and in the various countries. Evans *et al.*,<sup>12</sup> in a multicenter study on colonic cancer from the United States, found that duration of symptoms before admission was less than one month in 41 per cent of 11,655 patients. Peloquin,<sup>13</sup> managing patients with acutely obstructed and perforated bowels, reported duration less than two months in 52.7 per cent of his patients. According to McDermott *et al.*,<sup>3</sup> from Australia, symptom delay was less than three months in 45 per cent of his patients affected by rectal cancer, whereas in Wilson and Behrs<sup>14</sup> experience, the same delay was observed in 31 per cent of their patients with sigmoid and rectal cancer. As far as Europe is concerned, data are available from Irvin and Greaney<sup>2</sup> who described a delay less than five months in 45 per cent of 335 patients with colorectal neoplasms.

In a previous report from Italy concerning rectal cancer, Pescatori *et al.*<sup>15</sup> found duration of symptoms less than three months in 110 patients (23.5 per cent), whereas in this study, the same interval was observed in 28 per cent of the patients. The average interval between onset of symptoms and hospitalization seemed to be shorter in the United States than in the United Kingdom if we compare the period of two and 5.3 months<sup>7,9</sup> with a period of 7.3 and 5.6 months (rectum and colon, respectively).<sup>16</sup> Most of this delay occurred outside the hospital, and delays attributable to both patient and family doctor were almost equal in duration.<sup>17</sup> Irvin and Greaney<sup>2</sup> showed no significant difference between their symptomatic patients having a shorter or a longer clinical history, whereas McDermott *et al.*,<sup>3</sup> looking at rectal cancer patients, reported a significantly better five-year survival rate in patients with a shorter history. On the other hand, Copeland *et al.*<sup>4</sup> and Slaney<sup>5</sup> demonstrated that the

TABLE 6. Correlation between Pathologic Staging and Results of Surgical Treatment

	Stage A		Stage B		Stage C		Stage D		Stage A+B		Stage C+D		X <sup>2</sup>	P
	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Per Cent	Per Cent	Per Cent	Per Cent		
Radical operations	8	100	45	98	55	96	6	12	98	56	3794.43	<0.000001		
Complications	1	12	9	20	22	39	4	8	19	25	11.16	<0.001		
Mortality	0	0	1	1	4	7	10	23	2	13	197.39	<0.0001		
Five-year survival	7	88	26	68	70	45	0	0	72	21	25.67	<0.0001		

TABLE 7. Causes of Postoperative Complications and Mortality

	Postoperative Complications			Postoperative Deaths		
	Number	Per Cent	Per Cent Patients	Number	Per Cent	Per Cent Patients
Anastomotic dehiscence	11	24	7	5	33	3
Heart failure	10	22	6	6	40	4
Wound sepsis	7	16	4			
Pneumonia	6	13	4	2	13	1
Rectal bleeding	3	7	2			
Intestinal obstruction	3	7	2	1	7	0.6
Colostomy stricture	3	7	2			
Renal failure	2	4	1	1	7	0.6
TOTALS	45	100	28	15	100	9

longer the history of symptoms before the patient comes to operation, the better, on the average, are the prospects for survival.

In our series, the group of patients whose symptoms lasted more than six months had significantly better prognosis, more radical operations, lower postoperative mortality, and higher five-year survival.

The chance of a curative resection and five-year survival is strictly correlated with the pathologic staging as shown by many authors (Table 8).

Our study demonstrated a lack of correlation between duration of symptoms and pathologic staging. A shorter clinical history does not correspond to a more localized stage of the tumor, as suggested also

by Irvin and Greaney.<sup>2</sup> On the contrary, a shorter clinical history is generally associated with poorly differentiated rectal cancers.<sup>17</sup>

This explains why early diagnosis of symptomatic disease does not guarantee a better prognosis. In fact, in the determination of the spread of cancer cells, the biologic virulence of the tumor and resistance of the host are of much greater importance than the length of time the tumor has existed.

A better prognosis can be achieved by means of a presymptomatic diagnosis, since it leads to detection of the tumor in a more localized pathologic stage.

An overall five-year survival of 75 per cent was observed by Gilbertsen and Wangenstein<sup>24</sup> in patients operated upon for asymptomatic rectal cancer, an

TABLE 8. Five-Year Crude Survival Rate for Operated Colorectal Cancer (Dukes' Classification)

	Year	Stage A	Stage B	Stage C	Stage D	Total
Gilbertsen <sup>18</sup>	1959	83	68	45	0	32
Floyd <i>et al.</i> <sup>16</sup>	1966	70	50	25	5	23
Copeland <i>et al.</i> <sup>4</sup>	1968	71	61	39* and 13†		37
Hawley <sup>19‡</sup>	1972	82	69	54		
Hight <i>et al.</i> <sup>20</sup>	1973	68	53	44	0	44
Welch and Donaldson <sup>7</sup>	1974		64§	34		
Mzabi <i>et al.</i> <sup>10</sup>	1976	71	49	26	0	32
Gill and Morris <sup>21</sup>	1978	94	40	19	4	26
Evans <i>et al.</i> <sup>12‡</sup>	1978		57§	37	3	36
Alarcon and Greenwood <sup>9</sup>	1979	78	61	41	7	44
Corman <i>et al.</i> <sup>22</sup>	1979	81	62	35	0	
Bulow <sup>23  </sup>	1980	79	68	39		32
Present study	1981	88	68	45	0	38

\* Involvement into but not through muscle.

† Involvement through muscle.

‡ Colonic cancer.

§ A+B.

|| Under 40 years of age.

impressive result if compared with the five-year survival rate of 32 and 23 per cent reported for symptomatic patients in that period.<sup>16,18</sup>

One hundred eighteen patients (73 per cent) had the tumor localized in the rectum and in the sigmoid; this finding is consistent with the reports of many authors.<sup>8,9</sup>

Recent reports have noted a change in distribution of colorectal carcinoma in that tumors have been developing more proximally than had been seen previously,<sup>25</sup> but other authors noted no change in the first decade.<sup>22</sup> For prognosis, investigators disagree about the interference of the neoplasm's location in the large bowel. Gibrertsen<sup>18</sup> and Copeland *et al.*<sup>4</sup> found that patients with right-sided tumors had a better prognosis than those with lesions in the left colon. Sheperd and Jones<sup>6</sup> found the reverse. Welch and Donaldson<sup>7</sup> observed no significant difference in the prognosis at different sites.

In our series, better surgical results and more favorable prognoses have been achieved in right-sided tumors. This finding can be explained by the fact that the majority of patients treated by emergency procedures had left-sided cancer; moreover, tumors of the rectum may require a difficult anastomosis and are more likely to involve adjacent organs with a higher malignancy.

Only 13 of our patients (8 per cent) had emergency operations. Most of them were acutely obstructed; a prevalence of obstruction on perforation is commonly described in the literature.<sup>7,13</sup>

An increase of postoperative mortality is a constant and obvious finding following an emergency procedure. It varies from 11<sup>10</sup> to 21 per cent,<sup>7</sup> 32 per cent,<sup>13</sup> and 35 per cent.<sup>2</sup>

In our series, a postoperative mortality of 31 per cent was observed. We could see no difference in five-year survival between emergency and elective cases, as shown by others.<sup>13,21,23</sup>

Emergency procedures may decrease curative resectability rates by increasing the occurrence of uncleaned large bowel, which makes primary resection and anastomosis less safe.

Radical operations in elective surgery are most likely to be performed; the percentage is generally over 70 per cent in the literature<sup>4,12</sup> and 71 per cent in our study. Postoperative complications are rather frequent in colorectal surgery. They range from 12 to 21 per cent or more in the different series,<sup>7,9</sup> sepsis being the most frequent often due to an anastomotic dehiscence (28 per cent in Alarcon and Greenwood's experience,<sup>9</sup> 24 per cent in our series). The most frequently reported postoperative mortality varies between 4 and 7 per cent<sup>4,7,11,12,21</sup> and depends on a

series of factors: percentage of emergency patients in the considered cases, occurrence of free perforation within the emergencies, specific training of surgeons in colorectal surgery, number of junior surgeons who performed the operations, and other factors.

One third of our patients had lesions limited to the bowel wall. The percentage of localized colorectal cancers (A and B) varies in the different series, from 29.5 per cent<sup>12</sup> to 33 per cent and 45 per cent.<sup>9</sup> The five-year survival rate is considerably higher in Dukes' A and B cases (Table 8); 75 per cent of patients whose colorectal cancer was detected by presymptomatic diagnosis belong to these stages.<sup>26-28</sup> Periodic screening is therefore required in high-risk patients.

For the outcome of surgical treatment of colorectal cancer in symptomatic patients, our study indicates a better prognosis for those who are affected by right-sided tumors (not acutely obstructed or perforated) with a longer clinical history and localized pathologic staging.

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### Announcement

#### CONTINUING MEDICAL EDUCATION SEMINAR

A continuing medical education seminar entitled "Current Controversies in Crohn's Disease" will be held at the Baptist Memorial Hospital, Memphis, Tennessee, April 30 and May 1, 1982. Attendance is limited to 250 persons. The Program Director is Richard O. Bicks, M.D. AMA PRA Category I accreditation is pending. For additional information, contact: Anne Wallace, Educational Support Services, Baptist Memorial Hospital, 899 Madison Avenue, Memphis, Tennessee 38146. Telephone: 1-800-238-6893.