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Prophylactic Surgery for Patients with Longstanding Ulcerative Colitis. Which Option? Histopathological and Clinical Implications

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Abstract

Patients with longstanding chronic ulcerative proctocolitis are at risk to develop colorectal cancer Conflicting views as regards surveillance, the indications for surgery and type of preventive procedure exist. For permanent prevention of cancer development complete removal of all potential malignant colorectal mucosa has to be done. Panprocto-colectomy with a conventional ileostomy or continent ileostomy removing all colorectal mucosa should therefore eliminate further risks of colorectal cancer.

Colectomy and ileorectal anastomosis is a controversial issue. While many surgeons today are reluctant to use the technique, emphasising the persistent cancer risk, others consider the operation a viable alternative when used on a selective basis. The long-term risk of cancer in the rectal stump is the main strong argument .

In restorative proctocolectomy, i.e. proctocolectomy with construction of an ileopouch anal anastomosis residual rectal mucosa is left behind irrespective of technique used and is therefore at risk for cancer development. Quite a few cancers have been reported to occur in these patients but controversy exists as regards the origin of these tumours but the risk for cancer development is very low.

Biopsies from ileal pouches demonstrate various histopathological changes from nearly normal mucosa, to inflammation and atrophy, inflammatory cell changes, dysplasia as well as development of carcinoma. Grading of type and atypia is a challenge to reproduce and requires the participation of experienced gastrointestinal histopathologists.

Abbreviations

UC: Ulcerative colitis
CI: Continent ileostomy
IRA: Ileorectal end-to-end anastomosis
IPAA: Ileopouch anal anastomosis

Introduction

Colorectal cancer is far from being the commonest complication of ulcerative colitis (UC), but it is the one that has been most extensively studied, and the literature on the subject exceeds that dealing with other complications of the disease. The

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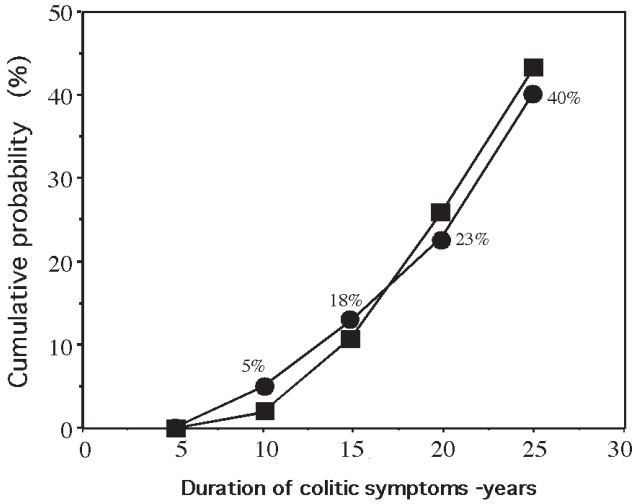

Figure 1. Cumulative risk of cancer in longstanding total colitis. Cumulative probability for cancer related to duration of colitis symptoms in years [3, 4].

cumulative risk of cancer in patients with total colitis rises slowly at first to around 4% after 10 years of colitic symptoms. However, after 10 years of colitis, the cumulative risk increases more and more sharply to reach the startling level of 40–48% after 25 years of colitic symptoms [1–4] (Figure 1). Similar results have recently been presented by others [3, 5–7] demonstrating that those with total or extensive colitis (extending proximal to the splenic flexure), colitis of 8 years or more, a family history of colorectal cancer, primary sclerosing cholangitis and an early age of onset of colitis have the greatest risk of developing carcinoma. Primary sclerosing cholangitis occurs in about 2.5 to 6% of patients with UC and adds a considerable cancer risk compared with UC in general [8]. The mean interval from diagnosis of primary sclerosing cholangitis to dysplasia or cancer is only 2.9 years. Colorectal cancer associated with primary sclerosing cholangitis is more likely to be proximal, to be diagnosed at a more advanced stage, and to be fatal [1, 3, 7]. How should these patients be followed-up , should prophylactic surgery be used ? If so, when should it be recommended and with all options present today what form should any prophylactic surgery take?What is the role for histopathology?

Cancer screening and colonoscopy surveillance

In the past the indication for prophylactic colectomy for patients with longstanding UC was mainly based on the disease history and the clinical risk factors mentioned above. Today with the availability of colonoscopy and the recognition of the dysplasia-precancer-cancer sequence, colonoscopy with serial colonoscopic examinations and mucosal biopsies is considered to allow for a more adequate individual assessment of the cancer risk. Thus prophylactic surgery should be reserved for patients whose biopsy findings are indicative of heightened cancer risk based on the joint interpretation by the clinician and the histopathologist.

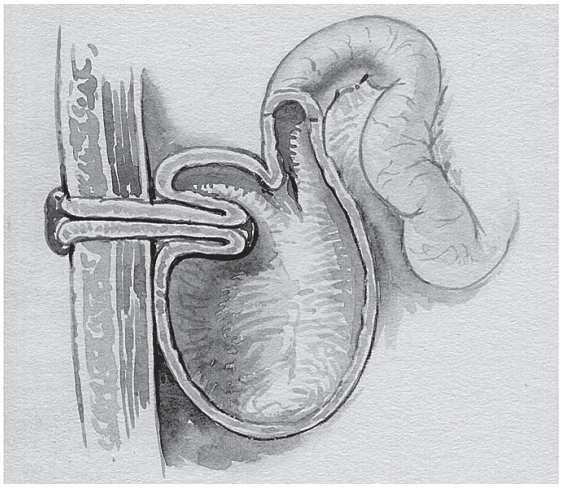

Figure 2. Principles for continent ileostomy (CI).

Prophylactic surgery – three options?

Panproctocolectomy and ileostomy

For prevention of cancer development in patients with ulcerative proctocolitis complete removal of all potential malignant colorectal mucosa is a prerequisite. Before advent of the surgical options of our days panproctocolectomy with construction of a conventional ileostomy was the standard procedure for cancer prophylaxis in patients with longstanding UC. Such an operation eliminates further risks of colorectal cancer. Although cancer in the ileostomy in these patients has been demonstrated to occur many years after surgery this is probably a different state of affairs [9]. Bowel metaplasia may occur where gut contents come into regular contact with the squamous epithelium of the skin, an important step in the development of these rare tumours. The ileostomy cancer develops at the mucocutaneous junction of the ileostomy and chronic irritation caused by trauma and/or chemical agents from stoma appliances or adhesives may be factors in the unclear aetiology. It seems very likely that the sole report of cancer developing in a continent ileostomy (CI) (Figure 2) may have a similar explanation [10].

Colectomy and ileorectal end-to-end anastomosis (IRA)

Conflicting results have been presented as regards the indications for colectomy with IRA for UC. Although many surgeons today are still reluctant to use the technique, emphasising not only the persistent cancer risk but also the poor function [11, 12] others consider the operation a viable alternative when used selectively in patients without signs of mucosal dysplasia and whose rectum is not severely affected by inflammation or fibrosis [13–15]. Using the colectomy and IRA procedure for a condition that almost invariably involves an inflamed rectum certainly seems illogical However, in many cases, the proctitis often settles spontaneously or after local treatment or recurs periodically. The time “bought” by IRA will get

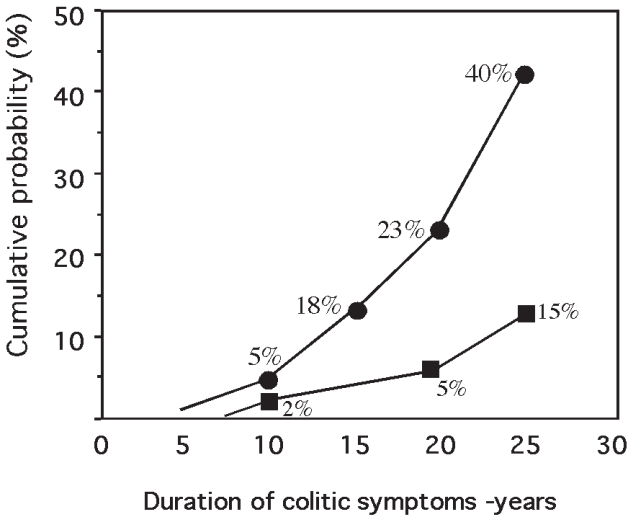

Figure 3. Cumulative probability of cancer development in longstanding total colitis before (upper curve [3]) and after IRA surgery (lower curve [23]).

many young people through their formative years of education, allowing them to plan for a family and a professional career. The long-term risk of cancer in the rectal stump is the main strong argument that has been put forward against the use of this operation however – a risk that increases with the duration of the disease and with the passage of time after the colectomy. The cumulative probability of cancer development approaches 5% and 15% after 20 and 25 years of observation, respectively (Figure 3) [3, 16]. The pathology findings is equvalent to that found in the IPAA situation.

Restorative proctocolectomy – Ileopouch anal anastomosis (IPAA)

IPAA or restorative proctocolectomy i.e. construction of a reservoir of distal ileum and an ileo-anal anastomosis is the currently most popular option for surgical treatment of ulcerative proctocolitis. There is no stoma or need for an external bag and the normal route of defecation is preserved i.e. a normal body image In the conventional technique colectomy is combined with endo-anal mucous proctectomy and the ileal pouch is hand-sewn to the pectinate line (Figure 4A). In the currently most popular technique the abdominal dissection is carried out down to the levator muscle, the rectum is severed at this level and the ileal pouch is connected to the rectal stump by a stapling device (Figure 4B). In analogy with the traditional total proctocolectomy surgery this procedure has been considered a curative and cancer-prophylactic procedure since all diseased mucosa is completely removed .

Its place as a cancer prophylactic procedure may in fact be questioned. An increasing number of cancers have been reported in these patients and the incidence is expected to rise as the length of follow-up increases (Table 1) [17–19].

Chronic inflammation in the ileal mucosa (pouchitis) is a frequent complication in the CI and has proved subsequently to be so even in the IPAA [20]. A case of adenocarcinoma in the CI [10] and sporadic reports of dysplasia in the ileal pouch mucosa have currently appeared in the literature, suggesting that the morphologi-

Table 1. Published pelvic pouch cancers in the world literature (M-ectomy: mucosectomy)

Author	Disease duration (years) at the time of IPAA	IPAA procedure	PAD Colorectal specimen at the time of IPAA	Time (years) from IPAA to neoplasia	Differerentiation of the pouch cancer	Proposed origin of the pouch cancer
Stern 1990	28	M-ectomy	Cancer cecum	3	High grade	Residual rect. mucosa
Puthu 1992	17	M-ectomy	Dysplasia	6	Average	Residual rect. mucosa
Rodrigues 1995	18	M-ectomy	Dysplasia	4	High grade	Residual rect. mucosa
Vieth 1998	20	Not stated	Cancer transv. colon	2	Average	Pouch mucosa?
Iwama 2000	21	M-ectomy	Dysplasia	2	Average	Pouch mucosa?
Heuschen 2001	26	M-ectomy	Cancer desc. colon	4	High grade	Pouch mucosa?
Laureti 2002	20	M-ectomy	Cancer sigm. colon	2	High grade	Residual rect. mucosa
Bentrem 2003	30	M-ectomy	Cancer asc. colon	13	High grade	Pouch mucosa?
Hassan 2003	10	M-ectomy	Dysplasia	2	Average	Pouch mucosa?
Negi 2003	10	M-ectomy	Dysplasia	5	High grade	Residual rect. mucosa
Lee 2005	27	M-ectomy	Dysplasia	2	Average-low	Lower pouch mucosa
Lee 2005	12	M-ectomy	Cancer	6.5	Not stated	Residual rect. mucosa
Lee 2005	4	M-ectomy	UC, no dysplasia	16	Average	Residual rect. mucosa
Sequens 1997	16	Stapled	Rectal cancer	2	Average	Residual rect. mucosa
Rotholz 2001	13	Stapled	Dysplasia	7	High grade	Residual rect. mucosa
Baratsis 2002	24	Stapled	Cancer cecum	2	High grade	Residual rect. mucosa
Hyman 2002	13	Stapled	Rectal cancer	6	High grade	Residual rect. mucosa
Bell 2003	15	Stapled	Dysplasia	12	High grade	Residual rect. mucosa
Knupper 2006	20	Stapled	No dysplasia	3	Low-grade	Pouch mucosa?

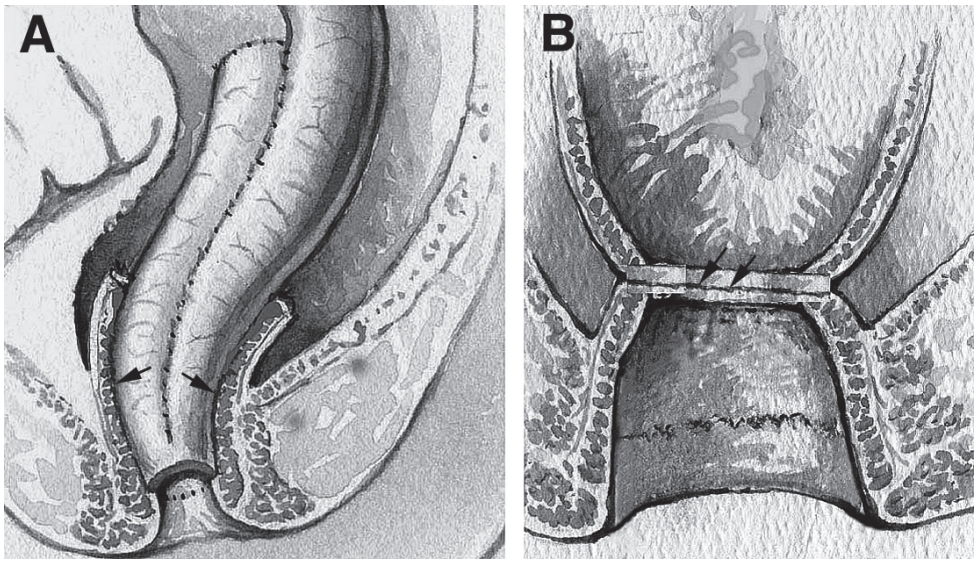

Figure 4. Principles for IPAA. A. IPAA with anastomosis to the dentate line with surrounding muscular cuff after rectal-anal mucosectomy. Arrows indicate problem areas for remnant colonic epithelium at risk for dysplasia and carcinoma development. B. IPAA above the dental line and anal transformation zone performed with a staple technique. Larger area of preserved colonic mucosa at risk for potential malignancy development.

cal transformation of the ileal pouch mucosa might result in cellular dysplasia and eventually carcinoma [21, 22]. The atrophic colon-like mucosa in the ileal pouch is hypothetically considered a potentially premalignant condition with risk for subsequent development of advanced neoplastic transformation. Dysplasia and aneuploidy as demonstrated by these authors is suggested to reflect a different pathway of an atrophic mucosa-dysplasia carcinoma sequence. However, the results from two recent long term studies both on CI patients and subsequently on IPAA patients from our group are reassuring [18, 23].

In our group biopsies from 40 patients with CI [23] and 45 patients with IPAA [18] were studied. Tissue was fixated in 4% buffered formaldehyde, imbedded in paraffin, cut at 3–4 μm and stained with haematoxylin-eosine, PAS for neutral mucins, Alcian blue/high iron diamine (HID/AB) for sialomucins and sulphomucins content.

Due to the well known difficulties and controversies surrounding the crucial histopathological diagnosis of dysplasia two sets of histopathologists is usually required in order to establish inter and intra reproducibility. In our studies two sets of histopathologists from Gothenburg and Manchester with special interest in the subject evaluated the same biopsies independently. Grading of dysplasia was according to established international criteria [24]. Morphological changes in the different forms of pouch mucosa were grouped into three types according to Veress et al [22, 25]. Type A: 51%, normal mucosa and few inflammatory cells. Type B: 40%, transient atrophy with temporary moderate to severe inflammation followed

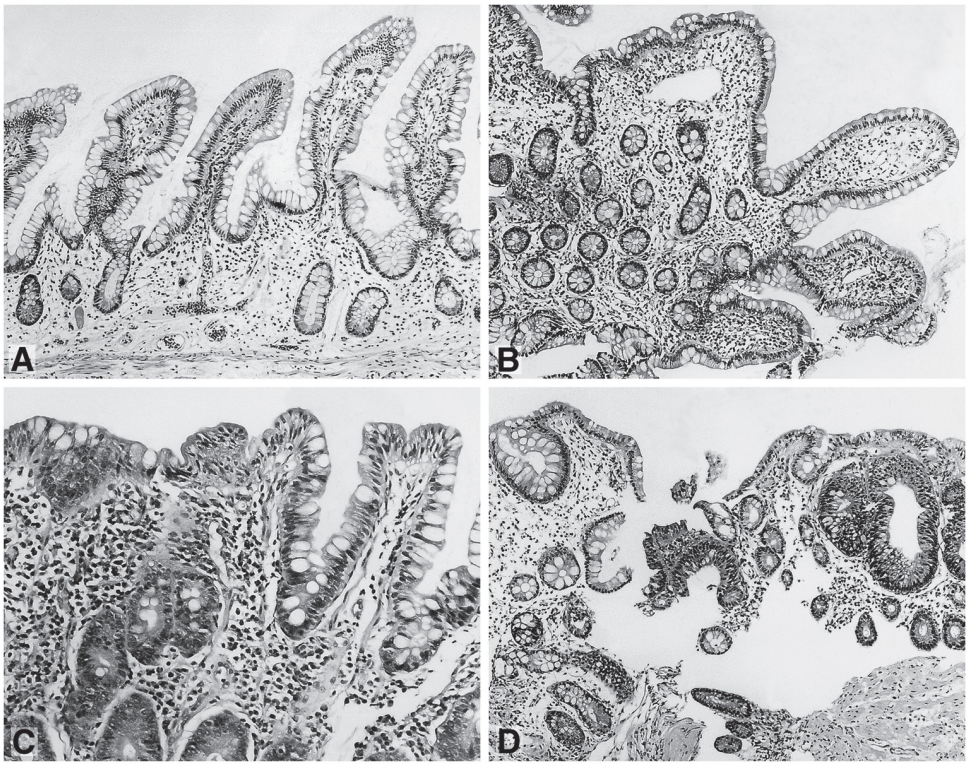

Figure 5. Histopatological features of a CI mucosa. A. Normal ileal mucosa with few inflammatory cells and slender villi, type A. B. Mucosa with blunt shortened villi and increased inflammatory cells in lamina propria, type B. C. Atrophic mucosa, type C, within some glands low-grade dysplasia (arrow). D. Higher magnification of a dysplastic area (arrow).

by architectural normalisation. However the villi are normally reduced in height, sometimes blunt and inflammatory cells are slightly increased. Type C: 9%, persistent villous atrophy accompanied by severe pouchitis and sometimes eroded surface with inflammatory cells in the mucosa (Figure 5 and 6). Carraro et al [21] and Stallmach et al [26] have also published similar grading systems, dividing the patients into three groups. A 45%, B 26%, C 8% and A 73%, B 20%, C 7% respectively. In the atrophic situation inflammation and "colonisation" of the ileal mucosa takes place with transformation of neutral mucins and sialomucins into sulphomucins according to the mucin stains. Usually this is not a fully developed colonic pattern but more of a complete type with a mixture of neutral, sialomucins and a variable amount of sulphated mucins. This transition is considered a marker for malignancy transformation on a molecular level, but far from all with these changes develop carcinoma [27, 28]. In most reports this mucinous transformation is not a common feature and when found is usually of incomplete type. Changes of amino-, oligopeptidase and Maltase have also been registered reflecting a functionally and morphologically adaptation towards a colonic pattern [29]. For CI only reactive cellular changes are usually observed but in our study with follow-up for 30 years

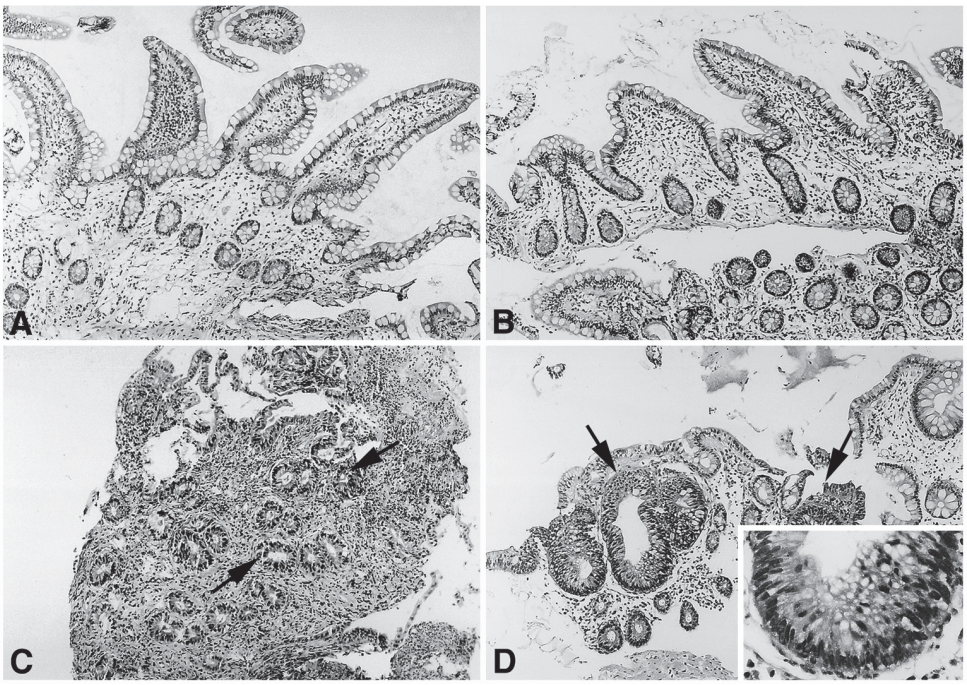

Figure 6. Histopathological features of an IPAA mucosa. A. Normal ileal mucosa with few inflammatory cells, type A. B. Mucosa with blunt shortened villi and increased number of inflammatory cells within epithelia and lamina propria, type B. C. Blunt shortened villi with partial atrophy, intense inflammatory cell reaction in lamina propria as well as gland and mucin atrophy (arrows), type C. D. In some areas dysplastic glands (arrows) with low-grade dysplasia (insert).

two cases of low-grade dysplasia were found [23] (Figure 5). Only one case of carcinoma is on record after longstanding chronic pouchitis [10].

In order to understand the reaction pattern possible with the IPAA procedure it is important to consider the anatomical situation that is outlined in Figure 6A–C. Figure 7A gives an overview of the anal fold (*), cloacogenic epithelium (C) and the beginning of the colonic mucosa (B). Figure 6B illustrates the transformation zone between cloacogenic epithelium and colonic mucosa proper. Figure 6C illustrates the transformation zone between anal squamous epithelium and the cloacogenic one. Note the undulating and deep folds making it difficult to completely remove epithelial structures.

For IPAA several reports have documented atypia, dysplasia, different molecular aberrations, as well as genetic changes [18, 21, 22, 25]. In our study of 45 patients operated with IPAA followed for 18 years, besides atrophy, inflammation and change of mucins towards sulphomucins, only 2 patients demonstrated low-grade dysplasia (Figure 7) [18].

Until the year 2005 only 19 cases of carcinoma developing in relation to IPAA have been reported (Table 1) [17–19]. Of these, 13 were clearly related to residual rectal mucosa sometimes remaining behind after either the endo-anal mucosectomy

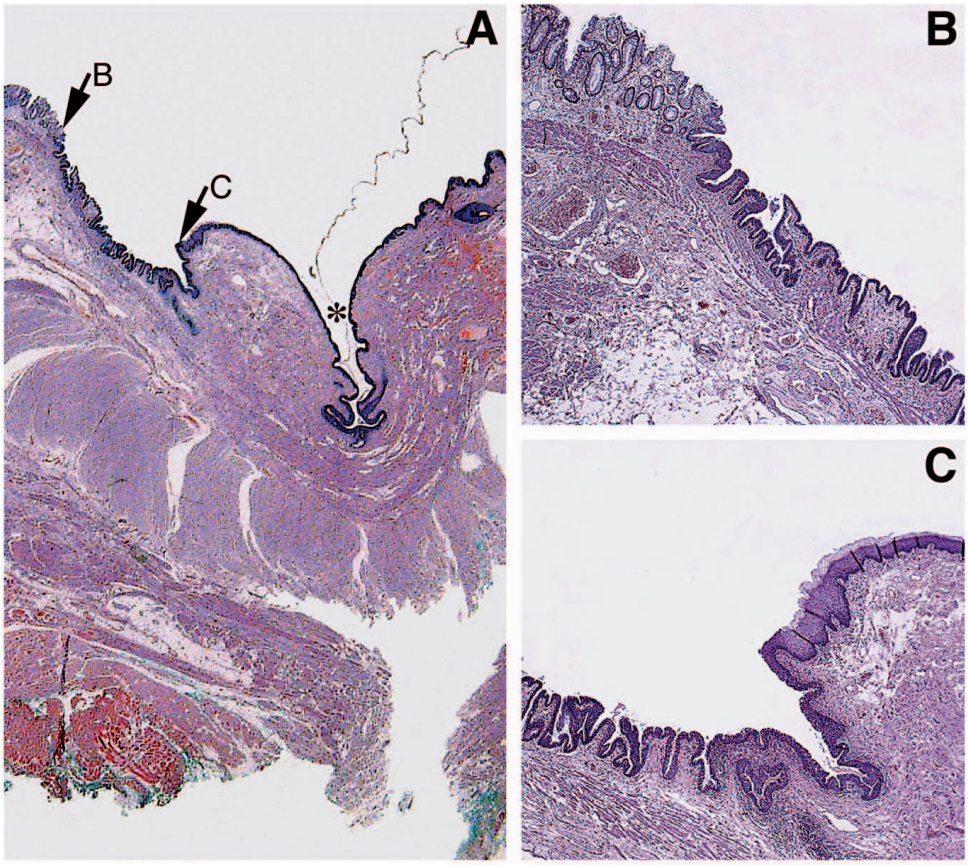

Figure 7. Normal anatomy of the anal-colonic region. A. (Overview): *Skin-anal fold. Beginning of colonic mucosa proper (arrow B). Beginning of the anal squamous mucosa and cloacogenic epithelium (arrow C). B. (Upper right): higher magnification of the area indicated by arrow B: Cloacogenic mucosa-colonic mucosa region. C. (Lower right): higher magnification of the area indicated by arrow C: Anal squamous mucosa-cloacogen border region. Note the undulating and deep folds making it difficult to completely remove epithelial structures.

or the non-mucosectomy technique. However, those reports claiming that cancer may have originated in the ileal pouch mucosa include a variety of circumstances making this claim questionable, as histopathology and illustrations in published articles is not easy to evaluate.

Discussion

The ileal reservoir mucosa adapts to the new environment in UC patients to a variable degree. The villi can be basically intact, be lower and broadened or develop severe atrophy. In order to grade the biopsies according to Veress it is best to have two or three different biopsies at different times in combination with clinical data.

This is especially important when trying to evaluate the difference between type B and C within a short period after surgery. Even if cell changes, dysplasia and DNA aberrations occur in all types it is the type C that is claimed to demonstrate the highest frequency of erosions, inflammatory changes and subsequent development of dysplasia and carcinoma. In a series of papers the Veress group have described all these features including DNA aneuploidy and genetic aberrations except carcinoma [22, 25]. In our group CI patients were followed for 30 years [23]. Besides reactive cellular changes only two cases of low-grade dysplasia were detected but no carcinoma.

The published reports on cancer developing in the IPAA patients operated for UC reflect a quite different issue however [17, 18]. Irrespective of technique used IPAA leaves residual rectal mucosa behind. Dysplasia in these rectal mucosal remnants with subsequent cancer development has proved to be a risk of the procedure, reflecting the continuous risk of malignant transformation in the chronically inflamed rectal mucosa (Figure 4, 6 and 7). Thus, it has been demonstrated that even after a careful macroscopically complete mucosectomy, islets of remnants of rectal mucosa are left behind in about 20 % of the cases (Table 1, Figure 4 and 7 [30–32]). In the alternative technique, where the ileal pouch is stapled to the top of the anal canal, varying amounts of rectal mucosa as well as the anal transitional zone mucosa remain preserved. The rectal stump may even include part of lower rectum in technically demanding cases.

In our study of IAPP patients who were followed for 18 years [18] the over all incidence of mucosal dysplasia in the ileal pouch mucosa proved to be low and no case of high-grade dysplasia or carcinoma was observed. Considering an observation time of an average 18 years in that study, and the comparatively large series of patients these results imply that dysplastic and neoplastic transformation within the ileal pouch mucosa is extremely rare regardless of the type of adaptation.From the rough morphological descriptions given in most papers it is difficult to evaluate if the ileal mucosa is the primary carcinoma target or not.

It is convincingly demonstrated that this risk of carcinoma development is increased in patients with a long history of antecedent UC and with the diagnosis of dysplasia or cancer in the operative specimen at the time of colectomy [17, 18]. Therefore, although there are reports suggesting that an IPAA is a successful surgical approach for UC patients with coexisting colorectal cancer [33] it is doubtful if such an approach should be recommended. Although some colorectal surgeons may question the need for routine surveillance for cancer in the IPAA patients [34] these observations imply that despite that the cancer risk after IPAA may well be less than after the IRA procedure similar endoscopy surveillance should still be motivated. Dysplasia or early cancer that arises from the residual rectal tissue in the muscular cuff after mucosectomy may then favourably be detectable.

Finally, endoscopy surveillance with deep random biopsies of the anal canal mucosa should be taken and therafter handled by a histopathologist well acquainted with the subtle features of pouch and anal pathology.

References

1. Devroede GJ, Taylor WF, Sauer WG, Jackman RJ, Stickler GB (1971) Cancer risk and life expectancy of children with ulcerative colitis. N Engl J Med 285: 17–21.
2. Devroede GJ, Taylor WF (1976) On calculating cancer risk and survival of ulcerative colitis patients with the life table method. Gastroenterology 71: 505–509.
3. De Dombal FT, Watts JM, Watkinson G, Goligher JC (1966) Local complications of ulcerative colitis: stricture, pseudopolyposis and carcinoma of colon and rectum. Br Med J 5501:1442–1447.
4. Kewenter J, Ahlman H, Hultén L (1978) Cancer risk in extensive ulcerative colitis. Ann Surg 188: 824–828.
5. Eaden J, Abranis KR, Mayberry JF (2001) The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48: 526–535.
6. MacDougall PM (1964) The cancer risk in ulcerative colitis. Lancet 2: 655–658.
7. Hulten, L, Kewenter J, Åhren, C (1972) Precancer and carcinoma in chronic ulcerative colitis. A histopathological and clinical investigation. Scand J Gastroenterol 7: 663–669.
8. Shetty I, Rybicki L, Brzezinski A, Carey WD, Lashner BA (1999) The risk for cancer or dysplasia in ulcerative colitis patients with primary sclerosing cholangitis. Am J Gastroenterol 94: 1643–1649.
9. Quah HM, Samad H, Maw A (2005) Ileostomy carcinomas a review: the latent risk after colectomy for ulcerative colitis and familial adenomatous polyposis. Colorectal Disease 7: 538–544.
10. Cox CL, Butts DR, Roberts MP, Wessels RA, Bailey HR (1997) Development of invasive adenocarcinoma in a long-standing continent ileostomy: report of a case. Dis Colon Rectum 40: 500–503.
11. Parc R, Legrand M, Frileux P, Tiret E, Ratelle R (1989) Comparative clinical results of ileal-pouch anal anastomosis and ileorectal anastomosis in ulcerative colitis. Hepatogastroenterol 36: 235–239.
12. Pastore RL, Wolff BG, Hodge D (1997) Total colectomy and ileorectal anastomosis for inflammatory bowel disease. Dis Colon Rectum 40: 1455–64.
13. Khubchandani IT, Sandfort MR, Rosen L, Sheets JA, Stasik JJ, Riether RD (1989) Current status of ileorectal anastomosis for inflammatory bowel disease. Dis Colon Rectum 32: 400–403.
14. Leijonmarck CE, Löfberg R, Öst Å, Hellers G (1990) Long-term results of ileorectal anastomosis in ulcerative colitis in Stockholm County. Dis Colon Rectum 33: 195–200.
15. Tonelli F, Batignani G (1989) Continenza e modificazioni della pressione del canale anale e della distensibilita rettale dopo ileorettoanastomosi. Chirurgia 2: 289–296.
16. Baker WN, Glass RE, Ritche JK, Aylett SO (1978) Cancer of the rectum following ileorectal anastomosis for ulcerative colitis. Br J Surg 65: 862–868.
17. Lee SW, Sonoda T, Milsom JW (2005) Three cases of adenocarcinoma following restorative proctocolectomy with hand-sewn anastomosis for ulcerative colitis: a review of reported cases in the literature. Colorectal Dis 7: 591–597.
18. Börjesson L, Willén R, Haboubi N, Duff SE, Hultén L (2004) The risk of dysplasia and cancer in the ileal pouch mucosa after restorative proctocolectomy for ulcerative proctocolitis is low: a long-term term follow-up study. Colorectal Dis 6: 494–498.
19 Knupper N, Straub E, Terpe HJ, Vestweber KH (2006) Adenocarcinoma of the ileoanal pouch for ulcerative colitis – a complication of severe chronic atrophic pouchitis? Int J Colorectal Dis (on-line January 2006).
20. Svaninger G, Nordgren S, Öresland T, Hulten L (1993) Incidence and characteristics of pouchitis in the Kock continent ileostomy and the pelvic pouch. Scand J Gastroenterol 28: 695–700.
21. Setti-Carraro P, Ritchie JK, Wilkinson KH, Nicholls RJ, Hawley PR (1994) The first 10 years' experience of restorative proctocolectomy for ulcerative colitis. Gut 35: 1070–1075.
22. Gullberg K, Stahlberg D, Liljeqvist L, Tribukait B, Reinholt FP, Veress B, Löfberg R (1997) Neoplastic transformation of the pelvic pouch mucosa in patients with ulcerative colitis. Gastroenterol 112: 1487–1492.
23. Hultén L, Willén R, Nilsson O, Safarani N, Haboubi N (2002) Mucosal assessment for dysplasia and cancer in the ileal pouch mucosa in patients operated on for ulcerative colitis – a 30-year follow-up study. Dis Colon Rectum 45: 448–452.

24. Riddell RH, Goldman H, Ransohoff DF, Appelman HD, Fenoglio CM, Haggitt RC, Åhren C, Correa P, Hamilton SR, Morson BC et al (1983) Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical applications. Hum Pathol 14: 931–968.
25. Veress B, Reinholt FP, Lindquist K, Lofberg R, Liljegvist L (1995) Long-term histomorphological surveillance of the pelvic ileal pouch: dysplasia develops in a subgroup of patients. Gastroenterol 109: 1090–1097.
26. Stallmach A, Moser C, Hero-Gross R, Muller-Molaian I, Ecker KW, Feifel G, Zeitz M (1999) Pattern of mucosal adaptation in acute and chronic pouchitis. Dis Colon Rectum 42: 1311–1317.
27. Sylvester PA, Wong NA, Myerscough N, Warren BF, Corfield AP, Thomas MG, Durdey P (2002) Mucin expression in the ileoanal reservoir reflects incomplete mucosal adaptation. J Pathol 197: 28–36.
28. Garcia-Armengol J, Hinojosa J, Lledo S, Roig JV, Carcia-Granero E, Martinez B (1998) Prospective study of morphologic and functional changes with time in the mucosa of the ileoanal pouch: functional appraisal using transmucosal potential differences. Dis Colon Rectum 41: 846–853.
29. Kawaguchi AL, Dunn JC, Saing MS, Cortina G, Fonkalsrud EW (2000) Functional and morpho logic changes of the ileal mucosa after ileoanal pouch procedure. J Am Coll Surg 190: 310–314.
30. Sequens R (1997) Cancer in the anal canal (transitional zone) after restorative proctocolectomy with stapled ileal pouch-anal anastomosis. Int J Colorectal Dis 12: 254–255.
31. Duff SE, O´Dwyer ST, Hultén L, Willén R, Haboubi NY (2002) Dysplasia in the ileo-anal pouch. Colorectal Dis 4: 420–429.
32. O'Connell PR, Pemberton JH, Weiland LH, Beart RW Jr, Dozois RR, Wolff BG, Telander RL (1987) Does rectal mucosa regenerate after i1eoanal anastomosis? Dis Colon Rectum 30: 1–5.
33. Remzi FH, Preen M (2003) Rectal cancer and ulcerative colitis: does it change the therapeutic approach? Colorectal Dis 5: 483–485.
34. Herline AJ, Meisinger LL, Rusin LC, Roberts PL, Murray JJ, Coller JA, Marcello PW, Schoetz DJ (2003) Is routine pouch surveillance for dysplasia indicated for ileoanal pouches? Dis Colon Rectum 46: 156–159.

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