

# Modifying the natural history of gastrointestinal diseases in Europe as a result of early diagnosis: From eosinophilic esophagitis to inflammatory bowel disease

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated inflammatory disease, characterized by esophageal dysfunction symptoms and transmural infiltration of the esophagus by eosinophils.<sup>1</sup> Since the first reports in the early 90s, the incidence and prevalence of EoE have skyrocketed in developed countries, especially over the past decade.<sup>2</sup> As such, EoE is currently the most prevalent cause of dysphagia and food impaction in children and adults younger than 50 years-old.<sup>1</sup> Updated epidemiologic studies have shown prevalence figures as high as one in 1,000 children and adults in Spain<sup>3,4</sup> and the US.<sup>5</sup>

The natural history of untreated EoE represents a steady progression from an inflammatory to a fibrostenotic phenotype. Four big retrospective studies published between 2013 and 2018 nicely demonstrated that the duration of untreated EoE, expressed as diagnostic delay, constitutes the major risk factor for esophageal remodeling and stricture formation in EoE.<sup>6-9</sup> At this point, the next question would be whether these potential complications might be minimized with increasing awareness leading to early diagnosis. In this issue of the United European Gastroenterology (UEG) Journal, Navarro and colleagues provide a clear answer through a detailed analysis of the EoE CONNECT database.<sup>10</sup> Briefly, this project comprises a prospectively-maintained registry, formerly promoted by the UEG as a part of the Link Award program "Harmonizing diagnosis and therapy of Eosinophilic Oesophagitis across Europe (HaEoE-EU)", later transferred in 2016 to EUREOS, the European Consortium for Eosinophilic Diseases of the GI Tract. After analyzing 1132 patients from Spain, Italy, Denmark, and France, the authors demonstrate a dramatic reduction in diagnostic delay for EoE, from 12.7 years (before 2007, when no guideline was available) down to 0.7 years (after publication of the last set of guidelines in 2017,<sup>1</sup> endorsed by the UEG). The earlier diagnosis resulted in a significantly lower proportion of patients with stricturing or mixed phenotypes at baseline (41% before 2007 vs. 16% after 2017). As expected, patients diagnosed before 2007 also underwent a significantly higher number of endoscopic procedures, likely for diagnostic confirmation or endoscopic dilation.

The aforementioned results observed in EoE resemble some aspects also found in inflammatory bowel disease (IBD). Both are immune-mediated diseases, leading to chronic structural damage of the gastrointestinal tract, with a peak incidence in young adults. Diagnostic delay has been recently demonstrated to be as short as 3 months or below for IBD in prospective multicenter studies from Spain<sup>11</sup> and Italy.<sup>12</sup> Despite these advances, recent data from the European Epi-IBD study highlighted that around one third of patients with Crohn's disease already show complications – strictures, fistulae, abscesses – at disease onset.<sup>13</sup> In addition, around half of all patients will eventually develop a stricturing or fistulizing phenotype within 10 years, especially when ileal or perianal disease are present at baseline.<sup>14</sup> Unlike EoE, it seems altogether that we are still far from modifying the natural history by early detection of symptomatic IBD (secondary prevention). Growing interest has been lately focused on disease detection at preclinical (presymptomatic) stages in IBD,<sup>15</sup> which will hopefully identify earlier those individuals at higher risk of a complicated disease course, or even help in preventing the disease.



Undoubtedly, the present study from Navarro and colleagues<sup>10</sup> provides an optimistic compelling proof on how resources spent on educational initiatives and disease awareness for secondary prevention may result in significant improvements in the disease course and patients' lives. However, this kind of initiatives may still be insufficient for complex disorders like IBD. Primary prevention (intervening before the disease or its effects occur), which is currently becoming a hot topic in IBD, should also be a priority in EoE, aiming at deciphering why staple foods consumed since the Neolithic Era like milk, wheat, and eggs, have led to a new allergic disorder just over the past 3 decades. We are sure that the future holds many new insights that will improve our understanding of both disorders.

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Javier Molina-Infante<sup>1,2</sup>   
Iago Rodríguez-Lago<sup>3,4</sup> 

<sup>1</sup>Gastroenterology Department, Hospital Universitario de Cáceres, Cáceres, Spain

<sup>2</sup>Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid, Spain

<sup>3</sup>Gastroenterology Department, Hospital Universitario de Galdakao, Biocruces Bizkaia Health Research Institute, Galdakao, Spain

<sup>4</sup>School of Medicine, University of Deusto, Bilbao, Spain

#### Correspondence

Iago Rodríguez-Lago, Gastroenterology Department, Hospital Universitario de Galdakao, 48960 Galdakao, Spain.  
Email: [iago.r.lago@gmail.com](mailto:iago.r.lago@gmail.com)

#### DATA AVAILABILITY STATEMENT

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

#### ORCID

Javier Molina-Infante  <https://orcid.org/0000-0003-1204-0571>

Iago Rodríguez-Lago  <https://orcid.org/0000-0003-1133-4578>

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