VOLUME 22 · NUMBER 3 · FEBRUARY 1 2004

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Surveillance of Duodenal Adenomas in Familial Adenomatous Polyposis Reveals High Cumulative Risk of Advanced Disease

Jean-Christophe Saurin, Christelle Gutknecht, Bertrand Napoleon, Annick Chavaillon, René Ecochard, Jean-Yves Scoazec, Thierry Ponchon, and Jean-Alain Chayvialle

From the Federation des Specialites Digestives and Service d'Anatomie Pathologique, Hopital E. Herriot; and Departement de Biostatistiques, Hospices Civils de Lyon, Lyon, France.

Submitted June 6, 2003; accepted November 24, 2003.

The study has been presented in part as an oral communication at the Digestive Disease Week in Orlando, FL, May 18, 2003.

Authors' disclosures of potential conflicts of interest are found at the end of this article.

Address reprint requests to J.C. Saurin, MD, Service d'Hepatogastroenterologie, Pavillon I, Hôpital Edouard Herriot, 5 Place d'Arsonval, 69437 Lyon cedex 03, France; e-mail: saurin@lyon.inserm.fr.

0732-183X/04/2203-493/$20.00

DOI: 10.1200/JCO.2004.06.028

ABSTRACT

Purpose
The development of high-grade dysplasia (HGD) on duodenal or jejunal adenomas and of late-stage (stage IV) duodenal polyposis are major clinical events for familial adenomatous polyposis (FAP) patients. Our aim was to determine their respective frequency, risk factors, and cumulative risk.

Patients and Methods
A prospective, optimized, endoscopic surveillance protocol was applied to 58 FAP patients in a university hospital. The number, size, and histology of duodenojejunal polyps were assessed, and the Spigelman's score was calculated at each endoscopy. Cox regression and linear regression analysis were used to determine risk factors for HGD development and the cumulative risk of stage IV duodenal polyposis, respectively.

Results
During a median (± standard deviation) follow-up of 47.9 ± 15.6 months, 35 patients with at least two consecutive examinations had 107 duodenojejunal examinations. The Spigelman's score increased in 21 patients (60.0%), and HGD developed in 12 patients (34.2%). High initial Spigelman's score (> 7 points), but not age or *APC* mutation site, was a risk factor for HGD development. Estimated cumulative risk of developing stage IV duodenal polyposis was of 42.9% at age 60 (95% CI, 35.7% to 50.0%) and 50.0% at age 70 (95% CI, 42.9% to 57.1%).

Conclusion
This prospective series shows a higher duodenal polyposis progression rate and cumulative risk of late-stage (stage IV) duodenal polyposis in FAP patients compared with previous series. These results suggest that current modalities for surveillance and management of these patients need revision.

J Clin Oncol 22:493-498. © 2004 by American Society of Clinical Oncology

INTRODUCTION

Proximal small bowel cancer is one of the two leading causes of death (the other being desmoid tumors) in familial adenomatous polyposis (FAP) patients with previous colectomy [1,2]. Cancer of the proximal small bowel in FAP develops from pre-existing adenomas, which are present in approximately 100% of patients in the duodenum. These duodenal adenomas can be classified through macroscopic and histologic criteria in five stages (0 to IV) following the Spigelman's classification. In a large series, 44% of FAP patients presented with a severe duodenal polyposis (stage III or IV) and were considered at higher risk of developing duodenojejunal cancer. Currently, two strategies are under discussion in FAP patients with duodenal polyposis. First, patients with advanced adenomas (larger than 1 cm) or with high-grade dysplasia (HGD) may be referred for endoscopic treatment by several means, the most common being mucosectomy [3]. Second, these patients may be simply followed up until they develop very advanced duodenal polyposis (stage IV) or duodenal cancer and treated at that time by pancreaticoduodenectomy (PD) [4,5]. The selection of the appropriate strat-

egy depends on the rate at which patients develop indicators of cancer risk, such as stage IV polyposis and/or HGD; high frequency of these indicators would support the use of early endoscopic treatment to avoid frequent high-risk surgery.

Regarding the natural history of duodenal adenomas, most series show a rather low frequency of duodenal polyposis progression with time. However, most series are retrospective and do not use the Spigelman's score, which makes the comparison difficult [6-8]. Moreover, in recent series, there is a striking discrepancy between the slow progression reported in the course of standardized endoscopic follow-up and the actual development of advanced cancer, mostly in patients with late-stage but also in patients with early-stage polyposis [6,9]. Therefore, a prospective evaluation is required to clarify the rate of duodenal polyposis progression in FAP patients, the frequency at which HGD is expected to appear within duodenal adenomas, and the life-time risk for stage IV polyposis development. The present study was undertaken to assess these rates and risks using a standardized and optimized endoscopic follow-up.

PATIENTS AND METHODS

Study Design and Patients

In 1995, we initiated a prospective follow-up study of duodenojejunal polyposis in FAP patients that included all consecutive patients. The study was approved by the review board of the Federation des Specialites Digestives of the E. Herriot Hospital in Lyon, France. Written informed consent was obtained from all patients before endoscopic examination. Fifty-eight patients from 41 different families were included. The diagnosis of FAP was based on the presence of more than 100 colonic polyps (all patients), the presence of extracolonic manifestations of FAP (all patients), a family history of FAP (all but four patients), and the knowledge of a genetic defect within the *APC* gene (33 of 41 families, 80%). Descriptive data on the severity of the duodenal polyposis and its relationship with age and patient genotype have been reported previously for the first 41 patients [10]. Among the 58 patients, eight were offered a treatment (endoscopic, five patients; surgical, three patients) of the duodenal polyposis after the first endoscopy (presence of large adenomas with HGD in all eight patients), whereas 15 patients have only been examined once to date. Thus, the present report focuses on the 35 patients (median age, 39 years; range, 21 to 63 years; 20 different families) who have undergone at least two consecutive examinations of the duodenum and proximal jejunum. Of these 35 patients, seven patients were referred to us for the surveillance of advanced duodenal or rectal polyposis, and 28 were not referred but had been observed at our institution for several years. The site of the *APC* mutation was identified in 29 patients (82.8%). As described elsewhere [10], 18 patients had a mutation between codons 279 and 1309, and 11 patients had a mutation outside this region, including two patients with complete deletion of the *APC* gene.

Endoscopic Protocol

All endoscopies of the proximal small bowel were performed under general anesthesia (total intravenous anesthesia, a common procedure in France for complex gastrointestinal endoscopic procedures), using a side-viewing endoscope (TJF 140; Olympus, Hamburg, Germany) for the examination of the duodenal papilla and then a forward-viewing enteroscope (SIF-100; Olympus) without use of an overtube. Indigo-carmine (0.5%) dye was systematically used. At each endoscopy, the number and maximal size of small bowel polyps were recorded from the following three different segments: proximal duodenum (first and second parts), distal duodenum (third and fourth parts), and proximal jejunum (two to three first jejunal loops within reach of the enteroscope). The size of the largest polyp in each segment was estimated with the use of open-biopsy forceps. The number and maximal size of polyps in these three segments were reported on standardized data collection forms at the time of endoscopy, which included a schematic diagram of the proximal small bowel. Biopsies were systematically obtained from the duodenal papilla (on the apex) and from large (at least 10 mm) polyps and from most polyps of more than 5 mm in diameter. Histologic results were subsequently reported. The stage of small bowel polyposis was graded using the Spigelman's score (range, zero to 12 points) and classification (stage 0 to IV, Table 1). The polyposis in the proximal duodenum (first and second part) was staged according to the Spigelman's classification [11]. According to the updated Vienna classification of gastrointestinal epithelial neoplasia (low-grade dysplasia or HGD) [12], the Spigelman's score was modified by attributing one point for low-grade and three points for HGD. Cases showing HGD were reviewed blindly by two different pathologists, and all the histologic material available for each patient was retrospectively reviewed and graded by our reference pathologist (J.-Y.S.); only those patients with a concordant diagnosis of HGD were retained. Patients were hospitalized for 24 hours after endoscopy, blood amylase levels were routinely checked 24 hours after biopsies of the duodenal papilla, and results were reviewed retrospectively. Other complications of endoscopy were recorded prospectively.

Table 1. Modified Spigelman's Score and Classification

Factor	Score		
	1 Point	2 Points	3 Points
No. of polyps	1-4	5-20	> 20
Polyp size, mm	1-4	5-10	> 10
Histology	Tubulous	Tubulovillous	Villous
Dysplasia	Low grade	—	High grade

NOTE. Classification: no polyp, stage 0; 1 to 4 points, stage I; 5 to 6 points, stage II; 7 to 8 points, stage III; 9 to 12 points, stage IV.

Expression of the Results and Statistical Analysis

Age, number of examinations, length of follow-up, and Spigelman's score were presented as mean (± standard deviation). Complications of endoscopy were presented as the proportion (percentage) of total number of examinations. Endoscopic findings (number, size, and histology of polyps) were presented as proportion (percentage) of patients. Independent predictive factors of increasing score and of occurrence of HGD were assessed. Tested factors included age at first examination (all 2-year intervals between 32 and 40 years were tested), genetic *APC* background (considering two groups with or without *APC* mutation within the 279 to 1309 codon interval, previously shown to correlate with severity of the duodenal polyposis in FAP patients) [10],

Table 2. Patients in the Different Stages of Duodenal Polyposis, According to the Spigelman's Classification, at Original and Last Examination: Evolution of Score, Stage, and Degree of Dysplasia on Adenomas

	Stage I		Stage II		Stage III		Stage IV	
	No.	%	No.	%	No.	%	No.	%
All patients								
Stage at first examination	3	8.5	11	31.4	16	45.7	5	14.2
Stage at last examination	3	8.5	6	17.1	11	31.4	15	42.8
Patients in the same stage								
Increasing score	0	0	5	45.4	12	75.0	4	80.0
Increasing stage	0	0	5	45.4	9	56.2	—	—
Development of high-grade dysplasia	0	0	1	9.0	8	50.0	3	60.0

and original Spigelman's score (all values from 6 to 9 were tested, Table 1). Independent factors of occurrence of HGD were tested first using Kaplan-Meier cumulative analysis and log-rank tests and then using a Cox multivariate model. A mover-stayer regression model was used to estimate both the probability associated with increased Spigelman score and the efficacy of the predictors [13]. In this model, we hypothesized that patients with a stable score during the follow-up would remain stable on a long-term basis. Attention was paid to patient origin, by distinguishing patients referred for management of duodenal polyposis from patients who were observed in our institution for several years; the latter group was considered as representative of the general population of FAP patients in terms of age and Spigelman's score. The mover-stayer regression model does not make any a priori assumption; for each patient, the probability to be a stayer (stable score over time) or a mover (increasing score) is estimated using the patient's series of scores and the overall trend of both the stayer and the mover groups of other patients. The Markov Chain Monte Carlo method has been used for this analysis [14]. Because several surgical and medical teams support the idea that FAP patients with stage IV duodenal polyposis should be treated with PD [5,9,15], the life-time cumulative risk of developing advanced (stage IV) duodenal polyposis was estimated using the results of the above mover-stayer regression model. SAS software (SAS/STAT User's Guide, Version 6, 1990; SAS Institute, Cary, NC) was used for all standard analyses. BUGS software (BUGS: Bayesian inference using Gibbs sampling; MRC Biostatistics Unit, Cambridge, United Kingdom) was used for the mover-stayer regression model. A P value $< .05$ was considered significant.

RESULTS

Since 1995, 35 patients with FAP underwent at least two consecutive examinations of the duodenojejunum. The mean ($\pm$ standard deviation) age of the cohort was 37 $\pm$ 10.2 years. Patients had a mean of 3.1 $\pm$ 0.8 examinations (total, 107 examinations). One examination (0.9%) resulted in a delayed (72 hours) cervical hematoma and perforation justifying emergency surgery, which was resolutive without sequel. No complications related to general anesthesia were observed. No patient developed symptoms of pancreatitis, despite systematic biopsies at the site of the duodenal papilla, but an asymptomatic amylase increase ($< 2 \times$ the normal range) was observed in 18 (30%) of 60 available tests.

Duodenal and Jejunal Polyposis Progression

The 28 nonreferred patients had a mean original Spigelman's score of 7.0 (95% CI, 6.4 to 7.7). The mean baseline score interval between the seven referred and the 28 nonreferred patients was of 1.9 (95% CI, 0.4 to 3.4; $P = .02$). During a mean follow-up of 47.9 $\pm$ 15.6 months, the mean Spigelman's score of all 35 patients increased from 6.9 $\pm$ 1.6 to 7.9 $\pm$ 2.1. The Spigelman's score increased in 21 patients (60%; six of seven referred *v* 15 of 28 nonreferred patients; $P =$ not significant). The mean annual score increase was of 0.35 (95% CI, 0.26 to 0.48) in these 21 patients. Table 2 shows the Spigelman's score and stage progression in the 35 patients. During the follow-up, the polyp count in the different segments of the proximal small bowel increased in 12 patients (34.2%; in the proximal duodenum of eight patients, in the distal duodenum of six patients, and in the jejunum of seven patients). Polyp size increased in 18 patients (51.4%; at the duodenal papilla of six patients, in the proximal duodenum distinct from the duodenal papilla of 13 patients, in the distal duodenum of five patients, and in the jejunum of one patient). Large (> 1 cm) adenomas were present at first examination in six patients (17.1%); during the follow-up, none of these large adenomas regressed, two of these six patients developed large adenomas in another segment of the proximal small bowel, and large adenomas developed in 11 patients (31.4%). A diagnosis of HGD was made in 13 patients (37.1%), on biopsy specimens of a 5-mm duodenal adenoma at first examination in one patient who refused endoscopic mucosectomy and was followed up for 50 months until an increase in size of the adenoma and endoscopic resection and during the follow-up in 12 patients (34.2%); HGD was localized at one site in 10 of these patients (duodenal papilla, three patients; proximal duodenum, five patients; distal duodenum, one patient; and first jejunal loop, one patient) and was present at several sites in two patients (proximal duodenum and jejunum in both patients). Except for the patient with HGD

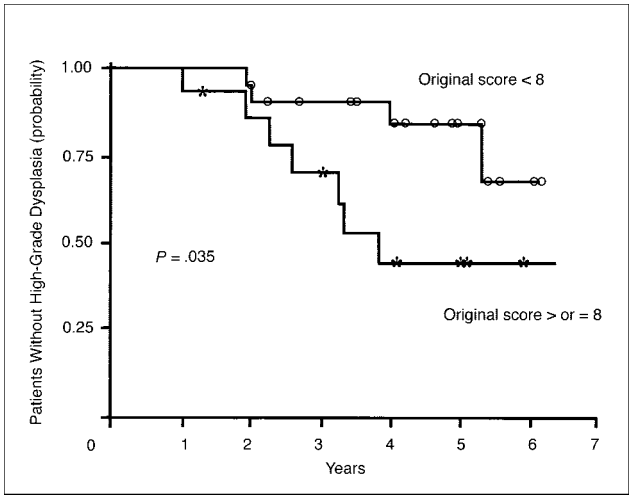

Fig 1. Probability, for familial adenomatous polyposis patients, of remaining free of high-grade dysplasia on duodenal adenoma biopsy specimens during the follow-up, as a function of the Spigelman's score (according to the study definition) calculated at original examination. *P* value was calculated using the log-rank test.

at initial examination, HGD was always diagnosed within large (> 1 cm) adenomas. The 13 patients with confirmed HGD underwent endoscopic resection (ampullectomy in four patients and mucosectomy in eight patients) or surgical resection (jejunal resection in one patient); histologic examination of the resected specimens confirmed the presence of HGD in all patients but did not reveal any evidence of invasive carcinoma. The number of patients with increasing polyp number, size, or worsening dysplasia was not statistically different when comparing referred and nonreferred patients.

Risk of HGD

The development of HGD is an important component of the Spigelman's classification (Table 1) and a decisive criterion for decision of endoscopic resection of duodenal adenomas [3,16,17]. In an attempt to identify factors predictive of HGD development, we did not observe any significant association with patient age at first examination (any value between 32 and 40 years of age) or with *APC* mutation site (18 patients whose mutation was located between codons 279 and 1309 were compared to 11 patients with a mutation outside this interval). However, an original Spigelman's score equal to or greater than 7 ($P = .032$) or 8 ($P = .035$) was predictive of HGD development (Fig 1).

Risk of Advanced Duodenal Polyposis

The present prospective data were used for calculating the life-time risk of developing stage IV duodenal polyposis. The regression model predicted a proportion of patients with a stage IV duodenal polyposis of 42.9% at age 60 (95% CI, 35.7% to 50.0%) and of 50.0% at age 70 (95% CI, 42.9% to 57.1%).

DISCUSSION

The data presented here provide information on the progression of duodenal polyposis in FAP patients in a single-center prospective study with an optimized surveillance protocol. The Spiegelman's score, which quantifies the severity of this duodenal polyposis, increased during the follow-up in 50% of patients, and HGD developed in 32% of the patients. This rate of progression seems to be higher than reported in previous series published on this topic (Table 3) [6,7,15]. This discrepancy may result from differences in populations under study and/or from a different methodology of duodenal examination. However, the group of FAP patients studied here does not seem to differ from previous reports regarding patients' mean age (37 years *v* 42 years, respectively), male to female ratio, position of *APC* mutations, and even the proportion of patients with advanced duodenal polyposis at first examination as detailed in three of six series (stage III, 45.7% *v* 35.9% to 38.5% in previous series; stage IV, 14.2% *v* 7% to 14% in previous series). Some of our patients were referred from primary

Table 3. Selected Studies of Duodenal Polyposis Progression in Familial Adenomatous Polyposis Patients

Characteristic	Current Study	Björk et al [9]	Groves et al [6]	Nugent et al [15]	Burke et al [7]	Matsumoto et al [8]
Study type	P	R	P	P	R	R
No. of subjects	35	180	99	70	114	18
Mean age, years	37	—	42	42	—	—
Male sex, %	57.1	—	55.2	55.7	—	38.8
Mean follow-up, months	47.9	72	—	40	51	196
Stage progression, % of patients	40.0	—	16.6	14.3	—	—
Stage IV polyposis*						
Initial examination, %	14	7.8	9.6	14.3	—	—
Final examination, %	35	—	14.0	17.1	—	—
Invasive carcinoma, No.	0	5	6	3	1	0

Abbreviations: P, prospective; R, retrospective.
*See Table 1.

centers, but this is also likely to be the case in other studies performed in reference centers. Some patients with attenuated disease may not have medical follow-up; our series, like previous ones, reflects only the situation of classical FAP. However, there are important methodologic differences between our series and others. First, our series uses a prospective study design, which is the case for only two of the five previously published series. It is noteworthy that these two other series were reported by the same team, were prospective, and most likely correspond to a single group of patients [6,15]. Thus, most of the results available on the progression of duodenal polyposis in FAP patients are retrospective, and the largest series are derived from cancer registration in different countries [5,9]. Second, the type of endoscope used in our study, as well as the endoscopic procedure, is more sophisticated than in most other studies, which have used either a simple forward-viewing [5,9] or a lateral-viewing endoscope [6,15,18]. Only one series is based on the use of axial and lateral-viewing endoscopes during the same examination [7]. Importantly, no series other than ours makes use of indigo-carmine coloration and general anesthesia. There is accumulating evidence that indigo-carmine dye is a powerful method to detect flat neoplastic lesions [19,20], as are most duodenal adenomas in FAP patients, although its usefulness in FAP patients has not been demonstrated. As for general anesthesia, which is a requirement in France for all difficult endoscopic procedures, we consider, as suggested in the more recent prospective series published on the topic [6], that it allows a precise and comfortable examination of all segments of the duodenum and proximal jejunum in this difficult situation of duodenal polyposis. A randomized prospective study comparing duodenal examination in FAP patients with or without general anesthesia is required to confirm this hypothesis. Thus, the important differences concerning the percentages of patients with late-stage polyposis, mostly at the end of the follow-up, compared with previous series are explained by these methodologic differences. However, we believe that this does not represent an overestimation of polyposis severity, but rather, it indicates better identification of true neoplastic lesions.

The use of an optimized methodology for duodenal polyposis surveillance in FAP patients deserves further justification because no consensus has emerged from previous studies on this matter [7,16,21]. The use of a lateral-viewing endoscope is generally recommended to examine and biopsy the duodenal papilla, which is a major site of neoplastic progression in this disease. Moreover, the use of lateral- and axial-viewing endoscopes at the same time under general anesthesia has been recommended at least for patients with advanced polyposis. Because the main objective of these surveillance programs is prevention or at least early detection of cancer, results of previous series are rather troubling. Among four recent series (including two prospective studies from the same hospital and two retrospective studies, Table 3), a total of 15 patients with duodenal cancer were reported; in most cases, these patients were not diagnosed at screening but at onset of symptoms, and 11 (73.3%) of these patients had at least locally advanced disease because they died as a result of cancer [6,9,15]. Moreover, these advanced cancers developed in four (36.3%) of 11 patients with duodenal polyposis who were evaluated at stage III or lower stages. One explanation for such poor results is that simple surveillance of duodenal polyposis in FAP patients is not sufficient and that surgery is justified in advanced cases (stage IV, maybe stage III when considering the reported occurrence of cancers at early stages). This is in contrast with the efficiency of colonic surveillance in patients with Lynch syndrome, despite the fact that these patients are also prone to develop flat adenomas that rapidly progress into cancer [22]. Another interpretation, as suggested by some authors [6], would be that these surveillance programs are not satisfying, which argues in favor of a more extensive approach, such as the one developed here. We plan to confirm the suitability of our approach by extending the follow-up of the present series. To date, none of our patients developed duodenal adenocarcinoma during a 48-month median follow-up, and complete resection of large adenomas with HGD using mucosectomy or surgery never revealed invasive carcinoma.

Therapeutic decisions concerning duodenal polyposis in FAP patients involve complex issues. A decision analysis model has been developed, based on retrospective data from polyposis registries in the Netherlands and Denmark [5]. In this model, the cumulative risk of developing stage IV duodenal polyposis was evaluated at 11%, a low rate justifying prophylactic PD in this situation, despite the 5% death rate of PD (only death, and not severe morbidity related to PD, was considered in the analysis) [23]. The cumulative risk of stage IV duodenal polyposis has been evaluated at 20% [9] and 30% [6] at ages 60 and 65 years, respectively, in two recent series and reaches 40% at age 60 and 50% at age 70 in our study. These results argue in favor of a new decision analysis model because the clinical complications of PD may overcome the benefit of surgery whenever approximately one third to half of patients with FAP should undergo prophylactic PD. Far beyond the scope of this study is the evaluation of therapeutic endoscopy in FAP patients with advanced duodenal polyposis. However, the high cumulative risk of stage IV polyposis supports further studies on endoscopy as an alternative to surgery in the prevention of duodenal cancer.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

REFERENCES

1. Arvanitis ML, Jagelman DG, Fazio VW, et al: Mortality in patients with familial adenomatous polyposis. Dis Colon Rectum 33:639-642, 1990

2. Nugent KP, Spigelman AD, Phillips RK: Life expectancy after colectomy and ileorectal anastomosis for familial adenomatous polyposis. Dis Colon Rectum 36:1059-1062, 1993

3. Hirasawa R, Iishi H, Tatsuta M, et al: Clinicopathologic features and endoscopic resection of duodenal adenocarcinomas and adenomas with the submucosal saline injection technique. Gastrointest Endosc 46:507-513, 1997

4. Penna C, Bataille N, Balladur P, et al: Surgical treatment of severe duodenal polyposis in familial adenomatous polyposis. Br J Surg 85:665-668, 1998

5. Vasen HF, Bulow S, Myrhoj T, et al: Decision analysis in the management of duodenal adenomatosis in familial adenomatous polyposis. Gut 40:716-719, 1997

6. Groves CJ, Saunders BP, Spigelman AD, et al: Duodenal cancer in patients with familial adenomatous polyposis (FAP): Results of a 10 year prospective study. Gut 50:636-641, 2002

7. Burke CA, Beck GJ, Church JM, et al: The natural history of untreated duodenal and ampullary adenomas in patients with familial adenomatous polyposis followed in an endoscopic surveillance program. Gastrointest Endosc 49: 358-364, 1999

8. Matsumoto T, Iida M, Nakamura S, et al: Natural history of ampullary adenoma in familial adenomatous polyposis: Reconfirmation of benign nature during extended surveillance. Am J Gastroenterol 95:1557-1562, 2000

9. Björk J, Akerbrant H, Iselius L, et al: Periampullary adenomas and adenocarcinomas in familial adenomatous polyposis: Cumulative risks and APC gene mutations. Gastroenterology 121:1127-1135, 2001

10. Saurin JC, Ligneau B, Ponchon T, et al: The influence of mutation site and age on the severity of duodenal polyposis in patients with familial adenomatous polyposis. Gastrointest Endosc 55:342-347, 2002

11. Spigelman AD, Williams CB, Talbot IC, et al: Upper gastrointestinal cancer in patients with familial adenomatous polyposis. Lancet 2:783-785, 1989

12. Schlemper RJ, Riddell RH, Kato Y, et al: The Vienna classification of gastrointestinal epithelial neoplasia. Gut 47:251-255, 2000

13. Goldstein H: Kendall's Library of Statistics: Multilevel Statistical Models. London, United Kingdom, Arnold, 1995

14. Gilks WR, Richardson S, Spiegelhalter DJ: Markov Chain Monte Carlo in Practice. London, United Kingdom, Chapman and Hall, 1996

15. Nugent KP, Spigelman AD, Williams CB, et al: Surveillance of duodenal polyps in familial adenomatous polyposis: Progress report. J R Soc Med 87:704-706, 1994

16. Bleau BL, Gostout CJ: Endoscopic treatment of ampullary adenomas in familial adenomatous polyposis. J Clin Gastroenterol 22:237-241, 1996

17. Desilets DJ, Dy RM, Ku PM, et al: Endoscopic management of tumors of the major duodenal papilla: Refined techniques to improve outcome and avoid complications. Gastrointest Endosc 54:202-208, 2001

18. Matsumoto T, Iida M, Kobori Y, et al: Progressive duodenal adenomatosis in a familial adenomatous polyposis pedigree with APC mutation at codon 1556. Dis Colon Rectum 45:229-233, 2002

19. Kiesslich R, von Bergh M, Hahn M, et al: Chromoendoscopy with indigocarmine improves the detection of adenomatous and nonadenomatous lesions in the colon. Endoscopy 33:1001-1006, 2001

20. Kiesslich R, Fritsch J, Holtmann M, et al: Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. Gastroenterology 124:880-888, 2003

21. Bulow S, Alm T, Fausa O, et al: Duodenal adenomatosis in familial adenomatous polyposis. DAF Project Group. Int J Colorectal Dis 10:43-46, 1995

22. Jarvinen HJ, Aarnio M, Mustonen H, et al: Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. Gastroenterology 118:829-834, 2000

23. Strasberg SM, Drebin JA, Soper NJ: Evolution and current status of the Whipple procedure: An update for gastroenterologists. Gastroenterology 113:983-994, 1997

Familial adenomatous polyposis (FAP) is an autosomal dominant genetic disorder that predisposes to a number or malignant disorders [1,2]. Clinically, FAP presents with an abnormalâ€¦ Expand. Conditions. Duodenal Cancer, Duodenal Polyposis, Familial Adenomatous Polyposes. Intervention. Diagnostic Test.Â Surveillance of duodenal adenomas in familial adenomatous polyposis reveals high cumulative risk of advanced disease. J. Saurin, C. Gutknecht, +5 authors J. Chayvialle. Medicine. Familial Adenomatous Polyposis: Causes. Overview The exact causes of colorectal cancer are not known. However, studies have shown that genetics, diet, and lifestyle may affect the risk of developing colorectal cancer. Family History Family history is one of the most significant risk factors for colorectal cancer. People who have cancer, colorectal cancer, non-cancerous colon polyps, or inflammatory bowel disease are at increased risk.Â Estrogen replacement therapy Studies show that ERT (estrogen replacement therapy) may reduce the risk of colorectal cancer by one half in postmenopausal women. The decision to take estrogen should be based on discussions of the benefits and risks with your doctor. Â© Copyright 2001-2013 | All Rights Reserved. Familial adenomatous polyposis (FAP) is a rare inherited cancer predisposition syndrome characterized by hundreds to thousands of precancerous colorectal polyps (adenomatous polyps). If left untreated, affected individuals inevitably develop cancer of the colon and/or rectum at a relatively young age.Â Affected Populations. Familial adenomatous polyposis affects males and females in equal numbers. It occurs in approximately one in 5,000 to 10,000 individuals in the United States and accounts for about 0.5% of all cases of colorectal cancer.Â Removal of duodenal polyps is sometimes recommended if they cause symptoms, are large or contain large numbers of abnormal cells (dysplasia). This is to prevent them from becoming cancerous. Familial adenomatous polyposis (FAP) syndrome is a complex entity, which includes FAP, attenuated FAP, and MUTYH-associated polyposis. These patients are at significant risk for colorectal cancer and carry additional risks for extracolonic malignancies. In this guideline, we reviewed the most recent literature to formulate recommendations on the role of endoscopy in this patient population.Â Surveillance of duodenal adenomas in familial adenomatous polyposis reveals high cumulative risk of advanced disease. J Clin Oncol. 2004; 22: 493-498. View in Article. Scopus (105). PubMed. Crossref. Familial adenomatous polyposis (FAP) is an inherited autosomal dominant syndrome that is caused by germline mutations in one copy of the adenomatous polyposis coli (APC) gene. These mutations lead to the development of a variable number of colorectal polyps during the second and third decade of life[1,2]. APC is a tumor suppressor gene that is located on the long arm of chromosome 5 (5q21-22) and is composed of 15 exons.Â The macroscopic appearance of duodenal adenomas in patients with FAP varies widely[21,29-31].Â Moreover, random duodenal biopsies revealed adenomatous tissue in 28 patients who did not have visible polyps at endoscopy.