# Carcinoma of the Colon

Cancer Specific Long-term Survival. A Series of 615 Patients Treated by One Surgeon

ERIC PIHL, M.D., PH.D., F.R.C.P.A.,\* EDWARD S. R. HUGHES, M.D., M.S., F.R.A.C.S.,† FRANCIS T. MCDERMOTT, M.D., F.R.A.C.S.,† BARRIE J. MILNE, B.A.,‡ JENNIFER M. N. KORNER, B.A.,† ANN B. PRICE†

The cancer specific survival in 615 patients undergoing resection for carcinoma of the colon is presented. The patients were operated on and managed by one surgeon between 1950-1977. Computer analysis has been made of the prospectively collected data. Results are presented as median survival in months and as percentage survivors at 5, 10, 15 and 20 years. Curative resection gave a cancer specific survival at the seventyfifth percentile of 66 months, corresponding to 76% survival at five years and 67% at 20 years. Age and sex were not significant prognostic factors. Dukes' Stages A, B and C had five-year survivals of 88%, 78% and 60% respectively, after curative resection. The median survival after palliative resection was 14 months. Site of the primary tumor within the colon was of significant prognostic importance only when the poor survival in tumors of the transverse colon was compared with the favorable survival in those of the splenic flexure, ascending, descending and sigmoid colon.

**I**<sup>N</sup> VICTORIA, AUSTRALIA, cancer of the colon causes 19.1 deaths per 100,000 inhabitants a year and 13% of all cancer deaths, male to female ratio being 0.8.<sup>1</sup>

We have recently reported on the cancer-specific long-term survival in 1061 patients with carcinoma of the rectum,<sup>12</sup> all treated with curative or palliative resection by one surgeon (E.S.R.H.). The purpose of the present paper is to report on cancer survival in a series of 615 patients with carcinoma of the colon, treated and followed-up by the same surgeon over the same period of time. Because all operations were performed by one surgeon, the difficulties in analyzing survival data consequent to surgeon-related variables<sup>5</sup> are minimized.

Supported by grants from the Anti-Cancer Council of Victoria, and the Potter Foundation, Melbourne, Australia.

Submitted for publication: December 13, 1979.

From the Departments of Pathology and Immunology, and Surgery, and the Computer Centre, Monash University, Melbourne, Victoria, Australia

The data also provides a baseline for adjuvant therapeutic trials.

## **Patients and Methods**

The series consisted of 615 patients, mostly from the state of Victoria, who were referred from other doctors for treatment, between 1950-1977, and who after investigation had resection of a single primary adenocarcinoma or undifferentiated carcinoma of the colon. All resections were performed by one surgeon (E.S.R.H.). In this series only tumors at a distance greater than 18 cm from the anal verge have been considered as colonic. Benign tumors, carcinoma in situ, carcinoma of the appendix, malignant tumors other than adenocarcinomas or undifferentiated carcinomas, and patients with more than one carcinoma of the colon and rectum (synchronous or metachronous), were not included. Patients who were treated with a definitive local excision. or were inoperable or had a laparotomy with or without palliative bypass, were also excluded.

Of the 615 patients 269 were male and 346 were female (ratio: 0.8), mean age 61  $\pm$  12 and 60  $\pm$  13 years respectively. Deaths from postoperative complications occurring within three months of the operation (44; 7.2%) were not included in the survival analysis, leaving 571 evaluable cases. In 434 (76%) of 569 patients the resection was considered curative, *i.e.* there was no evidence of metastasis to distant organs nor of residual local tumor at the end of the operation; in two patients the aim of the operation was not recorded. The site of the tumor was recorded as assessed at operation.<sup>8</sup>

0003-4932/80/0700/0114 \$00.70 © J. B. Lippincott Company

<sup>\*</sup> Department of Pathology and Immunology.

<sup>†</sup> Department of Surgery.

<sup>‡</sup> Computer Centre.

Reprint requests: E. Pihl, M.D., Department of Pathology and Immunology, Monash University Medical School, Commercial Road, Prahran, Victoria, Australia 3181.

Operative specimens were examined as reported previously,<sup>12</sup> using Dukes' staging scheme for cases treated with curative resection.<sup>2,3</sup> Tumors invading adjacent organs (D<sub>1</sub>) or with spread to distant organs (D<sub>2</sub>) were classified as Stage D; in 42 patients staging information was not available. Tumor differentiation was recorded according to conventional criteria<sup>13</sup> and was considered as good, intermediate, poor, or none in 45, 413, 78 and three cases respectively. In 32 patients no differentiation data were available.

Follow-up information was obtained at regular outpatient visits, one, three, six and 12 months postoperatively, followed by annual visits. The details of the follow-up procedures have been reported previously.<sup>8</sup> All 615 patients, selected as detailed above, were consecutive and completely documented to the end of the follow-up period.

The total data were coded in a form suitable for computer analysis by the method of Kaplan and Meier<sup>10</sup> and by contingency table analysis. Differences between survival curves were analyzed by the Wilcoxon test according to Gehan.<sup>6</sup> By this method cases are classified as either "Fails" (uncensored data) or "Non-fails"

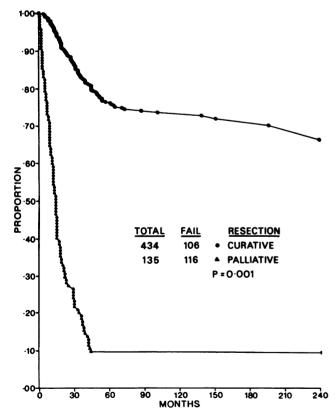


FIG. 1. Cancer specific survival after curative and palliative resection. The upper curve (curative) shows that 67% of these patients have survived the rectal cancer, the last death so far at 19.8 years. The lower curve shows that only 9% of patients treated with palliative resection have survived, all deaths from recurrence having occurred within 44 months.

 
 TABLE 1. Cancer Specific Survival\* in Relation to Resection Aim, Patient's Sex, Age, and Tumor Stage

	No. of Patients	Seventy-fifth Percentile Survival in Months†	Percent of Cancer Survivors at years:				
			5	10	15	20	‡
Resection							
Curative	434	66	76	73	71	67	0.001
Palliative	135	7 (14)	9	9	9	9	
Males	243	24	59	57	53	52	NS§
Females	328	25	61	58	56	54	
Age							
<40 years	32	26	64	61	60	60	NS NS
40-64 years	317	28	62	59	54	53	
≥65 years	222	21	57	56	56	56	
Stage							
Ă	109	216	88	86	82	70	0.000
В	208	100	78	74	74	74	0.006
Ċ	90	31	60	59	59	59	0.003
D	97	7 (14)	10	10	10	10	0.001
Total	571	24	60	58	56	53	

\* Analysed according to Kaplan and Meier<sup>10</sup> and Gehan.<sup>6</sup>

† Figures in parentheses refer to median survival, when reached.

‡ p values refer to Wilcoxon analysis of survival curves.

§ Not significant.

<sup>II</sup> Palliative cases (26) not included in Stages A, B, and C.

(censored data). Fails were defined as deaths due to recurrence of the colonic cancer, non-fails being patients known to be alive, or having died from causes other than the colonic cancer.

## **Results**

At the end of the follow-up period (February, 1978), 226 (37%) of the colon cancer patients were alive, 223 (36%) had died from recurrence, 44 (7%) had died from postoperative complications and two from late treatment complications; 13 patients (2%) had died from cancer other than of the large intestine, 101 (16%) had died from causes other than cancer. The cause of death was unknown in six (1%) patients. A total of 135 patients, including four originally considered as palliative, survived for more than 10 years, 63 patients survived more than 15 years, and 18 for more than 20 years. There were 12 deaths from confirmed recurrent cancer more than five years after removal of the colonic primary; four of these occurred between 10 and 19.8 years.

The median cancer specific survival for the whole series and for curative resections has not been reached. At the seventy-fifth percentile the respective survivals were 24 and 66 months. For curative resections this corresponds to five-, ten- 15- and 20-year survivals of 76, 73, 71, and 67% respectively (Table 1). After palliative resection the median cancer survival was 14 months; the significantly better survival prospects after curative resections are shown in Figure 1.

Age and sex did not relate significantly to cancer survival (Table 1).

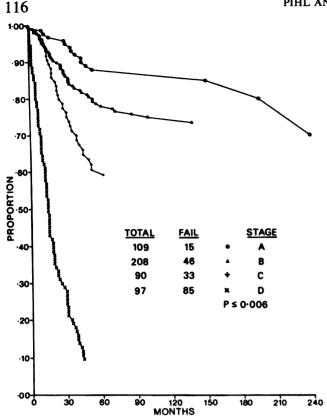


FIG. 2. Cancer specific survival in relation to tumor staging. Proportionally more deaths from recurrences occur later in patients with initially less extensive tumor spread. A total of 18 patients were still alive 20 years after resection. Staging information was available in 16 of the original tumors; the numbers in Stages A, B, C and D, being 6, 6, 3 and 1, respectively.

There was a highly significant association between cancer specific survival and tumor staging (Table 1, Fig. 2). The median survivals in Stages A, B and C (curative resections) have not been reached; at the seventy-fifth percentile the corresponding figures were 18, 8.3 and 2.6 years, *i.e.* five-year survivals of 81, 78 and 60% respectively. The long-term, 20-year survival figures are uncertain because of the small numbers, being 70  $\pm$  11% (SD), 74  $\pm$  4% and 60  $\pm$  6% in Stages A, B and C respectively. The five-year survival in

 TABLE 2. Cancer Specific Five-Year Survival\*

 in Relation to Colonic Tumor Site

	Total No. of Patients	Five-year Survival (Per Cent ± SD)
Cecum	43	71 ± 7
Ascending	35	$80 \pm 7$
Hepatic flexure	19	$74 \pm 10$
Transverse	63	$63 \pm 7$
Splenic flexure	15	$80 \pm 9$
Descending	58	$79 \pm 6$
Sigmoid	201	$77 \pm 3$

 $\ast\,$  Curative resections, only. Survival analysis according to Kaplan and Meier.  $^{10}$ 

Dukes' Stage C-1 was  $61 \pm 6\%$  in comparison with  $48 \pm 15\%$  in Stage C-2, although the difference was not significant when analyzed according to Gehan<sup>6</sup> (p = 0.15). The median survival in Stage D was 14 months (Table 1). Eight of the patients with Stage D tumors have survived for more than five years, five of these were considered curative cases at the operation.

The survival implications of site of the primary tumors are not immediately obvious (Table 2), although those of the transverse colon appeared to have the worst prognosis and those of the splenic flexure the best. If tumors proximal to the midtransverse colon are considered right-sided, 81 (59%) of 137 patients operated on prior to February 1973, excluding deaths from unrelated causes, survived for at least five years, in comparison with 158 (60%) of 262 patients with leftsided tumors ( $\chi^2 = 0.01$ , NS). Similarly, if right-sided tumors and those of the remaining part of the transverse colon (excluding the splenic flexure) are considered proximal 91 (57%) of 161 patients with proximal tumors survived for five years in comparison with 148 (62%) of 238 with tumors of the distal part ( $\chi^2$ = 1.06, NS).

Tumor differentiation related significantly to survival (Table 3), being predictably best in those of good differentiation and worst in those of poor.

#### Discussion

Cancer survival has been analyzed in a series of 615 patients with carcinoma of the colon resected by one surgeon. Of these, 571 (93%) patients survived the postoperative period. Twelve patients died from confirmed recurrences later than five years after the resection. The cancer specific survival at the seventyfifth percentile, following curative resection was 66 months. The corresponding five-, ten-, 15- and 20-year survivals were 76, 73, 71, and 67% respectively. Age and sex were not significant prognostic factors. Site of the primary cancer was associated with marginal survival differences, which did not reach statis-

 TABLE 3. Cancer Specific Five-Year Survival\*

 in Relation to Tumor Differentiation

	Good	Dif	n†	
		Inter- mediate	Poor	None
No. alive at				
five years/Total	14/18	193/310	18/43	1/2
Per cent	78	62	42	_

 $\chi^2 = 9.0, p = 0.03 (3 \text{ d.f.}).$ 

\* Patients operated on prior to February 1973. Postoperative and deaths within 5 years unrelated to colonic cancer not included. † Differentiation information not available in 32 cases. tical significance when one site was compared with the nearest proximal or distal, or the right side with the left or the proximal colon with the distal colon. Tumor staging<sup>2,3</sup> was a highly significant prognostic factor; cancer specific five-year survival was 88, 78 and 60% in Stages A, B and C respectively.

A comparison of results obtained in this series of 615 colonic cancer patients with those in a similar follow-up series of 1061 cases of rectal cancer,<sup>12</sup> all 1676 resected by the same surgeon (E.S.R.H.), shows that colonic site is marginally more favorable than rectal. The overall five-year survival was 60% in the colon in comparison with 56% in the rectum. Curative resection of colonic cancer gave a cancer specific survival at the seventyfifth percentile of 66 months in comparison with 45 months in the rectum, or five-year survival percentages of 76 and 69, respectively. This could be explained by the higher proportion Stage C tumors in the rectum (32%; colon 18%). Another partial explanation appears to be the larger proportion of long-term survivors with colonic (59%) compared to rectal (37%) Stage C tumors. Furthermore, proportionally more rectal than colonic cancers recurred after five years. The latter has been reported earlier.9

Our finding of a more favorable survival in colonic than in rectal carcinoma is in agreement with that of Godwin and Brown<sup>7</sup> and with Prorok.<sup>14</sup>

Our survival data for colonic carcinoma are difficult to compare with those of other surgical series, because only few authors have distinguished between rectal and colonic site in relation to prognostic factors. Murray and co-workers,11 like us, reported a much better fiveyear survival (49%) after curative resection of Stage C colonic carcinoma, than is generally reported in colorectal series. Falterman, et al.4 reporting on survival after resection in 2313 patients with colorectal carcinoma, found a five-year survival of 47%, in 923 curative resections, in comparison with our corresponding figures of 76% for the colon and 69% for the rectum. Welch and Donaldson<sup>15</sup> found a five-year survival after curative resection of 50-59% for tumor sites in the colon and 54% for the rectum. Although such differences between our series and those reported in the literature may be explained in several different ways, including the selection of patients, another major factor

may be the generally lower survival figures that can be expected in series involving several surgeons using different techniques, as has been shown by Fielding et al.<sup>5</sup>

In conclusion, our series shows that the better survival in colonic as distinct from rectal carcinoma is partly due to a larger proportion of rectal Stage C cases, to proportionally fewer late recurrences in colonic carcinoma, and to a much better long-term survival in Stage C of the colon than in the rectum.

#### Acknowledgments

The authors thank Mrs. E. A. Debney, S.R.N., and Miss B. Moynihan, S.R.N. for their valuable contributions to patient care, follow-up, and data recording. We also thank the National Large Bowel Cancer Project, Houston, Texas. U.S.A. for advice with the data analysis.

### References

- 1. Australian Bureau of Statistics. Causes of Death, Melbourne, 1978.
- 2. Dukes CE. The classification of cancer of the rectum. J Pathol Bacteriol 1932; 35:323.
- Dukes CE. Cancer of the rectum. In Smithers DW, Dukes CE (eds.) Neoplastic Disease at Various Sites III. Livingstone, Edinburgh, 1960; pp. 59-68.
- Falterman KW, Hill CB, Markey JC, et al. Cancer of the colon, rectum and anus: a review of 2313 cases. Cancer 1974; 34:951.
- Fielding LP, Stewart-Brown S, Dudley HAF. Surgeon-related variables and the clinical trial. Lancet 1978; 2:778.
- Gehan EA. Generalized Wilcoxon test for comparing arbitrarily singly censored samples. Biometrika 1965; 52:203.
- Godwin JD, Brown CC. Some prognostic factors in survival of patients with cancer of the colon and rectum. J Chronic Dis 1975; 28:441.
- Hughes ESR. Long-term study of large-bowel cancer. Med J Aust 1976; 2:365.
- 9. Hughes ESR, Cuthbertson AM. Recurrence after curative excision of carcinoma of the large bowel. JAMA 1962; 182:1303.
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1978; 53:457.
- 11. Murray D, Hreno A, Dutton J, Hampson LG. Prognosis in colon cancer: a pathologic reassessment. Arch Surg 1975; 110:908.
- Pihl E, Hughes ESR, McDermott FT, et al. Carcinoma of the rectum: cancer specific long-term survival. A series of 1061 cases treated by one surgeon. Cancer 1980; 45:196.
- Pihl E, Malahy MA, Khankhanian N, et al. Immunomorphologic features of prognostic significance in colorectal carcinoma. Cancer Res 1977; 37:4145.
- Prorok PC. Survival for cancers of the digestive system. DHEW Publ. No. (NIH). 78-1541, 1978.
- 15. Welch JP, Donaldson GA. Recent experience in the management of cancer of the colon and rectum. Am J Surg 1974; 127:258.