Survival with Carcinoma Arising in Mucosal Ulcerative Colitis

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Adenocarcinoma of the colon is a well-recognized complication of total chronic ulcerative colitis. The incidence increases with time, and the carcinoma arising in chronic ulcerative colitis has developed a bad clinical reputation in terms of aggressive behavior. The survival statistics of patients with cancer arising in chronic ulcerative colitis are compared with statistics for a group of noncolitic patients with equivalent clinicopathologic staging treated at the same institution. When grouped by extended Duke's classification and compared with carcinoma arising without ulcerative colitis, there was no statistical difference in survival rates. The overall results are worse because of a higher percentage of patients with incurable disease at the time of operation. With improved surveillance and methods of detecting premalignant changes, the necessity for prophylactic proctocolectomy should decline.

ADENOCARCINOMA OF THE COLON is a well-recognized complication of total colonic ulcerative colitis. The incidence of carcinoma increases with time, following an apparently safe period of approximately ten years.

Some physicians choose to follow mucosal ulcerative colitis (MUC) patients at risk with serial colonoscopic examinations and multiple endoscopic biopsies. A proctocolectomy is then advised when colon biopsy specimens show premalignant dysplastic changes or carcinoma in situ.

This mode of therapy raises the question of whether the biological aggressiveness of carcinoma arising in MUC is the same as that in patients with isolated colon cancer. Carcinoma developing in chronic MUC has a bad clinical reputation in terms of aggressive behavior.

The objective of this study is to examine the long-term survival of patients with cancer arising in MUC in relation to the clinicopathologic staging (extended Duke's classification) at the time of diagnosis (Table 1). The survival statistics are compared with those of a group of noncolitic patients with equivalent clinicopathologic staging treated at the same instutition.

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Materials and Methods

From February 1950 to June 1979, 79 patients underwent operation at the Cleveland Clinic for carcinoma arising in MUC. Data have been collected on sex, age, onset and duration of symptoms, pathologic staging of tumor, and surgical procedure performed. Follow-up is complete. Survival has been grouped according to an extension of Duke's classification and compared with survival of a separate group of patients treated for carcinoma of the colon at the same institution from 1950 to 1964.[1,2] Survival rates were calculated using the actuarial method, and life tables were prepared to show correction for age using the U.S. Life Tables.[3]

Results

There were 56 men and 23 women with 100% follow-up. The age range at the time of detection of the carcinoma was from 22 years to 73 years (Fig. 1). The mean duration of the symptoms before the discovery of the carcinoma was 17 years (Table 2). Proctocolectomy and subtotal colectomy were the most common operative procedures performed. The remaining procedures were performed for palliation in incurable situations (Table 3).

TABLE 1. *Extended Duke's Classification*

Duke's Classification	Characteristics
A	Tumor confined to bowel wall and its coats
B	Tumor through all coats of bowel (No metastases to lymph nodes; no distant spread)
C	Tumor metastases to regional lymph nodes (No clinical or radiological evidence of distant spread)
D	Tumor spread beyond primary site or lymph nodes (Adjacent organ invasion present; peritoneal, liver or distant organ metastases present)

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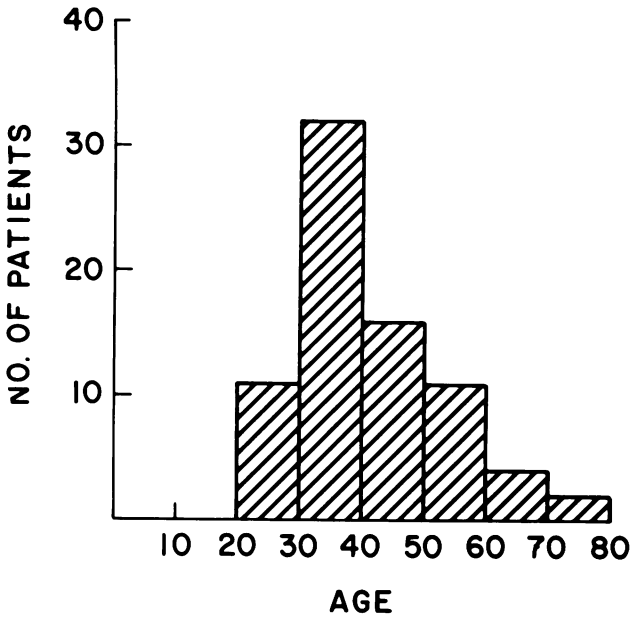

FIG 1. Age at detection of carcinoma

There were three operative deaths: two due to an intraoperative myocardial infarction and the third to a postoperative pulmonary embolus. Thirty-five deaths were attributable to the carcinoma of the colon, one to carcinoma of the bile duct, and eight were unrelated deaths; three patients are presently alive with carcinomatosis—all had disseminated disease at operation (Table 4).

The cancers were distributed throughout the large bowel, but most were located more distally. Three patients had multiple carcinomas. Of the 79 patients, 11 had carcinoma in situ, 13 with Duke's A, 15 with Duke's B, and 12 with Duke's C carcinomas. Twenty-eight patients had distant metastases (Stage D) when they underwent operation. Patients with carcinoma in situ have been excluded for the purpose of comparison with the figures from our institution. All patients with carcinoma in situ were alive after five years, with no evidence of disease.

The percentage of Duke's A cases was slightly higher than that in the group of carcinoma arising without MUC. In the Duke's B and C groups, the percentages were less in the group of carcinoma arising in MUC.

TABLE 2. *Carcinoma in Ulcerative Colitis, Duration of Symptoms*

Modified Dukes'	Number of Patients	Average Duration
In Situ	11	17 years
A	13	18 years
B	15	20 years
C	12	15 years
D	28	16 years

TABLE 3. *Carcinoma in Ulcerative Colitis*

Primary Procedure	Number
Proctocolectomy	24
Subtotal colectomy	27
Ileostomy	11
Biopsy	9
Abdominoperineal proctectomy	3
Fulguration	2
Intraoperative death	1
No operation	2

A higher percentage of patients had metastatic disease at the time of surgery in the group with carcinoma arising in MUC than in the noncolitic group (Table 5).

The five-year survival rate was 41%. For the 13 patients in Class A, the age-corrected five-year survival rate was 94%, as compared with 98.9% for those with carcinoma in the noncolitic group. Only one patient with carcinoma in MUC died in the five-year period. This was not a cancer-related death, and there was no evidence of metastatic disease at the time of death (Fig. 2).

Fifteen patients had Duke's B carcinomas arising in MUC. The age-corrected five-year survival was 59%, as compared with 84.9% in the noncolitic group. Three deaths were cancer-related. In each case the carcinoma had invaded the pericolic fat to a depth of 5 mm. Three other deaths were not attributable to the carcinoma (Fig. 3).

Twelve patients had Duke's C carcinomas. The age-corrected five-year survival rate was 57%, as compared with 67.3% in the noncolitic group. Four patients died of metastases, two patients were alive at follow-up one year after radical resection with metastases, and one patient died 12 years postoperatively with no evidence of disease (Fig. 4). No patient with less than three lymph nodes involved developed late metastases, but all patients with more than three lymph nodes involved developed widespread metastases.

Twenty-eight patients had distant metastases at the time of operation. This is the largest group in the study. In only three patients, no visible tumor remained at the completion of surgery. Three-year survival was zero

TABLE 4. *Carcinoma in Ulcerative Colitis*

Cause of Death	Number
Carcinoma related	35
Operative	
Myocardial infarction	2
Pulmonary embolus	1
Carcinoma of bile duct	1
Unrelated	8
	47

TABLE 5. *Carcinoma in Ulcerative colitis*

Modified Duke's Classification	Carcinoma in U.C.	Carcinoma
A	19%	15%
B	22%	32%
C	18%	23%
D	41%	30%

(Fig. 5). One patient was alive with metastases at the time of follow-up less than one year after surgery.

Nineteen patients had a previously unsuspected carcinoma that was detected by pathologic examination of the resected specimen. Of these six were carcinomas in situ, five Duke's A, six Duke's B, and two Duke's C carcinomas. Barium enema is notoriously unreliable in the early detection of carcinoma arising in MUC due to the characteristically flat configuration of the tumor and its propensity to spread submucosally. Colonoscopy has provided the opportunity for earlier recognition of these neoplasms.

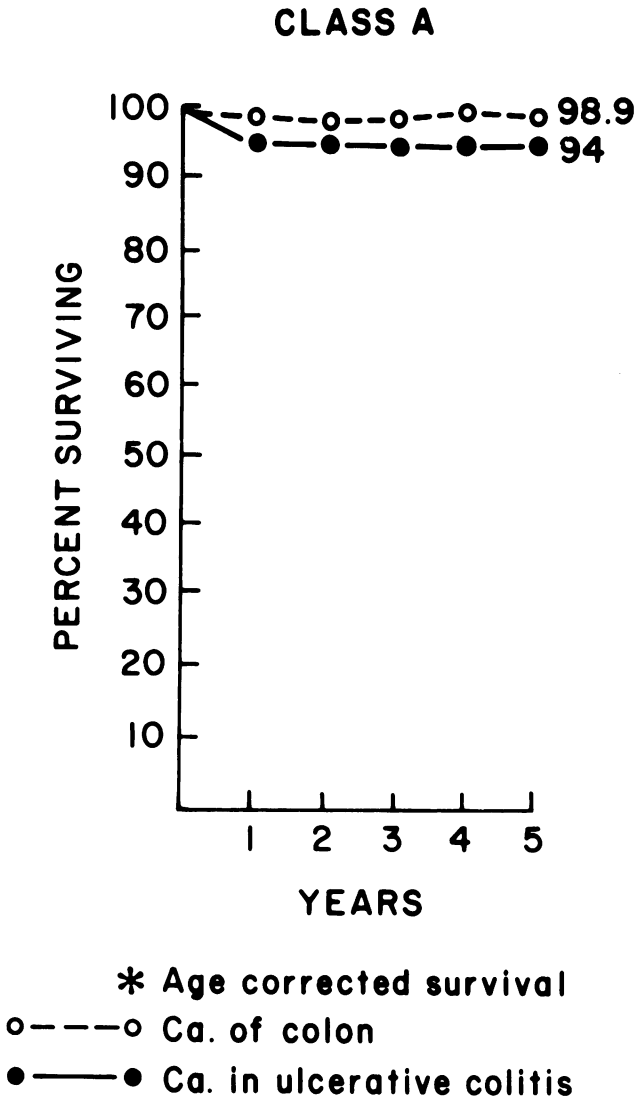

FIG. 2. Life Table A.

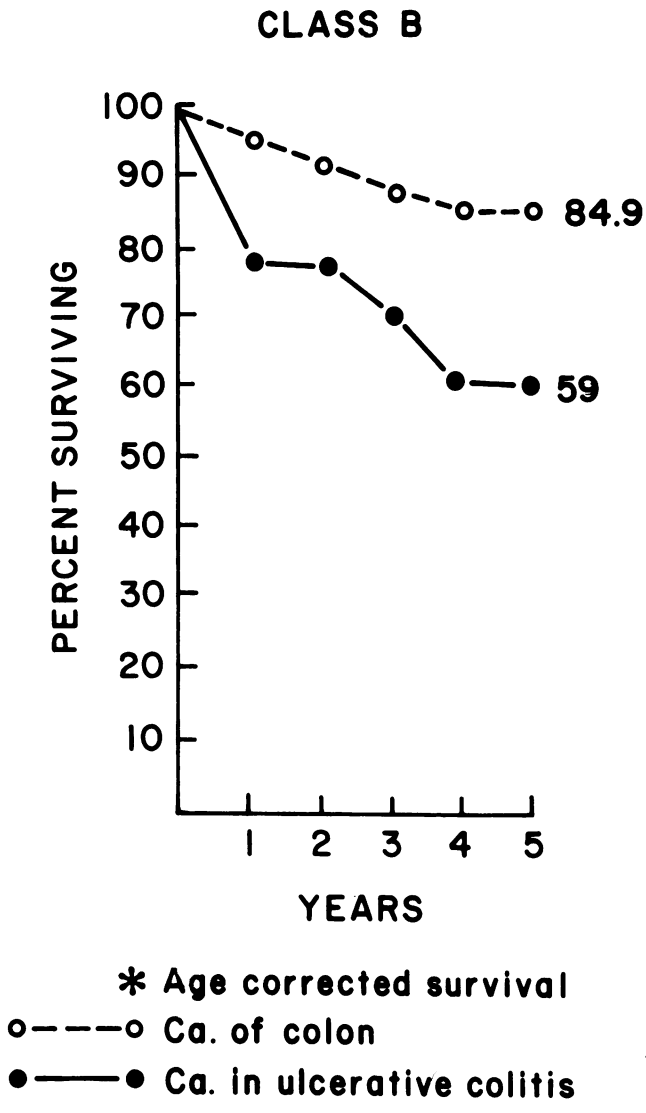

FIG. 3. Life Table B.

Discussion

MUC is unequivocally identified as one of the conditions that predispose to carcinoma of the colon.[4-13] The reported prevalence of carcinoma in ulcerative colitis varies depending on the duration of the colitis and on the method of collecting data for statistical evaluation.[14] Kewenter et al.[15] calculated the cumulative incidence of carcinoma in colitis to be 34%, 25 years after the onset of colitis, and 43% if the colitis developed before the patients were 25 years old. It has been suggested that most patients who have had extensive colitis

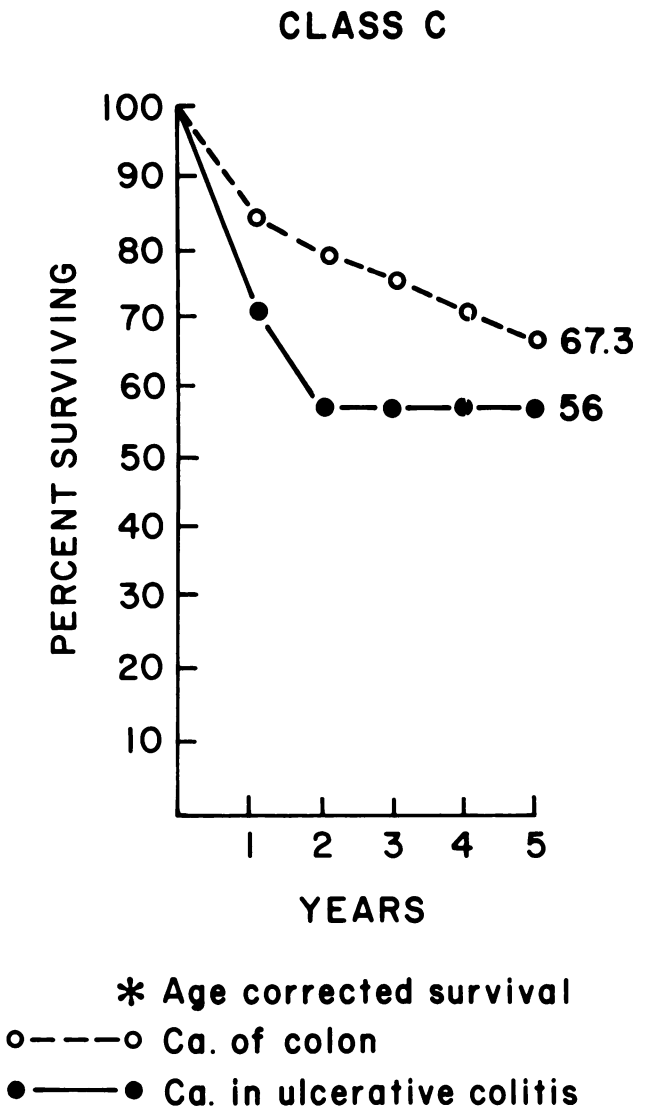

FIG. 4. Life Table C.

longer than 10 years should be advised to have colectomy for cancer prophylaxis.[16,17] The danger appears greater when ulcerative colitis develops before the patients are 20 years old. Patients with total or near total colonic involvement are principally at risk.

The prognosis of cancer in ulcerative colitis is generally regarded as poor. Slaney and Brooke,[18] from a review of the literature, gave a five-year survival figure of 18.6%. Michener et al.[19] found a five-year survival of 13% in children in whom the disease began before they were 15 years old and who subsequently developed carcinoma. Hinton[20] reported a 40% five-year survival for all patients with carcinoma arising in ulcerative colitis. The overall survivals are poor because of the advanced stage of the disease in a large number of patients. Hughes et al.[21] more recently compared carcinomas arising in patients with colitis with matched controls from a population without colitis. They found a five-year survival rate of 55.1% in the group with colitis and 46.9% in the group without colitis; the difference is not statistically significant. VanHeerden and Beart,[22] in a study from the Mayo Clinic, found a five-year survival rate of 41.7% in patients with cancer arising in mucosal colitis. When matched with a noncolitic population with cancer, they found no statistical difference in the five-year survival. Beahrs et al.[23] recognized that when the patient was asymptomatic and before complications developed, or when the lesion was precancerous, the disease was almost always localized, and that with adequate treatment the results were excellent. Morson and Pang[11] called attention to precancerous changes in epithelial dysplasia in rectal biopsy

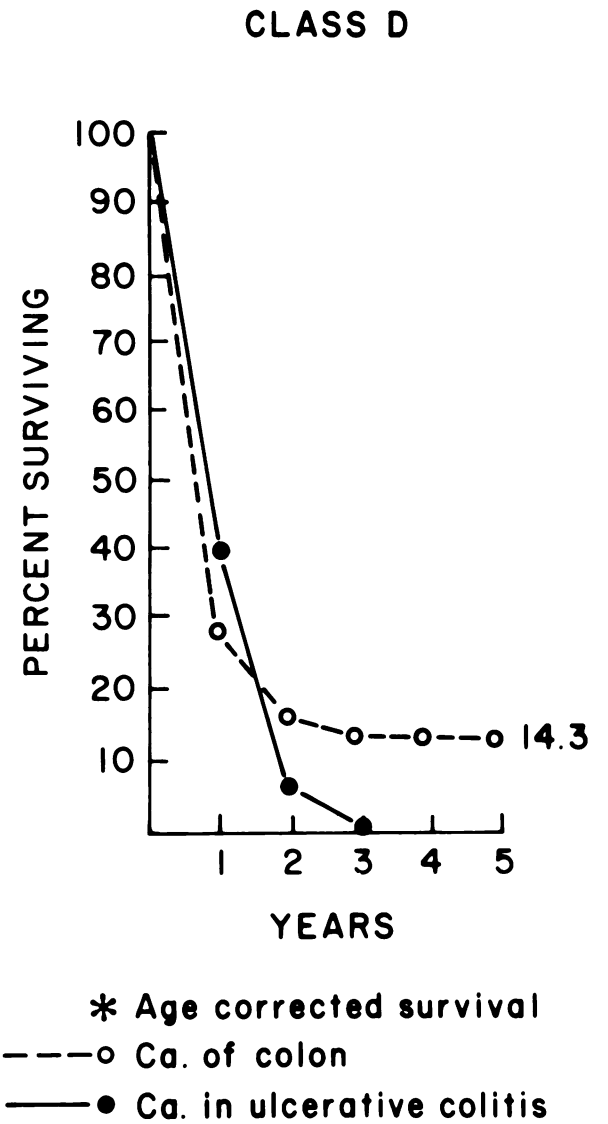

FIG. 5. Life Table D.

specimens, and this has been extended to multiple colonic biopsies taken through the colonoscope. This has modified our thoughts on the necessity for prophylactic proctocolectomy. Lennard-Jones et al.,[24] in following 229 patients with mucosal biopsies, found five patients with carcinoma of the colon. Colectomy was performed for severe dysplasia, or moderate dysplasia and clinical disability. There were five Duke's A carcinomas in four patients and one Duke's B. All patients were well seven months to ten years after surgery at the time of reporting. The data suggest that the short-term risk of carcinoma is very low if severe dysplasia is absent from colonic or rectal biopsy specimens. In every case in this series, the coincident carcinoma found with severe dysplasia was confined to the bowel wall, with a good chance of cure.

The data from our study support the concept that adenocarcinoma of the colon arising in MUC behaves in much the same way as adenocarcinoma in a noncolitic patient. When grouped by an extended Duke's classification and compared with carcinoma arising without MUC, there was no statistical difference in survival rates. The overall results are worse because of the higher percentage of patients with incurable disease at the time of operation. With improved surveillance and methods of detecting premalignant changes, the necessity for prophylactic protocolectomy should decline.

When surgery is required for intractability of symptoms, ileorectal anastomosis will often provide a good functional result. The rectum is still susceptible to the development of carcinoma,[25-28] but with proper surveillance the risk seems less than had been previously believed and compares favorably with the morbidity associated with a permanent ileostomy of any type or an ileo-anal anastomosis.

A suggested routine for surveillance is an annual colonoscopic examination with multiple colonic mucosal biopsies. If premalignant dysplastic changes are found, the examination should be repeated in three months. If these biopsy specimens again reveal dysplastic changes, serious consideration should be given to surgical excision. If no dysplasia is found on the repeat biopsies, annual examinations should be resumed.

On this program of management, the need for excision is based on established histologic criteria. With the proposed frequency of examinations, the risk of an incurable malignancy developing is minimized, and prophylactic colectomy can be avoided.

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