

## The natural history of extraintestinal manifestations after surgery in inflammatory bowel disease: Never give up!

The incidence of inflammatory bowel disease (IBD) is increasing worldwide, and its prevalence is expected to reach up to 1% of the population in many regions over the following decades.<sup>1</sup> This is crucial as we need to shape the healthcare assistance that will be delivered to these patients in the near future. Despite the main clinical manifestations of IBD are focused in the gut, approximately 25%–40% of patients develop at least one extraintestinal manifestation (EIM) during the disease course.<sup>2</sup> The frequent involvement of the joints, skin, eyes, and the hepatobiliary area, among others, leads to multiple symptoms, decreased quality of life and higher costs.<sup>3</sup> Thus, IBD units will need to provide a comprehensive and individualized evaluation to an increasing number of patients with multiple comorbidities that require a tight collaboration with rheumatologists and dermatologists.<sup>2</sup>

In recent decades, the use of immunosuppressive and biologic agents in ulcerative colitis patients has been associated with decreased colectomy rates,<sup>4</sup> but the overall influence of medical therapy in the natural history of the disease still remains controversial. Nevertheless, surgical resection is no longer curative in IBD. A significant proportion of patients with Crohn's disease develop some degree of postoperative recurrence and pouchitis is still the most frequent complication after ileal pouch-anal anastomosis.<sup>5</sup> The burden of the disease during the perioperative period is now supported by the observations made in this issue by the Swiss cohort, where one in every seven patients can develop de novo EIM during follow-up, with a 50% risk 8 years after surgery.<sup>6</sup> Additionally, between 42% and 67% of prior EIM can persist after colectomy in ulcerative colitis and Crohn's disease, respectively. These findings suggest that an important proportion of EIM have an independent course from the intestinal disease activity. Notably, rates of EIM persistence are usually higher in CD, perhaps due to a more pronounced systemic inflammatory burden and the increased probability of disease recurrence.


Fortunately, the available treatment options for both diseases have increased in recent years.<sup>7</sup> Multiple new molecules with different mechanisms of action have been included in our armamentarium. However, while they are highly efficacious in treating the uncontrolled inflammatory process located in the gut, not all of these drugs have the same influence over EIM.<sup>8</sup> The balance between gut-selectivity and the capacity of reaching extradigestive organs is

crucial in this subgroup of patients. In accordance with the results published from the Swiss cohort, this should be also considered after surgery. While around half of patients with peripheral arthritis (43%) can recover after colectomy, they are still the most frequent EIM persisting or developing de novo after surgery. Therefore, when a prophylactic treatment is planned after intestinal resection or colectomy, we should also consider the efficacy of the drug on these comorbidities.

Nonetheless, the choice of the best treatment for an individual patient remains a challenge for clinicians. As for today, precision medicine is still developing in IBD, so the current decision-making process is mainly based on clinical data. In addition, there is no gold-standard treatment for patients with IBD and concomitant rheumatologic conditions, even though they are the most prevalent EIM observed in our clinic. This subgroup of patients has been frequently underrepresented in clinical trials, and the same can be applied in subjects with prior surgery. Hence, evidence on the best holistic medical management of IBD coexisting with certain comorbidities or even its prevention after surgery is still limited.

In conclusion, the results from the Swiss cohort reinforce that IBD is a chronic disorder requiring long-term follow-up and tight monitoring on these subgroup of patients. We would like to acknowledge Roth and colleagues for their findings that should be considered among the established recommendations from the European Crohn's and Colitis Organisation on the best management of EIM.<sup>9</sup> The early identification of these complications is still an important issue,<sup>10</sup> but our understanding of the natural history of the immune-mediated comorbidities around IBD has grown quickly along with the significant improvement of medical therapy.

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