

Surgical management of ulcerative colitis

Andreas M. Kaiser, Robert W. Beart Jr.

Division of Colon and Rectal Surgery, University of Southern California, Keck School of Medicine, Los Angeles, USA

Summary

As long as our understanding of ulcerative colitis is too limited to allow a more specific, disease-targeted treatment, surgery will play an important role in the management of these patients. Careful interdisciplinary evaluation and counselling of patients with ulcerative colitis will permit to achieve the goals on an individual basis with maximum safety. Restorative proctocolectomy with an IPAA

has evolved as the procedure of choice among four basic surgical options because it appears to be safe and carries a low mortality. Although the associated morbidity is not negligible, functional results are generally good and patient satisfaction is high.

Keywords: ulcerative colitis; surgery; quality of life; pouch; ileostomy

Introduction

Ulcerative colitis is a complex chronic disease that belongs to the group of idiopathic inflammatory bowel diseases. It is characterised by a relapsing and remitting course of an acute ulcerating inflammation of the colorectal mucosa. Although our knowledge has greatly improved over the last decades, many fundamental aspects of the pathophysiology and optimal management of ulcerative colitis have yet to be elucidated. For this reason, treatment largely remains unspecific and primarily directed towards the relief of symptoms although

it is hoped that evolving understanding will permit more specific treatments in the future. Approximately 30–45% of patients with ulcerative colitis will at some point require operative treatment [1]. It is beyond the scope of this review to evaluate all the latest basic science and clinical research findings in detail, nonetheless our goal is to outline the role of current standard procedures and the various additional surgical options in the management of these patients.

General information

Epidemiology

The incidence of ulcerative colitis in Western countries is about 5–16 new cases per 100,000 per year with an onset most commonly but not exclusively between 15–45 years of age [2–9]. The prevalence ranges from 50–220 cases per 100,000. Familial, geographic, ethnic and cultural variations have been identified [5, 10]. In contrast to Crohn's disease, ulcerative colitis is favourably affected by

the use of nicotine, but the significance of this negative association remains unclear [11–13].

Pathology

The morphological picture of ulcerative colitis is distinct from that of Crohn's disease although there is a histopathological overlap in 15% of the patients (indeterminate colitis) [14]. Ulcerative colitis is characterised by a superficial acute inflammation that is – except for toxic megacolon – limited to the mucosa and submucosa. Large mucosal erosions and ulcers are present with margins that may protrude into the lumen and form pseudopolyps. Crypt abscesses characteristically develop and may penetrate the superficial submucosa. Vascular congestion and haemorrhage are additional prominent features of acute episodes whereas chronicity is characterised by distortion of the crypt architecture (gland branching, shorten-

Abbreviations

UC	ulcerative colitis
PC	proctocolectomy
TC	total abdominal colectomy
IPAA	ileal pouch-anal anastomosis
IRA	ileo-rectal anastomosis
IS	ileostomy (Brooke type)
CIS	continent ileostomy
PSC	primary sclerosing cholangitis
FAP	familial adenomatous polyposis

ing, loss of parallel arrangement), Paneth cell metaplasia, and infiltration of the lamina propria with mononuclear cells.

The rectum is invariably affected, and the confluent inflammation with superficial ulceration extends proximally. However, sequential endoscopies, performed in the course of treatment of patients with ulcerative colitis, reveal histological patchiness of inflammation and rectal sparing in up to 27% [15, 16]. There is a sharp demarcation between the affected distal colon and the more proximal unaffected colon. Based on the extent of colonic involvement, the disease may thus be categorised into [1]:

- proctitis/proctosigmoiditis (45–60%);
- left-sided colitis (distal to the splenic flexure);
- extensive colitis (involving the transverse colon);
- pancolitis (20%).

Ulceration in the distal ileum occurs in 10% of patients with pancolitis (backwash ileitis) and should not be mistaken for Crohn's disease. Although backwash ileitis does not alter the surgical approach and typically disappears upon removal of the colon [17], more recent data suggest a higher susceptibility of these patients to develop 'pouch'-itis [18].

At any time, about 50% of patients are relatively asymptomatic, 30% present with mild symptoms, and 20% have moderate to severe symptoms [19]. Many patients experience periods of complete remission, however, the cumulative probability of remaining relapse-free is only around 20% after two years and decreases to less than 5% after 10 years. Chronically involved segments of the colon lose their normal haustral folds and take on a foreshortened, flat, and rigid pipe-like appearance (burned out colitis).

Symptoms and diagnosis

The clinical manifestations of ulcerative colitis vary with the severity of the disease in which frequent exacerbations and remissions are the rule.

Typical complaints at presentation include diarrhoea and passage of mucous and blood per rectum. Certain patients may experience urgency incontinence when the diarrhoea becomes very explosive. General physical findings are unspecific and directly related to the duration and presentation of the disease. Anorexia, weight loss, growth retardation, anaemia, general debility, abdominal pain, and fever are associated with a long-standing or fulminant course of the disease.

The first steps towards establishing the diagnosis of ulcerative colitis are rigid or flexible sigmoidoscopy. In order to evaluate the extent of the disease, colonoscopy with serial biopsies has replaced the historically predominant radiographic studies and is now considered the best staging and diagnostic procedure, in spite of the increased risk of perforation in acute disease. Endoscopic examination reveals confluent disease extending proximally from the rectum with oedematous, hyperaemic and very friable mucosa. Depending on the clinical picture on presentation (emergency), plain abdominal films of the abdomen may be indicated to rule out perforation or colonic dilatation (toxic megacolon). Unfortunately, however, the extent of the colonic diameter does not accurately predict perforation [20]. Contrast studies of the colon, such as barium or gastrograffin enema, may reveal the mucosal pattern as well as foreshortening strictures of the colon. However, these procedures are contraindicated in patients with acute disease as they may precipitate deterioration with toxic dilatation. The role of newer imaging techniques such as MRI and PET scans has not yet been defined, but they may play a role in the future if they prove to be useful for the detection of fistulas or skip lesions, for assessing the disease activity, and for the differentiation between Crohn's disease and ulcerative colitis [21, 22].

The differential diagnosis of ulcerative colitis includes, among others, Crohn's disease, indeterminate colitis, ischaemic colitis, diverticulitis, and infectious colitis. Negative stool cultures should therefore be obtained.

Complications of the disease

Toxic megacolon

The incidence of this complication ranges between 5–7% of patients with ulcerative colitis, and is usually associated with pancolitis. Around 50% of the patients present with megacolon during their first attack of ulcerative colitis [23, 24]. The patients become acutely ill with fever, tachycardia, leukocytosis, abdominal tenderness and distention. On examination, the abdomen is tender to palpation in the region of the colon, and there may be signs of an acute abdomen. Mortality of toxic megacolon has historically been reported to range from 15–30% but has fallen drastically in recent years in parallel with a more aggressive clinical ap-

proach. Fatal outcome is closely related to a delay of surgery, as well as to the occurrence of multiple organ dysfunction syndrome (MODS) [25], and of colonic perforation at presentation, the latter being responsible for excessive mortality rates of up to 40–60% as compared to 2–3% without perforation [26–28].

Perforation

Colonic perforation complicates ulcerative colitis in about 3–5% and typically occurs in the setting of toxic megacolon [20, 26]. Perforation may also be seen at a much lower frequency of about 1% in the absence of colonic dilatation and

is most commonly located in the sigmoid colon [29]. Some of these cases may be related to instrumentation of the colon (eg, colonoscopy). Despite its low incidence, free perforation is associated with more deaths than any other complication [20, 28] and should therefore be avoided with early surgery. Corticosteroid medication may mask the symptoms otherwise associated with faecal peritonitis.

Bleeding

Although rectal bleeding is the most common complaint of patients with ulcerative colitis, massive haemorrhage is a relatively rare complication [30]. Establishing whether the source of bleeding is proximal or distal to the beginning of the rectum is crucial for the clinical management.

Cancer

Ulcerative colitis is an established risk factor for developing colorectal cancer [31]. In addition, an association with a higher incidence of lymphoma with a standardised incidence ratio of up to 8.8% has been suggested [32, 33], but also questioned by other studies [34]. The extent of colonic involvement and the duration of the disease are positively correlated with cancer risk [35]. Age and extent of disease at diagnosis are independent risk factors, whereas the disease activity does not appear to be correlated with cancer risk [31]. In addition, a positive family history of colorectal cancer and the presence of primary sclerosing cholangitis are independent hazards [36-41]. The true incidence of colitis-associated cancer, however, is still a matter of controversy and varies considerably between population-based studies and studies carried out at tertiary referral centers [31, 37, 42-44]. After 10 years follow-up, 5% of patients have developed cancer. The risk after 10 years increases with 2% per year and reaches about 25% after 20 years.

In contrast to sporadic colon cancer, cancers in ulcerative colitis may not develop from colono-

scopically recognisable adenomatous polyps but rather arise from flat plaque-like dysplastic epithelium. This may be indistinguishable from adjacent non-dysplastic mucosa at endoscopy, particularly in the presence of extensive mucosal alterations with pseudopolyps. Severe dysplasia on colonoscopic biopsy is associated with a cancer present in the colon in 50% of patients [45, 46]. Cancers superimposed on ulcerative colitis are often multifocal (20%), poorly differentiated (50%), and present in an advanced stage (Stage III or more) [46, 47].

Benign strictures are observed in less than 10% of patients with chronic ulcerative colitis [48, 49], and the presence of a stricture under these circumstances should be considered malignant until proved otherwise. A colectomy should be strongly advised even if biopsies are unrevealing or showing "only" dysplasia.

Extraintestinal manifestations

Extracolonic manifestations are present in 15-25% of the patients and involve the skeleton, the skin, the eyes or the liver [50, 51]. They include peripheral arthritis (15-20%), ankylosing spondylitis and sacroiliitis (1-6%), skin lesions (pyoderma gangrenosum, erythema nodosum), hepatobiliary disease (pericholangitis, primary sclerosing cholangitis 3-5%), ocular (anterior uveitis, iritis, episcleritis), and cardiac complications (pericarditis). In children, chronic disease may result in retarded growth and development. Whereas peripheral arthritis, skin complications and episcleritis often occur parallel with the course of the colitis, spondylitis, sacroiliitis, cholangitis, and uveitis appear to be more independent from the bowel disease and hence do not respond to resection of the colon.

Patients with ulcerative colitis are at increased risk to develop thromboembolic complications, which appear to be related to a hypercoagulatory state [52]. In some patients, colectomy causes the hypercoagulopathy to resolve.

Medical management

The medical management of ulcerative colitis will not be discussed in detail in this review, as there are excellent summaries on the subject in the literature [53-57]. Drugs in several different pharmacological categories are available to control the patients' symptoms, suppress the disease activity and maintain remission. Antidiarrhoeal and antispasmodic agents may be sufficient for otherwise asymptomatic individuals; in patients with acute exacerbations, they are contraindicated in order to prevent precipitation of toxic dilatation. Enemas containing corticosteroids or 5-ASA (mesalamine, olsalazine, sulfasalazine) are effective for patients with limited disease (proctitis, left-sided colitis) but are of little value for patients with more ex-

tensive disease or pancolitis. Oral administration of 5-ASA and of prednisone are effective for the treatment of mild to moderate ulcerative colitis and to maintain its remission in 75-80% of the patients [58]. More severe forms of the disease with systemic signs and symptoms or severe abdominal pain may preferably be treated with parenteral steroids or ACTH. The patients may require hospitalisation, intravenous nutritional support, and transfusions. Association of corticosteroids with long-term toxicity as well as steroid-refractory disease have led to a more frequent use of immunosuppressive drugs. Cyclosporine A [59, 60], azathioprine or 6-mercaptopurin [61] will frequently induce and maintain remission although the latter

may take three to six months to establish an effect. More recent developments include treatment with nicotine [62], thalidomid, or infliximab, as well as several other emerging biological modifiers [63,

64]. The use of antibiotics remains controversial in the medical management except for fulminant/toxic colitis [65].

Surgical treatment – indications

Although the medical treatment for ulcerative colitis is similar to that for Crohn's disease, the surgical therapies differ completely. For this reason, it is imperative that surgical therapies are based on a diagnosis that has been confirmed histologically [14]. The surgical treatment in patients with ulcerative colitis should aim to:

- cure the patient of the disease and thereby minimise exposure to side-effects of medical therapy;
- perform a reconstruction with low morbidity whilst permitting a good quality of life.

The surgical approaches for achieving these goals are shown in Figure 1. They are divided into two major categories, dealing with the *resection* on the one hand, and *reconstruction* on the other. Several combinations between alternative choices in the two categories are possible, but basically four surgical pathways have evolved. Each of these four options carries a number of inherent advantages and

disadvantages (see Table 2), and a careful counseling of the patients is therefore necessary.

Considering that not all patients with ulcerative colitis will have problems with their disease and its conservative management, the central question is how to identify those who will benefit from surgery and determining the correct timing for surgery. The selection criteria have undergone considerable revision over the last two decades. In the past, when total proctocolectomy combined with ileostomy was the only surgical option, intervention was frequently delayed to the point where both lifestyle and health were remarkably compromised. The decision-making process has remained complex, not only for medical reasons but also because the patient is situated in the center between several independent parties trying to manipulate the patient in one or the other way (see Figure 2). Performing safe surgery requires a qualified surgeon who is familiar with the disease, the procedures, and their complications.

Figure 1
Overview of surgical modules and their combinations for the management of ulcerative colitis.

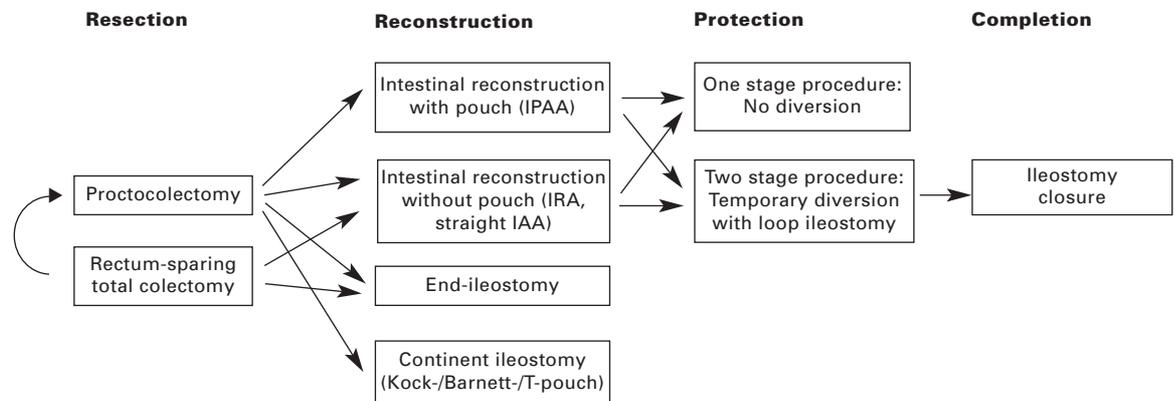
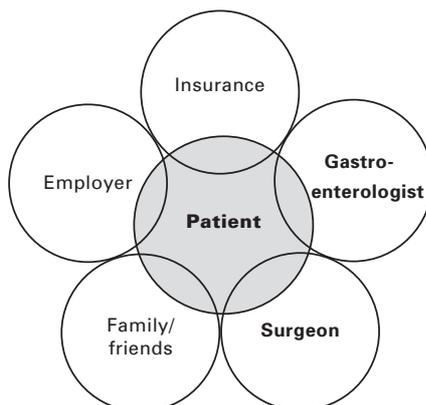


Figure 2
Complex interactions between the ulcerative colitis patient and his personal environment.



Based on the information provided in the previous sections, three categories of indications for surgery have evolved (see Table 1):

Life-threatening complications

These are certainly the most demanding to manage. The decision to carry out surgery under such circumstances, however, is usually not difficult to make. If a patient develops acute fulminant illness with toxic megacolon, a colonic perforation or massive bleeding and deteriorates despite maximised medical treatment, surgical intervention is unquestionably indicated [66–68].

For toxic megacolon, aggressive medical ther-

Table 1

Category system for indications to surgery in ulcerative colitis.

Category	manifestation
Life-threatening complications	toxic megacolon colonic perforation massive haemorrhage
Cancer-related	proven cancer presence of epithelial dysplasia in biopsies colonic "stricture" cancerophobia
"Unacceptable" disease despite adequate treatment	treatment refractoriness, frequent recurrences/flare-ups, extra-colonic manifestations chronic corticosteroid dependence side effects/intolerance/complications from medications, in particular steroids (catarract, Cushing, osteoporosis, hypertension, hyperglycemia, etc.) unacceptable life style (symptoms incompatible with expectations)

Table 2

Summary of the four surgical options, compared with regard to their advantages and disadvantages. For abbreviations: see footnote.

	PC/IPAA	TC/IRA	PC/IS	PC/CIS
Removing disease	+ to ++	(+)	++	++
Permanent stoma	-	-	+	+
External appliance	- / temp.	-	+	- to (+)
Continence	(+) to +	+	N/A	(+) to +
Continued symptoms of UC	(+)	++	-	-
Residual cancer risk	(+)	++	-	-
Maintenance operations necessary	(+)	+	-	++
Sexual dysfunction	(+)	-	(+)	(+)

apy and intensive care management are initiated and should include the use of corticosteroids, immunosuppressants (e.g. cyclosporine), and antibiotics. Sulfasalazine may be administered but has not been of significant value in the setting of fulminant colitis. If a patient does not show a response within three to five days or even worsens during this period, an emergency operation should be performed. Even if the conservative management of a severe attack has been successful to a certain point, the risk for a subsequent colectomy is over 83% [26, 69]. In these situations, the threshold for a surgical intervention should be rather low, and medical management should to be regarded as a preparation for imminent surgery.

Even in the case of an emergency operation, surgical resection of the diseased organ is the preferred strategy, because it will eliminate the source of sepsis. If a patient is in an acceptable general condition, an attempt to perform a complete excision (proctocolectomy with reconstruction and diversion) may be appropriate in experienced hands [70]. More often, however, a total abdominal colectomy with end-ileostomy, sparing the rectum and the pelvic dissection, are preferable [71]. Such an operation is safe and does not run the risk of an immediate reconstruction on the one hand, avoids the "burning of bridges" on the other, and means that a restorative completion proctectomy with pull-through procedure may still be performed after the recovery of the patient [72].

Turnball blowholes are of historical rather

than practical interest [73, 74] and have never been used in our hands. In this approach, which avoids resecting a friable colon, the colon is decompressed and vented by a skin-level right transverse and sigmoid colostomy as well as an ileostomy.

As has previously been mentioned, massive haemorrhage is a rather uncommon complication of ulcerative colitis [30]. It may be defined as a need for transfusing more than a 6 units of packed erythrocytes without cessation of the bleeding. In this situation, proctocolectomy with or without reconstruction is the operation of choice since sparing the rectum can result in missing the source of continued bleeding in 12% of patients [75].

Overall, emergency colectomy has shown an obvious trend towards safer surgery and the associated mortality has dropped from 19-30% [76, 77] to 0-1% in most of the recent series [70, 78].

Cancer risk, cancer or cancerophobia

Patients with symptomatic ulcerative colitis for more than 7 years should enter a surveillance programme and undergo two-yearly or better annual colonoscopy with multiple biopsies looking for epithelial dysplasia [79]. Once dysplasia is present, the likelihood of cancer is 20% [47]. Severe dysplasia on biopsy is associated with colorectal cancer in 40-50% of patients [80]. Consequently, prophylactic proctocolectomy is considered when any evidence of dysplasia is found.

However, three points of concern regarding the validity of the dysplasia-cancer transformation

model and the surveillance concept have to be mentioned [81, 82]. First, about 2% of patients, who have regular colonoscopies, will fall through the net and will develop cancer of the large intestine [83, 84]. Second, about 25% of ulcerative colitis patients with colorectal carcinoma do not show dysplasia in their colon except in close proximity to the cancer [47, 85]. And third, 18% of patients with a history of inflammatory bowel disease of less than eight years develop cancer [86].

Whether the practice of surveillance is adequate and cost-effective in reducing colitis-associated cancer mortality remains to be demonstrated [29, 82, 87–89]. Physicians as well as patients participating in surveillance programs, should be aware of the limitations of colonoscopy and biopsy as a means of reducing the risk of cancer in ulcerative colitis [90–92]. A proportion of patients with significant fears regarding this uncertainty, will choose to have a surgical resection earlier rather than to run a risk of developing cancer.

Disease refractory to treatment

“Intractability to medical therapy” is the third reason for surgical intervention in patients with ulcerative colitis who do not present with either of the two conditions outlined above. Objective parameters indicating failure of medical treatment include chronic steroid dependence with recurrent flare-ups of the colitis as soon as the prednisone

dose is tapered, or intolerance to and side effects of the prescribed drugs. In the absence of such objective criteria, the indication for surgery is commonly difficult to pinpoint on the basis of mere figures and should take the particular aspects of the individual patient into consideration. For this reason the term “unacceptability of the disease” appears to be more appropriate. What unacceptable means, can only be defined by the patients themselves. Neither the treating physicians nor any individual other than the patient can define an adequate quality of life, how many bowel movements are acceptable, how many social activities may be missed, what level of anaemia or how much pain are tolerable, and so forth.

Given that an adequate trial of medical therapy has previously been provided, it is important to assure that patients in this indication category should be well informed about the surgical options. There is however, neither need for, nor benefit from urging a patient to have an operation. Typically patients themselves reach a point where the day-to-day reality no longer meets their expectations, when they get tired of “organising their lives around the bathroom”. The patient’s active decision to overcome this extended experience of frustration will eventually allow them to better accept potential side effects of proctocolectomy.

Principle of elective surgery – eliminating the disease

From a theoretical standpoint, the inflamed bowel may either be completely or partially resected, or it may be rested by proximal diversion. Limited resections, in which proximal uninvolved portions of the colon were preserved, generally failed and have therefore been abandoned [93]. Over the last two decades, the surgical approach has become more defined but also more aggressive with the aim of providing the patient with a definitive solution. The surgeon should have a clear plan (as outlined in Table 2 and Figure 1) before starting an operation, but at the same time retain enough flexibility to change the approach in case of unexpected intraoperative findings (e.g. stigmata of Crohn’s disease or presence of cancer). The following two types of resection have established themselves for the treatment of ulcerative colitis.

Proctocolectomy (PC)

Proctocolectomy has evolved as the resection of choice in about 90% of patients with ulcerative colitis [94–97]. This resection eliminates all possibly affected colon from the caecum to the distal rectum and therefore involves a pelvic dissection down to the anus. Rectal mucosectomy, which once was routine, has mostly been replaced by a full thickness stapler dissection of the distal rectum at the level of the levator muscles, leaving the anal

transition zone with a circular cuff of about 1cm of rectal mucosa behind. The rationale for this approach is the ease and speed with which the procedure may be carried out, as well as avoidance of damage to the anal sphincter mechanism. In addition, it was argued that it would reduce the risk of impaired anorectal sensation although a functional difference between the staple and hand technique could not be confirmed [98, 99]. The disadvantage of this procedure is that the cuff needs to be surveyed at regular intervals (anoscopy with biopsy) and may be the source of anal dysfunction in certain patients. The manual technique with complete excision of the rectal mucosa is nowadays reserved for special situations such as the presence of a rectal cancer, patients with FAP, or technical difficulties.

Although proctocolectomy cures the patient of ulcerative colitis and improves the general health and function considerably, it has some disadvantages, and patients will never be able to lead a completely normal life [94, 97]. They will be left with the small intestine, which cannot replace the colon’s capacity for thickening and storing stools. The pelvic dissection and the manipulation around the anus may impair the hypogastric and pudendal nerve function and cause damage to the anal sphincter mechanism.

Rectum-sparing total colectomy (TC)

In this procedure, the whole colon is excised to the point of confluence of the colonic taenia which indicates the beginning of the rectum. The advantage of this approach is that it is simple and quick (e.g., emergency colectomy), avoids the pelvic and anal dissection and therefore leaves open the possibility for immediate, or later, reconstruction. The rationale for an elective rectum-sparing total colectomy has come from studies that have shown better bowel control with the rectum still in place than after proctocolectomy with ileo-anal anastomosis [100–102]. The disadvantage of this operation is that it leaves the rectal mucosa behind with the potential risk of recurrent disease and/or malignant transformation [103, 104]. Regular surveillance is required, and a completion proctocolectomy may later become necessary [101, 104].

Candidates are those 10% of all patients who have a rectum that is relative spared and has preserved its distensibility (as determined by measurement of the rectal compliance) [15, 16]. Careful patient selection and information are very important for an indication to this procedure, which is more the exception than the rule.

Oncological aspects

The finding of a colitis-associated cancer in the colon or rectum needs special consideration [45]. In this case, the surgical procedure does not only have to address the inflammatory disease but also needs to follow oncological criteria which may or may not include chemoradiation. The surgical strategy under these circumstances depends on:

- tumour location or locations (colon vs. rectum);
- tumour staging (localised vs dissemination, e.g., peritoneal carcinomatosis, distant metastases);
- whether the tumour has been identified or sus-

pected preoperatively or whether it is found incidentally during surgery;

- whether the tumour is obstructing.

The surgical treatment for localised cancers of the colon remains the same as for the underlying colitis [45, 46, 105], however based on the pathological staging of the tumour, adjuvant chemotherapy may be necessary. In the treatment of advanced disease patients should undergo neoadjuvant treatment before surgery whenever possible, unless they do not wish to proceed with a restorative operation, this is in contrast to sporadic rectal cancer, where the advantages of neoadjuvant vs. postoperative-adjuvant chemoradiation are still contested. In patients with rectal cancer superimposed on ulcerative colitis (or FAP), pelvic irradiation with a new ileal pouch in place should be avoided as it will result in scarring of the pouch and a poor functional outcome. Ideally 4–6 weeks after completion of the preoperative chemoradiation, a proctocolectomy should be performed including mucosectomy of the transitional zone and diversion with a loop ileostomy. In cases where the tumour lies very distal in the rectum the operation may have to be performed as an abdomino-perineal resection.

In the presence of metastatic disease from an unidentified colorectal cancer with no evidence of an imminent obstruction, resection is not recommended [45]. These patients require extended periods of chemotherapy during which diarrhoea is a common adverse effect. In order to avoid aggravation of side effects with unmanageable fluid shifts, preservation of colonic length is therefore advised.

Colorectal cancer arising in ulcerative colitis has a prognosis similar to cancer in the absence of colitis if equivalent stages are compared, but colitis-associated cancer is more often diagnosed at a later stage.

Principles of surgery – reconstruction

The most significant advance in surgical technique and management of ulcerative colitis involves reconstruction after a resection. In the past, end-ileostomy was the only surgical option for treatment of ulcerative colitis, yet was at the same time often unacceptable for many patients. Nowadays, a spectrum of choices with or without a permanent ileostomy are offered (see Figure 1).

Reconstruction after the removal of the diseased organ may be performed either by restoring the intestinal continuity or by diverting the faecal stream through an ileostomy. The resection will either control or eliminate the disease, whereas the reconstruction attempts to establish a postoperative state which meets the patient's short and long term physical and emotional requirements. These include (A) a quick recovery from acute bouts of

debilitating chronic illness as well as from the operation itself, (B) the acceptability and ease in dealing with intestinal function, bowel movements or a stoma, and (C) preserving the potential for surgical adjustments once the body has fully recovered. Since the choice of the best procedure may, at times, end in a compromise, it is of crucial importance that the advantages and disadvantages of the various options are discussed with the patient before surgery (see Table 2).

Restoration of intestinal continuity

The goal of restoring intestinal continuity is to avoid a permanent stoma and to maintain the anal route of evacuation. If the rectum has been removed, a faecal storage area has to be created (reservoir or pouch) in order to reduce diarrhoea

and to improve continence and hence quality of life [106, 107].

Ileo-rectal anastomosis (IRA)

In patients with a preserved rectum (as outlined in previous section), the creation of a pouch is unnecessary. Instead, a straight end-to-end ileo-rectal anastomosis (IRA) is performed [102]. Damage to autonomic innervation and the anal sphincter mechanism are avoided.

Ileo-anal anastomosis (IPAA, IAA)

The so-called ileo-anal pull-through procedure (also referred to as “restorative” proctocolectomy) is the method of choice for the majority of patients [95]. Severe faecal incontinence and preoperative evidence of Crohn’s disease are contraindications for an ileo-anal pull-through procedure. Though 7% of patients with a preoperative diagnosis of ulcerative colitis have histological evidence of Crohn’s disease in the final pathology, if clinical features of Crohn’s disease are absent, these patients may still respond favourably to an ileo-anal procedure [108–110]. Older patients need careful evaluation but the procedure is not necessarily associated with a poor outcome [111].

Although various designs of ileal pouches have been described (J, S, W, H, etc.), the ileal J-pouch has become the most common configuration because of its simplicity and a comparable function. A 12–15 cm pouch is created by folding the terminal ileum and fusing the two limbs to form one space. The tip of the pouch may either be stapled or sewn by hand [98, 99] down to the transitional cuff or the anal canal (IPAA, ileal pouch-anal anastomosis). If the pelvic floor is difficult to reach with a standard approach, the small bowel mesentery may have to be lengthened [112]. Alternatively, an S-pouch may be used [113], but this configuration often results in a functional outlet obstruction if the efferent limb is too long [114]. In rare cases where neither pouch configuration reaches the pelvis, the planned pouch has to be abandoned and a straight ileo-anal anastomosis (IAA) is carried out. The overall satisfaction and continence rate achieved by IAA are nonetheless considerably lower than for a pouch. Anastomotic complications may furthermore necessitate creation of an ileostomy in 32% of patients [107, 115].

While the ileo-anal anastomosis frequently needs to be protected by a temporary diverting loop ileostomy to allow the pouch and/or anastomosis to heal, the ileorectal anastomosis hardly ever requires such a two-stage procedure. In the past, the two-stage procedure was routine in all patients undergoing an IPAA, but recent series suggest that a one-stage procedure without temporary diversion is possible in a selection of patients [116–118]. Its major advantage is that both a second operation (ileostomy take-down) as well as ileostomy-associated morbidity (20%) can be avoided. The disadvantage of a one-stage procedure, on the other hand, is a more difficult adjust-

ment period in the immediate postoperative period caused by the change in bowel habit and the fact that the new pouch is more rigid during the period of postoperative swelling and scarring. The period spent in hospital is roughly the same for the one-stage procedure as for the combined duration of hospitalisation of the two-stage procedure. Patients who are malnourished, on corticosteroids, very obese, or in whom intraoperative technical difficulties arise, do not qualify for a one-stage procedure. However, an ileostomy should be discouraged in patients with portal hypertension (primary sclerosing cholangitis) in order to avoid peristomal varices [119].

Take-down of the temporary ileostomy should not be carried out within 6 weeks of the primary surgery. Requirements are that (A) the pouch has healed, as evidenced by the radiographic absence of a leak or stricture on a barium pouchogram [120], (B) the patient’s general health and nutritional status have returned to normal, and (C) the patient has been completely weaned off steroids. Evidence of pouch-related complications is found in 4–12% of patients after IPAA [121–124]. A second operation surgery to salvage the pouch is warranted and successful in two thirds of these patients [124]. Delaying the ileostomy closure until pouch-related problems are solved has not been associated with deleterious effects on pouch function [125].

Intestinal diversion

End ileostomy (Brooke)

In the past, proctocolectomy with an end-ileostomy, as described by Brooke [126], was the “gold standard” by which any other operation for ulcerative colitis had to be judged. Today, the creation of a Brooke ileostomy is chosen in patients who either do not qualify for a restorative procedure or who prefer a stoma. With the exception of a Hartmann-type rectum-sparing emergency colectomy with diversion, the ileostomy will be permanent. Its advantages are the absence of an anastomosis and a predictable functional result without anal incontinence [127]. Its disadvantages, however, include the need for an external ileostomy device, which has to be emptied several times per day, as well as the psychological and social implications of a permanent ileostomy [128]. In addition, device-related problems such as leakage and skin irritation are not uncommon [129].

Continent ileostomy (Kock-/Barnett pouch, T-pouch)

The concept of a continent ileostomy was first described in 1969 by Kock, who developed a high volume/low pressure reservoir with an intussuscepted nipple valve [130, 131]. The principal design allows faecal material to accumulate in a pouch and to be emptied at the patient’s convenience by means of a tube intermittently introduced into the pouch, thus avoiding an appliance over the stoma. Functioning Kock pouches have achieved high levels of acceptance [132, 133], but the pro-

cedure has also been associated with numerous complications, with 15–40% of patients requiring surgical pouch revisions [134]. In the ensuing years, the pouch was subject to many modifications [135, 136], which primarily attempted to overcome the fundamental flaws associated with the valve. Valve dysfunction was mostly due to the pulling apart of the intussuscepted nipple which led to an unsatisfactorily high incidence of leakage and difficulties in intubating the pouch [137–141].

We have very recently described a completely new valve design which does not disintegrate [142]. The so-called T-pouch appears to be a promising alternative for patients who desire a continent stoma after a previous proctocolectomy with a Brooke ileostomy, and for patients who have either failed with or are not candidates for a restorative proctocolectomy [143]. Contraindications include Crohn's disease, morbid obesity, short-bowel syndrome, and excessive adhesions.

Outcome and quality of life

Over the last 20 years, the mortality of elective surgery in ulcerative colitis has dropped significantly to less than 1%, and a good functional outcome is expected in 93–95% of all patients [144]. Procedure-related parameters defining the outcome are the absence of a stoma, a low number of bowel movements per day, the absence of daytime and/or nighttime leakage, and the patient's ability to discriminate between wind and stool. More important than the number of bowel movements, however, is the ability to delay them until it is socially convenient. Other factors adding to the patient's quality of life include avoidance of disability, intact sexual function, independence from medical institutions, as well as a low long-term risk of complications, dysfunction, and maintenance operations. Procedure-related advantages and disadvantages are summarised in *Table 2*.

Once, patients have recovered from surgery and passed the adjustment period, the functional outcome appears to remain stable over years [97]. The majority of patients are continent [106] and

typically report an average of 5–7 bowel movements per day and one at night. Supportive management is important and includes the administration of bulking fibers and drugs for slowing intestinal transit as well as local application of a barrier ointment (eg, Zinc oxide) to the anus to protect the perianal skin from maceration by intestinal contents.

Despite some controversial results, most patients share the belief that the quality of life is better with an ileal pouch-anal anastomosis than with a permanent ileostomy [144, 145]. Patients who have undergone an ileo-anal procedure experience fewer restrictions on sporting activities as well as sexual function than patients with Kock pouches. Patients with a Kock pouch are less restricted in the above-mentioned activities than are patients with a Brooke ileostomy, but are more limited with regard to traveling. However, the choice of surgical procedure does not result in a significant difference with regard to the patients' social life, recreation, work, and family [128, 146].

Procedure-related complications

Perioperative morbidity

Any of the procedures performed in ulcerative colitis is associated with a number of general surgical complications, most of which will respond to non-surgical management. Since PC/IPAA has become the most frequently performed procedure, we will limit our discussion to complications inherent to this technique.

Minor perioperative complications after PC/IPAA are common (63%), but surgical re-exploration is required in only about 24% of the patients [123]. The most common complications include small bowel obstruction (17–20%) [147, 148], wound infections (5.8%), and bleeding (3.8%) [123].

Procedure-related complications (see *Table 3*), on the other hand, involve leaks in the pouch or at the anastomosis with or without pelvic sepsis, development of an abscess or of fistulas, and complications related to the ileostomy. A leak may become evident as diffuse peritonitis, an abscess,

or as a fistula with pouch-vaginal or pouch-perineal fistulas, the latter being associated with a high rate of pouch failures [149, 150]. In the two largest series, 73 of 1508 patients (4.8%) and 46 of 1680 patients (2.7%) were reported to have developed pelvic abscess and sepsis after ileal pouch-anal anastomosis [121, 123, 151]. Although salvage surgery including repeat ileal pouch-anal anastomosis has been performed in the majority of patients, 17–26% of this subset eventually lost their pouch [121, 124, 151]. In case of true pouch failure, the surgical options include conversion to a Brooke ileostomy or a continent ileostomy (as has been described in previous sections) [142, 143].

Pouch fistulas may occur even in the absence of Crohn's disease and despite good surgical techniques. Yet, a re-evaluation of the histopathological findings is warranted [149, 150]. In spite of the fact that treatment of fistulas depends a great deal on their clinical presentation, they generally respond best to surgical revision. Pouch-vaginal fis-

Table 3

Comparison of functional outcome in large series.

Institution	publication	years	total number of patients	% with UC	mortality (%)	pelvic sepsis	definitive pouch failure	satisfaction rate (%)	number of bowel movements	day-time leakage	night-time leakage	one or more episodes of pouchitis
Mayo Clinic [184]	1998	1981–94	1310	87	0.2	7 → 3	9	91	6	7	12	48
Cleveland Clinic Ohio [123]	1995	1983–93	1005	85	1	6.8	3.4	93	6	12	29	25
Lahey Clinic [185]	1998	1980–96	628	84		6.5	2.5		6.6		28.7	
University of Utah [122]	1997	1983–97	510	87	0		0.78	95	5.8			26
University of Minneapolis [186]	1992	1980–90	253			5.1	9.9					31
St. Mark's Hospital, UK [187]	1990	1977–87	205		1		6	93	3 to 5		2	20
Auckland [188]	1999	1982–97	201	88	1.6	5	9	90	4.7			44
Hôpital Saint-Antoine, Paris [189]	1996	1983–93	171	0	0.6	4			5.2		0	
Birmingham, UK [190]	1993	1984–92	168		0	12	30 → 4					
University of Göteborg, Sweden [191]	1989	1981–87	100		0	5	3	97	7		30	

tulas, whose spontaneous healing is rare, occur in up to 7% percent of women after IPAA. In these cases, delaying the ileostomy closure or creation of a new ileostomy is appropriate in combination with adequate local debridement and fistula repair [152].

Morbidity associated with ileostomy and ileostomy take-down

Ileostomy complications include episodes of small bowel obstruction, high stoma output with risk of dehydration, stoma prolapse, parastomal abscess formation and fistulisation, development of a peristomal hernia, retraction or stenosis of the ileostomy, and skin irritation [153]. While most of these circumstances necessitate surgical revision in patients with a permanent Brooke ileostomy [154], conservative management with a temporary diverting ileostomy attempts to bridge the gap until the ileostomy can eventually be closed. At the time of the ileostomy closure, episodes of small bowel obstruction (5–25%) or anastomotic complications are the most frequently encountered problems [155].

Pouchitis

Pouchitis is the most frequent long-term complication after an ileal pouch-anal anastomosis or a continent ileostomy in patients with ulcerative colitis. It occurs in up to 50% of ulcerative colitis patients within 10 years after surgery and is responsible for the loss of 1–4% of the pouches. The pathogenesis of pouchitis remains unclear [156–158]. Plausible theories either focus on a nutritional aetiology or suggest a bacterial over-

growth within the pouch although identification of organisms typically associated with pouchitis has failed. However, more recent studies suggest that administration of probiotics such as *Lactobacillus* may reduce the risk of recurrent pouchitis [159, 160]. Steroid administration, on the other hand, has not been of any value in cases of true pouchitis; a recurrence of the underlying colitis is therefore unlikely. Pouch emptying is not part of the aetiological mechanism since these pouches empty as well as those of patients who do not experience symptoms of pouchitis [161].

Although there may be a non-specific inflammation on endoscopy and histopathology [162], the correlation of morphological findings with functional parameters is poor. For this reason, the diagnosis of pouchitis is primarily based on the following clinical criteria [163]:

- the pouch must be intact and not be defunctionalised by a diverting ileostomy;
- there must be a sudden change in the clinical course (onset of diarrhoea, fever, malaise, urgency, incontinence);
- evidence of a pouch stricture, or other reasons for pelvic symptoms such as Crohn's disease, pelvic abscess, or pouch fistula must be ruled out;
- bacteriology must be negative;
- patient should respond to metronidazole.

After the initiation of antibiotic treatment with metronidazole, symptoms will subside in a majority of patients. In refractory cases, pouch bacteriology and cytomegalovirus status should be re-evaluated, and long-term antibiotic treatment may

be necessary. Metronidazole, however, carries a risk of intolerance and side effects, such as a metallic taste and polyneuropathy with paresthesias. Alternative drugs for treating an acute episode of pouchitis, include ciprofloxacin or bismuth preparations. As has previously been mentioned, the administration of probiotics has elsewhere been shown to prevent recurrent pouchitis [159, 160], although this has not been our experience.

The diagnosis of Crohn's disease in recurrent pouchitis should only be made if re-examination of the original proctocolectomy specimen shows typical pathological features of Crohn's disease, or if Crohn's disease arises in parts of the gastrointestinal tract distant from the pouch, if biopsies taken from the pouch contain active enteritis with granulomas, or if the excised pouches show the characteristic features of Crohn's disease, including granulomas [164].

Potpourri

Primary sclerosing cholangitis and liver transplantation

Primary sclerosing cholangitis (PSC) associated with ulcerative colitis is more common in men than women and may precede intestinal manifestations by as much as 7 years [168]. Some PSC patients respond favourably to colectomy, but a majority shows progression of their hepatic disease even after proctocolectomy [169].

Complications of ulcerative colitis-associated PSC include a higher incidence of cancers of the biliary tract and the colorectum [170]. About 1% of the PSC patients develop biliary cirrhosis requiring an orthotopic liver transplantation. While the ulcerative colitis activity could be expected to be suppressed by the immunosuppressive medications, 50% of the patients thus treated show a worsening of their intestinal symptoms [171]. In addition, the risk of developing colorectal cancer appears to be higher under immunosuppression [172]. For this reason, close follow-up of these patients is of utmost importance.

Sexual dysfunction

Sexual dysfunction in patients with ulcerative colitis is not uncommon [173] and may be attributed to factors such as the general health status, drug toxicity (sulfapyridine), psycho-social implications either of the disease or the stoma, as well as to intraoperative injury to the pelvic autonomic nerves. Assessing the causative role of surgery is difficult because both male and female patients have reported improved sexual functioning after proctocolectomy [173, 174]. While almost 50% of males report preoperative impotence, postoperatively only 3–14.6% complain of impotence and 2–3% have retrograde ejaculation [175–177]. In as many as 20% of female patients, dyspareunia persists after an ileoanal anastomosis, albeit to a lesser degree than preoperatively [175].

Anorectal dysfunction, cuff dysplasia

Poor anorectal function may be related to recurrent inflammation of the retained transitional cuff mucosa triggered by the underlying ulcerative colitis (14.7%) [165, 166]. Alternatively, a stricture, which occurs in 4–11% of patients with IPAA, has to be excluded because it may result in pouch outlet obstruction with dilatation of the pouch with symptoms of overflow urgency and frequent bowel movements.

The incidence of dysplasia in the retained anal transition-zone mucosa is low [165]. Frequent follow-up with biopsies is recommended in patients whose cuff has been preserved. For persistent or recurrent dysplasia, a completion mucosectomy is recommended [167].

Pregnancy

Ulcerative colitis as such does not appear to reduce fertility, but it might increase the risk for preterm labor or spontaneous abortion [178, 179]. The impact of abdominal and pelvic surgery with IPAA on postoperative fertility in women of child-bearing age is still unknown [180]. Moreover, pregnancy and birth may be expected to have a negative impact on the pelvic floor, faecal continence and pouch function. An analysis by the Mayo Clinic, however, found no difference in pouch function between woman with or without children [181, 182].

Current controversies

Several aspects of surgical management of ulcerative colitis have not yet been completely defined and require further analysis. Among these are the manner in which the patient with indeterminate colitis, older age and co-morbid medical conditions should be surgically treated, the use of mucosectomy, temporary ileostomy, and whether laparoscopy should be promoted for proctocolectomy [183].

We are indebted to Petra R. Lott, PhD, for her support in the preparation and editing of this manuscript.

Correspondence:

Andreas M. Kaiser, M.D.
Assistant Professor of Surgery
Division of Colon and Rectal Surgery
Keck School of Medicine
University of Southern California
1450 San Pablo Street, DEI 5400
Los Angeles, CA 90033
USA
e-mail: akaiser@surgery.usc.edu

References

- 1 Farmer RG, Easley KA, Rankin GB. Clinical patterns, natural history, and progression of ulcerative colitis. A long-term follow-up of 1116 patients. *Dig Dis Sci* 1993; 38:1137-46.
- 2 Andres PG, Friedman LS. Epidemiology and the natural course of inflammatory bowel disease. *Gastroenterol Clin North Am* 1999; 28:255-81, vii.
- 3 Brostrom O. Ulcerative colitis in Stockholm County - a study of epidemiology, prognosis, mortality and cancer risk with special reference to a surveillance program. *Acta Chir Scand* 1986 (Suppl.); 534:1-60.
- 4 Bernstein CN, Blanchard JF, Rawsthorne P, Wajda A. Epidemiology of Crohn's disease and ulcerative colitis in a central Canadian province: a population-based study. *Am J Epidemiol* 1999; 149:916-24.
- 5 Lashner BA. Epidemiology of inflammatory bowel disease. *Gastroenterol Clin North Am* 1995; 24:467-74.
- 6 Niv Y, Abuksis G, Fraser GM. Epidemiology of ulcerative colitis in Israel: a survey of Israeli kibbutz settlements. *Am J Gastroenterol* 2000; 95:693-8.
- 7 Bjornsson S, Johannsson JH. Inflammatory bowel disease in Iceland, 1990-1994: a prospective, nationwide, epidemiological study. *Eur J Gastroenterol Hepatol* 2000; 12:31-8.
- 8 Stewenius J, Adnerhill I, Ekelund G, Floren CH, Fork FT, Janzon L, et al. Ulcerative colitis and indeterminate colitis in the city of Malmo, Sweden. A 25-year incidence study. *Scand J Gastroenterol* 1995; 30:38-43.
- 9 Shivananda S, Lennard-Jones J, Logan R, Fear N, Price A, Carpenter L, et al. Incidence of inflammatory bowel disease across Europe: is there a difference between north and south? Results of the European Collaborative Study on Inflammatory Bowel Disease (EC-IBD). *Gut* 1996; 39:690-7.
- 10 Corrao G, Tragnone A, Caprilli R, Trallori G, Papi C, Andreoli A, et al. Risk of inflammatory bowel disease attributable to smoking, oral contraception and breastfeeding in Italy: a nationwide case-control study. Cooperative Investigators of the Italian Group for the Study of the Colon and the Rectum (GISC). *Int J Epidemiol* 1998; 27:397-404.
- 11 Guslandi M. Nicotine treatment for ulcerative colitis. *Br J Clin Pharm* 1999; 48:481-4.
- 12 Birtwistle J. Quitting smoking could increase your risk of surgery for ulcerative colitis. *Br J Th Nurs* 1995; 5:27-8.
- 13 Thomas GA, Rhodes J, Green JT. Inflammatory bowel disease and smoking—a review. *Am J Gastroenterol* 1998; 93:144-9.
- 14 Moum B, Ekbom A, Vatn MH, Aadland E, Sauar J, Lygren I, et al. Inflammatory bowel disease: re-evaluation of the diagnosis in a prospective population based study in south eastern Norway. *Gut* 1997; 40:328-32.
- 15 Kleer CG, Appelman HD. Ulcerative colitis: patterns of involvement in colorectal biopsies and changes with time. *Am J Surg Path* 1998; 22:983-9.
- 16 Kim B, Barnett JL, Kleer CG, Appelman HD. Endoscopic and histological patchiness in treated ulcerative colitis. *Am J Gastroenterol* 1999; 94:3258-62.
- 17 Gustavsson S, Weiland LH, Kelly KA. Relationship of backwash ileitis to ileal pouchitis after ileal pouch-anal anastomosis. *Dis Colon Rectum* 1987; 30:25-8.
- 18 Schmidt CM, Lazenby AJ, Hendrickson RJ, Sitzmann JV. Preoperative terminal ileal and colonic resection histopathology predicts risk of pouchitis in patients after ileoanal pull-through procedure. *Ann Surg* 1998; 227:654-62; discussion 663-5.
- 19 Hendriksen C, Kreiner S, Binder V. Long term prognosis in ulcerative colitis - based on results from a regional patient group from the county of Copenhagen. *Gut* 1985; 26:158-63.
- 20 Greenstein AJ, Barth JA, Sachar DB, Aufses AH, Jr. Free colonic perforation without dilatation in ulcerative colitis. *Am J Surg* 1986; 152:272-5.
- 21 Bicik I, Bauerfeind P, Breitbart T, von Schulthess GK, Fried M. Inflammatory bowel disease activity measured by Positron-emission Tomography. *Lancet* 1997; 350 (9073):262.
- 22 Durno CA, Sherman P, Williams T, Shuckett B, Dupuis A, Griffiths AM. Magnetic resonance imaging to distinguish the type and severity of pediatric inflammatory bowel diseases. *J Pediatr Gastroenterol Nutr* 2000; 30:170-174.
- 23 Jalan KN, Sircus W, Card WI, Falconer CW, Bruce CB, Crean GP, et al. An experience of ulcerative colitis. I. Toxic dilatation in 55 cases. *Gastroenterology* 1969; 57:68-82.
- 24 Norland CC, Kirsner JB. Toxic dilatation of colon (toxic megacolon): etiology, treatment and prognosis in 42 patients. *Medicine* 1969; 48:229-50.
- 25 Caprilli R, Latella G, Vernia P, Frieri G. Multiple organ dysfunction in ulcerative colitis. *Am J Gastroenterol* 2000; 95:1258-62.
- 26 Heppell J, Farkouh E, Dube S, Peloquin A, Morgan S, Bernard D. Toxic megacolon. An analysis of 70 cases. *Dis Colon Rectum* 1986; 29:789-92.
- 27 Greenstein AJ, Sachar DB, Gibas A, Schrag D, Heimann T, Janowitz HD, et al. Outcome of toxic dilatation in ulcerative and Crohn's colitis. *J Clin Gastroenterol* 1985; 7:137-43.
- 28 Fry PD, Atkinson KG. Current surgical approach to toxic megacolon. *Surg Gyn Obst* 1976; 143:26-30.
- 29 Koobatian GJ, Choi PM. Safety of surveillance colonoscopy in long-standing ulcerative colitis. *Am J Gastroenterol* 1994; 89:1472-5.
- 30 Pardi DS, Loftus EV, Jr., Tremaine WJ, Sandborn WJ, Alexander GL, Balm RK, et al. Acute major gastrointestinal haemorrhage in inflammatory bowel disease. *Gastrointest Endosc* 1999; 49:153-7.
- 31 Ekbom A, Helmick C, Zack M, Adami HO. Ulcerative colitis and colorectal cancer. A population-based study. *N Engl J Med* 1990; 323:1228-33.
- 32 Greenstein AJ, Mullin GE, Strauchen JA, Heimann T, Janowitz HD, Aufses AH, Jr., et al. Lymphoma in inflammatory bowel disease. *Cancer* 1992; 69:1119-23.
- 33 Abulafi AM, Fiddian RV. Malignant lymphoma in ulcerative colitis. Report of a case. *Dis Colon Rectum* 1990; 33:615-8.
- 34 Loftus EV, Jr., Tremaine WJ, Habermann TM, Harmsen WS, Zinsmeister AR, Sandborn WJ. Risk of lymphoma in inflammatory bowel disease. *Am J Gastroenterol* 2000; 95:2308-12.
- 35 Gillen CD, Walmsley RS, Prior P, Andrews HA, Allan RN. Ulcerative colitis and Crohn's disease: a comparison of the colorectal cancer risk in extensive colitis. *Gut* 1994; 35:1590-2.
- 36 Nuako KW, Ahlquist DA, Mahoney DW, Schaid DJ, Siems DM, Lindor NM. Familial predisposition for colorectal cancer in chronic ulcerative colitis: a case-control study. *Gastroenterology* 1998; 115:1079-83.
- 37 Karlen P, Lofberg R, Brostrom O, Leijonmarck CE, Hellers G, Persson PG. Increased risk of cancer in ulcerative colitis: a population-based cohort study. *Am J Gastroenterol* 1999; 94:1047-52.
- 38 Shetty K, Rybicki L, Brzezinski A, Carey WD, Lashner BA. The risk for cancer or dysplasia in ulcerative colitis patients with primary sclerosing cholangitis. *Am J Gastroenterol* 1999; 94:1643-9.
- 39 Brentnall TA, Haggitt RC, Rabinovitch PS, Kimmey MB, Bronner MP, Levine DS, et al. Risk and natural history of colonic neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis. *Gastroenterology* 1996; 110:331-8.
- 40 Marchesa P, Lashner BA, Lavery IC, Milsom J, Hull TL, Strong SA, et al. The risk of cancer and dysplasia among ulcerative colitis patients with primary sclerosing cholangitis. *Am J Gastroenterol* 1997; 92:1285-8.
- 41 Kornfeld D, Ekbom A, Ihre T. Is there an excess risk for colorectal cancer in patients with ulcerative colitis and concomitant primary sclerosing cholangitis? A population based study. *Gut* 1997; 41:522-5.
- 42 Gilat T, Fireman Z, Grossman A, Hachon D, Kadish U, Ron E, et al. Colorectal cancer in patients with ulcerative colitis. A population study in central Israel. *Gastroenterology* 1988; 94:870-7.
- 43 Palli D, Trallori G, Saieva C, Tarantino O, Edili E, D'Albasio G, et al. General and cancer specific mortality of a population based cohort of patients with inflammatory bowel disease: the Florence Study. *Gut* 1998; 42:175-9.
- 44 Ransohoff DF. Colon cancer in ulcerative colitis. *Gastroenterology* 1988; 94:1089-91.
- 45 Taylor BA, Wolff BG, Dozois RR, Kelly KA, Pemberton JH, Beart RW, Jr. Ileal pouch-anal anastomosis for chronic ulcerative colitis and familial polyposis coli complicated by adenocarcinoma. *Dis Colon Rectum* 1988; 31:358-62.
- 46 van Heerden JA, Beart RW, Jr. Carcinoma of the colon and rectum complicating chronic ulcerative colitis. *Dis Colon Rectum* 1980; 23:155-9.
- 47 Connell WR, Talbot IC, Harpaz N, Britto N, Wilkinson KH, Kamm MA, et al. Clinicopathological characteristics of colorectal carcinoma complicating ulcerative colitis. *Gut* 1994; 35:1419-23.
- 48 Gumaste V, Sachar DB, Greenstein AJ. Benign and malignant colorectal strictures in ulcerative colitis. *Gut* 1992; 33:938-41.

- 49 Lashner BA, Turner BC, Bostwick DG, Frank PH, Hanauer SB. Dysplasia and cancer complicating strictures in ulcerative colitis. *Dig Dis Sci* 1990; 35:349-52.
- 50 Voigt E, Griga T, Tromm A, Henschel MG, Vorgerd M, May B. Polymyositis of the skeletal muscles as an extraintestinal complication in quiescent ulcerative colitis. *Int J Colorect Dis* 1999; 14:304-7.
- 51 Greenstein AJ, Gennuso R, Sachar DB, Heimann T, Smith H, Janowitz HD, et al. Extraintestinal cancers in inflammatory bowel disease. *Cancer* 1985; 56:2914-21.
- 52 Talbot RW, Heppell J, Dozois RR, Beart RW, Jr. Vascular complications of inflammatory bowel disease. *Mayo Clin Proc* 1986; 61:140-5.
- 53 Sands BE. Therapy of inflammatory bowel disease. *Gastroenterology* 2000; 118:S68-82.
- 54 Robinson M. Medical therapy of inflammatory bowel disease for the 21st century. *Eur J Surg* 1998 (suppl.):90-8.
- 55 Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults. American College of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol* 1997; 92:204-11.
- 56 Stein RB, Hanauer SB. Medical therapy for inflammatory bowel disease. *Gastroenterol Clin North Am* 1999; 28:297-321.
- 57 Marion JF, Present DH. The modern medical management of acute, severe ulcerative colitis. *Eur J Gastroenterol Hepatol* 1997; 9:831-5.
- 58 Sachar DB. Maintenance therapy in ulcerative colitis and Crohn's disease. *J Clin Gastroenterol* 1995; 20:117-22.
- 59 Lichtiger S, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, et al. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. *N Engl J Med* 1994; 330:1841-5.
- 60 Kornbluth A, Present DH, Lichtiger S, Hanauer S. Cyclosporin for severe ulcerative colitis: a user's guide. *Am J Gastroenterol* 1997; 92:1424-8.
- 61 Linn FV, Peppercorn MA. Drug therapy for inflammatory bowel disease: Part II. *Am J Surg* 1992; 164:178-85.
- 62 Sandborn WJ. Nicotine therapy for ulcerative colitis: a review of rationale, mechanisms, pharmacology, and clinical results. *Am J Gastroenterol* 1999; 94:1161-71.
- 63 Sandborn WJ, Hanauer SB. Antitumour necrosis factor therapy for inflammatory bowel disease: a review of agents, pharmacology, clinical results, and safety. *Inflamm Bowel Dis* 1999; 5:119-33.
- 64 Sands BE. Novel therapies for inflammatory bowel disease. *Gastroenterol Clin North Am* 1999; 28:323-51.
- 65 Peppercorn MA. Are antibiotics useful in the management of nontoxic severe ulcerative colitis? *J Clin Gastroenterol* 1993; 17:14-7.
- 66 Hawley PR. Emergency surgery for ulcerative colitis. *World J Surg* 1988; 12:169-73.
- 67 Katz JA. Medical and surgical management of severe colitis. *Sem Gastrointest Dis* 2000; 11:18-32.
- 68 Muscroft TJ, Warren PM, Asquith P, Montgomery RD, Sokhi GS. Toxic megacolon in ulcerative colitis: a continuing challenge. *Postgrad Med J* 1981; 57:223-7.
- 69 Grant CS, Dozois RR. Toxic megacolon: ultimate fate of patients after successful medical management. *Am J Surg* 1984; 147:106-10.
- 70 Ziv Y, Fazio VW, Church JM, Milsom JW, Schroeder TK. Safety of urgent restorative proctocolectomy with ileal pouch-anal anastomosis for fulminant colitis. *Dis Colon Rectum* 1995; 38:345-9.
- 71 Aeberhard P. [Toxic megacolon: surgical timing important:]. *Zentralbl Chir* 1998; 123:1365-9.
- 72 Jamart J, Boissel P, Debs A, Grosdidier J. Total colectomy with ileorectal anastomosis in surgical management of toxic megacolon. *Langenbeck Arch Chir* 1983; 360:159-65.
- 73 Turnbull RB, Jr., Hawk WA, Weakley FL. Surgical treatment of toxic megacolon. Ileostomy and colostomy to prepare patients for colectomy. *Am J Surg* 1971; 122:325-31.
- 74 Turnbull RB, Jr., Weakley FL, Hawk WA, Schofield P. Choice of operation for the toxic megacolon phase of nonspecific ulcerative colitis. *Surg Clin North Am* 1970; 50:1151-69.
- 75 Robert JH, Sachar DB, Aufses AH, Jr., Greenstein AJ. Management of severe haemorrhage in ulcerative colitis. *Am J Surg* 1990; 159:550-5.
- 76 Van Heerden JA, McIlrath DC, Adson MA. The surgical aspects of chronic mucosal inflammatory bowel disease (chronic ulcerative colitis). *Ann Surg* 1978; 187:536-41.
- 77 Sirinek KR, Tetrick CE, Thomford NR, Pace WG. Total proctocolectomy and ileostomy: procedure of choice for acute toxic megacolon. *Arch Surg* 1977; 112:518-22.
- 78 Fleshner PR, Michelassi F, Rubin M, Hanauer SB, Plevy SE, Targan SR. Morbidity of subtotal colectomy in patients with severe ulcerative colitis unresponsive to cyclosporin. *Dis Colon Rectum* 1995; 38:1241-5.
- 79 Anonymous. Ulcerative colitis and colon carcinoma: epidemiology, surveillance, diagnosis, and treatment. The Society for Surgery of the Alimentary Tract, American Gastroenterological Association American Society for Liver Diseases, American Society for Gastrointestinal Endoscopy, American Hepato-Pancreato-Biliary Association. *J Gastrointest Surg* 1998; 2:305-6.
- 80 Rosenstock E, Farmer RG, Petras R, Sivak MV, Jr., Rankin GB, Sullivan BH. Surveillance for colonic carcinoma in ulcerative colitis. *Gastroenterology* 1985; 89:1342-6.
- 81 Woolrich AJ, DaSilva MD, Korelitz BL. Surveillance in the routine management of ulcerative colitis: the predictive value of low-grade dysplasia. *Gastroenterology* 1992; 103:431-8.
- 82 Collins RH, Jr., Feldman M, Fordtran JS. Colon cancer, dysplasia, and surveillance in patients with ulcerative colitis. A critical review. *N Engl J Med* 1987; 316:1654-8.
- 83 Lennard-Jones JE, Morson BC, Ritchie JK, Williams CB. Cancer surveillance in ulcerative colitis. Experience over 15 years. *Lancet* 1983; 2:149-52.
- 84 Sachar DB. Clinical and colonoscopic surveillance in ulcerative colitis: are we saving colons or saving lives? *Gastroenterology* 1993; 105:588-97.
- 85 Ransohoff DF, Riddell RH, Levin B. Ulcerative colitis and colonic cancer. Problems in assessing the diagnostic usefulness of mucosal dysplasia. *Dis Colon Rectum* 1985; 28:383-8.
- 86 Mayer R, Wong WD, Rothenberger DA, Goldberg SM, Madoff RD. Colorectal cancer in inflammatory bowel disease: a continuing problem. *Dis Colon Rectum* 1999; 42:343-7.
- 87 Delco F, Sonnenberg A. A decision analysis of surveillance for colorectal cancer in ulcerative colitis. *Gut* 2000; 46:500-6.
- 88 Karlen P, Kornfeld D, Brostrom O, Lofberg R, Persson PG, Ekbohm A. Is colonoscopic surveillance reducing colorectal cancer mortality in ulcerative colitis? A population based case control study. *Gut* 1998; 42:711-4.
- 89 Gyde S. Screening for colorectal cancer in ulcerative colitis: dubious benefits and high costs. *Gut* 1990; 31:1089-92.
- 90 Solomon MJ, Schnitzler M. Cancer and inflammatory bowel disease: bias, epidemiology, surveillance, and treatment. *World J Surg* 1998; 22:352-8.
- 91 Bernstein CN, Shanahan F, Weinstein WM. Are we telling patients the truth about surveillance colonoscopy in ulcerative colitis? *Lancet* 1994; 343:71-4.
- 92 Corman ML. Understanding surveillance colonoscopy. *Lancet* 1994; 343:556-7.
- 93 Varma JS, Browning GG, Smith AN, Small WP, Sircus W. Mucosal proctectomy and colo-anal anastomosis for distal ulcerative proctocolitis. *Br J Surg* 1987; 74:381-3.
- 94 Pemberton JH, Kelly KA, Beart RW, Jr., Dozois RR, Wolff BG, Ilstrup DM. Ileal pouch-anal anastomosis for chronic ulcerative colitis. Long-term results. *Ann Surg* 1987; 206:504-13.
- 95 Beart RW, Jr. Sphincter saving operations for chronic ulcerative colitis. *Adv Surgery* 1990; 23:195-209.
- 96 Beart RW, Jr. Proctocolectomy and ileoanal anastomosis. *World J Surg* 1988; 12:160-3.
- 97 McIntyre PB, Pemberton JH, Wolff BG, Beart RW, Dozois RR. Comparing functional results one year and ten years after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Dis Colon Rectum* 1994; 37:303-7.
- 98 Reilly WT, Pemberton JH, Wolff BG, Nivatvongs S, Devine RM, Litchy WJ, et al. Randomized prospective trial comparing ileal pouch-anal anastomosis performed by excising the anal mucosa to ileal pouch-anal anastomosis performed by preserving the anal mucosa. *Ann Surg* 1997; 225:666-76; discussion 676-7.
- 99 McIntyre PB, Pemberton JH, Beart RW, Jr., Devine RM, Nivatvongs S. Double-stapled vs. handsewn ileal pouch-anal anastomosis in patients with chronic ulcerative colitis. *Dis Colon Rectum* 1994; 37:430-3.
- 100 van Duijvendijk P, Slors JF, Taat CW, Oosterveld P, Vasen HF. Functional outcome after colectomy and ileorectal anastomosis compared with proctocolectomy and ileal pouch-anal anastomosis in familial adenomatous polyposis. *Ann Surg* 1999; 230:648-54.

- 101 Soravia C, O'Connor BI, Berk T, McLeod RS, Cohen Z. Functional outcome of conversion of ileorectal anastomosis to ileal pouch-anal anastomosis in patients with familial adenomatous polyposis and ulcerative colitis. *Dis Colon Rectum* 1999; 42:903-8.
- 102 Leijonmarck CE, Lofberg R, Ost A, Hellers G. Long-term results of ileorectal anastomosis in ulcerative colitis in Stockholm County. *Dis Colon Rectum* 1990; 33:195-200.
- 103 Farnell MB, Van Heerden JA, Beart RW, Jr., Weiland LH. Rectal preservation in nonspecific inflammatory disease of the colon. *Ann Surg* 1980; 192:249-53.
- 104 Oakley JR, Lavery IC, Fazio VW, Jagelman DG, Weakley FL, Easley K. The fate of the rectal stump after subtotal colectomy for ulcerative colitis. *Dis Colon Rectum* 1985; 28:394-6.
- 105 Ziv Y, Fazio VW, Strong SA, Oakley JR, Milsom JW, Lavery IC. Ulcerative colitis and coexisting colorectal cancer: recurrence rate after restorative proctocolectomy. *Ann Surg Oncol* 1994; 1:512-5.
- 106 Goes R, Beart RW, Jr. Physiology of ileal pouch-anal anastomosis. Current concepts. *Dis Colon Rectum* 1995; 38:996-1005.
- 107 Taylor BM, Beart RW, Jr., Dozois RR, Kelly KA, Phillips SF. Straight ileoanal anastomosis v ileal pouch-anal anastomosis after colectomy and mucosal proctectomy. *Arch Surg* 1983; 118:696-701.
- 108 Hyman NH, Fazio VW, Tuckson WB, Lavery IC. Consequences of ileal pouch-anal anastomosis for Crohn's colitis. *Dis Colon Rectum* 1991; 34:653-7.
- 109 Panis Y, Poupard B, Nemeth J, Lavergne A, Hautefeuille P, Valleur P. Ileal pouch/anal anastomosis for Crohn's disease. *Lancet* 1996; 347:854-7.
- 110 Pezim ME, Pemberton JH, Beart RW, Jr., Wolff BG, Dozois RR, Nivatvongs S, et al. Outcome of «indeterminant» colitis following ileal pouch-anal anastomosis. *Dis Colon Rectum* 1989; 32:653-8.
- 111 Tan HT, Connolly AB, Morton D, Keighley MR. Results of restorative proctocolectomy in the elderly. *Int J Colorect Dis* 1997; 12:319-22.
- 112 Goes RN, Nguyen P, Huang D, Beart RW, Jr. Lengthening of the mesentery using the marginal vascular arcade of the right colon as the blood supply to the ileal pouch. *Dis Colon Rectum* 1995; 38:893-5.
- 113 Tuckson WB, Fazio VW. Functional comparison between double and triple ileal loop pouches. *Dis Colon Rectum* 1991; 34:17-21.
- 114 Fonkalsrud EW, Bustorff-Silva J. Reconstruction for chronic dysfunction of ileoanal pouches. *Ann Surg* 1999; 229:197-204.
- 115 Rintala RJ, Lindahl H. Restorative proctocolectomy for ulcerative colitis in children - is the J-pouch better than straight pull-through? *J Ped Surg* 1996; 31:530-3.
- 116 Galandiuk S, Wolff BG, Dozois RR, Beart RW, Jr. Ileal pouch-anal anastomosis without ileostomy. *Dis Colon Rectum* 1991; 34:870-3.
- 117 Gorfine SR, Gelernt IM, Bauer JJ, Harris MT, Kree I. Restorative proctocolectomy without diverting ileostomy. *Dis Colon Rectum* 1995; 38:188-94.
- 118 Dolgin SE, Shlasko E, Gorfine S, Benkov K, Leleiko N. Restorative proctocolectomy in children with ulcerative colitis utilizing rectal mucosectomy with or without diverting ileostomy. *J Ped Surg* 1999; 34:837-9; discussion 839-40.
- 119 Kartheuser AH, Dozois RR, Wiesner RH, LaRusso NE, Ilstrup DM, Schleck CD. Complications and risk factors after ileal pouch-anal anastomosis for ulcerative colitis associated with primary sclerosing cholangitis. *Ann Surg* 1993; 217:314-20.
- 120 Malcolm PN, Bhagat KK, Chapman MA, Davies SG, Williams NS, Murfitt JB. Complications of the ileal pouch: is the pouchogram a useful predictor? *Clin Radiol* 1995; 50:613-7.
- 121 Farouk R, Dozois RR, Pemberton JH, Larson D. Incidence and subsequent impact of pelvic abscess after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Dis Colon Rectum* 1998; 41:1239-43.
- 122 Dayton MT, Larsen KP. Outcome of pouch-related complications after ileal pouch-anal anastomosis. *Am J Surg* 1997; 174:728-31; discussion 731-2.
- 123 Fazio VW, Ziv Y, Church JM, Oakley JR, Lavery IC, Milsom JW, et al. Ileal pouch-anal anastomoses complications and function in 1005 patients. *Ann Surg* 1995; 222:120-7.
- 124 Galandiuk S, Scott NA, Dozois RR, Kelly KA, Ilstrup DM, Beart RW, Jr., et al. Ileal pouch-anal anastomosis. Reoperation for pouch-related complications. *Ann Surg* 1990; 212:446-52; discussion 452-4.
- 125 Hyman NH, Fazio VW, Tuckson WB, Lavery IC. Consequences of delayed ileostomy closure after ileal pouch-anal anastomosis. *Dis Colon Rectum* 1992; 35:870-3.
- 126 Brooke BN. Ileostomy. *Surgery* 1968; 64:678-80.
- 127 Morowitz DA, Kirsner JB. Ileostomy in ulcerative colitis. A questionnaire study of 1, 803 patients. *Am J Surg* 1981; 141:370-5.
- 128 Kohler LW, Pemberton JH, Zinsmeister AR, Kelly KA. Quality of life after proctocolectomy. A comparison of Brooke ileostomy, Kock pouch, and ileal pouch-anal anastomosis. *Gastroenterology* 1991; 101:679-84.
- 129 Carlstedt A, Fasth S, Hulten L, Nordgren S, Palselius I. Long-term ileostomy complications in patients with ulcerative colitis and Crohn's disease. *Int J Colorect Dis* 1987; 2:22-5.
- 130 Kock NG, Darle N, Kewenter J, Myrvold H, Philipson B. The quality of life after proctocolectomy and ileostomy: a study of patients with conventional ileostomies converted to continent ileostomies. *Dis Colon Rectum* 1974; 17:287-92.
- 131 Kock NG. Intra-abdominal "reservoir" in patients with permanent ileostomy. Preliminary observations on a procedure resulting in faecal "continence" in five ileostomy patients. *Arch Surg* 1969; 99:223-31.
- 132 Little VR, Barbour S, Schrock TR, Welton ML. The continent ileostomy: long-term durability and patient satisfaction. *J Gastrointest Surg* 1999; 3:625-32.
- 133 Ojerskog B, Kock NG, Nilsson LO, Philipson BM, Ahren C. Long-term follow-up of patients with continent ileostomies. *Dis Colon Rectum* 1990; 33:184-9.
- 134 Dozois RR, Kelly KA, Ilstrup D, Beart RW, Jr., Beahrs OH. Factors affecting revision rate after continent ileostomy. *Arch Surg* 1981; 116:610-3.
- 135 Barnett WO. Modified techniques for improving the continent ileostomy. *Am Surg* 1984; 50:66-9.
- 136 Cohen Z. Evolution of the Kock continent reservoir ileostomy. *Can J Surg* 1982; 25:509-14.
- 137 Fazio VW, Tjandra JJ. Technique for nipple valve fixation to prevent valve slippage in continent ileostomy. *Dis Colon Rectum* 1992; 35:1177-9.
- 138 Arai Y, Okada Y, Matsuda T, Hida S, Takeuchi H, Kihara Y, et al. Afferent nipple valve malfunction caused by anchoring collar: an unexpected late complication of the Kock continent ileal reservoir. *Journal of Urology* 1991; 145:29-32; discussion 33.
- 139 Meijer DW, Klopper PJ. Construction of a stable nipple valve with processed dermal sheep collagen for continent ileostomy and urostomy. *Urological Research* 1990; 18:353-5.
- 140 Orangio GR, Bronsther B, Abrams M, Wise L. A new type of continent ileostomy. Results of an animal study. *Dis Colon Rectum* 1984; 27:238-43.
- 141 Dozois RR, Kelly KA, Beart RW, Jr., Beahrs OH. Improved results with continent ileostomy. *Ann Surg* 1980; 192:319-24.
- 142 Kaiser AM, Stein JP, Beart Jr. RW. T-pouch: a promising new valve design for a continent ileostomy. *Dis Colon Rectum* 2001; submitted for publication.
- 143 Ecker KW, Haberer M, Feifel G. Conversion of the failing ileoanal pouch to reservoir-ileostomy rather than to ileostomy alone. *Dis Colon Rectum* 1996; 39:977-80.
- 144 Pemberton JH, Phillips SF, Ready RR, Zinsmeister AR, Beahrs OH. Quality of life after Brooke ileostomy and ileal pouch-anal anastomosis. Comparison of performance status. *Ann Surg* 1989; 209:620-6; discussion 626-8.
- 145 Fazio VW, O'Riordain MG, Lavery IC, Church JM, Lau P, Strong SA, et al. Long-term functional outcome and quality of life after stapled restorative proctocolectomy. *Ann Surg* 1999; 230:575-84; discussion 584-6.
- 146 Emblem R, Larsen S, Torvet SH, Bergan A. Operative treatment of ulcerative colitis: conventional proctectomy with Brooke ileostomy versus mucosal proctectomy with ileoanal anastomosis. *Scand J Gastroenterol* 1988; 23:493-500.
- 147 Marcello PW, Roberts PL, Schoetz DJ, Jr., Coller JA, Murray JJ, Veidenheimer MC. Obstruction after ileal pouch-anal anastomosis: a preventable complication? *Dis Colon Rectum* 1993; 36:1105-11.
- 148 Francois Y, Dozois RR, Kelly KA, Beart RW, Jr., Wolff BG, Pemberton JH, et al. Small intestinal obstruction complicating ileal pouch-anal anastomosis. *Ann Surg* 1989; 209:46-50.
- 149 Lee PY, Fazio VW, Church JM, Hull TL, Eu KW, Lavery IC. Vaginal fistula following restorative proctocolectomy. *Dis Colon Rectum* 1997; 40:752-9.

- 150 Gecim IE, Wolff BG, Pemberton JH, Devine RM, Dozois RR. Does technique of anastomosis play any role in developing late perianal abscess or fistula? *Dis Colon Rectum* 2000; 43:1241-5.
- 151 Fazio VW, Wu JS, Lavery IC. Repeat ileal pouch-anal anastomosis to salvage septic complications of pelvic pouches: clinical outcome and quality of life assessment. *Ann Surg* 1998; 228:588-97.
- 152 Paye F, Penna C, Chiche L, Tiret E, Frileux P, Parc R. Pouch-related fistula following restorative proctocolectomy. *Br J Surg* 1996; 83:1574-7.
- 153 Senapati A, Nicholls RJ, Ritchie JK, Tibbs CJ, Hawley PR. Temporary loop ileostomy for restorative proctocolectomy. *Br J Surg* 1993; 80:628-30.
- 154 Weaver RM, Alexander-Williams J, Keighley MR. Indications and outcome of reoperation for ileostomy complications in inflammatory bowel disease. *Int J Colorect Dis* 1988; 3:38-42.
- 155 Hasegawa H, Radley S, Morton DG, Keighley MR. Stapled versus sutured closure of loop ileostomy: a randomized controlled trial. *Ann Surg* 2000; 231:202-4.
- 156 Kuhbacher T, Schreiber S, Runkel N. Pouchitis: pathophysiology and treatment. *Int J Colorect Dis* 1998; 13:196-207.
- 157 Sandborn WJ, McLeod R, Jewell DP. Medical therapy for induction and maintenance of remission in pouchitis: a systematic review. *Inflamm Bowel Dis* 1999; 5:33-9.
- 158 Nicholls RJ, Banerjee AK. Pouchitis: risk factors, etiology, and treatment. *World J Surg* 1998; 22:347-51.
- 159 Sartor RB. Probiotics in chronic pouchitis: restoring luminal microbial balance. *Gastroenterology* 2000; 119:584-7.
- 160 Gionchetti P, Rizzello F, Venturi A, Brigidi P, Matteuzzi D, Bazzocchi G, et al. Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis: a double-blind, placebo-controlled trial. *Gastroenterology* 2000; 119:305-9.
- 161 O'Connell PR, Pemberton JH, Brown ML, Kelly KA. Determinants of stool frequency after ileal pouch-anal anastomosis. *Am J Surg* 1987; 153:157-64.
- 162 Stallmach A, Moser C, Hero-Gross R, Muller-Molaian I, Ecker KW, Feifel G, et al. Pattern of mucosal adaptation in acute and chronic pouchitis. *Dis Colon Rectum* 1999; 42:1311-7.
- 163 Beart RW, Jr. Pouchitis. *Br J Surg* 1995; 82:566-7.
- 164 Goldstein NS, Sanford WW, Bodzin JH. Crohn's-like complications in patients with ulcerative colitis after total proctocolectomy and ileal pouch-anal anastomosis. *Am J Surg Path* 1997; 21:1343-53.
- 165 Thompson-Fawcett MW, Mortensen NJ, Warren BF. "Cuffitis" and inflammatory changes in the columnar cuff, anal transitional zone, and ileal reservoir after stapled pouch-anal anastomosis. *Dis Colon Rectum* 1999; 42:348-55.
- 166 Lavery IC, Sirimarco MT, Ziv Y, Fazio VW. Anal canal inflammation after ileal pouch-anal anastomosis. The need for treatment. *Dis Colon Rectum* 1995; 38:803-6.
- 167 Ziv Y, Fazio VW, Sirimarco MT, Lavery IC, Goldblum JR, Petras RE. Incidence, risk factors, and treatment of dysplasia in the anal transitional zone after ileal pouch-anal anastomosis. *Dis Colon Rectum* 1994; 37:1281-5.
- 168 Broome U, Lofberg R, Lundqvist K, Veress B. Subclinical time span of inflammatory bowel disease in patients with primary sclerosing cholangitis. *Dis Colon Rectum* 1995; 38:1301-5.
- 169 Cangemi JR, Wiesner RH, Beaver SJ, Ludwig J, MacCarty RL, Dozois RR, et al. Effect of proctocolectomy for chronic ulcerative colitis on the natural history of primary sclerosing cholangitis. *Gastroenterology* 1989; 96:790-4.
- 170 Broome U, Lofberg R, Veress B, Eriksson LS. Primary sclerosing cholangitis and ulcerative colitis: evidence for increased neoplastic potential. *Hepatology* 1995; 22:1404-8.
- 171 Papatheodoridis GV, Hamilton M, Mistry PK, Davidson B, Rolles K, Burroughs AK. Ulcerative colitis has an aggressive course after orthotopic liver transplantation for primary sclerosing cholangitis. *Gut* 1998; 43:639-44.
- 172 Papatheodoridis GV, Hamilton M, Rolles K, Burroughs AK. Liver transplantation and inflammatory bowel disease. *Journal of Hepatology* 1998; 28:1070-6.
- 173 Weber AM, Ziegler C, Belinson JL, Mitchinson AR, Widrich T, Fazio V. Gynecologic history of women with inflammatory bowel disease. *Obstetrics & Gynecology* 1995; 86:843-7.
- 174 Metcalf AM, Dozois RR, Kelly KA. Sexual function in women after proctocolectomy. *Ann Surg* 1986; 204:624-7.
- 175 Dozois RR, Nelson H, Metcalf AM. [Sexual function after ileo-anal anastomosis]. *Annales de Chirurgie* 1993; 47:1009-13.
- 176 Tiainen J, Matikainen M, Hiltunen KM. Ileal J-pouch-anal anastomosis, sexual dysfunction, and fertility. *Scand J Gastroenterol* 1999; 34:185-8.
- 177 Damgaard B, Wettergren A, Kirkegaard P. Social and sexual function following ileal pouch-anal anastomosis. *Dis Colon Rectum* 1995; 38:286-9.
- 178 Hudson M, Flett G, Sinclair TS, Brunt PW, Templeton A, Mowat NA. Fertility and pregnancy in inflammatory bowel disease. *International Journal of Gynaecology & Obstetrics* 1997; 58:229-37.
- 179 Baird DD, Narendranathan M, Sandler RS. Increased risk of preterm birth for women with inflammatory bowel disease. *Gastroenterology* 1990; 99:987-94.
- 180 Counihan TC, Roberts PL, Schoetz DJ, Jr., Collier JA, Murray JJ, Veidenheimer MC. Fertility and sexual and gynecologic function after ileal pouch-anal anastomosis. *Dis Colon Rectum* 1994; 37:1126-9.
- 181 Farouk R, Pemberton JH, Wolff BG, Dozois RR, Browning S, Larson D. Functional outcomes after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Ann Surg* 2000; 231:919-26.
- 182 Nelson H, Dozois RR, Kelly KA, Malkasian GD, Wolff BG, Ilstrup DM. The effect of pregnancy and delivery on the ileal pouch-anal anastomosis functions. *Dis Colon Rectum* 1989; 32:384-8.
- 183 Marcello PW, Milsom JW, Wong SK, Hammerhofer KA, Goormastic M, Church JM, et al. Laparoscopic restorative proctocolectomy: case-matched comparative study with open restorative proctocolectomy. *Dis Colon Rectum* 2000; 43:604-8.
- 184 Meagher AP, Farouk R, Dozois RR, Kelly KA, Pemberton JH. J ileal pouch-anal anastomosis for chronic ulcerative colitis: complications and long-term outcome in 1310 patients. *Br J Surg* 1998; 85:800-3.
- 185 Breen EM, Schoetz DJ, Jr., Marcello PW, Roberts PL, Collier JA, Murray JJ, et al. Functional results after perineal complications of ileal pouch-anal anastomosis. *Dis Colon Rectum* 1998; 41:691-5.
- 186 Gemlo BT, Wong WD, Rothenberger DA, Goldberg SM. Ileal pouch-anal anastomosis. Patterns of failure. *Arch Surg* 1992; 127:784-6; discussion 787.
- 187 Nicholls RJ. Restorative proctocolectomy with ileal reservoir: indications and results. *Schweizerische Medizinische Wochenschrift Journal Suisse de Medecine* 1990; 120:485-8.
- 188 Neilly P, Neill ME, Hill GL. Restorative proctocolectomy with ileal pouch-anal anastomosis in 203 patients: the Auckland experience. *Austr N Zealand J Surg* 1999; 69:22-7.
- 189 Kartheuser AH, Parc R, Penna CP, Tiret E, Frileux P, Hannoun L, et al. Ileal pouch-anal anastomosis as the first choice operation in patients with familial adenomatous polyposis: a ten-year experience. *Surgery* 1996; 119:615-23.
- 190 Keighley MR, Grobler S, Bain I. An audit of restorative proctocolectomy. *Gut* 1993; 34:680-4.
- 191 Oresland T, Fasth S, Nordgren S, Hulten L. The clinical and functional outcome after restorative proctocolectomy. A prospective study in 100 patients. *Int J Colorect Dis* 1989; 4:50-6.

The many reasons why you should choose SMW to publish your research

What Swiss Medical Weekly has to offer:

- SMW's impact factor has been steadily rising, to the current 1.537
- Open access to the publication via the Internet, therefore wide audience and impact
- Rapid listing in Medline
- LinkOut-button from PubMed with link to the full text website <http://www.smw.ch> (direct link from each SMW record in PubMed)
- No-nonsense submission – you submit a single copy of your manuscript by e-mail attachment
- Peer review based on a broad spectrum of international academic referees
- Assistance of our professional statistician for every article with statistical analyses
- Fast peer review, by e-mail exchange with the referees
- Prompt decisions based on weekly conferences of the Editorial Board
- Prompt notification on the status of your manuscript by e-mail
- Professional English copy editing
- No page charges and attractive colour offprints at no extra cost

Editorial Board

Prof. Jean-Michel Dayer, Geneva
 Prof. Peter Gehr, Berne
 Prof. André P. Perruchoud, Basel
 Prof. Andreas Schaffner, Zurich
 (Editor in chief)
 Prof. Werner Straub, Berne
 Prof. Ludwig von Segesser, Lausanne

International Advisory Committee

Prof. K. E. Juhani Airaksinen, Turku, Finland
 Prof. Anthony Bayes de Luna, Barcelona, Spain
 Prof. Hubert E. Blum, Freiburg, Germany
 Prof. Walter E. Haefeli, Heidelberg, Germany
 Prof. Nino Kuenzli, Los Angeles, USA
 Prof. René Lutter, Amsterdam, The Netherlands
 Prof. Claude Martin, Marseille, France
 Prof. Josef Patsch, Innsbruck, Austria
 Prof. Luigi Tavazzi, Pavia, Italy

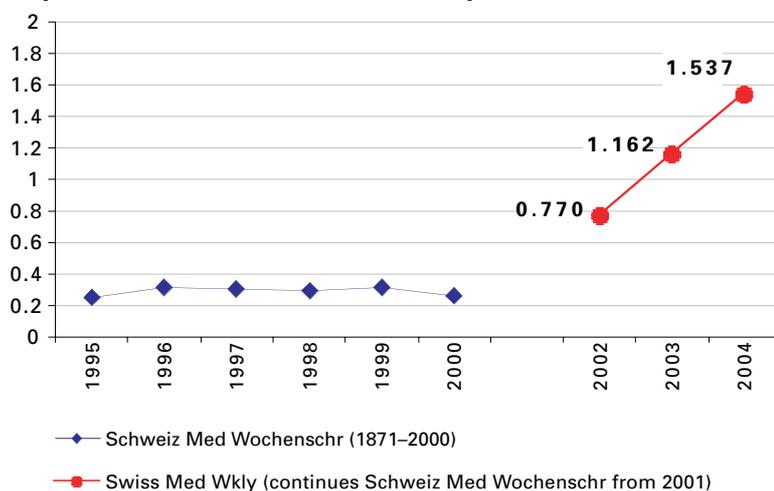
We evaluate manuscripts of broad clinical interest from all specialities, including experimental medicine and clinical investigation.

We look forward to receiving your paper!

Guidelines for authors:

http://www.smw.ch/set_authors.html

Impact factor Swiss Medical Weekly



All manuscripts should be sent in electronic form, to:

EMH Swiss Medical Publishers Ltd.
 SMW Editorial Secretariat
 Farnsburgerstrasse 8
 CH-4132 Muttenz

Manuscripts: submission@smw.ch
 Letters to the editor: letters@smw.ch
 Editorial Board: red@smw.ch
 Internet: <http://www.smw.ch>