Surgical Treatment and Long-Term Outcome of Patients with Familial Adenomatous Polyposis: 16 Years Experience at the Tel Aviv Sourasky Medical Center

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Abstract

Background: Restorative proctocolectomy eliminates the risk of colorectal cancer in patients with familial adenomatous polyposis. Complications and extra-intestinal manifestations are inherent to the procedure.

Objectives: To evaluate operative procedures, complications, early and late results and long-term functional outcome in FAP patients operated in our department.

Methods: The study group included all patients with FAP who were operated between 1988 and 2003. Demographic data, length of follow-up, complications, colorectal cancer, pouch function and extracolonic manifestations were recorded.

Results: Median age at surgery was 33 years (range 13–61 years). The final operative breakdown was: 48 proctocolectomies, 41 ileal pouch-anal anastomoses, 2 Kock's pouch, 5 permanent ileostomies, and 2 colectomies with ileorectal anastomosis. There was no perioperative mortality. Early and late complications occurred in 20 and 9 patients, respectively. Twelve patients required reoperation. Colorectal carcinoma was diagnosed in eight patients, three of whom were in an advanced stage. The mean follow-up was 74 months (range 3–288 months). Four patients were lost to follow-up. Extracolonic manifestations developed in 38 patients, including desmoid tumors (in 12), duodenal adenomas (in 9), pouch adenomas (in 5), and rectal stump adenomas (in 3). Two patients died (4%) because of desmoid tumor and malignant fibrous histiocytoma. At last follow-up, 37 IPAA patients have (median) six bowel movements/24 hours and good fecal control.

Conclusions: Restorative proctocolectomy can be performed with low mortality, acceptable morbidity, and good functional results. Patients should be closely followed after surgery for development of other manifestations of the syndrome. Relatives of the affected patients should be referred to a specialist multidisciplinary clinic.

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Familial adenomatous polyposis is an autosomal dominant condition caused by germline mutation of the *APC* gene on chromosome 5. The clinical diagnosis is usually based on hundreds of adenomatous polyps carpeting the entire colon. If left untreated, the vast majority of patients will develop colorectal cancer by the age of 40 years [1]. The development of screening, surveillance and prophylactic colectomy has led to a decrease in colorectal cancer prevalence and overall improvement in prognosis [2]. Proctocolectomy and ileal pouch anal anastomosis is emerging as the treatment of choice. Colectomy with ileorectal anastomosis is also a sound option in selected patients. The main concern is the risk of rectal cancer after IRA on the one hand and the possible higher morbidity and inferior function after IPAA on the other.

Patients may develop extracolonic manifestations expressed as adenomatous polyps of the duodenum and the ileal pouch that are susceptible to malignant transformation, as well as desmoid tumors that have an unpredictable and aggressive nature and pose a difficult management problem.

The aim of the present study is to report our 16 year experience with the treatment of FAP patients at the Tel Aviv Sourasky Medical Center.

Patients and Methods

Included in the study group were all FAP patients who underwent surgery in our department between January 1988 and December 2003. Data were collected from operative notes, hospital charts, and outpatient clinic records. They included demographics, background diseases, indications for and types of operative interventions, early and late complications, length of hospital stay, readmissions, further interventions and medical treatment during follow-up.

Results

We treated a total of 50 patients with FAP: 25 males and 25 females, with a median age at operation of 33 years (range 13–61 years). Eight patients were referred to us after some surgical procedure at other hospitals. An *APC* mutation was established in 31 patients. Eight patients were diagnosed as having phenotypic Gardner syndrome expression and one as having Turcot syndrome type 2. The mean follow-up was 74 months (range 3–288 months). Four patients were lost to follow-up.

Surgical outcome

IPAA was eventually performed in 41 patients, of whom 22 had a double-stapled IPAA and 19 underwent mucosectomy with hand-sewn ileoanal anastomosis. IPAA was performed in one stage in 11 patients and in two stages in 28. Two patients had a three-stage procedure: they were converted from IRA and Hartman's pouch with ileostomy to IPAA. A J-pouch was constructed in 39 patients and an

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FAP = familial adenomatous polyposis
IPAA = ileal pouch-anal anastomosis
IRA = ileorectal anastomosis

S-pouch in 2 patients. Two patients had an IRA. Seven patients underwent proctocolectomy and permanent ileostomy – three of them because of advanced cancer that was found during operation, and two had been operated on in the pre-IPAA era and had a Kock's pouch reconstruction. The remaining two patients had undergone IRA or Hartman's pouch and ileostomy and had failed conversion to IPAA because of a mesenteric desmoid tumor in one and technical difficulties in the other.

The median postoperative hospital stay was 11 days (range 7–23 days). Patients with protective ileostomy underwent closure after a median of 99 days after pouch construction (range 34–317 days). Twenty-one patients developed complications and 10 had more than one complication. There was no perioperative mortality. Early postoperative complications (IPAA and ileostomy closure) occurred in 20 patients; only 10 complications were specific [Table 1]. The most common (61%) were septic (pelvic sepsis, wound infection, urinary tract infection). Four patients had small bowel obstruction for which two required reoperation. Another two patients underwent surgery in the postoperative period – one due to anastomotic bleeding after ileostomy closure and one for suspected small bowel ischemia.

Nine patients developed late complications [Table 2]: eight had small bowel obstruction requiring readmission to hospital and two of them required reoperation. Two patients had scar exploration for wound complications and two had ileoanal anastomotic stricture that required dilatation under anesthesia. One patient developed pouch perineal fistula and was found to have Crohn's disease.

Table 1. Early postoperative complications (including restorative proctocolectomy and ileostomy closure)

Complication	No. of patients (No. of patients operated)
Urinary tract infection	3
Urinary retention	1
Wound infection	5
Line sepsis	1
Prolonged ileus	1
Acute abdomen	1 (1)
Pneumonia	1
Pulmonary embolism	1
Small bowel obstruction	4 (2)
Pelvic sepsis/peripouch collection	3
Anastomotic bleeding	1 (1)
Anastomotic leak	1 (1)
Pouch bleeding	1
Total	20

Table 2. Late complications

Complication	No. of patients (No. of patients operated)
Small bowel obstruction	8 (2)
Wound sinus/pain	2 (2)
Pouch perineal fistula	1 (1)
Ileoanal anastomotic stricture	2 (2)
Total	9

Colorectal cancer

Eight patients (16%) were diagnosed with colorectal cancer. It was the first presentation of the syndrome in three patients: two underwent urgent surgery for large bowel obstruction due to obstructing tumors. The colorectal cancer was discovered at colectomy in four patients and the cancer developed in the rectal stump during the follow-up period in one patient. Distribution by TNM stage was as follows: stage I in 3 patients, stage II in 2 patients, stage III in 2 patients and stage IV in one patient. Four patients had one or more synchronous cancer. Patients were treated with adjuvant chemotherapy according to the standard of care in colorectal cancer. At a median follow-up of 7 years and 4 months (range 15 months to 15 years) all eight patients are alive. One patient has tumor recurrence and one receives adjuvant chemotherapy.

Extracolonic manifestations

Extracolonic manifestations were diagnosed in 38 patients (76%) [Table 3]. Twelve patients were found to have 14 desmoid tumors of which 7 were treated surgically and 7 are being controlled medically. Of 41 patients who had upper gastrointestinal endoscopy, 11 developed duodenal and/or ampullary adenomas. Three had endoscopic polypectomy and one patient underwent a Whipple operation. Twenty-nine patients underwent pouchoscopy and 5 of them had pouch adenomas with low-grade dysplasia that were resected endoscopically. Three of 17 patients with stapled IPAA had adenomas with low-grade dysplasia in the residual anorectal mucosa. Two polyps were resected endoscopically and one surgically; there was no evidence of invasive cancer.

Table 3. Extracolonic manifestations

Manifestation	No. of patients (38)	Surgery
Syndrome		
Gardner	8	
Turcot	1	
Upper gastrointestinal polyps (20 patients)		
Stomach	13	
Duodenum	14	4
Periampullary	1	1
Papilla	4	3
Osteomata	15	1
Desmoid tumor	12	7
Malignant fibrous histiocytoma	1	1
Fibrous bone dysplasia	1	
Thyroid nodule	1	
Papillary cancer of thyroid	1	1
Pinealoblastoma	1	1
Skin fibromata	3	
Benign brain cyst	1	
Retinal hyperpigmentation	1	
Pouch adenoma	5	
Adenoma in anorectal mucosa	3	3

Mortality

There was no postoperative mortality associated with surgery. Two patients died during follow-up. One patient who had been lost to follow-up was admitted 5.5 years after IRA because of an acute abdomen and underwent emergent surgery. She had small bowel perforation due to an aggressive mesenteric tumor that was found on histology to be a malignant fibrous histiocytoma. She died several months later due to intra-abdominal tumor spread. The other patient died from a huge intra-abdominal desmoid that caused deep vein thrombosis and fatal pulmonary embolism 9 months after IPAA.

Bowel function post-IPAA

At last follow-up, 38 patients have a pouch, which is functioning in 37. One patient is awaiting ileostomy closure. Three patients were lost to follow-up. The median 24 hour and night-time stool frequency was 6 (range 3–16) and 0.8 (range 0–3), respectively. Two patients had perianal soreness. Most of the patients (92%) had complete daytime continence as well as complete night-time continence (86%). Four patients reported fecal incontinence once per 1 or 2 weeks, and three patients (9%) used pads on a regular basis. Three patients could not defer defecation for more than 10 minutes, while two patients required antidiarrheal medications. There was no difference between the stapled versus the handsewn IPAA group.

Discussion

FAP patients should undergo prophylactic surgery in order to extirpate the large bowel, which carries a 100% risk of developing cancer [3]. The overall incidence of colorectal cancer in our series was high (16%), compared to the 8.6% reported by the Mayo Clinic group [4]. The reason is most probably a lack of awareness on the part of the patients as well as community healthcare workers of the need to refer the relatives of affected patients to clinical and genetic diagnosis. The median age at surgery in our series was 33 years and the median age of patients at the time of cancer diagnosis was 46, reflecting a delay in diagnosing FAP.

Preservation of the rectum was a matter of debate when the only two available options were total proctocolectomy with permanent ileostomy or total abdominal colectomy and IRA, with the latter still carrying a significant risk of cancer in the rectal stump and thus requiring lifelong surveillance [5,6]. The advent of IPAA has solved the issue to some extent by removing the mucosa at risk of cancer while preserving transanal fecal flow. Studies comparing IRA and IPAA are ambiguous. Proponents of IRA cite the relatively low morbidity, good functional results and ease of surveillance as benefits of the technique [7–10]. Other studies have failed to show a greater morbidity or poorer functional outcome for IPAA [11–13]. Church et al. [14] found that IRA performed since the advent of the pouch era carries a much lower rate of proctectomy and rectal cancer than IRA performed when IPAA was not an option. One of the reasons for this is proper patient selection and IRA being carried out only on mildly affected patients. Delayed IPAA after IRA has been proposed by Phillips and Spigelman [15]. The major difficulty with this approach is that second proctectomy and IPAA may not always be feasible because of desmoid tumor, as was seen in the present study and the study by Penna et al. [16]. We contend that the treatment of choice should be restorative proctocolectomy.

Our complication rate of 51%, taking into account minor/major and general/specific complications, is comparable with results reported in large groups of patients [7,10,12,16]. Small bowel obstruction is a common complication after major abdominal surgery. The reported risk after IPAA ranges from 13% to 35% [17,18]. The current study showed a 32% risk, with most episodes occurring late. Reoperation was required in 10% of the patients, a figure comparable to that found by Parc and colleagues [19]. The surgical management requires special training and should be undertaken in centers that are experienced in the care of these patients.

As in other series, desmoid tumors have a substantial contribution to late morbidity and mortality. The reported incidence ranges between 8.9 and 17% [20,21], while our incidence was 26%. The mortality rate of this manifestation in our group of patients was 14%, and it varied between 2 and 22% in larger series of patients reported in the literature [19,21,22]. FAP patients are also at risk for developing duodenal cancer. Our finding of one patient out of 50 (2%) who developed periampullary adenocarcinoma concurs with the figures reported by Bjork et al. [23].

Functional results of IPAA in patients with FAP were studied in large groups of patients during relatively long follow-up periods and found to be satisfactory [4,24]. Our patients' median stool frequency of six bowel movements in 24 hours compares favorably with previous reports [19,25].

Conclusion

FAP is an entity with diverse clinical manifestations that could lead to mortality at a young age unless identified and treated in time. The prognosis could probably be improved by referring the relatives of the index patients to a specialist multidisciplinary clinic that is experienced in the evaluation, treatment and follow-up of these patients.

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I cannot think that the world as we see it is the result of chance; and yet I cannot look at each separate thing as the result of Design... I am, and shall ever remain, in a hopeless muddle.

Charles Darwin (1809-1882), British naturalist who originated the concept that living things evolve by natural selection. His views, as expressed in his famous Origin of Species aroused bitter controversy because they conflicted with the account of the Creation in the Bible.

Capsule

Shark cartilage and cancer – no bite?

For more than a decade, shark cartilage has been touted as a rich source of anticancer agents. Although shark cartilage extracts have not yet shown efficacy against cancer in controlled clinical trials, the general public – especially cancer patients desperate for a cure – appear to have embraced the idea. Ecologists fear that continued growth of the shark cartilage industry could have a negative impact on shark populations, which are vulnerable to overfishing. One of the main justifications given for studying the anticancer activity of shark cartilage is the assertion that sharks rarely develop cancer. Ostrander et al. provide evidence that this assumption may be incorrect. Gathering information from the National Cancer Institute's "Registry of Tumors in Lower Animals" and from the scientific literature, they identified 42 cases of tumors in sharks and their close relatives, about one-third of which were malignant. The authors point out the need for systematic surveys to determine the true incidence of cancer in sharks.

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