The Risk of Cancer Following Colectomy and Ileorectal Anastomosis for Extensive Mucosal Ulcerative Colitis

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A retrospective study was performed on 89 patients who underwent total colectomy and ileorectal anastomosis for extensive mucosal ulcerative colitis between the years 1957 and 1977 in order to determine the risk of developing cancer of the rectum. The 30-day operative mortality rate was 0%. Of the 84 patients available for follow-up study, four patients, (4.8%) developed a carcinoma of the rectum. The risk of cancer per patient-year was zero in the first decade, 1/206 in the second decade, and 1/116 in the third decade. The cumulative risk of developing cancer was 0% at 10 years, 2.1% ± 2.1% at 15 years, 5.0% ± 3.5% at 20 years, and 12.9% ± 8.3% after 25 years of disease. Patients with cancer or precancer in the colon at the time of colectomy appear to be at high risk for the later development of rectal cancer.

PATIENTS WITH EXTENSIVE ulcerative colitis requiring surgery have traditionally been treated by protocolectomy and ileostomy. This operation has been advocated on the grounds that 1) only total removal of the colon and rectum provides absolute assurance that the patient will be free of the risk of developing cancer, 2) most patients have rectums which are so ravaged by ulcerative colitis that they are unsuitable for an ileorectal anastomosis, and 3) retention of diseased rectum will lead to continued systemic manifestations of the disease (*e.g.* arthritis, hepatic dysfunction, pyoderma gangrenosum, etc.). This radical approach has certain obvious drawbacks, however. Removal of the rectum necessitates the construction of an ileostomy and subjects the male patient to the risk of sexual dysfunction. Many of the patients who have this disease are young, and have not yet had time to marry and to raise children. Thus, they often object strenuously to an operation which they fear will make them socially unacceptable and which might impair their ability to have offspring, preferring instead to suffer the continual bouts of severe diarrhea, bleeding, and the side effects of steroid drugs. It is not surprising, therefore, that some surgeons have favored a more conservative approach, sparing the rectum whenever possible. It is the purpose of this paper to determine the risk of cancer in patients with extensive mucosal ulcerative colitis who have been treated by total colectomy and ileorectal anastomosis.

Patients and Methods

The charts of the 89 patients treated at the Cleveland Clinic between January 1, 1957 and December 31, 1977 were reviewed. All patients had total colectomy and ileorectal anastomosis (IRA) for extensive mucosal ulcerative colitis, as determined by clinical criteria with proctoscopic and colonoscopic findings, barium enema, and pathologic examination of the excised colons. Eighty-eight patients had total colonic involvement, and one patient had sparing of the proximal ascending colon. Patients with granulomatous (transmural) colitis and with nonspectific colitis were excluded from this study. With the exception of three patients who had subtotal colectomies prior to referral to the Cleveland Clinic for IRA, all of the pathologic material was reviewed by one pathologist to ascertain the accuracy of the original diagnosis and to grade the specimens for dysplasia according to the criteria described by Morson.[1] Confirmation of the diagnosis of ulcerative colitis in the remaining three patients rests on the review by Cleveland Clinic pathologists of slides prepared elsewhere and on review of the subsequent tissue obtained at the time of IRA and later rectal biopsies.

The risk of cancer was calculated in two different ways to allow comparison with other series in the literature. The number of patient-years of disease was measured by subtracting the date of onset of disease (as determined from the patient's chart) from the date the patient was last known to have a rectum free of cancer. When a follow-up examination could not be performed, patients were contacted by letter or by

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Submitted for publication: July 3, 1980.

0003-4932/81/0100/0009 $00.80

TABLE 1. *Operative Procedures*

Procedure	Number of Patients
One-stage elective procedures	
total colectomy and IRA	20
Staged procedures	
total colectomy, IRA and ileostomy	20
colectomy and sigmoid mucous fistula, or closure of rectal stump, and ileostomy with later IRA	20
ileostomy, followed by later colectomy and IRA	4
ileostomy and "blowhole" colostomy followed by colectomy and IRA	4
ileostomy done elsewhere followed by colectomy and IRA	1
colostomy done elsewhere with subsequent colectomy and IRA	1
colectomy and ileostomy, later IRA	1
ileostomy and exteriorization of colon perforation done elsewhere, subsequent colectomy and mucous fistula followed by IRA	1
colectomy and ileostomy done elsewhere subsequent IRA	1
colectomy and ileosigmoid anastomosis done elsewhere, subsequent sigmoid resection and IRA	1
right hemicolectomy with later left colectomy and IRA	2

telephone. Whenever possible, confirmation of the status of the patient's health was also received from his personal physician. The follow-up interval was terminated as of December 31, 1979. When the month of onset of disease was not recorded, it was assumed to be July. The duration of disease was then rounded off to the nearest year. To allow comparison with the figures of Baker et al.,[2] the risk of carcinoma per patient-year of disease was calculated for each decade. Thus, patients who entered the study in March 1965 with a history of four years of disease beginning in January 1961, and a last recorded follow-up visit free of cancer in April 1978, contributed ten patient-years to the first decade (0–10), and seven patient-years to the second decade (10–20). It is to be noted that this differs from the technique used by De-Dombal[3] and by Lennard-Jones[4] who calculated the risk per patient-year *under observation.*

The cumulative probability of survival (P) without developing carcinoma of the rectum was also calculated according to the method of Cutler and Ederer,[5] with estimation of the standard deviation by Greenwood's formula.[5] A life table was constructed with the following constraints. Patients not seen in 1978 or 1979 ("lost") were considered as withdrawn without cancer as of the time of their last follow-up visit. Patients who underwent proctectomy for benign disease, who died of an unrelated disease without rectal cancer, or who were alive in 1978 or 1979 were also considered withdrawn without evidence of cancer. The cumulative risk of developing rectal cancer Q is then expressed as $1 - P$. As noted by Devroede[6] and others, this actuarial analysis provides a more accurate estimate of the actual cancer risk.

Patients were considered to be candidates for ileorectal anastomosis if the rectum was found to be distensible and soft without severe narrowing. Patients with normal or granular appearing rectal mucosa and who were in satisfactory medical condition usually underwent one-stage total colectomy and ileorectal anastomosis (33 patients). Those patients who required operation for severe toxicity, who were nutritionally depleted, or who had severe rectal inflammation were treated by staged procedures (56 patients). The presence of rectal pseudopolyps was not considered a contraindication to IRA. A variety of staged procedures were used (Table 1). Twenty of the patients undergoing staged procedures had toxic megacolon. Thirteen of these patients were initially treated by subtotal colectomy, ileostomy, and either creation of a sigmoid mucous fistula or oversewing of the rectal stump, four patients initially had diverting ileostomy and "blowhole" colostomy, and three had a diverting ileostomy alone, followed by delayed colectomy and IRA. The operative mortality and morbidity statistics are summarized in Table 2. No patient died during the surgical procedure in either group. The relatively low morbidity rate (15%) in the staged group illustrates the rationale for delaying large operative procedures in critically ill patients.

A total of 51 males and 38 females were operated on between 1957 and 1977. The average age of onset of disease was 23.2 years (range: 6–57) for the male patients and 22.4 years (range: 5–53) for the female patients. Five patients were lost to follow-up study within six months of operation. These patients were excluded from the cancer risk analysis. The average age at onset of disease in the remaining 84 patients was 22 years (Fig. 1). The average age at operation was 29.3 years (range: 5–57 years), and the average duration of the follow-up period was 7.7 years after IRA (range: 0.1–30 years). The average length of disease was 15.4 years. (range: 1–46 years).

Five patients underwent ileorectal anastomoses between 1957 and 1959, 32 patients between 1965 and 1969, 22 patients between 1970 and 1974, and 17 patients between 1975 and 1977.

Seven patients with carcinoma of the colon at the time of colectomy were included in the study since they remained at risk for developing a carcinoma of

TABLE 2. *Operative Mortality and Morbidity Rates in 89 Patients Undergoing Colectomy and IRA*

	One-stage Colectomy and IRA	Staged Procedures
Number of patients	33	56
Acute toxic megacolon	0	20
Operative complication rate	16.1%	15.2%
Anastomotic leak rate	9.1%	0%
Operative mortality rate	0%	0%

FIG. 1. The age distribution of 84 operation survivors at onset of disease. Solid blocks: female patients. Striped blocks: male patients.

the rectum. Their outcomes are summarized in Table 3. None of these patients had lymph node involvement, and their average survival time was 8.9 years.

Results

The overall outcome of the 84 patients undergoing cancer risk analyses is shown in Table 4. Sixty-four per cent of the group have functioning IRAs and have satisfactory or good control of bowel movements. Severe diarrhea was a common problem during the first six months after operation, but sibsided with time in more than 80% of the patients. Four of the 56 patients in the staged group were unable to achieve closure of ileostomy because of continued severe rectal inflammation. All of these patients underwent proctectomy, as did 14 other patients (21.4% of the group). There were no deaths after proctectomy. The reasons for proctectomy are given in Table 5. The most common cause was continued symptoms, *e.g.* rectal bleeding, diarrhea, and tenesmus. No patient required proctectomy for systemic effects of ulcerative colitis per se, although two patients did subsequently develop sclerosing cholangitis (one progressing to a bile duct cancer). Six patients had "prophylactic" proctectomy (two with moderate or severe dysplasia of the rectal mucosa and the four patients whose ileostomies could not be closed), and two patients had proctectomy for malignant disease. Six patients (7.1%) were lost to follow-up study (no contact in 1978 or 1979), and seven patients (8.4%) died. The causes of death are listed in Table 6.

Four patients developed carcinoma of the rectum during the study period (4.8%). Two patients had advanced lesions (Dukes' C and D) at the time of discovery, and they subsequently died of metastatic cancer (Table 7). A third patient had proctectomy for a Dukes' A lesion and is living with no evidence of recurrence. In this patient rectal biopsy specimens demonstrated moderate dysplasia at one and two years prior to surgery, and severe dysplasia two months prior to surgery. The fourth patient had local excision and fulguration of the base of a poorly differentiated signet-cell carcinoma, and died of sepsis and mycosis fungoides more than five years later without recurrent disease.

TABLE 4. *Overall Outcome at the End of Follow-up in 84 Patients having Colectomy and IRA*

	Number of Patients	Per Cent
Alive and well with functioning IRA	54	64.3
Died (cancer of the rectum)	2	2.4
Died from other causes	5	6.0
Proctectomy	18	21.4
Lost to follow-up	5	6.0

TABLE 3. *Outcome of Patients with Colon Cancer at the Time of Colectomy*

Age	Sex	Stage	Location	Years of Symptoms	Survival-years	Follow-up Study
53	M	A	Transverse colon	28	18	NED
57	M	B	Transverse colon	0	2	Died (cancer)
33	M	B	Transverse colon	15	16	NED
35	F	A	Sigmoid colon	10	6 weeks	Died—pulmonary embolus
57	M	CA in situ (villous tumor)	Rectum	0	15	NED
31	M	A	Sigmoid colon	12	5	NED proctectomy for severe dysplasia
56	M	B	Transverse colon	35	6	Rectal cancer locally excised 6 months post colectomy Died of mycosis fungoides and sepsis. NED

NED: no evidence of disease.

TABLE 5. *Reasons for Proctectomy*

Reason	Number of Patients
Carcinoma	2
Symptoms	10
Cancer prophylaxis	6
	18

TABLE 6. *Causes of Death in 84 Operation Survivors*

Cause of Death	Number of Patients
Related	
cancer of the colon	1
cancer of the rectum	2
pulmonary embolus	1
Nonrelated	
mycosis fungoides	1
respiratory failure	1

The risk of carcinoma per patient-year is shown in Table 8. As described earlier, the risk is calculated per patient-year beginning at the onset of symptoms rather than per patient-year under observation. There were no instances of carcinoma in patients having the disease for less than 10 years. Between 10 and 20 years the risk was 1/206, and between 20 and 30 years, the risk was 1/116. The figure for disease greater than 30 years, 1/29, should be interpreted with caution since it is based on only three patients. The annual incidence of colon and rectal carcinoma in the state of Ohio is approximately 0.0006 (or 1 case per 1667 persons per year).‡ Thus, the risks in the second and third decades are nine times and sixteen times the average annual risk. If a matched control group§ is taken as a basis for comparison, the excess risk is 781 times greater at 15 years, and 305 times greater at 25 years. It should be stressed, however, that the individual risk for a given patient is still quite small, and much smaller than if the total colon were left in place. Table 9 compares the cancer risk after IRA found in our patients and in Aylett's series[2] with patients having extensive colitis described by DeDombal[3] and Lennard-Jones.[4] While it is clear that the risk is less when one compares the IRA patients to patients having extensive colitis in DeDombal's series (the risk being diminished by approximately one-fourth), the figures of Lennard-Jones appear to predict approximately the same incidence of carcinoma regardless of whether or not the colon is left in place. As Baker et al.[2] noticed, however, the patients in Lennard-Jones' series are not strictly comparable since he excluded all patients

‡ Based on American Cancer Society Statistics, 1980.[7]

§ Figures courtesy of Dr. A. Flynn, Cleveland Clinic Cancer Center based on the 3rd National Cancer Survey, 1975.

TABLE 8. *Incidence of Rectal Cancer Per Patient—Year from Onset of Disease*

Years of Disease	Patient-years	Number of Patients with Cancer	Incidence of Cancer per Patient-year	Risk per Patient-year
<10	769	0	0	0
10–19	412	2	0.005	1/206
20–29	116	1	0.009	1/116
>30	29	1	0.034	1/29

TABLE 9. *Comparison of Risk of Cancer*

Total Colon Years of Disease	Extensive U.C.		Colectomy and IRA	
	DeDombal	Lennard-Jones*	Baker	Present Series
<10	1/282	0	0	0
10–19	1/50	1/200	1/206	1/185
>20	1/17	1/60	1/117	1/74

* Patients with dysplasia or carcinoma and patients requiring surgery excluded.

TABLE 7. *Follow-up Study of Patients Developing Rectal Carcinoma*

Age	Sex	Years of Symptoms	Stage	Survival (Years)	Treatment and Follow-up
56	M	35.5	?	5.5	Local excision Died NED mycosis fungoides
32	F	24	D	1.4	Laparotomy showed liver metastases Died (cancer)
31	M	15	C	0.4	Proctectomy Died (cancer)
30	F	14	A	0.6	Proctectomy Living NED

NED: no evidence of disease.

TABLE 10. *Probability of Survival without Rectal Cancer from the Onset of Disease in 84 Patients having Colectomy and IRA**

Duration of Disease (Years)	No. of Patients	Incomplete Year of Follow-up	Corrected No. at Risk	Observed Number with Cancer	Proportion with Cancer	Proportion without Cancer	Cumulative Proportion without Cancer	SD
					q_i	p_i	$P = p_1p_2p_n$	
9–	68	4	66	0	0	1.000	1.000	—
14–	49	4	47	1	0.0213	0.9787	0.9787	0.0211
17–	35	2	34	1	0.0294	0.9705	0.9499	0.0354
19–	28	5	25.5	0	0.000	1.000	0.9499	0.0354
24–	12	0	12	1	0.0833	0.9167	0.8708	0.0825
29–	3	0	3	0	0.000	1.000	0.8708	0.0825
34–	2	0	2	0	0.000	1.0000	0.8708	0.0825
35–	2	0	2	1	0.5000	0.5000	0.4354	0.3106
39–	1	0	1	0	0.000	1.000	0.4354	0.3106

* Abbreviated to show figures at ten years and each year in which a carcinoma was found.

presenting with dysplasia, carcinoma, and severe symptoms requiring surgical therapy.

A more accurate estimate of the cancer risk may be obtained by using the life-table method[5] to compare our patients to those in Kewenter's series of patients with extensive ulcerative colitis[8] (Table 10). The cumulative risk of developing cancer $Q = 1 - P$ is shown graphically in Figure 2 and enumerated in Table 11. The cumulative risk at 25 years is only 12.9% ± 8.3%, compared to Kewenter's figures of 33.7% ± 8.6%. For all years, the risk was significantly less for patients having total colectomy and IRA than when the colon was left in place ($z > 2.33$, $p < 0.01$).

Dysplasia

Following the detailed description of "precancerous" epithelial changes in patients with ulcerative colitis by Morson and Pang in 1967,[9] several investigators tried to predict the probability of colonic cancer on the basis of epithelial dysplasia in the colon and rectum. Lennard-Jones[4] showed that severe dysplasia was rather uncommon, occurring in approximately 6% of his patient. Dobbins noted that "precancer" on rectal biopsy was associated with a colonic cancer in 32% of patients.[10] It would, thus, seem reasonable to attempt to correlate epithelial changes in the extirpated colon with the subsequent development of rectal dysplasia or cancer.

Epithelial dysplasia of the colon and rectum was graded as mild, moderate, or severe depending on whether the upper one-third, upper two-thirds, or entire glands displayed nuclear anisocytosis and hyperchromatism, as well as loss of nuclear polarity and the normal goblet cell configuration of colonic mucosa. Since dysplastic changes were often patchy, only the highest degree of dysplasia was considered.

Of the 84 colectomy specimens, 62 (73.8%) showed no dysplasia, ten (11.9%) showed mild dysplasia, two (2.4%) showed moderate dysplasia, and three (3.6%) showed severe dysplasia. Seven patients (8.3%) had colonic cancers (Table 3). Forty-six of these patients had subsequent microscopic evaluation of the rectal epithelium. Of these, 37 (80.4%) had no dysplasia, one (2.2%) had mild dysplasia, two (4.4%) had moderate dysplasia, four (8.7%) had severe dysplasia, and four developed rectal cancer (8.7%).

Thirty-three patients whose colons showed no dysplasia had subsequent rectal biopsy. Of these, only three (9%) developed cancer or "precancer" (moderate or severe dysplasia). One patient developed rectal cancer, one severe dysplasia, one moderate dysplasia, two mild dysplasia, and the other 28 had no dysplasia. Of the ten patients having mild colonic dysplasia, one patient developed rectal cancer, one patient had moderate rectal dysplasia, seven patients had no rectal dysplasia, and one patient had no biopsy performed. Hence, two out of nine (22.2%) patients evaluated with mild colonic dysplasia had rectal cancer or precancer. The group having moderate or severe colonic dysplasia and colonic cancer is detailed in Table 12. Seven of the ten patients who survived who had cancer or precancer of the colon had rectal biopsies. Five of these seven (71.4%) developed cancer or precancer of the rectum. While it is difficult to draw firm conclusions from this small number of patients, there seems to be an evident trend towards rectal dysplasia and cancer when the colon has been previously involved with such changes, and it would seem that we are justified

TABLE 11. *Cumulative Risk of Developing Carcinoma in Extensive Mucosal Ulcerative Colitis*

Years Since Onset	Total Colon Kewenter	Colectomy and IRA		
		Baker	Present Series	
<10	3% ± 1.7%	0	0	
10–15	9.6% ± 3.5%	1.4% ± 0.7%	2.1% ± 2.1%	$p < 0.01$
15–20	24.2% ± 6.6%	6.1% ± 1.7%	5.0% ± 3.5%	$p < 0.01$
20–25	33.7% ± 8.6%	9.2% ± 2.2%	12.9% ± 8.3%	$p < 0.01$

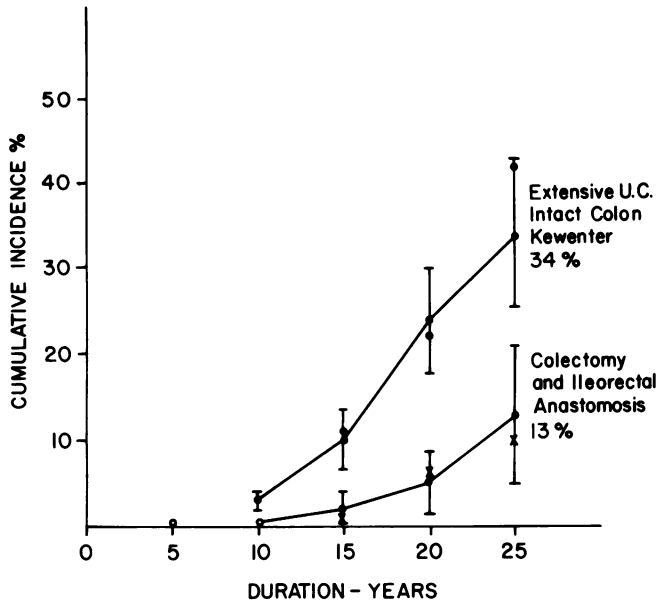

FIG. 2. The cumulative risk of developing carcinoma in extensive mucosal ulcerative colitis following colectomy and ileorectal anastomosis compared to the risk without surgery. ×: Baker et al. ○: DeDombal et al.

in regarding such patients as being at increased risk for the development of rectal carcinoma when compared to the group as a whole. Thus, we consider severe colonic dysplasia and colonic cancer as a contraindication to ileorectal anastomosis.

We also would recommend that yearly rectal biopsy specimens be taken from multiple sites in all patients having ulcerative colitis for a period of more than ten years. Patients who have had an IRA performed after having previous moderate or severe colonic dysplasia or cancer, and patients with moderate or severe rectal dysplasia, should probably have biopsies performed every six months, followed by proctectomy if dysplastic changes persist.

Summary

We have reviewed a series of 89 patients having colectomy and ileorectal anastomosis for mucosal ulcerative colitis. The operation can be performed with a low risk of mortality and an acceptable morbidity. Twenty-one per cent of the patients required subsequent proctectomy, and the overall incidence of carcinoma was 4.8%. The cumulative risk of developing a rectal cancer was 12.9% ± 8.3% after 25 years, significantly less than when the colon is left intact. Colectomy and ileorectal anastomosis appears to be a satisfactory alternative to total proctocolectomy and ileostomy when the rectal mucosa is distensible. Pre-existing colonic cancer or severe colonic dysplasia should be considered a relative contraindication to the prevention of the rectum. Close follow-up of all patients with proctoscopy and rectal biopsy is imperative.

TABLE 12. *Patients having Cancer or Precancer at the Time of Colectomy*

Colon	Subsequent Rectal Biopsies Examination
Cancer	Severe dysplasia
Cancer	Died—no biopsies
Cancer	Alive—no biopsies
Cancer	Severe dysplasia—proctectomy
Cancer *in situ*	Alive—no biopsies
Cancer	Died
Cancer	Cancer of the rectum, severe dysplasia proctectomy
Severe dysplasia	Severe and moderate dysplasia
Severe dysplasia	No dysplasia (one biopsy)
Severe dysplasia	Cancer
Moderate dysplasia	No biopsy—lost to follow-up
Moderate dysplasia	No dysplasia

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