Risk Factors for Rectal Cancer Morbidity and Mortality in Patients with Familial Adenomatous Polyposis After Colectomy and Ileorectal Anastomosis

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PURPOSE: The aims of the study were to investigate the effects of ileorectal anastomosis and the follow-up program on rectal cancer morbidity and mortality and to identify risk factors that predict the fate of the rectal stump. METHODS: One hundred ninety-five patients with familial adenomatous polyposis on whom an ileorectal anastomosis was performed between 1957 and the end of 1995 were included. Median follow-up time was 14 (range, 1-39) years. The cumulative risks of rectal cancer and rectal excision were estimated using survival analysis. RESULTS: Eighteen patients (9.2 percent) developed cancer, 17 in the retained colorectal segment and one on the ileal side of the anastomosis, and nine died of their cancer during the study period. The cumulative rectal cancer morbidity and mortality 20 years after ileorectal anastomosis was 12.1 percent (95 percent confidence interval = 5.7-18.5) and 7 percent (95 percent confidence interval = 2-12), respectively. The cumulative age-dependent risk of rectal cancer was 22.9 percent (95 percent confidence interval = 11.4-34.5) and 25.7 percent (95 percent confidence interval = 13.2-38.2) at the ages of 60 and 70 years, respectively. The corresponding cumulative mortality was 11.1 percent (95 percent confidence interval = 2.9-19.3) at the age of 70 years. Patients with dense polyposis at colectomy had an increased risk for cancer in the retained colorectal segment compared with patients with intermediate or sparse polyposis (P = 0.04). Sixty-six patients (34 percent) had their rectum removed, and the cumulative rectal excision rate 35 years after ileorectal anastomosis was 65.5 percent (95 percent confidence interval = 53-78). CONCLUSION: Patients on whom ileorectal anastomosis was performed had, despite the high rectal excision rate, a substantial risk of developing cancer in the retained colorectal segment, with an ensuing high mortality. Our results indicate that patients with dense polyposis should undergo restorative proctocolectomy as primary operation for familial adenomatous polyposis. In younger patients with intermediate or sparse polyposis and good expected follow-up compliance, ileorectal anastomosis still is an alternative. [Key words: Familial adenomatous polyposis; Colectomy and ileorectal anastomosis; Colorectal cancer]


Familial adenomatous polyposis (FAP) is a genetic disorder passed on in an autosomal dominant fashion with an estimated gene frequency of approximately 1/13,000 to 1/24,000.1-3 The disease is caused by mutations in the adenomatous polyposis coli (APC) gene located on chromosome 5q21.4-6 The main pathognomonic feature is the development of numerous adenomatous polyps in the colon and rectum. Adenomas occur in all carriers of the mutated APC gene because penetrance is estimated to be complete.2 The colorectal cancer (CRC) morbidity among unidentified affected subjects is estimated to be 100 percent.

The establishment of national and regional registries and the early detection of affected subjects in families with FAP have dramatically decreased CRC incidence.7-9 The Swedish national screening program for FAP has been successful in terms of identifying and informing families with FAP. This is a prerequisite for detecting and treating patients with FAP before they have developed CRC, thereby reducing CRC morbidity and mortality.

Panproctocolectomy is obviously the most efficient prophylactic treatment for CRC. In spite of this, colectomy and ileorectal anastomosis (IRA) has been the most commonly used prophylactic surgery, providing

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a good functional outcome and a low complication rate.

However, data has been published from several registries about an increased risk of rectal cancer development in those operated on with IRA, despite regular endoscopic follow-up.\textsuperscript{10-16} Restorative proctocolectomy (RPC) and ileal pouch-anal anastomosis (IPAA) have gradually replaced IRA as the primary prophylactic treatment of CRC in FAP.\textsuperscript{17-18} An important reason for this is the reported morbidity and mortality in rectal cancer among the IRA-operated. Factors proposed as predicting increased risk are length of the postoperative period, chronological age, length of the retained rectum, and dense polyposis at diagnosis.\textsuperscript{11-16}

The aim of this study was to investigate all patients with FAP in Sweden on whom IRA was performed during a 40-year period to evaluate the effect of IRA and of the surveillance program on morbidity and mortality in colorectal cancer. It was also to study the predictive value of known risk factors to optimize the treatment of these patients.

**PATIENTS AND METHODS**

One-hundred ninety-five patients (99 males) with FAP in the Swedish Polyposis Registry on whom IRA was performed between 1957 and the end of 1995 were studied. The IRA operations were performed throughout the country at several Swedish hospitals, although most operations were performed at St Erik's Hospital in Stockholm until it was closed down in 1985. The colorectal surgery for FAP in Sweden during this period is illustrated in Figure 1. The length of follow-up after IRA was 1 to 39 years, and the median follow-up time was 14 years. Forty-eight of the patients were probands who were diagnosed because of symptoms, and 147 were call-up patients who were diagnosed by screening of at-risk subjects. Four of the IRA-operated patients had a previous colon cancer and had undergone segmental resections 9 (range, 4–18) years earlier. Twenty-six of the 195 patients had colon cancer at the time of IRA, and seven of these died of their cancers during the study period. The remaining 19 patients who were still alive at the end of the study period had a median follow-up time of 11 (range, 1–25) years. Six patients died of FAP-associated malignancies other than CRC, and 12 patients died of nonrelated causes during the study period. Ninety-eight patients with IRA were still alive at the end of December 1995, and two were lost to follow-up.

Data on the number of polyps at the time of colectomy was collected from surgical and pathology reports. It was available for 170 patients: 21 had less than 100 polyps (sparse), 58 had more than 100 but less than 1,000 polyps (intermediate), and 91 had more than 1,000 polyps (dense). The number of polyps was calculated by examining the open specimen of the colon. Only patients with more than 1,000 carefully counted polyps or polyposis that almost covered the normal mucosa were defined as patients with dense polyposis.

Patients were examined endoscopically with extirpation or fulguration of polyps at 6-month to 12-month intervals. The diagnosis of adenoma or cancer was made after histologic examination of the specimens.

Cumulative risks were calculated from the date of IRA or from birth (age-dependent risk) using Kaplan-Meier analysis. End points were date of diagnosis of cancer, date of rectal cancer-related death, or date of rectal excision. Subjects were censored at December 31, 1995, date of death (not rectal cancer-related), or at last date of follow-up. The variability of the values calculated from the Kaplan-Meier analysis was expressed as 95 percent confidence interval (CI). The log-rank test was used to compare the influence of polyp density and gender on the cumulative rectal cancer morbidity, rectal cancer mortality, and rectal excision rate. Fisher's exact probability test was used for categorical data, comparing the groups with and without rectal cancer according to polyp density, age, and length of the retained colorectal segment.

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**Figure 1.** Patients operated on with colectomy and ileo-rectal anastomosis (IRA), panproctocolectomy and ileal pouch-anal anastomosis (IPAA), and panproctocolectomy and ileostomy (figures in brackets refer to patients operated on with colectomy and continence ileostomy ad modum Kock) for familial adenomatous polyposis (FAP) in Sweden, 1957–1996.