The Predictive value of Microscopic Inflammation beyond The Endoscopic Margin at diagnosis in Ulcerative Colitis Outcomes

1. Abstract

Ulcerative colitis is an inflammatory bowel disease that starts in the rectum and may extend to the entire colon. The classification of disease extent is based on the Montreal classification, which divides patients in 3 major subgroups: inflammation limited to the rectum (E1), inflammation of left-sided colon distal to the splenic flexure (E2) and extensive colitis, proximal to the splenic flexure (E3). This classification system has prognostic and therapeutic implications. However, the Montreal classification of UC extent is based only on the endoscopic appearance of disease at diagnosis. Current guidelines recommend that a minimum of two biopsies from at least five sites along the colon, are obtained and collected in separate vials at the time of diagnosis. It is quite frequent to find histological inflammation above the endoscopic margin, but the prognostic value of this finding remains unknown, despite strong evidence suggesting that during follow-up histology is an important prognostic factor. Therefore, we designed a multicenter, retrospective study, with the goal of understanding the prognostic value, if any, of the presence of histological inflammation above the endoscopic margin at the time of diagnosis in medium and long-term outcomes. Patients with an incident diagnosis of proctitis (E1) or left-sided colitis (E2) from different medical centers from 01/01/2000 to 31/12/2015 will be included, as long as their endoscopy and histological data at diagnosis is available. The histology slides at the moment of diagnosis will be retrieved and analyzed by an expert gastrointestinal pathologist using a validated score. Clinical outcomes during follow-up will be recorded. We propose to test whether the microscopic features beyond the endoscopic margin at the index colonoscopy have any impact on patient outcomes, including proximal extension of the disease, higher frequency of clinical relapses, higher therapeutic requirements, colectomy or hospitalization rates, etc.

2. Synopsis

Protocol title	The Predictive value of Microscopic Inflammation beyond The Endoscopic Margin at diagnosis, in Ulcerative Colitis Outcomes
Objective	To assess the prognostic value of histologic inflammation above the endoscopic margin in E1 and E2 patients at the time of diagnosis
Investigators	All Centers that may agree in participating
Study population	Subjects will be identified from each Hospital database, or from individual gastroenterology practices. Patients with ulcerative colitis located in the rectum, sigmoid and/or descending colon at the time of diagnosis will be selected, from 01/01/2000 to 31/12/2016
Methodology	Multicenter retrospective study
Inclusion criteria	1. Pediatric and adult patients with a diagnosis of proctitis or left-sided ulcerative colitis at the index colonoscopy (based on the endoscopic appearance) 2. The index colonoscopy and histology are available for consultation and review 3. The pathology slides at the moment of diagnosis are available for retrieval (at least from 3 different colonic segments) 4. Detailed information about disease course is available through medical chart consultation
Exclusion criteria	1. Patients who don't have a formal or definitive diagnosis of ulcerative colitis 2. Patients with ulcerative colitis who have pancolitis at diagnosis 3. Patients with proctitis or left-sided colitis that don´t have detailed clinical information during follow-up 4. Patients whose biopsies were done only after starting therapy
Primary endpoint	The impact of the presence of histological inflammation and the histologic features of colonic mucosa beyond or proximally to the endoscopic margin on the medium and long-term outcomes
Outcomes to be measured	1. Frequency of proximal extension of the disease 2. Number of hospitalizations per year for UC relapse 3. Requirement for therapy escalation a. Need for oral steroids b. Number of steroid courses every year c. Addition of thiopurines d. Need for IM/Biologics 4. Need for colectomy for refractory or complicated UC 5. Frequency of colorectal cancer 6. Associated mortality