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Editorial

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Do We Still Need Predictors of Disease Severity When Applying a Treat-to-Target Approach in Inflammatory Bowel Disease?

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In this issue of *Journal of Crohn and Colitis*, Fernando Magro and colleagues from the Portuguese IBD group [GEDII], report on a large multicentre retrospective study aiming at establishing a risk matrix for two major outcomes in ulcerative colitis: colectomy and progressive disease.[1] The authors must be commended for this work, which is one of the largest published so far with such an aim, and which uses a very well thought out and robust strategy of analysis, including a test cohort, an internal validation, and an external validation on a second cohort, and combining Bayesian network analysis with logistic regression to generate these risk matrices. Predicting bad outcome in ulcerative colitis remains an important objective of clinical and translational research, and it could have a major impact on the way one treats these patients. The authors have put their efforts into generating a simple model, based on clinical and demographic characteristics, easily usable by clinicians, with a calculator available online to allow its broad use by the medical and scientific community. Patients at the highest risk of colectomy were those previously hospitalized, with extensive colitis, not on an immunomodulator and being steroid-dependent. Patients at the highest risk of progressive disease were male patients with extensive colitis and younger than 40 at diagnosis. This work strongly confirms some variables already suggested in other studies, including population-based studies, particularly for the risk of colectomy.[2,3] This is particularly the case for the extensive colitis and the younger age at diagnosis. Beyond these extreme risk profiles, the matrices generated allow assessment of variable degrees of risk for these outcomes based on the corresponding characteristics. Finally, and probably the most interesting result of this work: using the calculator and the matrix proposed allows the clinician to calculate for each individual patient at any given time point in the disease course these risks, and thus integration of them into the discussion on the therapeutic strategy. Although these results represent a significant advance in our knowledge of the natural history of ulcerative colitis and may give insight into how to best manage our patients, the study has some limitations, already partly highlighted by the authors in their paper. These limitations can be classified into three categories: methodological, practical and conceptual.

From a methodological point of view, if the colectomy can be considered as a robust and fully relevant outcome when studying ulcerative colitis course, progressive disease may be much more difficult to define. In the present study, the authors chose factors associated with tissue remodelling, such as strictures, mucosal bridges, pseudopolyps, lead pipe, or shortening or haustral markings, but they also included here colectomy, multiple hospitalisations, multiple steroid courses, and the need to upgrade or switch immunomodulator or biologic therapy. This thus represents a very heterogeneous definition, for which the clinical relevance may not be obvious.

From a practical point of view, if one takes the profile associated with the highest risk of colectomy [including extensive colitis, steroid dependence and absence of immunomodulator], it is clear that in such a situation, a clinician following the ECCO or other guidelines would upgrade the treatment and use an immunomodulator or a biologic. Therefore, the added value of the risk matrix on the therapeutic choice will probably be low. Such added value may be higher for less extreme situations, but the risk associated will also be lower and the decision not necessarily easier to make. The added value may be higher for the progressive disease risk matrix, since the patient characteristics [including male gender, extensive colitis and diagnosis before 40 years of age] may not necessarily by themselves trigger the use of an immunomodulator and/or a biologic. Having in mind the risk of developing progressive disease [up to 70%] in this situation, and despite the limitations highlighted [associated with the definition of this outcome], this could represent a sufficient argument for early starting of an immunomodulator and/or biologic.

The main limitation is maybe conceptual and reflects a paradigm shift that has occurred recently. If the search for predictors of disease outcome has been very active over the last decade in inflammatory bowel disease, it may become obsolete or much less important when one is implementing a treat-to-target strategy. A strategy based on predictors is heavily dependent on the quality and the strength of

these predictors and is associated with a risk of overtreatment and undertreatment linked to imperfect prediction. Compared with this, the treat-to-target approach has the big advantage that the strategy is rapidly and constantly corrected [through step-up or even de-escalation] to keep tight control of the disease, thanks to the monitoring.[4] With treat-to-target, whatever the initial treatment strategy, the risk of undertreatment and overtreatment remains low. As emphasized by the authors, there may be a complementarity between the predictive strategy and a treat-to-target approach: the initial treatment is based on the predictive assessment and is then constantly adapted based on the regular monitoring.

Despite the above-mentioned limitations, with their large and well-conducted multicentre study, Fernando Magro and colleagues have generated a tool that should be easy to use in routine practice and that may help the clinician to choose an initial treatment strategy after having assessed the patient. This initial treatment option should then be rapidly followed up by close monitoring and the treatment adapted according to a treat-to-target approach. Applying this and taking advantage of the increasing number of efficacious drugs available to treat ulcerative colitis, one may further decrease the risk of progressive disease and colectomy.

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Conflict of Interest

None declared.

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