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Incidental Finding of Terminal Ileum Inflammation on Screening Colonoscopy: Approach to Diagnosis and Workup

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Key Takeaways

Incidental terminal ileitis is identified in ~1.6% of screening colonoscopies.

Isolated terminal ileal inflammation without symptoms often resolves without treatment.

The presence of symptoms, not chronicity on biopsies, is the best predictor of isolated ileitis progressing to overt Crohn's disease.

Use a fecal calprotectin cutoff of $>200 \mu\text{g/g}$ to identify inflammation in isolated ileal Crohn's disease.

Introduction

The incidental finding of terminal ileal inflammation on screening or non-diagnostic colonoscopy poses a diagnostic and management dilemma for all gastrointestinal endoscopists. The question of whether this finding represents inflammatory bowel disease (IBD), namely Crohn's disease, is often postulated. This paper outlines a pragmatic approach to the evaluation and management of an incidentally identified finding of terminal ileitis on screening colonoscopy.

Review of the Literature

In Canada, colorectal cancer (CRC) screening is offered to asymptomatic average risk individuals aged 45/50–75 years (In 2026, the age to start screening in Canada varies by province with some offering screening at age 45 and others at age 50). Screening is primarily based on fecal immunochemical testing (FIT), with colonoscopy reserved for FIT positive individuals or those at increased risk of CRC.¹ Other jurisdictions have adopted age 45 as the start for average risk screening. However, patients undergoing screening colonoscopy are not always truly asymptomatic and may report symptoms of rectal bleeding, diarrhea, or abdominal pain. As these symptoms can be intermittent or gradual in onset, patients often downplay or ignore them. The differential diagnosis of a positive FIT result is broad, and includes any condition that leads to bleeding in the digestive tract, such as colon cancer, polyps, hemorrhoids, diverticulosis, and angiodysplasia. As both FIT and fecal calprotectin (FCP) can be used to identify mucosal healing in Crohn's disease,² individuals with a positive FIT result may also have bowel inflammation accompanied by an elevated FCP level.

The differential diagnosis of ileal inflammation and ulceration is broad and includes infection, drug-induced (e.g. nonsteroidal anti-inflammatory drug-related), intestinal tuberculosis (TB), Behçet's disease and malignancy, in addition to Crohn's disease.^{3,4} The presence or absence of symptoms—including abdominal pain, weight loss, diarrhea, bleeding, and oral or genital ulceration—are important in helping to determine if the findings represent Crohn's disease.

A systematic review reported a pooled prevalence of 1.6% (range, 0.04–6.77) for incidentally detected terminal ileitis on non-diagnostic colonoscopy among asymptomatic patients undergoing colon cancer screening, with terminal ileitis defined as 'macroscopic erythema, erosion, ulceration, or non-specific inflammation.'⁵ Long-term follow-up of one-quarter of these patients showed that progression to overt Crohn's disease was rare, although a small proportion subsequently developed symptoms. In a large (>40,000 patients) single-centre study of a CRC screening cohort that included FIT positive individuals or those undergoing surveillance colonoscopy for prior polyps, incidental IBD was found in 0.15% of procedures. Of these cases of incidental IBD, two-thirds (40/60) were Crohn's disease, and 39/40 had isolated ileal involvement.⁶ During a mean follow-up of ~2 years, only 3 Crohn's patients developed symptoms and were started on therapy after symptom onset. Notably, isolated terminal ileal ulcerations in asymptomatic individuals often improve or resolve without-treatment.^{7,8}

In a South Korean study of patients with symptomatic localized terminal ileitis at a referral hospital, a specific diagnosis was established in two-thirds of cases. Crohn's disease was the most common diagnosis (42%), followed by Behçet's disease (28%) and infection (14%), with drug-induced causes, TB, and other diagnoses accounting for the remainder.¹¹ Abdominal pain was present in most patients with Crohn's, disease, Behçet's disease, and non-TB infection, while diarrhea occurred in approximately half of those with Crohn's disease or infection. Oral ulceration was identified in most patients with Behçet's, disease, in one-sixth of those with Crohn's disease, and in 30% of those with infection. In contrast, genital ulcers were exclusively observed in those with Behçet's disease.¹¹

Role of Biopsy (Pathology), Fecal Calprotectin and Intestinal Ultrasound

The finding of ileal inflammation at endoscopy often prompts biopsy to assess the degree of inflammation and to identify histologic signs of chronicity. However, a biopsy study of individuals with endoscopic and histologic ileal abnormalities reported that the presence of symptoms was the best predictor of progression to Crohn's

disease ($p < 0.001$). In contrast, asymptomatic individuals with ileitis, even with chronicity findings on histology, rarely progressed to overt Crohn's disease.⁹

FCP is commonly used to determine mucosal healing in those with a known diagnosis of Crohn's disease. However, it is important to note that for those with isolated ileal disease, an FCP cutoff of 200 $\mu\text{g/g}$ may be more appropriate than the conventional cutoff of 250 $\mu\text{g/g}$.¹² Repeated assessment of symptoms and FCP testing at one year and thereafter as clinically indicated, can aid in ongoing monitoring for the development of Crohn's disease over time.

In a retrospective study of a subset of patients with non-specific ileitis identified at endoscopy who underwent intestinal ultrasound, no patient with a normal bowel wall thickness (< 3 mm) was subsequently diagnosed with Crohn's disease.¹⁰ Of the patients who met the criteria for nonspecific ileitis, 66 were followed up with another modality [median follow-up time of 370 days (IQR 173–911)]. Thirty-five patients were followed up with intestinal ultrasound (≤ 6 months from colonoscopy), and 31 had colonoscopy (52%, $n = 16$), a gastrointestinal ultrasound that was taken ≥ 6 months after the colonoscopy (29%, $n = 9$), or other cross-sectional radiology (19%, $n = 6$) [CT enterography (CTE) in 1 and magnetic resonance enterography (MRE) in 5]. Although the cohort included patients with iron deficiency anemia, only 5.4% ultimately developed Crohn's disease, with most diagnosed in the first year of follow-up at a median of 148 (range 27–603) days after colonoscopy. These findings raise the possibility of using intestinal ultrasound as an adjunct tool to exclude Crohn's disease in patients with incidental ileitis.

Management

It is important to remember that even when mild ileal Crohn's disease is diagnosed, current evidence does not support the use of biologics or small molecule therapies as first-line treatment. Because advanced therapies for Crohn's disease are approved for moderate-to-severe disease, the optimal approach to management of mild Crohn's disease, especially isolated ileal Crohn's disease, remains less clearly defined. Mild ileal Crohn's

disease is characterized by normal laboratory parameters, aside from mildly elevated biomarkers (FCP, c-reactive protein), a Simple Endoscopic Score for Crohn's disease score of 3–6, and the absence of significant systemic signs or weight loss.¹³ Budesonide 9 mg daily for 4–8 weeks is an appropriate treatment, followed by re-assessment at 3 months. Patients who respond can often be managed with supportive care (diet, antidiarrheals) and ongoing monitoring at one year.^{13–15} Symptomatic patients with ongoing inflammation may require additional therapy with prednisone, immunosuppressants, and/or advanced therapies. Re-assessment at one year or if symptoms develop is prudent.

Approach and Workup of Incidentally Found Terminal Ileitis

Figure 1 depicts an approach and monitoring strategy for diagnostic workup and management of patients with incidentally identified terminal ileitis.

Summary and Conclusions

The finding of terminal ileitis identified on screening colonoscopy has a broad differential diagnosis and should prompt a re-assessment for symptoms, including evaluation for extraintestinal manifestations of IBD and Behçet's disease. Available evidence suggests that only a minority of patients with incidentally identified mild ileitis on colonoscopy ($\sim 5\%$) will develop Crohn's disease. Initial evaluation should include laboratory assessment with a complete blood count, c-reactive protein, and FCP should also be completed. Because isolated ileal disease is often associated with lower FCP levels, a threshold of > 200 $\mu\text{g/g}$ might be more appropriate than conventional cutoffs. Asymptomatic patients rarely develop overt Crohn's disease, even if biopsies show signs of chronicity. Intestinal ultrasound assessment may further aid in risk stratification, with a bowel wall thickness < 3 mm suggesting a low likelihood of Crohn's disease. The presence of symptoms is the most important predictor of patients with incidentally diagnosed terminal ileitis progressing to overt Crohn's disease.

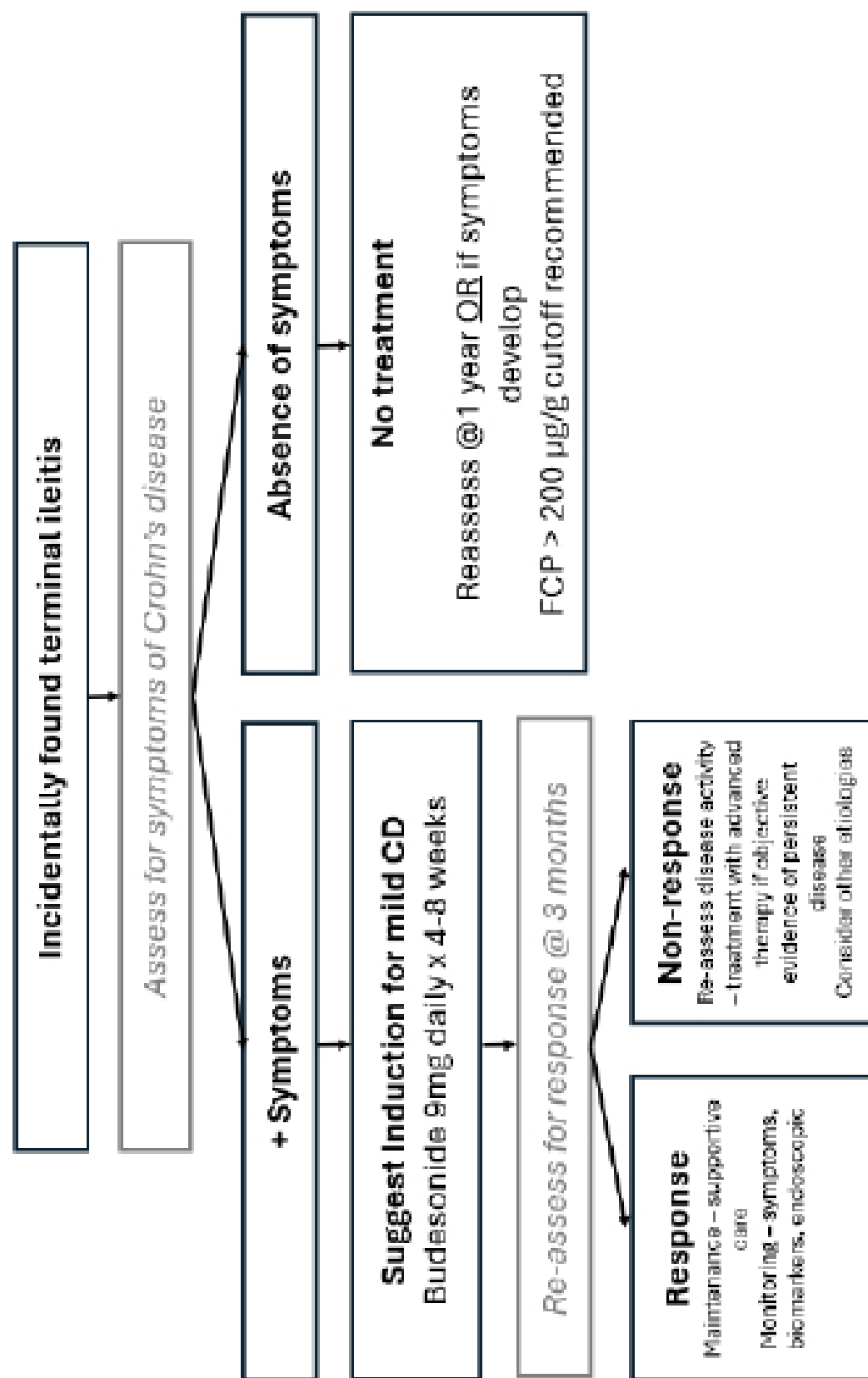


Figure 1. Pragmatic approach to incidentally identified findings of terminal ileitis; courtesy of Karen I. Kroeker, MSc, MD, FRCPC.

Abbreviations: CD: Crohn's disease; **FCP:** fecal calprotectin

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