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EDITORIAL

The Writing Is on the Wall: The Utility of Mural Stratification for Risk Stratification of Hospitalized Patients with Severe Ulcerative Colitis

Georgios I. Tsiaoussis[1] · Stelios F. Assimakopoulos[2] · Konstantinos C. Thomopoulos[3]

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Ulcerative colitis (UC), a form of inflammatory bowel disease (IBD), is a chronic inflammatory disease affecting the colonic mucosa, involving, in the majority of cases, the rectum and more proximal colonic segments in a continuous pattern. An assessment of disease severity based on clinical and laboratory studies is crucial in the formulation of a treatment plan for patients with symptoms suggestive of UC [1]. Within 2 years of diagnosis, 20% of patients with UC require hospitalization. Patients admitted to hospital should be evaluated for the severity and anatomical extent of disease in order to help predict the disease course. Pancolitis is associated with a higher rate of failure of medical treatment and an increased rate of colectomy [2]. Stool frequency, colonic dilatation, and hypoalbuminemia are predictors of failure of intravenous corticosteroid treatment, enabling early identification of patients with severe UC who could benefit from second-line medical therapy or surgery [3]. More specifically, this subgroup of patients should be treated early with intravenous glucocorticoids, fluids and electrolyte restoration, and broad-spectrum antibiotics without delay until the results of stool studies and cultures are available. Among those patients who are hospitalized, nearly one-third are unresponsive to intravenous corticosteroids, requiring rescue therapy with infliximab, cyclosporine, or emergent colectomy [4]. Patients with fulminant ulcerative colitis who do not respond by the third day of intensive treatment should be managed with either cyclosporine (CsA; a calcineurin inhibitor), or infliximab to induce and maintain remission or undergo rescue colectomy.

✉ Georgios I. Tsiaoussis
tsiaoussisgeorgios@yahoo.com

[1] Department of Gastroenterology, General Hospital of Karditsa, CP 43100 Karditsa, Greece

[2] Department of Internal Medicine, University Hospital of Patras, CP 26504 Patras, Greece

[3] Department of Gastroenterology, University Hospital of Patras, CP 26504 Patras, Greece

Patients with fulminant colitis who fail treatment with CsA or infliximab, either due to a failure to respond or due to relapse within four to 7 days of therapy initiation, or those with toxic megacolon who do not respond to therapy within 72 h, require colectomy. A multicenter retrospective study of the Cinergy Group in Canada showed that 18% of hospitalized patients with UC and 25% of steroid-refractory patients underwent rescue colectomy [5]. A cohort study by Kohn et al. in Italy showed that 9% of hospitalized patients with active UC underwent colectomy [6]. These discrepancies could be explained by differences in the cohort sample or by substantial geographic variation in the inpatient management and outcomes across different centers.

Response to steroids is defined by an improvement in stool frequency, rectal bleeding, abdominal pain, decreased C-RP, ESR, and albumin increment. The existing predictive indices that have been developed to stratify the risk of steroid failure in acute severe ulcerative colitis (ASUC) rely on the dynamic assessment of clinical status, laboratory measurements, and inflammatory markers after 3–5 days of therapy and consequently delay initiation of rescue therapy, thereby increasing overall morbidity [7–9].

In UC patients, the use of CT scanning can exclude alternate etiologies for symptoms and extra-intestinal IBD manifestations, assist in the noninvasive determination of the disease activity, extent, and severity, and identify disease complications such as toxic megacolon and perforation. The hallmark of active UC is the presence of colonic mural thickening (> 3 mm) and enhancement of wall thickness. Radiological features of UC may also include mural stratification as it is defined by the identification of two or three layers within the bowel wall, mesenteric hyperemia, fat deposition in the colonic wall, rectal narrowing, widening of the presacral space, and the stranding of perirectal fat. CT features have been significantly correlated with endoscopic severity accordingly to the Mayo UC score. Moreover, histological severity scores correlate with colonic wall thickening [10, 11]. Although there are

multiple applications for CT in UC patients, at present there is a paucity of published data assessing the contribution of radiographical evaluation to the prediction of the response to intensive medical therapy and the need for rescue medical or surgical treatment.

Given that published data are sparse, prospective trials are warranted to delineate predictive factors of steroid failure in order to prevent morbidity and obtain early control of disease activity. In this issue of *Digestive Diseases and Sciences*, Cushing et al. from Harvard Medical School showed that CT predictors at admission can be an important asset in stratifying patients according to their likelihood of inferior outcomes. Specifically, mural stratification was suggested as an independent risk index for the need for inpatient rescue therapy, as defined by medical therapy or colectomy, in hospitalized UC patients. This finding highlights the unique value of CT within the first 48 h of admission in predicting steroid-refractoriness (Fig. 1) that could aid the clinician in decision making and in selecting patients for early rescue medical or surgical therapy [12].

The study of Cushing et al.'s group contributes important new knowledge to the field of UC management. The authors evaluated the relationship between radiographic features and disease severity in UC, demonstrated the correlation between mural stratification and disease severity, and documented the independent predictive value of mural stratification on outcomes among hospitalized patients with severe UC, a group that is at high risk for poor outcomes. Mural stratification was found to be the only significant predictor of the responsiveness to initial intensive treatment with steroids when adjusting for potential confounders such as age, albumin, and C-RP according to multivariate analysis. These data add to the existing clinical and biological markers of ASUC outcomes, informing a more reliable prognostic model. Although there may has been a selection bias toward patients with more severe disease preferentially undergoing CT scanning, the investigators limited the study cohort to only those subjects who had a CT scan within 48 h of admission, eliminating the potential confounding effect of corticosteroid therapy on findings. Therefore, these findings

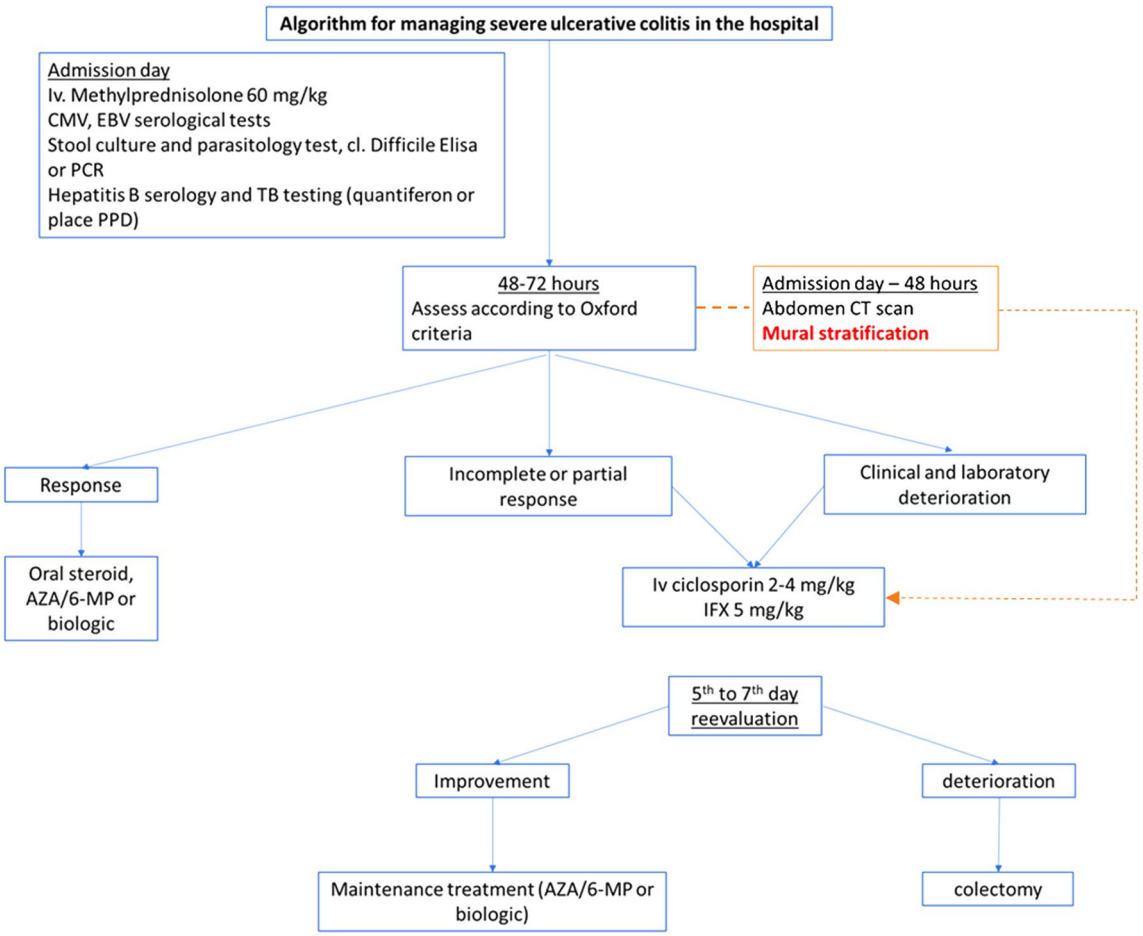

Fig. 1 Treatment algorithm for hospitalized patients with acute severe ulcerative colitis. CMV, cytomegalovirus; EBV, Epstein–Barr virus; TB, tuberculosis; PPD, purified protein derivative; AZA, azathioprine; 6-MP, 6-mercaptopurine; IFX, infliximab

are likely reflective of the disease activity and not influenced by subsequent therapy.

Despite the value of these findings, the current study is a retrospective analysis of a relatively small sample of subjects from a single center that may have limited the ability to detect more modest radiographic predictors of inpatient outcomes. Further studies would need to replicate these findings as well as determine the statistical precision and power of the imaging modality prior to widespread clinical implementation. Incorporation of radiological predictors into the existing decision-making algorithms may allow for improved risk stratification and standardized processes of care.

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