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## Reoperations at the ileostomy in Crohn's disease reflect inflammatory activity rather than surgical stoma complications alone

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**Abstract** After ileostomy construction for Crohn's disease reoperations due to ileal recurrences are thought to be unusually rare, whereas reconstructions of the ileostomy due to stoma complications are considered to be unusually frequent. It remains unclear why the natural course of a disease as well as outstanding results of a standardized surgical procedure should be perverted. Therefore reconstructions of the ileostomy in 92 patients colectomized during a 12.5-year period and followed up for 5.4 years were analyzed concerning preoperative indication and postoperative histology. In 28 patients (30.4%) a total of 42 reoperations were necessary. The clinical indication was prestomal recurrence in 5 reoperations (11.9%) and stoma complications in 37 (88.1%). In contrast, ileal recurrence was demonstrated histologically in 28 specimens (66.7%) and healthy ileum in the rest. There was a statistically significant association between fibrotic recurrence and stoma stenosis/retraction and a trend for association between penetrating recurrence and peristomal ulceration. The cumula-

tive risk for a first reoperation due to clinical recurrence was calculated at 3.3% and 14.0% at 5 and 10 years postoperatively, whereas the corresponding figures for stoma complications were 25.7% and 40.0%. In contrast, the cumulative risk that a recurrence was found histologically on the occasion of the reoperation was 23.0% and 35.0%, while the probability that the ileum was healthy in the case of a stoma complication remained low. In conclusion, most reoperations after ileostomy-construction in Crohn's disease are associated histologically with recurrent inflammation. The accentuation of the inflammatory recrudescence at the stoma itself or the prestomal ileum is decisive for the clinical presentation as stoma complication or intestinal complication. These findings reinforce both well known characteristics of the inflammatory disease and of established surgery.

**Keywords** Crohn's disease · Ileostomy · Stoma complications · Clinical recurrence · Histological inflammatory recrudescence

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### Introduction

Conservative procedures are generally advocated in the surgery of Crohn's disease [1]. Despite this interdisciplinary consensus a considerable number of patients with the inflammation mainly confined to the colon or the co-

lorectum must eventually accept the construction of an ileostomy [2]. On the one hand, the loss of continence is thought to be even beneficial in terms of long-lasting improvement in health [3]. Especially the reoperation rate due to inflammatory recurrence has been shown to be much lower than after ileorectostomy [4]. On the other

hand, the reoperation rate for function-threatening stoma complications is much higher in Crohn's disease than in other colonic disorders [5]. This is most important since the patient's quality of life depends on maintaining or restoring perfect stoma function [6]. Considering this aspect, it remains to be clarified why stoma complications are so frequent specifically in this type of inflammatory bowel disease. Since the operative technique of ileostomy construction in Crohn's disease does not differ from that in other diseases, it was the aim of this study to investigate the effect of the underlying inflammatory process on the development of stoma complications.

## Patients and methods

### Patients and study design

The observational study included 92 patients (34 men, 58 women; mean age  $33.0 \pm 10.3$  years) who had undergone ileostomy construction for Crohn's colitis. The data were collected prospectively in the Crohn's disease registry of the institution for retrospective analysis. Of these, 49 patients (53.3%) had subtotal colectomy and 43 (46.7%) proctocolectomy. Large-bowel resections were indicated for chronic intractable course of disease in 68.5% ( $n=63$ ), for severe acute attack of colitis with or without complications in 20.7% ( $n=19$ ), and for fulminant course of inflammation with or without toxic dilatation in 10.5% ( $n=10$ ). Operations were performed consecutively over a 12.5-year period, and patients participated in the regular follow-up program of the outpatient clinic for a mean period of  $5.4 \pm 3.1$  years (95% CI 4.8–6.1 years). During this period the same surgeon and the same stomatherapist intended to ensure both perfect stoma function and a life free of complications of recurrent ileal disease. Excluded from analysis were reoperations for both proximal and medical treatment of distal intestinal disease and conservative stomatherapy. The study was focused on any problem requiring reoperation at the distal ileum including the ileostomy.

### Reoperations

Indications for reoperations were classified as "complicated ileal recurrence" or "ileostomy-complication." In each reoperation the ileostomy was reconstructed after resection of more or less of the (neo-)terminal ileum either by a local procedure or via a laparotomy. The histological investigation of the specimens was classified as normal ileum or inflamed ileum signaling possibly recurrent disease. Signs of inflammatory penetration were differentiated from fibrotic scarification.

### Statistical analysis

The valid N method was used and performed with the programs Report (version 4.6) and "Testimate" (version 5.2) of IDV (Gauting, Germany). For all reconstructions of the ileostomy the correlations were examined between indications and the appropriate histology. Associations between absence or presence of stoma complications and the presence of penetrating or fibrotic inflammation was interpreted for binary data with Fisher's exact test. The probability of an association is presented with two-tailed 95% confidence intervals. The sequence of the reoperations was analyzed concerning both indication and histology. For the first reoperation cumulative probabilities were calculated separately for

both the clinical indication and the risk of inflammation to be found in the specimen. The data were actuarized using Kaplan-Meier evaluation method.

## Results

### Indications and histology

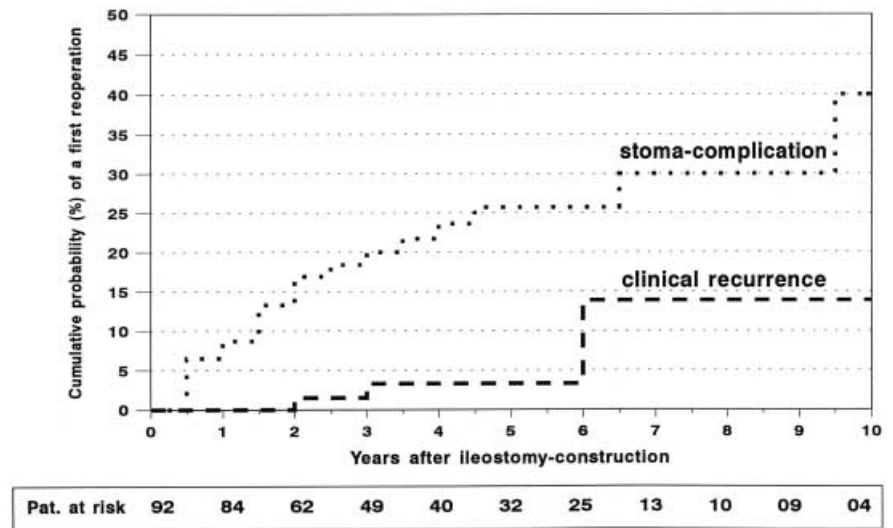
A total of 42 reconstructions of the ileostomy were performed, 5 (12%) for the indication of complicated ileal recurrence and 37 (88%) for stoma complications. However, in nearly two-thirds of cases histological investigation of the specimens revealed clear inflammation and clinical recurrence in each case. Histology revealed a healthy ileum in only about one-third ( $n=14$ ) of all stoma complications. The difference between stoma complication with histologically inflamed ileum and a clinical recurrence was that the inflammatory process developed at the stoma-forming ileum in the former and at the pre-stomal ileum in the latter indication.

The most common stoma complications were peristomal skin ulcerations ( $n=22$ ) and retraction of the prominent nipple ( $n=10$ ). In seven cases each the ileum was normal. Other stoma complications included three stenoses, one prolapse, one peristomal hernia. However, inflammation was present in each ileal specimen. The specific tendency of Crohn's inflammation (penetration and fibrosis) to provoke typical stoma complications (peristomal ulceration and retraction or stenosis) was evident. Of peristomal skin ulcerations 59.1% (13/22) were definitely identified as the result of a penetrating complication of the inflamed stoma-forming ileum whereas a fibrotic inflammation was found in 39.5% of retractions or stenoses (5/13). The probability of an association of a peristomal ulceration with an inflammatory penetration of the ileum was 68.4% (95% CI 43.5–87.4%), but with a fibrotic inflammatory process it was only 22.2% (95% CI 2.8–60.0%). A twofold one-tailed  $p$  value of 0.058 was calculated for this difference. On the other hand, the probability of an association of a retraction or a stenosis of the nipple with a fibrotic ileitis was 55.6% (95% CI 21.2–86.3%), but with a penetrating ileitis it was only 5.3% (95% CI 0.1–26.0%). This difference was statistically significant at a twofold one-tailed  $p$  value of 0.013 (Table 1).

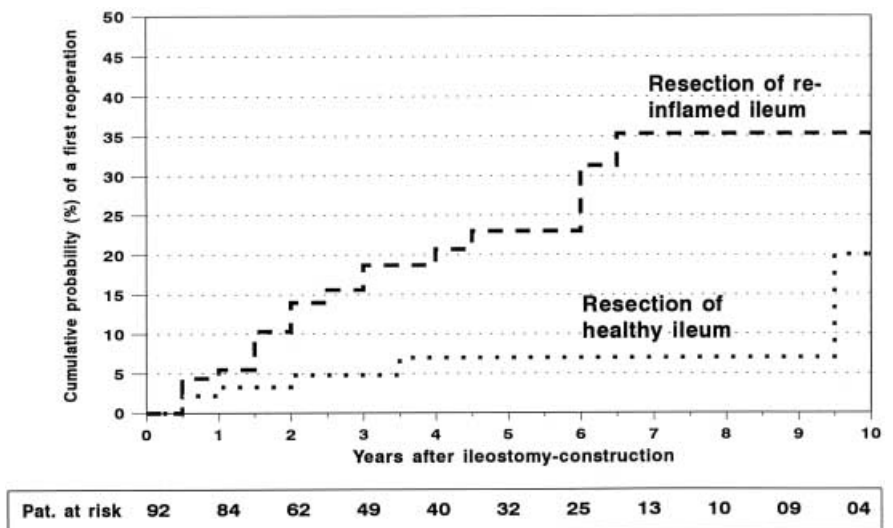
### Sequence of the reoperations

At least one reoperation was necessary in 28 patients (30.4%), two reoperations in 11 (11.9%), and three reoperations in 3 (3.3%). A complicated recurrence of the disease was the indication for a first reoperation in only 5 patients (5.4%). Clinically the sequence of the reoperations was started by the predominance of stoma compli-

**Fig. 1** Cumulative probability (%) of a first reconstruction of the ileostomy according to Kaplan-Meier product limit estimation method for various subgroups. *Dotted line* Reconstructions for clinical stoma complications; *dashed line* reconstructions for clinical recurrences



**Fig. 2** Cumulative probability (%) of a first ileal resection in Crohn's disease with preexisting ileostomy according to Kaplan-Meier product limit estimation method for various subgroups. *Dotted line* of healthy ileum; *dashed line* resections of re-inflamed ileum



**Table 1** Association between clinical indication for reconstruction of the ileostomy and histology of the resected ileum

	Total	No pathological findings	Inflammation with penetration	Inflammation and fibrosis
Prestomal recurrence	5		4	1
Ileostomy-complication	37	14	15	8
Skin ulceration	22	7	13*	2
Retraction	10	7	–	3**
Stenosis	3	–	1	2**
Prolapse	1	–	1	–
Peristomal hernia	1	–	–	1

\* $P=0.06$ , \*\* $P=0.01$ , Fisher's exact test

cations. However, inflammation was present in 78.6% of all first reoperations (22/28). The subsequent reoperations were indicated exclusively by stoma complications, but histological investigation shifted more and more in favor of healthy ileum (Table 2).

#### Cumulative probabilities

The risk that reoperation is induced by a clinical recurrence was calculated as 3.3% after 5 and 14.0% after 10 years, but at 25.7% and 40.0%, respectively, by a clin-

**Table 2** Clinical indications and pathology of the ileum in the sequence of the reoperations

	Total	Sequence of reoperations		
		First	Second	Third
Complicated recurrence	5	5		
Inflammation	5	5		
Stoma complication	37	23	11	3
Inflammation	23	17	5	1
Normal ileum	14	6	6	2
All indications	42	28	11	3
Inflammation	28	22	5	1
Normal ileum	14	6	6	2

ical stoma complication (Fig. 1). On the other hand, the risk of an inflamed segment of ileum being resected increased rather constantly to 23% after 5 years and 35% after 10 years. In contrast, the risk of having a healthy part of the ileum being resected was 7% after 5 years and increased only in the 10th year to 20.0% (Fig. 2).

## Discussion

The postoperative course of Crohn's disease is characterized by a high risk of relapsing inflammation [1, 7]. Now it is accepted that the true surgical recurrence is located at the neoterminal ileum orally of an ileocolic anastomosis [8, 9]. This study demonstrated by histological investigation that the postoperative recrudescence of the inflammatory process within the aboral small bowel persists after interruption of the ileocolic continuity. However, the deviation of the fecal stream gives quite another quality and, in addition, a more favorable dynamic of complication to the recurrence than does the anastomosis. It can be assumed that many complications of an ileostomy in Crohn's disease are closely linked to an inflammatory activity rather than to surgical insufficiencies of the stoma construction. Therefore high reoperation rates for stoma complications [5] and low reoperation rates for ileal recurrences [3, 4] require systematic clarification.

In this study the inflammatory state of the (neo)-terminal ileum after colectomy and ileostomy could be investigated histologically owing to the availability of resected ileal specimens on the occasion of any ileostomy reconstruction. As in to endoscopic surveys after ileocolonic anastomoses, any clear inflammation of the neoterminal ileum should be regarded as recurrence regardless of its severity [8, 9]. This also seems justified in ileostomy patients since inflammation in Crohn's disease is by definition nonspecific, and histological findings judged as typical are not at all mandatory. Keeping this in mind, mucosal and/or transmural inflammation was present in 23 of 37 stoma complications (62.2%) clinically not sus-

picious by all means for Crohn's recurrence. Moreover, a coincidence with inflammatory processes was found even in the rare cases of prolapse and peristomal hernia, which are primarily due to anatomical abnormalities or to surgical insufficiencies [6, 10]. In most cases, however, specific stoma complications were strikingly associated with the type of inflammation found histologically in the resected ileostomy. From the statistical point of view this was confirmed for the association of stenoses and retractions with fibrotic inflammation. Although much more frequent, the evident association of peristomal ulceration with penetrating ileal recurrence barely failed statistical significance since it was impossible to preoperatively differentiate fistulating from necrotizing skin ulcers of other origin such as peristomal pyoderma gangrenosum [11]. An inflammatory activity nevertheless probably plays a role in those cases as well [12]. This probably explains why these ulcerations are not observed in noninflammatory disorders [13].

The calculation of reoperation rates of course depends on preoperatively determined indications. Concerning complications of clinically manifest ileal recurrences our calculated cumulative risks at about 5% and 15% after 5 and 10 years for resection including reconstruction of the ileostomy confirm the results of similar studies published [3, 4]. There is no doubt that clinical recurrence usually is confirmed histologically, at least after the operation. In contrast, confusion may arise from stoma complications when trying to reconcile the indication for reoperation and the respective morphology in the same way. Keeping this difficulty in mind, the only comparable study reported in the literature, 10 years ago, refers to stoma complications excluding inflammatory recurrence by clinical means [5]. Applying the same statistical method, we confirmed that the risk for reoperation due to this indication continuously increases over the time. However, the cumulative probabilities after 5 and 10 years were only about one-half as high (25.7% and 40.0% vs. 60.0% and 75.0%) on the basis of some 90 patients each. Although the technical details of the ileostomy construction were not the subject of this study, the more favorable prognosis in our study appears to be the result of technical improvements during the past decade. We observed no cases of non-recurrence-related fistulas after the introduction of resorbable suture material [6]. Additionally, instabilities of the prominent nipple such as retraction/recession and prolapse decreased markedly when adopting to the stapler-stabilization technique [14].

From the technical point of view, resection of the complicated ileostomy and complete reconstruction of a new prominent nipple has proven the safest way to avoid repeated reoperations [10]. Moreover, this procedure offered the chance for histological investigations of ileal specimens. Consequently this study is, to our knowledge, the first investigation able to calculate the cumulative risk for having a reoperation at the ileostomy in Crohn's disease in

the presence of microscopic recurrent inflammation. It was shown that this probability increases until the 10th year to the range of 30–40%, figures that have also been calculated for the resection risk of the neoterminal ileum after ileocolic anastomosis [3, 4]. However, in ileostomy patients accentuation of the new inflammation determines whether the complication develops at the intra-abdominal (classical recurrence) or the preabdominal (stoma complication) ileum. Consequently the curve of the cumulative risk for resection of inflamed ileum (Fig. 2) nearly represents the addition of the curves for both clinical indications (Fig. 1). In contrast, the curve of the cumulative risk for resection of healthy ileum (Fig. 2) remains low over the period, suggesting that purely surgical stoma complications are the exception, provided that the technique has been performed correctly [6].

We conclude from our findings that the risk for developing (neo)terminal ileal recurrences after colectomy for Crohn's disease is higher than previously thought, even after construction of an ileostomy [15]. Moreover, it must

be acknowledged that our cumulative rates underestimate the true risk since noncomplicated recurrences were excluded from our analyses. To compare the natural course after deviation of the intestinal stream with the restoration of the intestinal continuity endoscopic and histological surveys are needed. However, one also must emphasize that the clinical severity of ileal recurrences after ileostomy construction usually runs a mild to moderate course compared to the ileocolic anastomosis. Moreover, the remaining small bowel is unlikely to develop inflammatory recurrences [2]. Therefore in the presence of stoma complications whole-gut investigations prior to reoperation of the stoma site may remain reserved to cases clinically suspicious for high intestinal lesions. Nevertheless our results indicate the need for an evaluation of medical prophylaxis in controlled clinical trials such as in patients with continuity-restoring resections [8].

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