Traditionally, the primary treatment goal in ulcerative colitis (UC) has been the achievement of clinical remission. However, over recent times, it has been shown that achieving endoscopic mucosal healing (MH) in UC is associated with improved clinical outcomes including prolonged remission, fewer hospitalisations and colectomies and improved quality of life when compared to achieving clinical remission alone. This has led to recommendations by both the FDA and the STRIDE working group that mucosal healing should be a therapeutic goal of treatment. However, the optimal target for mucosal healing, particularly in the trial setting, is yet to be defined or validated.

The article by Vuitton and colleagues aim to provide expert evidence-based guidelines on the appropriate endoscopic targets for remission and response in UC clinical trials. The recommendations were developed from a steering committee of 15 IBD specialists who undertook a literature review and Delphi-style vote. Ultimately, it was decided that a UCEIS score of 0 should define endoscopic remission and a decrease in Mayo endoscopic score of ≥1 or decrease in UCEIS of ≥2 should define endoscopic response. The definition of endoscopic remission as UCEIS score of 0 is a significant advance as most trials define mucosal healing as a less strict score of Mayo Endoscopic Sub-score ≤1. This is despite evidence that patients with a sub-score of 0 have significantly better outcomes compared to those who only achieve a score of 1. In addition, Vuitton et al. outline the important role of training endoscopists on precise definitions and scoring of lesions before clinical trials and the critical role of centralised readers in both UC and CD trials.

It is encouraging to see attempts being made to create stringent consensus guidelines to be adopted in clinical trials. Despite mucosal healing being accepted as the minimal treat-to-target therapeutic goal, thus far trials have used numerous scores and indices when defining mucosal healing and improvement, which makes outcomes difficult to interpret and comparison of results between trials not feasible. It is therefore important to have a standardised, validated UC endoscopic index that all trials adopt. In future, guidelines on standardised timing of these assessments would also be of benefit.

There are several limitations to this paper. It is confusing that two different scores are recommended to define endoscopic response but only the UCEIS is recommended for defining mucosal healing. This is consistent with the prior lack of consensus in this field; clearly from a practical point of view, it would be better to use one index. In addition, although a different question, histological outcomes have not been addressed. It has been shown that histological inflammation is common in patients with mucosal healing and portends a poorer prognosis and both the FDA and STRIDE now recommend including histological outcomes as an adjunctive goal in UC clinical trials.

Finally, there are several unanswered questions that remain if future trials are to adopt the UCEIS as their endoscopic index. These questions include (i) what UCEIS scores define mild, moderate and severe disease?; (ii) how responsive to change is the UCEIS after treatment?; (iii) do prospective studies using a UCEIS target of zero change natural history outcomes and finally (iv) is the UCEIS applicable to use with flexible sigmoidoscopy rather than full colonoscopy?

In conclusion, this study provides some consensus on definitions of endoscopic remission and response in UC clinical trials. This is important as mucosal healing guidelines have become more stringent with experts now agreeing that normal mucosa is required for endoscopic remission. The role of histological remission in further improving clinical outcomes requires further prospective evaluation.
Editorial: combining elastography with blood test for fibrosis assessment in chronic hepatitis C

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The imprecision and invasive nature of the liver biopsy has led to the development of several validated non-invasive fibrosis markers, which have decreased the need for liver biopsy in chronic hepatitis C patients. In the realm of highly effective oral therapies, management is affected by the presence or absence of severe fibrosis, which would warrant surveillance screening for hepatocellular carcinoma and oesophageal varices. Vibration controlled transient elastography (VCTE) is a validated non-invasive modality that is widely used with an AUROC of 0.90 for detecting advanced fibrosis. The limitation of VCTE is its potential overestimation of fibrosis, particularly in those with obesity or increased necroinflammatory activity.

In contrast, serologic markers have historically led to underestimation of fibrosis levels. Combination of VCTE with other markers have shown favorable results and have been proposed by national guidelines. Calés et al. evaluated the performance of a serologic test (FibroMeter V2G) with VCTE (Fibroscan) as two separate constitutive tests, as well as a single combined test (FibroMeter VCTE2G), for the detection of severe fibrosis in hepatitis C patients. They found increased accuracy with the combination test, compared to individual tests alone, especially when there was concordance between the tests, validating the recommendation of using combined tests. The authors conclude that if the constitutive tests are concordant, then the diagnosis can be accepted, and if discordant, FibroMeter VCTE2G should be pursued. However, in cases (3.2%) of strict discordance, the FibroMeter VCTE2G is unreliable for detecting severe fibrosis (accuracy of 44%) and requires alternative measures for fibrosis (i.e. liver biopsy). The authors projected a reduction in the liver biopsy rates from 28% to 1% with the use of this diagnostic algorithm.

This study validates EASL-ALEH and AASLD-IDS recommendations to combine biomarkers with VCTE and shows the combined test to have improved accuracy, especially when there is concordance, eliminating the need for an invasive liver biopsy in the majority of patients. However, the claim that the liver biopsy rate is reduced from 28% to 1% should be taken with some caution as the authors did not provide the invalid and failure rate of VCTE, one of major components in their combination test. Although VCTE has revolutionised the non-invasive measurement of fibrosis, unreliable results and failure to obtain results have been reported in 3% and 16% of cases, respectively, mostly due to obesity and operator experience. It would be important to see how the combined test performs in the United States population, which has a higher mean body mass index than this study cohort from France. While the accuracy of the FibroMeter VCTE2G is excellent, it still leaves 8% of patients misclassified, making it important that the clinician still thoroughly evaluates the patient’s clinical, radiologic and laboratory data. The role of this combination test in monitoring the progression or regression of fibrosis, as well as its applicability to other chronic liver disease is an important avenue for research.

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LINKED CONTENT
This article is linked to Calés and Boursier, and Calés et al papers. To view these articles visit https://doi.org/10.1111/apt.14032 and https://doi.org/10.1111/apt.13954.

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