Mistakes in the management of postoperative Crohn's disease and how to avoid them

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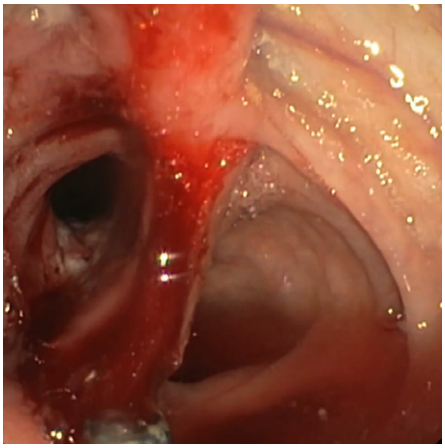
Crohn's disease is a chronic immune-mediated inflammatory condition that usually produces cumulative transmural intestinal damage. Disease-related complications, such as intestinal strictures and intra-abdominal penetrating complications (including enteric fistulae, inflammatory masses and abscesses), are mostly managed via a surgical approach, with ileocecal resection plus ileocolic anastomosis being the most common procedure.[1,2] Despite the curative intention of surgery, however, up to 70% of patients develop new mucosal lesions in the neoterminal ileum within the first year of intestinal resection if no preventive therapy is started early after surgery.[3] This postoperative recurrence (POR) can be described as endoscopic, clinical or surgical. Endoscopic POR—defined as the presence of mucosal lesions in the neoterminal ileum, as assessed by ileocolonoscopy—precedes the development of symptoms (clinical POR), which may lead to the need for new surgical resections (surgical POR).

Here we discuss the errors to avoid when managing patients with Crohn's disease in the postoperative setting. The discussion is based on evidence, whenever possible, as well as on our clinical experience and perception of the field.



Mistake 1 Failing to recommend smoking cessation

Many risk factors for POR have been reported, such as a penetrating disease pattern, prior intestinal resections and perianal disease (figure 1). However, active smoking alone has been repeatedly identified as a risk factor for POR in retrospective and prospective studies. Indeed, active smoking confers a 2.5-fold increase in the risk of POR compared with not smoking after surgery.[4] In addition, active smoking is the only risk factor that can be reverted, thus reducing the risk of POR.[5] Therefore, giving up smoking is the only preventive measure that is universally accepted and all patients who smoke should be advised to give up once intestinal resection is planned.

Mistake 2 Prescribing ineffective drugs for the prevention of postoperative disease recurrence

Nowadays, there are two accepted strategies for the management of Crohn's disease in the postoperative setting. With the first strategy, the treatment decision is driven by the findings of early endoscopic monitoring (preferably performed 6 months after surgery). Alternatively, the second strategy is to begin preventive therapy early after surgery (within the first 4 weeks). Although many drugs have been evaluated for their potential to prevent POR in randomized controlled trials (RCTs), regrettably, only thiopurines and anti-tumour necrosis factor agents (anti-TNFs)—but not aminosalicylates, corticosteroids or probiotics—demonstrated efficacy in preventing endoscopic and clinical POR. In fact, two recent guidelines on the management of postoperative Crohn's disease recommend the use of these drugs and no others for early prevention in patients who have risk factors for POR.[6,7]

Mistake 3 Monitoring faecal calprotectin concentrations too soon after surgery

Faecal calprotectin has proved to be a good surrogate marker of ileal mucosal lesions in Crohn's disease patients after they've undergone ileocecal resection and anastomosis.[8–10] However, faecal calprotectin levels can remain high during the first 2–3 months after surgery, probably related to the surgical insult.[11] For this reason, faecal calprotectin concentrations should not be measured during this early period to monitor the development of POR, although it is a useful noninvasive tool thereafter. Furthermore, it is also important to remember that there are many other gastrointestinal diseases, and some medication-related and even lifestyle factors, that can alter faecal calprotectin concentrations. These alternative influences should always be taken into account when interpreting faecal calprotectin concentrations.[12]

Mistake 4 Performing endoscopic monitoring too late after surgery

Currently, endoscopic examination of the terminal ileum remains the gold standard to define subclinical POR, with the severity of the endoscopic ileal lesions detected driving the need for treatment escalation, as outlined in the available guidelines.[6,7] Some prospective studies have observed that lesions were already present 6 months after surgery in most of the patients who went on to develop POR within the first year.[13,14] Moreover, in studies that have evaluated the efficiency of anti-TNF agents in cases of endoscopic POR, mucosal lesions were reverted in less than half of cases.[15] From this perspective, an endoscopic examination should be scheduled for 6 months after surgery as part of the discharge process, as doing so will ensure early detection of POR and treatment escalation in all Crohn's disease patients undergoing intestinal resection with anastomosis.

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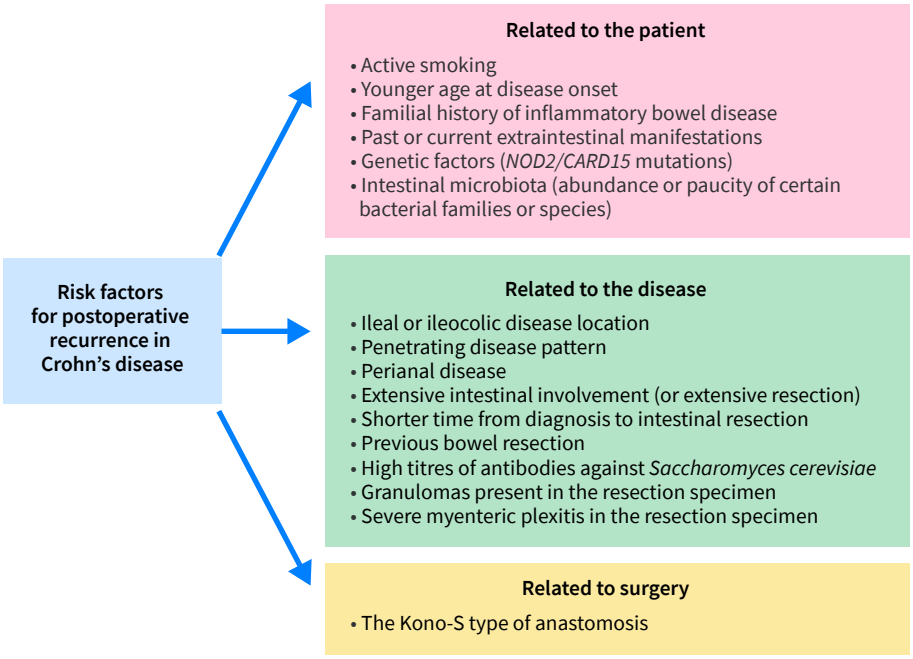

Figure 1 | Risk factors for postoperative recurrence in Crohn's disease.

Mistake 5 Using an inappropriate endoscopic score or performing an incomplete ileoscopy

The landmark study on the natural history of postoperative Crohn's disease showed that POR was a process that is almost exclusive to the neoterminal ileum, involving a length of intestine between 2 cm and 55 cm lying proximally to the ileocolic anastomosis.[3] Moreover, its authors developed the only existing endoscopic score for POR and correlated the severity of the observed lesions with the risk of clinical POR in the follow-up period.

In clinical practice, endoscopic monitoring to assess the development of POR must include the examination of at least the last 15 cm of the ileum and grade the lesions with the so-called Rutgeerts' endoscopic score (figure 2). When endoscopic examination is incomplete or the patient refuses it, other radiologic examinations, such as magnetic resonance enterography or intestinal ultrasonography, should be used as a replacement.[6]

Mistake 6 Discontinuing disease monitoring after an initial normal ileocolonoscopy

Although most patients who develop POR do so within the first year after surgery, patients who have no recurrent lesions at the first postoperative endoscopic examination remain at risk.[16] Globally, the risk of 'late' POR (i.e. later than 1 year after surgery) is suspected to be low and the use of invasive monitoring is, therefore, precluded unless clinical features are suggestive of POR. However, periodic determination of faecal calprotectin concentrations or ultrasonographic assessment seem to be useful in asymptomatic patients.[6]

Mistake 7 Neglecting to start or escalate therapy in case of endoscopic recurrence

The main goal of endoscopic monitoring is the early diagnosis of subclinical POR. An RCT demonstrated that treatment escalation in the case of endoscopic POR seen at an early endoscopic examination was associated with a higher rate of endoscopic remission in the follow-up period.[17] Although its benefit for intermediate lesions (i.e. Rutgeerts' score i2) is still under debate,[18] treatment escalation is strongly recommended in cases of severe endoscopic lesions (i.e. Rutgeerts' score i3 or i4).[6,7]

Rutgeerts' index	i0	i1	i2	i3	i4
Endoscopic findings	Normal ileal mucosa	Fewer than 5 aphthous ulcers	More than 5 aphthous ulcers with normal mucosa between them, or skip areas of larger lesions, or lesions confined to ileocolonic anastomosis	Diffuse aphthous ileitis with diffusely inflamed mucosa	Diffuse inflammation of the mucosa with large ulcers, nodules and/or narrowing

Figure 2 | Rutgeerts' endoscopic index for postoperative recurrence.

Mistake 8 Believing diarrhoea is synonymous with clinical recurrence

Ileocolonic resection is frequently associated with structural and functional changes in the gut. The removal of the ileocecal valve often induces intestinal bacterial overgrowth, and the resection of the terminal ileum may be followed by bile acid malabsorption (BAM). Both intestinal bacterial overgrowth and BAM are potential causes of chronic diarrhoea that should not be attributed to POR. Indeed, these conditions should be suspected when diarrhoea occurs soon after surgery (i.e. within days), particularly if there is no concomitant abdominal pain, fever and in the absence of raised inflammatory biomarkers. In this scenario, the empirical use of cholestyramine may be helpful. Moreover, patients with Crohn's disease may also present with symptoms of irritable bowel syndrome, and poor correlation between digestive symptoms and the presence of endoscopic lesions has been reported.[19] Therefore, the diagnosis of clinical POR should rely not only on digestive symptoms but also on morphological assessment.

Mistake 9 Assuming postoperative recurrence does not occur in patients who have a terminal ileostomy

For many decades the concept of POR was associated with ileocolic anastomosis and the involvement of changes in the microbiota, leading to the belief that POR did not occur in patients who had undergone a terminal ileostomy. However, there is a growing body of evidence that this phenomenon can also occur in ostomates.[20] No monitoring strategies for patients who have a terminal ileostomy are currently available, but clinicians should always be aware that it is possible for POR to develop in these patients.

Mistake 10 Underestimating the risk of vitamin B_{12} deficiency

After chronic iron deficiency and anaemia of chronic disease, vitamin B_{12} deficiency is a common cause of anaemia in patients with Crohn's disease. Risk factors for vitamin B_{12} deficiency include small-bowel involvement or resection (mainly ileal).[21] In fact, the European guidelines recommend assessing vitamin B_{12} levels at least once a year for Crohn's disease patients, and even more frequently for patients with extensive small-bowel resection, extensive ileal Crohn's disease or an ileal-anal pouch.[22]

Therefore, cobalamin levels should be assessed every 6–12 months in Crohn's disease patients who have undergone ileal resections—parenteral supplementation should be started if deficiency is noticed and in patients who have ileal resections of >30 cm.

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Your post-operative Crohn's disease briefing

UEG Week

- 'How to manage postoperative recurrence?' presentation in the 'Management of Crohn's disease' session at UEG Week Virtual 2020 [https://ueg.eu/library/session/management-of-crohns-disease/161/2825].
- 'Pre- and postsurgical management in Crohn's disease' presentation in the 'How to use drugs in IBD' session at UEG Week 2109 [https://ueg.eu/library/session/how-to-use-drugs-in-ibd/156/2124].
- 'Post-operative recurrence of Crohn's disease' session at UEG Week 2018 [https://ueg.eu/library/session/post-operative-recurrence-of-crohns-disease/153/1991].
- 'Post-operative management of Crohn's disease' session at UEG Week 2016 [https://ueg.eu/library/session/post-operative-management-of-crohns-disease/144/1579].

Standards and Guidelines

- Bemelman WA, et al. ECCO-ESCP Consensus on Surgery for Crohn's Disease. *J Crohn's Colitis* 2018; 12: 1–16 [https://ueg.eu/library/ecco-escp-consensus-on-surgery-for-crohn-s-disease/176354].
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