





Case Report

# Rethinking Intra-operative Management of Crohn's Disease: Intestinal Ultrasound Detects Microscopic Disease Unidentified at Ileal Margin Resection

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## Abstract

Crohn's disease is a chronic and relapsing inflammatory condition that often requires surgical intervention. Post-operative recurrence of Crohn's disease remains common after surgery occurring in up to 75% of patients. The role of disease-free surgical margins in post-operative recurrence has been debated, however, it has been identified as an independent risk factor for recurrence. We present a case of a woman with obstructive Crohn's disease who underwent ileocecectomy and was maintained on uninterrupted infliximab therapy. Despite operative and pathology reports describing grossly normal surgical margins, three months post-operation the patient was experiencing new intermittent lower abdominal pain and intestinal ultrasound revealed active ileitis involving a 10cm segment immediately proximal to the ileocolonic anastomosis. Due to concern of incomplete resection, microscopic re-evaluation of the margins was conducted and confirmed histologically positive margins of active Crohn's disease. Current guidelines have called for additional studies to examine the role of disease-free margins. Our case demonstrates the limitations of gross evaluation of disease-free margins and suggests a potential application of intestinal ultrasound intraoperatively for such assessment. While intestinal ultrasound has been utilized intraoperatively for colonic malignant margin identification, it has not yet been studied in inflammatory bowel disease and requires further evaluation.

## Keywords

Intestinal Ultrasound, Crohn's Disease, Post-operative Recurrence, Surgical Margins, Inflammatory Bowel Disease

## 1. Introduction

Post-operative recurrence (POR) of Crohn's disease (CD) occurs in up to 75% of patients within one year after surgery [1]. POR is a process whereby previously healthy intestinal segments develop new lesions subsequent to surgery [2]. While there are conflicting data over the necessity and feasibility of microscopically clean margins during ileocecal re-

section [3], studies have identified that microscopic inflammation at ileocecal resection margins is a serious and independent risk factor for POR [4]. Intestinal ultrasound is a non-invasive, highly accurate tool to assess disease activity [5] and has been well described in its accuracy of detecting post-operative disease recurrence in patients with CD [6].

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Here we present the case of a patient with CD who underwent an ileocecal resection that was suspected to be incomplete based on post-operative intestinal ultrasound (IUS) findings, confirmed by subsequent microscopic

## 2. Case Report

A 22-year-old woman with fibrostenotic and penetrating ileal and perianal CD presented with obstructive symptoms despite weekly adalimumab therapy. Point-of-care IUS identified sonographic evidence of active and chronic inflammation in the terminal ileum (TI), a TI stricture with proximal small bowel dilation, and two ileum to cecum fistulas. The patient's obstructive symptoms and IUS findings persisted despite switching to infliximab therapy and escalating dosing to 10 mg/kg every 8 weeks for 10 months. A preoperative colonoscopy confirmed ileocecal valve stenosis that could be traversed with an endoscopically and histologically colon.

The patient subsequently underwent a laparoscopic ileocectomy with a side-to-side, functional end-to-end ileocolonic anastomosis, during which 15.5cm of distal ileum and 7.3cm of proximal colon were removed. Histologic evaluation identified mildly active Crohn's enteritis, two ileocolonic measuring 1.2cm, and disease-free margin on gross evaluation. The patient had an unremarkable post-operative period and continued uninterrupted infliximab therapy for prevention of recurrence of CD. However, three months post-operation, the patient presented for follow-up with new intermittent lower abdominal pain for the last month. A point-of-care IUS exam showed sonographic evidence of active ileitis (thickened bowel wall to 5.5mm and mild hyperemia) involving a 10cm long segment immediately proximal to the ileocolonic anastomosis, which raised the clinician's suspicion for incomplete resection. The findings prompted a histologic re-examination of the previously resected ileal specimen in which microscopically positive margins were identified at the ileum (Figure 1(D) and (E)). A subsequent colonoscopy seven months post-operation revealed a patent side-to-side ileocolonic anastomosis characterized by erosion and erythema. Histology showed patchy mild active enteritis in the neo-TI and inflamed intestinal-type mucosa with erosion and reactive changes at the ileocolonic anastomosis, supporting the previous IUS findings.

## 3. Discussion

While evidence has demonstrated that gross evaluation be insufficient to identify positive margins, histologic assessment to ensure negative margins is not part of routine practice and clinical guidelines; however, the evidence to support these guidelines is limited. The only randomized evidence is from a 1996 randomized control trial by Fazio et al. that found no statistical significance between clinical or surgical POR in patients with positive compared to negative

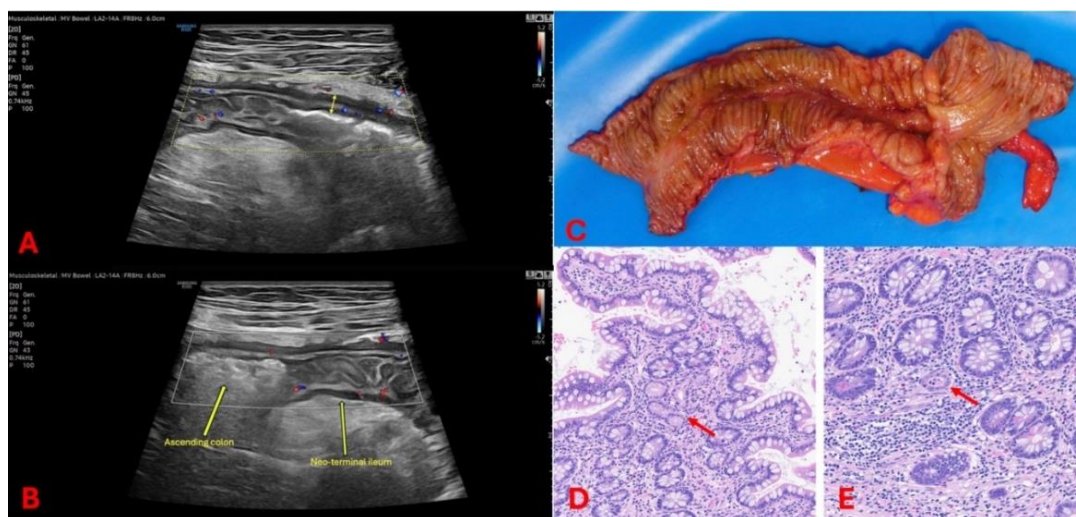
surgical margins [7]. However, no patients in this trial received prophylactic therapy post-operation, which is now part of guidelines [8], the follow-up period was limited, and the number of patients with positive margins was small.

Several recent studies have since found positive surgical margins to be associated with clinical, surgical, and endoscopic POR [9-12]. Multiple recent meta-analyses have also demonstrated that positive margins and other histologic findings, such as mesenteric plexus and granuloma, predict POR [13-15]. Alongside the mounting evidence of the risks associated with positive margins, the limitations of present studies, such as lack of standardized definition of histopathologic criteria, are well recognized and further supported by the recent European Crohn's and Colitis Organization 2017 guidelines stating the need for additional studies to examine the role of histology in preventing POR [6].

IUS has been shown to be an excellent tool in detecting POR with sensitivity of 90%, specificity 86.4%, and area under the curve of 0.923 [16]. Although the feasibility of intra-operative ultrasound has been established in other conditions and is utilized in colorectal surgery for malignant margin identification [17, 18], IUS for CD margin identification has not yet been studied. This case suggests the potential role of IUS in identifying residual disease in patients with who have undergone resection based on the current standard of removal of all macroscopically involved bowel.

Limitations of this study include its description of a singular case and identification of positive margins solely postoperatively and not intraoperatively. Generalizability of this is limited due to the presence of a dedicated IUS program, with IUS-experienced sonographers, which may not be available at other centers. However, the strengths of this study include it taking place at a tertiary IBD center in which a colorectal surgeon specializing in IBD performed the operation and identified the gross margins to be disease-free, an IBD expert pathologist who also initially identified the margins to be grossly disease-free, and an experienced sonographer in IUS who identified the residual disease post-operatively. We believe that the inability to grossly identify margins in a highly specialized center suggests the possibility of this being an underreported and underrecognized phenomenon in other centers.

Although this case suggests IUS may be useful in the intra-operative setting to assess disease extent and margin identification of CD, the methodology by which it may be performed is not yet described. However, methods may be extrapolated from colorectal neoplasia studies. In a 2009 study of IUS in malignant margin identification by Greif et al., the colon was instilled with saline solution after anesthesia administration and the bowel segments were scanned for detection of neoplastic margins [17]. We propose further exploration of this clinically important observation, as further study of both the application of intra-operative IUS in CD and role of positive margins in POR are needed.



**Figure 1.** Intestinal ultrasound images (A) of the neo-terminal ileum under color Doppler view demonstrating mild hyperemia, thickened bowel wall (double headed arrow), mesenteric fat hypertrophy, and a number of sinus tracts, suggestive of active inflammation (B) the ileocolonic anastomosis under color Doppler view demonstrating mild hyperemia, thickened bowel wall, and mesenteric fat hypertrophy. (C) Gross image of resected terminal ileum. (D) Ileal margin section with pyloric gland metaplasia (red arrow), consistent with chronic injury. (E) Ileal margin section with a crypt abscess (arrow), consistent with active disease.

## Abbreviations

POR	Post-Operative Recurrence
CD	Crohn's Disease
IUS	Intestinal Ultrasound
TI	Terminal Ileum

## Author Contributions

**Noa Krugliak Cleveland:** Conceptualization, Investigation, Writing – original draft, Writing – review & editing

**Lindsay Alpert:** Investigation, Writing – review & editing

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## Conflicts of Interest

NKC is a consultant for NeuroLogica and Johnson & Johnson. cmD, KBS, and LA declare no conflicts of interest.

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