

Editorial

A Simple Intestinal Ultrasound Score in Crohn's Disease: First Big Step Towards New Paradigms

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Despite diagnostic and therapeutic improvements, the limitations in defining and achieving treatment targets for Crohn's disease [CD] still exist. There is an unmet need for non-invasive reliable diagnostic tools to assess disease activity in CD and for tight monitoring of transmural involvement. Intestinal ultrasound [IUS] has been shown to be a reliable tool to determine transmural disease activity in CD with high reliability and reproducibility.^{1–3} No less important in this context is the preference of patients, who favour IUS as standard diagnostic tool as it connects directly and in real time their symptoms to objective measurements of intestinal inflammation.⁴ Consequently, the use of IUS as a first-line imaging modality as well as imaging tool to follow up active CD is highlighted in recent ECCO diagnostic guidelines.⁵

The regular use of IUS in monitoring the treatment depends on the utilization of standardized, validated and reliable activity measures reflecting disease activity. These are necessary requirements to demonstrate therapeutic response and transmural healing. These sonographic measures need to be repeatable, consistent and prospectively defined.

The study by Fredrik Saevik *et al.* in this issue introduces a simple ultrasound activity score for CD that consists of simple ultrasound parameters including bowel wall thickness and colour Doppler imaging. The simple ultrasound score correlates well with endoscopic disease activity. The current score has already been validated in a second cohort and correlates very well with SES-CD [Simple Endoscopic Score for Crohn's Disease] in both cohorts. Note that the lack of correlation between the IUS score and biochemical parameters is similar for other modalities including endoscopy.

Several studies have attempted to define CD disease activity with IUS, providing IUS activity scores. The study by Saevik *et al.* strengthens for the first time the relevance of standardized measurement of IUS findings to determine disease activity in CD. Attempts to develop simple scores with standardized measurements for disease activity, as demonstrated in the current study, are a crucial step for monitoring of CD.

The IUS index proposed in the Saevik study is not the first one developed to determine CD activity. However, these other scores have

not been validated, as summarized in a recent review.⁶ Consistent with previous findings, it appears that bowel wall thickness [BWT] and vascularity, assessed by Doppler signals, seem to be the most relevant parameters that should be included in an activity score. Interobserver variability is known to be particularly low for these parameters if they are determined in a highly standardized fashion.⁷ Standardization of measurement is a crucial factor for any parameter included in a score. Among several IUS parameters potentially correlated with disease activity, such as BWT, echostratification, length of BWT, vascularization assessed by colour Doppler, stenosis, fistula and fatty wrapping, BWT appears to be the most relevant. However, we have to consider that increased BWT may also reflect chronic fibrotic changes. The combination of this parameter with vascularization, which is more strictly related to neoangiogenesis and disease activity,⁸ included in this simple ultrasound activity score, allows us to distinguish increased BWT due to fibrotic changes from changes due to acute inflammatory activity. Other IUS findings which might be relevant for detecting an inflammatory process, such as echostratification and mesenteric fat, seem to be less important for this disease activity score, probably because they are less reliable and reproducible parameters, without clear standardized measures.

Considering the clinical context where the score may be used, it has to be evaluated if we need one single or more scores to determine disease activity and chronicity, severity of disease as well as response to treatment. It is questionable if an all-in-solution for a score that is suitable for any clinical situation is a realistic goal. From the current perspective it is more likely that we need different scores for different clinical situations in the future.

Before the simple ultrasound activity index for CD can be used in clinical practice and particularly in multicentre clinical trials, several aspects must be considered. First, the responsiveness, namely the ability to detect changes in response to treatment, needs to be tested in an independent randomized cohort and measurements in trials should be confirmed by central reading. Central reading has recently been implemented for IUS by the IBUS group and used for the Stardust IUS substudy trial.⁹ Interim analysis from that trial as



well as data from the TRUST-CD study suggest that response to treatment is variable and differs between small and large bowel.⁹ Whether the simple IUS score is of comparable value in the small bowel vs colon needs to be proven.

Second, the score should reliably assess not only the terminal ileum but also the entire small bowel, and also evaluate the lesions proximal to the reach of ileocolonoscopy. For this, enteroscopy, video capsule endoscopy or magnetic resonance enteroscopy [MRE] should be used as gold standard comparators in such a confirmatory study.

Last, but not least, the score should be included in randomized clinical trials to determine if it is effective for clinical decision-making. The limitations of current clinical and endoscopic scores in CD trials are well known and it is time for a new paradigm shift and new end points such as transmural healing.

If endoscopic disease activity in CD can be reliably determined by the use of a simple ultrasound score, and if such a score could also be used to strictly monitor disease activity, and detect deeper degrees of remission such as transmural healing, we should change our diagnostic algorithms. As IUS is a non-invasive examination needing no preparation, response as well as non-response to therapy can potentially be detected at a much earlier time point than can logistically be done by endoscopy. With IUS and the use of reliable IUS activity scores, we may come up with a cost-effective, safe and easy to use diagnostic tool that might reduce the number of invasive colonoscopies for determining and monitoring disease activity in CD patients in the near future.

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Conflict of Interest

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Author Contributions

T.K.: first draft of the editorial; C.M.: finalization of the editorial including further relevant aspects; G.M.: second draft of the editorial including new relevant aspects

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