Study proposes a novel index for predicting the course of ulcerative colitis

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The arrows in the images above indicate eosinophils, CD177-positive neutrophils, and CD40L-positive T cells. Credit: Prof. Zhanju Liu, Center for IBD Research, The Shanghai Tenth People's Hospital of Tongji University, China
Ulcerative colitis (UC) is an inflammatory bowel disease that causes irritation, inflammation, and ulcers in the tissues lining the large intestine. Known to be a long-term condition, UC can result in significant discomfort, abdominal pain, diarrhea, dietary restrictions, and weight loss, ultimately impairing patients' quality of life.

While the precise cause of UC is unclear, a complex interplay of immune responses to microbiota (intestinal microbial population), intestinal defects, genetic and environmental factors are often associated with the pathogenesis of UC. In the past, studies have shown that histological or mucosal healing (MH), also known as a decrease in intestinal tissue inflammation, is associated with favorable outcomes, reduced hospitalization, and reduced need for surgery. However, 30% of patients with UC continue to experience tissue inflammation, despite the resolution of symptoms.

To this end, associations between specific immune cell activation and intestinal disease activity have been well established. However, their role in the intestinal tract and potential association with tissue healing remains unexplored.

To bridge this research gap, a team of researchers from China, led by Professor Zhanju Liu, sought to develop a diagnostic criterion based on changes in infiltrating immune cells in the large intestine, associated with tissue healing in patients with UC. Sharing his views on the importance of such an index, Prof. Liu elaborates, "Importantly, the assessment of activated immune cell infiltrations in the colonic lamina propria may provide a rationale for the precision diagnosis of histological healing in UC patients."

The team's article appears in the Chinese Medical Journal.

The study was conducted between January 2017 and May 2022 across
hospitals in China. The researchers analyzed the clinical, endoscopic, and tissue data of 220 patients with UC who underwent treatment and successfully achieved healing. They analyzed the levels of the surface proteins CD177, CD64, CD40L, and CD69, which are the biomarkers of activated immune cells, namely neutrophils and T cells.

Further, they correlated the proportion of activated immune cells with six characteristic features of the colon, namely acute inflammatory cell infiltration, crypt abscesses (accumulation of inflammatory cells within the crypts of the intestine), depletion of the mucin layer in the intestine, surface integrity, chronic inflammatory cell infiltration, and crypt irregularities in the colon. Finally, they assessed the relationship between the levels of immune cell biomarkers, tissue healing, and long-term outcomes, including symptomatic recurrence after standard therapy.

Their results suggested that after the 18-month follow-up, a higher proportion of CD177-positive neutrophils, CD40L-positive T cells, and eosinophils were highly predictive of disease recurrence. Notably, patients who achieved histological healing had a lower proportion of inflammatory immune cells, compared to those who did not achieve healing.

Next, based on the threshold values of colonic CD177-positive neutrophils, eosinophils, and CD40L-positive T cells from healthy donors, the researchers developed a measure called the inflammatory cell enumeration index (ICEI). Patients with lower values than the established ICEI threshold, and without crypt abscesses, mucin depletion, surface epithelial damage, and crypt architectural irregularities, were considered as having achieved tissue healing.

Furthermore, the team found that ICEI could reliably stratify patients on the basis of those with healed tissue and those with active tissue. Notably, only 13.1% of patients from the healed group experienced a
recurrence, compared to 40.7% of patients from the group with active tissue. Further, ICEI combined with other established indices provided a more accurate prediction of histological healing and recurrence than either score alone.

While a standard and uniform format for grading mucosal inflammation is currently lacking, the proposed ICEI could serve as a good choice for predicting the prognosis of patients with UC. This can in turn help reduce overtreatment in clinical practice by helping in the evaluation of MH and identification of high-risk patients following clinical healing. Overall, these findings pave the way for the development of accurate prediction models for assessing the risk of recurrence in patients with UC.

Sharing his concluding thoughts on the clinical applications of their work, Prof. Liu says, "As clinical therapy goals in UC continue to evolve, from endoscopic MH to histopathological healing, the ICEI offers a valuable tool for assessing and predicting the prognosis of UC patients. These advancements will definitely contribute to a deeper understanding of UC and offer opportunities for more tailored and effective management strategies."


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