Risk of ileal pouch neoplasms in patients with familial adenomatous polyposis

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Abstract

Restorative proctocolectomy is the most common surgical option for patients with familial adenomatous polyposis (FAP). However, adenomas may develop in the ileal pouch mucosa over time, and even carcinoma in the pouch has been reported. We therefore reviewed the prevalence, nature, and treatment of adenomas and carcinoma that develop after proctocolectomy in the ileal pouch mucosa in patients with FAP. In 25 reports that were reviewed, the incidence of adenomas in the ileal pouch varied from 6.7% to 73.9%. Several potential factors that favor the development of pouch polyps have been investigated, but many remain controversial. Nevertheless, it seems certain that the age of the pouch is important. The risk appears to be 7% to 16% after 5 years, 35% to 42% after 10 years, and 75% after 15 years. On the other hand, only 21 cases of ileal pouch carcinoma have been recorded in the literature to date. The diagnosis of pouch carcinoma was made between 3 to 20 years (median, 10 years) after pouch construction. Although the risk of malignant transformation in ileal pouches is probably low, it is not negligible, and the long-term risk cannot presently be well quantified. Regular endoscopic surveillance, especially using chromoendoscopy, is recommended.

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Key words: Familial adenomatous polyposis; Restorative proctocolectomy; Ileal pouch; Ileal pouch-anal anastomosis; Ileo-rectal anastomosis; Adenoma; Adenocarcinoma; Pouch polyp; Pouch neoplasm

Core tip: To eliminate the risk of colorectal cancer, the majority of patients with familial adenomatous polyposis (FAP) are treated with restorative proctocolectomy and an ileal pouch-anal anastomosis. However, as these patients are followed-up for longer intervals, it has gradually become recognized that adenomas and adenocarcinomas may develop in the ileal pouch. If the standard-of-care surgery for FAP patients does not eliminate all cancer risk, surgical and follow-up strategies may need to be altered. In this review, we summarize the data from the published English literature regarding the incidence of adenomas and carcinomas in the ileal pouch after proctocolectomy in FAP patients.

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INTRODUCTION

Familial adenomatous polyposis (FAP) is an inherited, autosomal-dominant disease caused by a germline muta-
tion of the adenomatous polyposis coli gene (APC). The phenotype is characterized by the development of hundreds of colorectal adenomas, leading to a 100% lifetime risk of colorectal cancer. For this reason, a prophylactic colectomy is recommended for patients with FAP to prevent the development of colorectal cancer. The main surgical strategy in patients with FAP is restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA). As originally described by Parks et al., IPAA included an anal mucosectomy to eliminate the risk of malignancy in the remaining anorectal mucosa. However, many surgeons now prefer to preserve the anorectal transition zone (ATZ) during the double-stapled IPAA technique because of its simplicity and better functional outcome. The trade-off is a risk of neoplasia developing in the retained ATZ mucosa, with a 10%-15% incidence of adenoma. Another widely accepted surgical procedure is colectomy with ileorectal anastomosis (IRA), performed when there are few polyps in the rectum. The major advantage of IRA is preservation of the rectal innervation, with subsequent better quality of life. However, continuing endoscopic surveillance for adenomas in the rectum is necessary, and there is a 13%-25% cumulative risk of rectal cancer after 15-25 years despite surveillance. On the other hand, it has been thought that IPAA theoretically eliminates the risk of colorectal cancer and adenomas, and perhaps the need for further lower gastrointestinal surveillance. However, there are recent reports of adenomas or carcinomas developing not only in the residual rectal mucosa or anastomosis after IRA, but also in the ileal pouch mucosa after IPAA. In addition, there are several reports of cancers arising from the ileal pouch mucosa, as opposed to the anastomotic site, in patients with FAP.

The aim of this review is to describe the prevalence, nature, and treatment of adenomas and carcinoma developing in the ileal pouch mucosa after proctocolectomy in patients with FAP.

**INCIDENCE OF ILEAL POUCH ADENOMAS**

The basic premise underlying the popularity of IPAA in patients with FAP is that it results in a significantly lower risk of rectal cancer than IRA. Although this is likely to be true, the risk of pouch polyposis and pouch cancer has not been recognized so far. After the advent of pouch surgery, several reports of adenomatous polyps in the pouches of FAP patients have appeared in the literature. In 1982, Beart et al. first described a FAP patient with continent ileostomy, in whom a large sessile tubulovillous adenoma and multiple smaller adenomatous polyps developed. Since then, there have been at least 25 reports of ileal pouch adenomas developing in these patients (Table 1). We reviewed only those studies that clearly described adenomas appearing within the ileal pouch mucosa. These included 8 case reports, 7 retrospective studies, and 10 prospective studies. The incidence of adenomas in the ileal pouch varied from 6.7% to 73.9%. This variation in the prevalence of ileal pouch adenomatosis could be due to differences in the way endoscopy was performed in the various studies. Adequacy of bowel preparation, type of instrument employed, use of chromoendoscopy, and other miscellaneous factors influence the detection rates of pouch polyps. Good bowel preparation and a flexible video colonoscope are essential in identifying pouch polyps because most ileal adenomas are flat or sessile, measuring only 1 mm to 3 mm in diameter, and having a morphology different from large bowel adenomas. Therefore, a careful examination of the entire pouch, anal canal, and pouch-anal anastomosis should be performed. Although Polese et al. reported the prevalence of ileal pouch adenomas as 6.7%, these investigators used a rigid sigmoidoscope with enema preparation, without chromoendoscopy. These technical factors may explain the low prevalence of ileal pouch adenomas in the study by Polese et al.

The only meaningful estimates of adenoma incidence have come from prospective studies, with all 10 prospective studies showing that the incidence of pouch adenomas increases with the follow-up duration. The risk appears to be 7% to 16% after 5 years, 35% to 42% after 10 years, and 75% after 15 years. The great majority of pouch polyps described in the literature are small, tubular adenomas with mild atypia. The incidence of adenoma with advanced pathology (size > 1 cm, villous pattern, or moderate-to-severe dysplasia) is less. According to Banasiewicz et al., the estimated frequency of low-grade dysplasia 4 years after IPAA surgery is 4%, and increases to 50% after 15 years. The same percentage of patients, but with high-grade dysplasia, develop high-grade dysplasia 2.5 years later, that is to say, 17.5 years after IPAA, and with neoplasia 18.5 years after the above procedure. The full impact of pouch polyposis will not be fully understood until most pouch patients reach a follow-up duration of 20 to 40 years.

**RISK FACTORS FOR DEVELOPMENT OF ADENOMAS IN THE ILEAL POUCH**

**Phenotype**

At present it does not seem possible to predict who is at risk for developing polyps in the pouch. Some studies show that there is no apparent high-risk phenotype for the development of ileal polyps. However, other studies describe risk factors that favor the development of pouch polyposis. Parc et al. observed that patients with pouch polyps are younger, and have a longer follow-up period since IPAA, than patients without pouch polyps. A more aggressive disease requiring earlier surgery could explain these features. However, Groves et al. analyzed the risk factors by using logistic regression, and found that age was a more significant predictor of pouch adenomas than the follow-up period, sex, or type of primary or secondary procedures. Groves et al. reported that, in their experience, all patients older than 60 years...
will develop polyps in the pouch. Tonelli et al.\footnote{36} reported that an age of more than 50 years was associated with pouch adenomas, but not sex or elapsed time since restorative proctocolectomy.

Several studies found that the severity of duodenal polyposis was related to the presence of pouch adenomatous polyps. In a multivariate analysis of 118 FAP patients who had undergone surgery, Pommaret et al.\footnote{39} discovered that the presence of advanced duodenal adenomas was an independent risk factor for the development of pouch adenomas, in addition to follow-up duration. Tonelli et al.\footnote{36} found that patients affected by pouch adenomas had high polyp counts (> 1000) at colectomy, as well as duodenal adenomas.

Several potential factors that favor the development of pouch polyposis have been investigated; a number of them remain controversial, although it seems certain that the age of the pouch is important.

**Pathogenesis**

The mucosa of the ileal pouch may be subjected to not only the tumorigenic consequences of \textit{APC} gene mutations\footnote{53}, but also to luminal factors due to fecal stasis, which may also exert an important effect. Fecal stasis, such as occurs in a reconstructed pouch, may promote neoplastic changes in the ileal mucosa. Several authors have implicated colonic metaplasia of the ileal mucosa as a precursor for the development of ileal adenomas\footnote{59,51,52} and even carcinomas in the surgically constructed pouches of patients with FAP\footnote{53-55}. Colonic metaplasia was frequently recognized even in earlier descriptions of the changes observed in the ileal pouch mucosa. Some authors have considered colonic metaplasia as an adaptive response of the ileal pouch to its role as a neo-

### Table 1 Summary of 25 reports of ileal pouch adenomas in familial adenomatous polyposis

| Ref. | Study Year Operation | n  | Type of pouch | Findings | % of adenoma | Time to neoplasia |
|------|---------------------|----|---------------|----------|--------------|------------------|
| Beart et al.\cite{21} | Case 1982 Kock | Kock pouch 1 | Tubulovillous Adenomas | 6 yr |
| Wolfstein et al.\cite{22} | Case 1982 IAA | Soave | Adenomas in 2 pts | 1 yr and 3 yr |
| Shepherd et al.\cite{23} | Retro 1987 IPAA | 12 | N | Tubular Adenoma in 2 pts | 16.7 |
| Stryker et al.\cite{24} | Case 1987 Brooke ileostomy | Kock pouch 1 | Tubular Adenomas | 12 yr |
| Nugent et al.\cite{25} | Retro 1993 IPAA | 38 | N | Tubular Adenoma in 5 pts | 11.2 |
| Bertron et al.\cite{26} | Pros 1995 IAA | S/J-pouch 9/16, 1 N | Tubular Adenoma in 11 pts | 42.3 |
| Wu et al.\cite{27} | Pros 1998 IPAA | 5 | N | Adenomas | 20 |
| Valle et al.\cite{28} | Case 2001 IPAA | 20 Kock, 2 | J-pouch | 5 yr |
| Thompson-Fawcett et al.\cite{29} | Pros 2001 Kock, 5, IPAA 28 | 33 | N | Adenoma in 14 pts (with microadenoma 20 pts) | 42.4 (60.6) |
| Parc et al.\cite{30} | Pros 2001 IPAA | 85 | J-pouch | 30 pts (28 grossly visible, 2 microadenoma) | 35.3 |
| Polese et al.\cite{31} | Retro 2002 IPAA | 46 | S/W/J-pouch 2/1/43, Kock 1 | Adenoma in 2 of 30 pts | 6.7 |
| Beveridge et al.\cite{32} | Case 2004 IPAA | 2 | J-pouch 1, Kock 1 | 2 large VA, VA | 6 yr |
| Wasmuth et al.\cite{33} | Case 2004 IPAA | 1 | J-pouch | Adenomas with focal severe dysplastic change | 6 yr |
| Groves et al.\cite{34} | Pros 2005 Kock, 4, IPAA 56 | W/J-pouch 13/43, Kock 4 | Mild dysplasia 23, more advanced 11 | 56.7 |
| Nilubol et al.\cite{35} | Pros 2007 IPAA | 10 | N | Tubular Adenoma in 1 of 9 pts | 11.1 |
| Moussata et al.\cite{36} | Retro 2008 IPAA | 23 | N | Low-grade 16, high-grade 1 | 73.9 |
| Friederich et al.\cite{37} | Pros 2008 IPAA | 212 | N | Adenoma 74 pts, AAP 25 pts | 46.7 |
| Schulz et al.\cite{38} | Pros 2008 IPAA | 35 | N | Low-grade 8 | 22.8 |
| Tajika et al.\cite{39} | Retro 2009 Kock, 8, IPAA 16 | J-pouch 24 | 16 pts, (advanced 1, carcinoma 2) | 66.7 |
| Kang et al.\cite{40} | Case 2010 Kock | 2 | Kock pouch 2 | (the largest one is 15mm in size) | 15.8 |
| Banasiewicz et al.\cite{41} | Pros 2011 IPAA 165 | J-pouch 165 | Low-grade 13, high-grade 8, neoplasia 5 | 15.8 |
| Tonelli et al.\cite{42} | Pros 2012 IPAA 69 | S/J-pouch 25/29, SIMM 15 | Adenoma 25 pts, carcinoma 2 | 39.1 |
| Makni et al.\cite{43} | Case 2012 IPAA 1 | J-pouch 1 | Adenoma and carcinoma 2 | 14 pts |
| Wasmuth et al.\cite{44} | Retro 2013 IPAA 61 | N | Adenoma 14 pts | 23 |
| Pommarel\cite{45} | Retro 2013 IPAA 118 | J-pouch 57 pts (12 advanced Adenomas) | 48.3 |

Study: Type of study; Retro: Retrospective series; Pros: Prospective series; n: Number of patients in the study; IPAA: Ileal pouch-anal anastomosis; Kock: Kock continent ileostomy; N: Not described; AV: Anal verge; pts: Patients.

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rectum\textsuperscript{[18,19,36,57]}. Further investigations have shown that colonic transformation is only partial. Small-bowel brush border disaccharidase activity is preserved, as is the ability to absorb vitamin B12, D-xylene, phenylalanine, and bile acids\textsuperscript{[32,58-60]}. The mucosal changes described as colonic metaplasia are likely a response to chronic inflammation caused by changes in the luminal contents due to stasis. In FAP, these changes may, at least in theory, favor the development of adenomas in a region of the gut where they are not usually observed. There is an increase in the concentration of luminal short chain fatty acids to levels that are seen in the colon\textsuperscript{[34]}, an increase in anaerobic bacterial counts with a more colonic type flora\textsuperscript{[62,64]}, and increased deconjugation and dehydroxylation of bile acids by the anaerobic bacteria\textsuperscript{[64]}. In particular, deoxycholic acid and lithocholic acid, which are known carcinogens, have concentrations several times higher in an ileal pouch than in an end ileostomy\textsuperscript{[69]}. On the other hand, reduction of glutathione S-transferase (GST) detoxification activity in the pouch compared with the afferent ileal loop after IPAA may promote tumorigenesis\textsuperscript{[64]}.

\textbf{APC gene mutations}

FAP develops due to a dominant autosomal mutation of the \textit{APC} gene in more than 80\% of patients\textsuperscript{[66]}. Recently, it has been discovered that a biallelic mutation of the \textit{MUTYH} gene might exist in 5\% of patients with colorectal polyposis and 20\% of FAP patients, with no \textit{APC} mutation found\textsuperscript{[66]}. Many researchers have investigated \textit{APC} gene mutations in pouch patients with FAP, although none has demonstrated obvious genotype-phenotype correlations that would predict the development of pouch adenomas\textsuperscript{[28,30,36,49]}. Hence, the available evidence suggests that systematic surveillance of all patients who undergo IPAA is necessary. Targeted surveillance of a defined subgroup of patients is currently not feasible.

\textbf{Type of pouch and anastomosis}

There are different pouch configurations. Parks \textit{et al}\textsuperscript{[7]} originally devised a triple-limb \textit{S}-shaped pouch. This pouch was relatively complicated to construct, and suffered from kinking of the efferent limb if it was left too long\textsuperscript{[67]}. Alternative designs have included the high-capacity W-pouch, the H-pouch and the J-pouch. The majority of surgeons now favor the J-pouch due to ease of construction, economical use of the terminal ileum, and reliable emptying\textsuperscript{[68]}. Functional results are equal to those of other reservoir designs\textsuperscript{[69,70]}. The pouch is formed from the terminal 40 cm of ileum, using several applications of a linear-cutting stapler to join the anti-mesenteric borders of two 20-cm ileal limbs.

Several authors have shown that there is no apparent relationship between the development of pouch polyps and the type of ileal pouch construction\textsuperscript{[34]} or the suture used (hand-sewn or stapled)\textsuperscript{[25,28,36]}. However, other authors have reported that patients with a stapled IPAA are at a significantly increased risk of developing adenomas at the anastomotic site: 1.5\% to 20.9\% vs 27\% to 66\% for hand-sewn and stapled anastomoses, respectively\textsuperscript{[9,11,22,16,72,73]}. These data suggest that a hand-sewn IPAA may be a preferable strategy for decreasing the occurrence of adenomas at the anastomotic ileo-anal site. Recently, Wasmuth \textit{et al}\textsuperscript{[80]} evaluated the differences between adenoma formation at the anastomotic site and in the ileal pouch after IPAA, with or without mucosectomy. These investigators found that an occurrence of adenomas at the anastomotic site was significantly reduced after mucosectomy. However, there was no difference in the occurrence of ileal pouch adenomas between patients who underwent mucosectomy and those who retained a rectal mucosal remnant (8/39 vs 6/22; \textit{P} = 0.57)\textsuperscript{[68]}.

\textbf{Pouchitis}

In patients with ulcerative colitis, concern about the risk of neoplasia in ileal pouches was raised after observing a combination of histologic changes in the ileal mucosa of the pouch, including villous atrophy, inflammation and metaplasia\textsuperscript{[74,76]}. These transformations in the ileal pouches are likely caused by the chronic inflammatory state. The inflammatory process in pouchitis may lead to dysplasia\textsuperscript{[47]} and loss of heterozygosity, consistent with precancerous lesions of the colon\textsuperscript{[77]}. Thus, a dysplasia-to-neoplasia progression can occur in ileal pouches and can lead to cancer of the pouch. The cumulative risk of pouchitis is up to 50\% in patients with ulcerative colitis\textsuperscript{[78-81]}, with most patients experiencing at least one episode of pouchitis during the first ten years after surgical pouch construction. In contrast, the pouchitis rate is below 25\% in patients with FAP\textsuperscript{[34,20,33,36]}. Banasiewicz \textit{et al}\textsuperscript{[82]} analyzed the frequency and progression of dysplasia and inflammation in the intestinal pouch of FAP patients after restorative proctocolectomy. Although these authors diagnosed pouchitis in 20.6\% of patients after restorative proctocolectomy, no relationship was found between pouchitis and pouch dysplasia in FAP patients.

\textbf{THE PREVALENCE OF ADENOMAS IN THE PRE-POUCH ILEUM}

Although it is currently recognized that adenomas may develop in the ileal pouch, the risk of adenomas occurring in the afferent ileal loop above the pouch is unclear. The incidence of adenomas above the IPAA pouch was merely recognized previously, and it seemed to be low, with reported figures ranging from 4\% to 16\%\textsuperscript{[22,28,13,12,27]}. The majority of pre-pouch ileal adenomas have measured 4 mm or smaller. Pommeret \textit{et al}\textsuperscript{[9]} reported that only nine (6.5\%) of 118 patients had afferent ileal loop adenomas after an IPAA. The only independent predictive factor for the occurrence of afferent ileal loop adenoma was found to be the presence of pouch adenomas (OR: 2.16; 95\%CI: 0.17-26.98; \textit{P} = 0.007). Pommeret \textit{et al}\textsuperscript{[9]} concluded that because afferent ileum loop adenomas are rare and have an unclear pathologic significance, there is no justification for their systematic search, particularly among patients without any duodenal or pouch adeno-
mas. In cases of extensive pouch polyposis with a significant cancer risk, this viewpoint could allow clinicians to consider resection of the adenomatous pouch, with construction of a new one using the afferent ileum.

SURVEILLANCE OF THE ILEAL POUCH

Saurin et al described methods of surveillance and therapeutic indications in FAP patients following colectomy. Although there are no validated data in the literature, on the basis of expert opinion, endoscopic surveillance is performed at 6 mo, 1 year, and then every 2 years after surgery. In the presence of polyps with high-grade dysplasia, and/or polyps > 1 cm size, and/or presence of large polyp number (> 30), surveillance should be repeated every 6 mo. Many authors have performed pouch endoscopy every 6-12 mo after surgery. Optimum bowel preparation and the use of indigo carmine surface staining are necessary. The main utility of chromoendoscopy is to highlight the small lymphoid lesions that are characteristic of the terminal ileum in FAP patients, and to distinguish flat polyps (Figure 1). In the experience of the Dutch Registry, indigo carmine chromoendoscopy significantly increases the detection rates of adenomas < 5 mm in size. Investigators with the Dutch Registry found that 75.7% of FAP patients harbored adenomas in the pouch at a median follow-up duration of 8 years after IPAA. Because some patients have a stricture at the anal anastomosis, a pediatric colonoscope or gastroscope may sometimes be required.

TREATMENT OF ADENOMAS IN THE ILEAL POUCH

According to Saurin et al, no systematic endoscopic treatment of adenomas of the ileal pouch or afferent loop can be recommended. For large adenomas (> 1 cm), or in patients with high-grade dysplasia, endoscopic resection must be considered; however, a skilled team is needed because of the thin ileal mucosa. Our current strategy in patients with IPAA is regular follow-up starting at 1 year after surgery, and then every year thereafter. If adenomas are observed in the pouch, we recommend endoscopic resection or argon plasma coagulation where feasible, and then follow-up every 6 mo. Other reports also describe polypectomy of large polyps, and ablation by fulguration or electrocoagulation for small lesions. In patients having extensive pouch polyposis with no possibility of endoscopic treatment, together with invasive cancer, pouch excision and terminal ileostomy has to be considered.

Although there have been some reports suggesting the efficacy of nonsteroidal anti-inflammatory drugs (NSAIDs) in suppressing the development of ileal pouch adenomas, this has not been systematically studied.

THE PREVALENCE OF ADENOCARCINOMAS IN THE ILEAL POUCH

The progression from a dysplastic lesion in the ileal pouch to invasive carcinoma appears to be rare, occurring in no more than 1% of patients with ileal pouches. However, in the past few years, several cases of carcinoma have been observed after IPAA, although the majority of them occurred at the level of the anal canal. Patients with either hand-sewn or stapled IPAA are at risk for developing a carcinoma in any residual rectal mucosa that harbors dysplasia or is prone to dysplasia. To date, only 21 cases of ileal pouch carcinoma have been recorded in the literature (Table 2). No relationship has been found between the occurrence of pouch carcinoma and the shape (J or S) of the pouch, or the type (hand-sewn or stapled) of IPAA. These pouch cancers have clearly appeared in the ileal pouch, and not in the ATZ. The time elapsed between pouch construction and diagnosis of pouch carcinoma has been between 3 and 20 years (median, 10 years).

It is noteworthy that in at least seven patients, the development of advanced cancer was detected within a very short interval—within 1 year since last pouch endoscopy. Furthermore, in four of the patients, ileal polyps...
were not found during endoscopic follow-up until the development of pouch carcinoma. It seems that neoplasia that appears in the ileal pouch may not always follow the classic adenoma-carcinoma sequence. We strongly recommend a strict surveillance program for FAP patients, including annual flexible colonoscopy, irrespective of the phenotype and genotype.

**IRA vs IPAA**

In a review of 12 studies containing 1002 patients with FAP (53.4% IPAA, 46.6% IRA), Aziz et al\[3\] showed that bowel frequency, nocturnal defecation, and incontinence rates were significantly less in IRA patients, although fecal urgency was less among IPAA patients. There was no significant difference between IPAA and IRA in terms of sexual dysfunction, dietary restrictions, or postoperative complications. In their review, Aziz et al\[3\] could not identify any malignancies in IPAA patients, and rectal cancer was a diagnosis only in the IRA patients (5.5%). At the present time, IPAA anastomosis is recommended by a majority of surgical teams as the preferred option for FAP patients\[3,6,10,92,93\]. Although cancer formation after IPAA in patients with FAP may be rare, it is of concern that several of the recently reported patients had an advanced stage at diagnosis, with poor outcome.

Recent reports of a high frequency of adenomas after IPAA, together with favorable functional outcomes in patients who underwent IRA, may lead to reconsideration of the latter surgical option for some FAP patients, especially when quality of life and fertility criteria are taken into account\[3,10\]. In clinical practice, the results of preoperative evaluation of the rectal stump using indigo carmine chromoendoscopy are a major deciding factor. A limited number (< 10–20) of rectal polyps without any cancer would lead to preservation of the rectal stump in a majority of patients\[3,5\]. However, with the availability of better endoscopic instruments and resection techniques, and the possibility of enhanced post-operative surveillance, > 20 rectal polyps and/or non-invasive cancers can now also be managed endoscopically. So, there is a possibility that the criteria for IRA will expand in the near future. Of course, based on clinical and genetic data, a stepwise surgical strategy with a primary IRA followed at a later age by a secondary proctectomy and IPAA could be proposed\[5\].

An ongoing multicenter study in Japan is being conducted by Ishikawa et al\[3\] under the title “Intervention trial for colorectal cancer prevention by endoscopic polypectomy in patients with familial adenomatous pol-
The development of adenomas with high-grade dysplasia and carcinoma in the ileal pouch is an important issue because the choice between IPAA and IRA is based mainly on the expected low risk of cancer development after the former surgery. Although the risk of malignant transformation in ileal pouches is probably low, it is not negligible, and the long-term risk cannot presently be well quantified. IPAA will not prevent cancer development in the terminal remnant intestine, and patients who undergo IPAA require regular follow-up similar to patients who receive IRA. A detailed analysis of the phenotypes and mutations in the APC gene of patients with FAP may allow tailoring of the surgical options in the future.

CONCLUSION

The development of adenomas with high-grade dysplasia and carcinoma in the ileal pouch is an important issue because the choice between IPAA and IRA is based mainly on the expected low risk of cancer development after the former surgery. Although the risk of malignant transformation in ileal pouches is probably low, it is not negligible, and the long-term risk cannot presently be well quantified. IPAA will not prevent cancer development in the terminal remnant intestine, and patients who undergo IPAA require regular follow-up similar to patients who receive IRA. A detailed analysis of the phenotypes and mutations in the APC gene of patients with FAP may allow tailoring of the surgical options in the future.

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