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Editorial: ulcerative colitis submucosal fibrosis and inflammation: more than just strictures

Intestinal fibrosis is associated with chronic intestinal inflammation in IBD, generally reflecting long-lasting illness, where persistent tissue damage and healing result in scar tissue formation.[1] It has been stated that inflammation is required for the initiation of fibrosis, as both share the same distribution.[2] However, inflammation seems to play a minor role in fibrosis progression.[3] Transmural inflammation and fibrosis are common features of stricturing Crohn's disease (CD),[1] however, in ulcerative colitis (UC), both inflammation and extracellular matrix (ECM) deposition are generally restricted to the colonic mucosal and submucosal layers,[4,5] affecting deeper layers only after profound ulcers below to submucosa.[5] Fibrosis in UC is characterised by marked thickening of muscularis mucosae[6,7] and excessive ECM deposition in the submucosa,[8] seldom leading to strictures.[7] In UC, fibrosis has been related with ulcers and longer disease duration—the latter linked to higher risk of malignancy.[5] UC is now seen as a potentially progressive disease where fibrosis may lead to diffuse increased wall stiffness, resulting in motility abnormalities, anorectal dysfunction, rectal urgency and incontinence.[5]

In a recent issue of AP&T, Gordon and colleagues depicted the first comprehensive assessment of fibrosis in UC.[9] They studied 706 H&E and Masson Trichrome stained sections of 89 UC total colectomy or proctocolectomy specimens, which were compared to those of Crohn's colitis, diverticular disease and normal colons. Inflammation was graded according to Geboes score and fibrosis over a new UC submucosal fibrosis score (grading 0 to 4) for each segment, with the average designated as "fibrosis burden score." They further correlated the section studies results with histological findings on mucosal biopsies taken <4 weeks prior to surgery matched for colon location, with no endoscopic biopsy features predicting the degree of submucosal fibrosis.

The systematic approach used allowed the identification of clinical and pathological associations supporting the concept of inflammation-driven fibrogenesis in UC: submucosal fibrosis and muscularis mucosae thickening were restricted to involved segments of the colon, showing a gradient from proximal to distal colon; refractory disease was associated with higher degrees of fibrosis and muscularis mucosae thickening; and the degree, severity and histological aspects of active inflammation and chronic mucosal injury correlated with the grade of fibrosis. Importantly, the amount of fibrosis was not associated with disease duration but with severity of inflammation, which contrasts with previous studies. Likewise, no relation was found between the degree of fibrosis or average muscularis mucosae thickening and the length of the colon specimen, which contradicts the traditional view that submucosal fibrosis is responsible for the so called "lead pipe colon."

In summary, this paper comprehensively demonstrates that UC is a progressive disease characterised by submucosal fibrosis and muscularis mucosae thickening associated with both severity and chronicity of inflammation. We now have evidence to support that inflammation in UC drives not only an increased risk of colorectal neoplasia,[10] but also of intestinal fibrosis, reinforcing the importance of deep remission (including histological remission) as a therapeutic target in UC.

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Editorial: older-onset inflammatory bowel disease—is it time to start looking beyond a number?

In 2003, the Montreal Working Group expanded on the Vienna subclassification of inflammatory bowel disease (IBD) to distinguish adult from paediatric-onset disease.[1] Now an increasingly complex interplay between biology, prognosis, and therapy response has led to further stratification of Crohn's disease (CD) and ulcerative colitis (UC) in adults according to age of disease onset.

The number of older IBD patients is growing with nearly a quarter of IBD diagnoses made in patients ≥60 years old.[2,3] Concurrently, studies have identified clinical distinctions between older and adult-onset IBD.[2,4,5] Mañosa et al, in one of the largest retrospective multicenter studies examining older-onset IBD, found that compared to adult-onset disease, older patients have a less aggressive disease phenotype, but similar progression of disease.[6] A previous multicenter study has shown a decreased risk of disease progression in older-onset disease,[4] but this finding has not been consistent.[5] Mañosa et al showed less use of immune suppression and anti-TNF agents in elderly and similar rates of TNF-related complications between older-onset and adult-onset cases. They also found that older-onset UC patients were more likely to undergo surgery with similar post-operative complications between older-onset and adult-onset IBD patients. The authors conclude that in light of their findings in older-onset IBD, surgical management should be considered "as a real alternative" in UC and that therapeutic decisions in CD be similar to those with adult-onset disease.[6] However, in a population-based analysis, thiopurine use decreased the risk of surgery in older-onset UC.[7] In developing optimal treatment algorithms in older-onset IBD, the risk of surgical and medical complications needs to be determined by prospective studies examining appropriate therapeutic endpoints and drug efficacy. More definitive therapeutic strategies in older-onset IBD will be difficult to develop until then.

Even as recent data sheds further light on disease and therapy-related complications in older-onset IBD, the results fail to explain the worse disease outcomes in a less aggressive IBD phenotype in the elderly.[2,5,6] Future studies accounting for disease activity in