JOURNAL OF THE
ANUS, RECTUM AND COLON
dx.doi.org/10.23922 /jarc.2017-007
http://journal-arc.jp

REVIEW ARTICLE

Alternative treatments for prophylaxis of colorectal cancer in familial adenomatous polyposis

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Abstract:

Familial adenomatous polyposis (FAP) is a rare, hereditary disease characterized by the presence of 100 or more adenomas distributed throughout the colon and rectum. If untreated, colorectal cancer develops in almost 100% of FAP patients. As prophylactic treatment, proctocolectomy with ileal pouch-anal anastomosis remains the surgical treatment of choice. High rates of postoperative complications, however, have been reported with this procedure, including bowel dysfunction, incontinence, and reduced female fecundity. Some novel strategies for preventing hereditary colon cancers have been reported. This review summarizes alternative treatments, including the laparoscopic approach, chemoprevention, endoscopic management, and subtotal colectomy combined with endoscopic treatment, for prophylaxis of colorectal cancer in FAP patients.

Keywords:

familial adenomatous polyposis, total proctocolectomy, ileal pouch-anal anastomosis (IPAA), ileorectal anastomosis (IRA), chemoprevention, endoscopic management

J Anus Rectum Colon 2017; 1(3): 74-77

Introduction

Familial adenomatous polyposis (FAP) is a rare, hereditary, and complex disease characterized by the presence of 100 or more adenomas distributed throughout the colon and rectum[1]. FAP is the most common polyposis syndrome, with a prevalence of 1 per 10,000 births, and accounting for approximately 0.5%-1% of all colorectal cancer cases. Colorectal cancer will subsequently develop in almost 100% of FAP patients in the third or fourth decade of life if untreated[2]. To date, the only curative treatment for FAP is prophylactic surgery. Two major surgeries, total proctocolectomy with ileal pouch-anal anastomosis (IPAA) or total colectomy with ileorectal anastomosis (IRA), have been conducted for the prevention of colorectal cancer in FAP patients. In a review of the literature, Campos stated that the decision-making process should not be limited to the conventional confrontation of the pros and cons of colectomy with IRA or proctocolectomy with IPAA. Factors including age, genotype, family history, sphincter function, presence or risk of desmoid disease, potential complications of each procedure and chances of postoperative surveillance may be carefully evaluated in the process. Campos also emphasized that the definition of the best moment and the choice of appropriate procedures constitute individual decisions that must take into consideration the preferences of the patient and full information about the complex nature of the disease[3]. Several alternative treatments have recently been reported, and this review describes the standard therapy and alternative treatments for the prophylaxis of colorectal cancer in FAP patients.

Standard Surgery

Colectomy is the recommended treatment for prophylaxis of colorectal cancer in FAP patients. The timing of surgery for patients is usually around their late teens to early twenties. Surgical options include subtotal colectomy with IRA, total proctocolectomy with protective loop-ileostomy, or proctocolectomy with IPAA. The procedure for subtotal colectomy with IRA is relatively simple, less invasive, and maintains better function compared to total proctocolectomy.

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Received: February 9, 2017, Accepted: April 4, 2017

However, Koskenvuo reported the cumulative risk of rectal cancer was 24% at 30 years after colectomy with IRA[4]. Therefore, only a select number of FAP patients would be candidates for this treatment. Intensive endoscopic surveillance of the residual rectum should be continued approximately every 6 months, although no formal guidelines have been set.

Proctocolectomy with IPAA has emerged as the surgical treatment of choice, allowing for complete resection of the colorectal mucosa while preserving transanal defecation. However, IPAA has been associated with a higher rate of postoperative complications, such as bowel function, incontinence, and reduced female fecundity. The functional results of IRA and IPAA appear similar, insofar as the frequency of bowel movements and daytime soiling are concerned[5]. The fecundity of women with FAP after IPAA was recently reported by Olsen et al. to have dropped to 46% compared to preoperatively, while no change in fecundity was observed between before and after IRA[6]. Approximately 50% of patients with a retained rectum after IRA or ileal pouch after IPAA develop adenomatous disease, requiring frequent endoscopies, polypectomies, laser/cautery ablation, and additional operations[7-9].

Laparoscopic Approach

In recent years, surgical approaches have changed dramatically. Laparoscopic surgery for colorectal carcinoma has increased over time and has comprised >30% of all colorectal surgeries performed in Japan since 2008[10]. Some studies have reported the safety and feasibility of a laparoscopic approach for FAP, although previous studies have been based on relatively small cohorts. Due to the reduced invasiveness, laparoscopic surgery has been adopted not only for the treatment of colorectal cancer, but also for the prophylactic treatment of FAP[11]. Recently, Ueno et al. reported a multicenter retrospective cohort study comprising 23 specialist institutions for colorectal disease and a cohort of 282 FAP patients who underwent total colectomy or proctocolectomy between 2000 and 2012. They compared the clinical backgrounds and surgical outcomes of patients between the first and second halves of the study period. The number of patients undergoing laparoscopic surgery for FAP began to increase after 2008, remaining at or above 74% since 2010. The researchers observed no evidence in their study indicating that laparoscopic surgery was inferior to open surgery in terms of clinical outcomes such as morbidity, overall survival rate, stoma closure rate, or incidence of postoperative desmoid tumor[12]. Laparoscopic surgery is expected to offer many other advantages attributable to its minimal invasiveness, including reduced incidences of infertility[13,14] and desmoid tumors[15-18]. However, the efficacy and safety of laparoscopic surgery for FAP have yet to be confirmed. Appropriate clinical trials are demanded to clarify the clinical utility of laparoscopic approaches for FAP patients in future.

Chemoprevention

Despite the acceptance of prophylactic colectomy, there has always been an understandable desire to delay or prevent surgical treatment through the use of medical intervention[19]. Molecular studies have suggested that the inhibition of colorectal mucosal polyamines may represent a promising approach to prevent colorectal cancer. FAP is characterized by marked up-regulation of ornithine decarboxylase in normal intestinal epithelial and adenoma tissue, and reducing polyamines therefore offers a potential strategy to control the progression of FAP-related intestinal polyposis[9].

Sulindac, aspirin, cyclooxygenase-2 inhibitor, combinations of these agents, and other agents are all candidates for chemoprevention of FAP[19-36]. As conducting large studies with a large number of patients is difficult for FAP, scientific evidence is often based on observational and small phase II/III trials. Despite the fact that no chemopreventive strategies are available to replace surgery and endoscopic surveillance in these patients, such methods can be seen as an option in selected cases to delay the time of surgery or as secondary prevention if persistence of adenomas is seen after prophylactic surgery[37].

Endoscopic Management of FAP

Ishikawa et al. provided a retrospective review of endoscopic management for FAP patients who refused colectomy. Ninety patients were managed with repeated colonoscopies to remove numerous polyps between 2001 and 2012. A total of 55,701 polyps were resected by hot snare polypectomy or endoscopic mucosal resection, without adverse events such as bleeding or perforation. All these patients were treated endoscopically, without signs of recurrence during a median follow-up of 4.3 years. No invasive colorectal cancer was recorded during the study period. Two patients (2.2%) underwent colectomy because the polyposis phenotype had changed to dense polyposis. The authors concluded that endoscopic management of FAP is feasible and safe, offering no risk associated with surgery, preservation of normal bowel function, and no increased risk of desmoid tumor, in the medium term. However, they also stated that endoscopic management may also offer an alternative to surgery in FAP patients who decline colectomy or who want to postpone colectomy by a few years, but strong emphasis is required that their results should not be used to discourage FAP patients from prophylactic colectomy, which remains the standard treatment[38]. Several investigators have pointed out that endoscopic management can be challenging, as the risk of developing interval cancer cannot be completely avoided, even with the most careful procedures and the most advanced technologies[39,40]. To evaluate the utility and safety of thorough endoscopic polypectomy with FAP, the single-armed, nonrandomized, multicenter, prospective "Intervention trial for colorectal cancer prevention by endoscopic polypectomy in patients with FAP" is ongoing by a

Japanese study group (ID: UMIN000009365, https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000011005). In that trial, the subjects are patients who have (or had) 100 or more adenomas in the large intestine and who refused to undergo surgery despite being advised to do so, or patients who have undergone surgical resection of part of the large intestine but still have 10 cm or more of the large intestine, and who are 16 years old or older. Study outcomes are expected within several years. Along with endoscopic technology for the management of colonic lesions in FAP patients, strict patient selection criteria are major challenges for the future.

Conservative treatment is only acceptable under the condition that patients can receive intensive surveillance colonoscopy with a good quality. Patients must well understand the necessity of intensive surveillance, and be kept in a good physical and social condition. In addition, medical economy must be healthy in order to offer intensive surveillance colonoscopy to the patients.

Laparoscopic Subtotal Colectomy with Ileo-sigmoid Anastomosis Followed by Intensive Endoscopic Polypectomy for FAP

The aims of management for FAP patients are to prevent death from cancer and to preserve quality of life (QOL). The optimal treatment remains prophylactic proctocolectomy, while continued surveillance of the rectal remnant or ileoanal anastomosis seems warranted given the ongoing risks of adenomas and carcinomas within residual mucosa[41]. In addition, total proctocolectomy is a relatively highly invasive surgery. QOL issues encountered in patients after proctocolectomy include high stool frequency. Saida et al. reported 2 cases of laparoscopic subtotal colectomy with ileosigmoid anastomosis combined with subsequent postoperative intensive endoscopic polypectomy as minimally invasive treatment for FAP. These patients had sparse FAP and opted to undergo less invasive surgery, and so were selected for this procedure. More than 20 cm of colorectum remained with this procedure. Compared to the standard procedure, operative time was shorter, fewer complications were seen, and bowel function was better. After colectomy, frequent colonoscopy and polypectomies were performed at intervals of approximately 3-6 months, and no cancer was found during follow-up. They concluded that this procedure is a novel combined therapy that is less invasive and results in better QOL[42]. As of the time of writing, 4 patients have undergone this procedure, and surveillance is continuing (data not yet published; presented at the 71st General Meeting of the Japanese Society of Gastroenterological Surgery; July 14-16, 2015; Tokushima, Japan). In general, the risk of cancer development might be higher in their cases with this procedure compared to that with standard surgery, because the remnant colorectum is longer than IRA. In addition, the surveillance period seems not long enough. Therefore, careful and intensive surveillance is required as same as endoscopic management of FAP.

Conclusions

For FAP patients, the standard of care is prophylactic colectomy or proctocolectomy, followed by regular and lifelong endoscopic evaluation, polypectomies or ablation and additional operations[9]. Concerns remain, however, with regard to morbidity, postoperative bowel function, female fecundity and desmoid tumor. Studies of endoscopic options, chemoprevention, and other surgical procedures are ongoing. Some of these options, either alone or in combination with colectomy, may offer alternatives to standard surgical procedures for selected FAP patients.

Conflicts of Interest
There are no conflicts of interest.

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