

# Upper gastrointestinal Crohn's disease: What are we talking about?

Crohn's disease (CD) is a chronic inflammatory condition that can affect any part of the gastrointestinal (GI) tract, from the mouth to the anus.<sup>1</sup> While lower GI involvement is more commonly recognized, upper GI (UGI) CD is gaining increasing attention despite its relatively uncommon presentation in adults.

The prevalence of UGI involvement in CD varies widely, with reported rates ranging from 0.05% to 83%, due to differing definitions and diagnostic criteria across studies.<sup>2</sup> In fact, some studies report much higher rates when upper endoscopy is routinely performed, highlighting the potential underdiagnosis of this condition. Of note, a recent study found that while 41% of newly diagnosed adult CD patients had UGI involvement, only 32% had corresponding symptoms, raising questions about the utility of additional investigations, and thereafter treatment, when lesions are asymptomatic.<sup>3</sup> The lack of specific symptomatology likely contributes to the under-recognition of UGI CD, leading to either a delayed diagnosis until the disease progresses to the lower GI tract or the misattribution of symptoms to lower GI disease.

The definition of UGI CD is complex and varies across studies. In this issue of the *United European Gastroenterology Journal*, a scoping review by Yuan and colleagues attempts to address these inconsistencies by analyzing key guidelines and consensus papers in order to stimulate future research in this area.<sup>4</sup> The review highlights that while the Montreal classification primarily categorizes UGI CD as L4, affecting segments up to the proximal ileum, organizations like the European Crohn's and Colitis Organisation and the European Society of Gastrointestinal and Abdominal Radiology include the esophagus, stomach, and duodenum in their definitions of UGI CD.<sup>5,6</sup> Notably, the review also highlights the absence of a clear definition in pediatric guidelines, which is particularly concerning given that significant small intestine involvement in pediatric CD patients can lead to serious consequences such as growth failure and stricturing disease. Moreover, the importance of including biopsies from the UGI tract in clinical trials involving children is underscored, as this could lead to a more accurate assessment. In adults, on the other hand, the role of histological

findings in the absence of corresponding endoscopic or clinical evidence remains uncertain, complicating diagnostic and management strategies.

The precise definition of UGI CD is critical, as it influences diagnostic approaches, prevalence estimates, prognostic implications, and treatment responses. Regarding prognosis, CD involving the jejunum and proximal ileum often presents later in the disease course and is associated with a stricturing phenotype that frequently necessitates surgical intervention. This involvement has been identified as an independent risk factor for surgery, hospitalization, and overall complications, in contrast to disease located in the upper GI tract.<sup>2</sup> As to the diagnosis, CD assessment in the UGI tract still remains a significant task, particularly due to the limited accessibility of segments like the jejunum with standard endoscopic techniques. There is growing recognition that diagnosing CD beyond the duodenum may require more advanced diagnostic approaches, including capsule endoscopy, device-assisted enteroscopy, or MRI. Moreover, the endoscopic appearance of UGI lesions in CD is highly variable, ranging from aphthae, erosions, and ulcerations to bamboo joint-like lesions, strictures, and notch-like formations.<sup>7</sup> This variability has sparked debate about which is the best approach to diagnose UGI CD: whether UGI CD should be confirmed histologically, through endoscopic and radiologic findings alone, or if histology alone might suffice. Additionally, while there is a scoring system for capsule endoscopy in CD, no such scoring system exists for gastroscopy, further complicating a standardized diagnostic approach and management.

Finally, the uncommon occurrence of UGI involvement in CD has resulted in a scarcity of data concerning its pharmacological treatment. Clinical trials specifically evaluating the effectiveness of biologic therapies for UGI CD are scant, and evidence is often limited to case reports or case series.<sup>8</sup> Treatment strategies often focus on controlling coexisting distal disease.<sup>9</sup> Surgical intervention for UGI CD, particularly in cases of stricturing disease, presents additional challenges, with techniques such as Roux-en-Y gastrojejunostomy being utilized in some instances. However, the choice of this inter-

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vention is based on limited evidence and is not supported by established guidelines.<sup>10</sup>

In summary, the diagnosis and management of UGI CD are difficult due to limited evidence and the heterogeneous nature of the disease. Future studies should focus on standardizing definitions, understanding the impact of histological activity, and developing more effective treatment strategies for patients with UGI involvement. Standardized diagnostic criteria and targeted therapeutic strategies will be crucial at improving outcomes for this under-recognized subset of CD patients.

## KEYWORDS

definition, diagnosis, esophagus, gastric Crohn's disease

## AUTHOR CONTRIBUTIONS

Luisa Bertin, Brigida Barberio and Edoardo Vincenzo Savarino: collection and analysis of the data, draft of the manuscript, approving final version.

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## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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