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Short Communication

Miniprobe Based EUS as an Adjunct to Ileocolonoscopy in Patients with Crohn´S Disease

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Abstract

Background: Crohn´s disease (CD) is a chronic inflammatory condition characterized by a cumulative bowel damage over time. In order to change the course of the disease, treatment should strive to abrogate the inflammation. Hence, objective monitoring of the inflammatory activity and/or response to therapy is necessary. Endoscopic ultrasound using a miniprobe (mEUS) during ileocolonoscopy offers unique possibility to assess the endoscopic disease activity and the alterations in the intestinal wall at the very same occasion.

Patients and Methods: The study comprises 26 patients (18 women, 10 men), of these 18 suffered from Crohn´s disease (group A), whereas in eight symptomatic patients the suspicion of CD was not confirmed (group B). After endoscopic evaluation, the mEUS was performed using the ultrasonic Olympus 20 MHz UM-3R miniprobe catheter passed through the accessory channel.

Results: In group B wall stratification, featuring five distinct layers could typically be seen, but this was not a universal finding. The total wall thickness was ≤ 3.8 mm. In the group A the TWT ranged from 3.8 -10.2, mean 5.1 mm and the stratification appeared blurred. The mEUS was easily learned and it prolonged the procedure only marginally.

Conclusion: These preliminary data suggest that mEUS my become a valuable adjunct to endoscopic assessment of the Crohns patients. Nonetheless, more work is needed to standardize the procedure as well as to elucidate its contribution in clinical management of the patients with CD.

Keywords: *Inflammatory Bowel Disease; Inflammation; Endoscopy; Endoscopic Ultrasound*

Introduction

Crohn´s disease (CD) is a chronic inflammatory condition characterized by a cumulative bowel damage over time. As a result, about half of the patients require surgery for ill health and/or complications within 10 years after diagnosis [1]. It is well known that active inflammation may persist and lead to poor outcomes even in patients who are asymptomatic [2,3]. Therefore, if we are to change course of the disease, treatment should aim beyond resolution of symptoms and abrogate the inflammation. Hence, objective monitoring of the inflammatory activity and/or response to therapy is of paramount importance. At present ileocolonoscopy is considered gold standard for that purpose [4], and mucosal healing [5] has become the "target to treat" for contemporary treatment of CD. However, in CD, the inflammation afflicts the whole thickness of the bowel. Still, at present we have limited knowledge to which extend the endoscopic image mirrors healing of the mural inflammation.

Endoscopic ultrasound using a miniprobe (mEUS) during ileocolonoscopy offers the possibility to assess the endoscopic disease activity and the alterations in the intestinal wall at the very same occasion. Nonetheless, the experience with mEUS in CD is scarce. Herein, we report our preliminary findings with the method.

Patients and Methods

The study comprises 26 patients (18 women, 10 men), aged 25 - 76, mean 42 years. Of these 18 with CD (group A) were referred for ileocolonoscopy as part of evaluation aimed at adjustment of treatment. Eight other patients were referred because of symptoms suggestive of CD, but in whom the diagnosis of CD was reasonably excluded (group B). Three of these showed at least one abnormality on CT or MRI and/or laboratory signs of inflammation. The mEUS were performed using the ultrasonic Olympus 20 MHz UM-3R miniprobe catheter which provides B – mode 360-degree radial imaging perpendicular to the axis of insertion. The miniprobe was passed through the accessory channel and placed in the segment of interest. In order to achieve acoustic coupling quantity of water needed to get the miniprobe immersed was flushed into the lumen. Antispasmodics were not given to any of the patients.

The obtained images were estimated with respect to changes in the wall stratification as well as total bowel wall thickness (TWT) which was measured between the luminal hyperechoic zone and the outer limit of the hypoechoic zone of muscularis propria.

Results

The mEUS were successful in 20 patients, whereas we failed to obtain acceptable images in three of the patients with CD and in three of the patients in group B: in two patients, intense motility prevented constant immersion of the catheter, and in four the miniprobe was worn out or broken.

In the patients in the group B typical wall stratification, featuring distinct five layers, figure 1, was disclosed in three, whereas two showed partly blurred stratification, figure 2. The TWT varied from 2.0 to 3.8 mm.

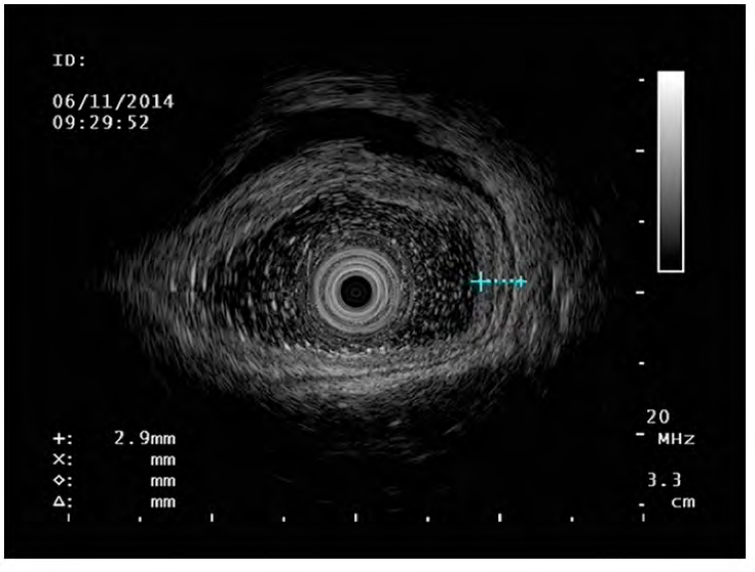

Figure 1: *Normal TWT and typical stratification of the intestinal wall.*

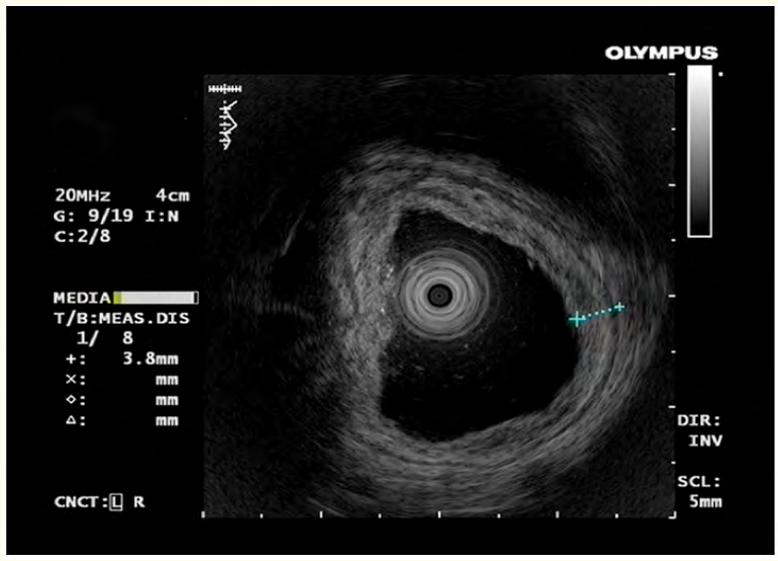

Figure 2: *TWT 3.8 mm and blurred stratification in a group B patient.*

Notably, in two patients in this group a TWT of 4.5 and 5.7 mm respectively was registered during the bowel contraction, but the TWT was normal on relaxation. Figure 3 a and b. The typical appearance in one of them is shown in figure 3 a and b. With exception of two patients in group A, who were in clinical as well as endoscopically remission, the TWT was 3.8 - 10.2, median 5.1 mm, and these also showed loss of stratification such that only three layers could be discerned: mostly the intestinal wall above m. propria appeared as one hyperechogenic layer contributing the most to the TWT, whereas m. propria showed normal appearance: figure 4. However, in some m. propria appeared markedly conspicuous, figure 5 or outright thickened, figure 6, comprising at about a third of the TWT. Marked sonographic thickening of m. propria, but normal mucosa and submucosa were observed in two patients with segmental narrowing fronted by endoscopically normal mucosa, example Figure 7a, b. In the two other patients who achieved clinical and endoscopic remission after anti – TNF therapy overall normal sonographic appearance was registered, figure 8 a, b. Nonetheless, corresponding to patchy areas of minimal endoscopic abnormalities such as solitary erosions and/or shortened villi the TWT was slightly increased and the stratification appeared blurred, figure 8 c.

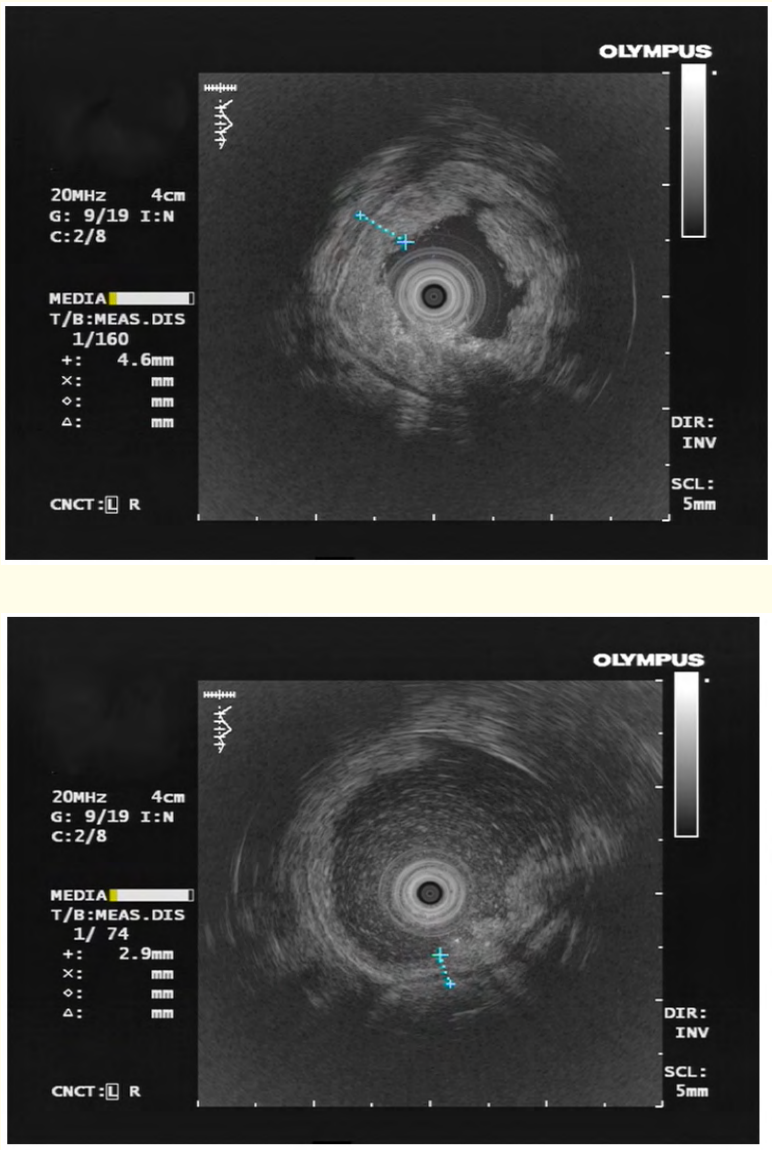

Figure 3: *a. mEUS appearance of intestinal wall during contraction in a group B patient. Increased TWT as well as blurred stratification, b. mEUS appearance in the same patient during relaxation. Normal TWT.*

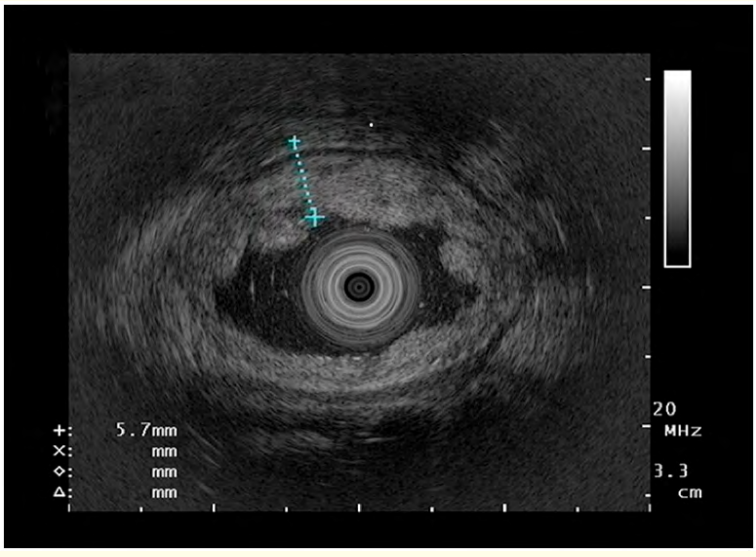

Figure 4: *Increased TWT and absent stratification in a group A patient. M. propria appears normal.*

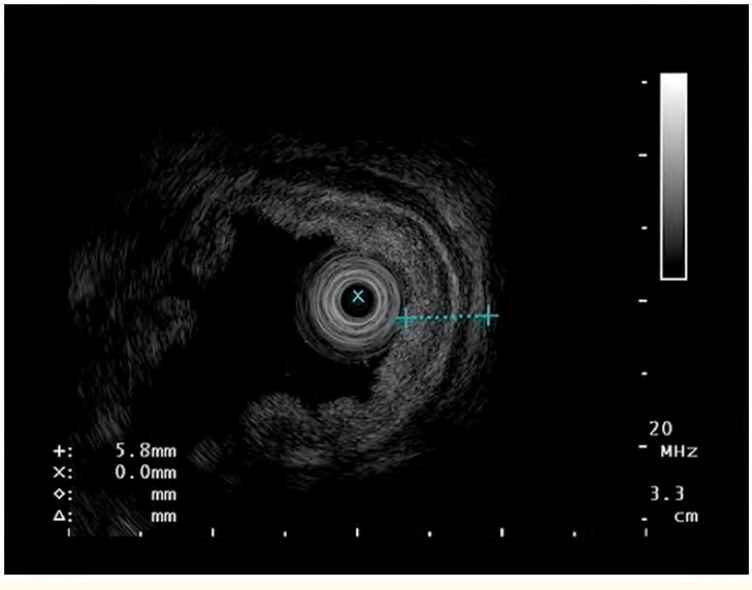

Figure 5: *Conspicuous m. propria in a group A patient.*

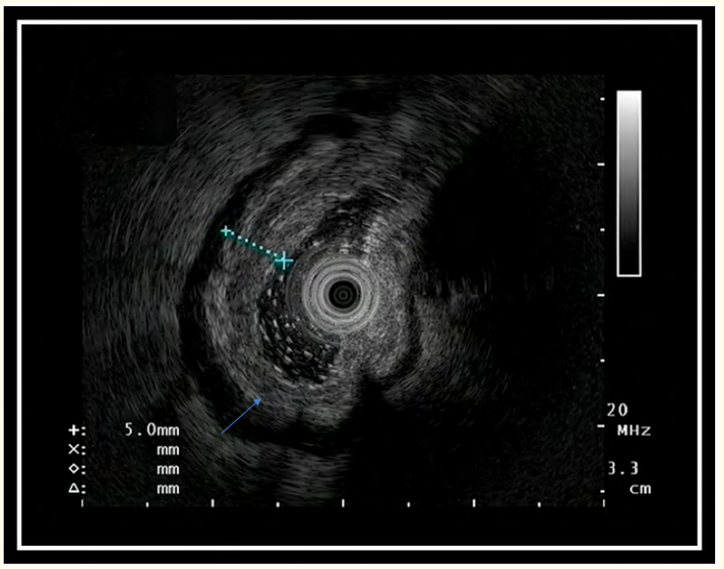

Figure 6: *Markedly thickened m. propria in a group A patient.*

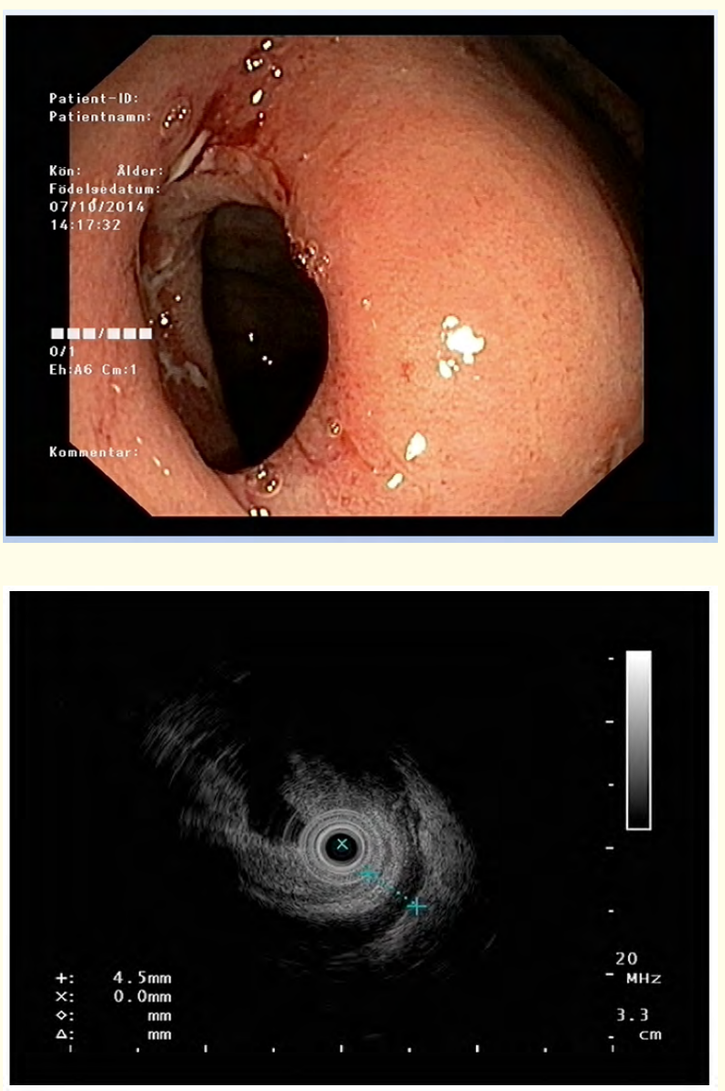

Figure 7: *a. Mucosa without active inflammation in a narrowed segment. b. m EUS shows normal mucosa/submucosa but thickened m. propria.*

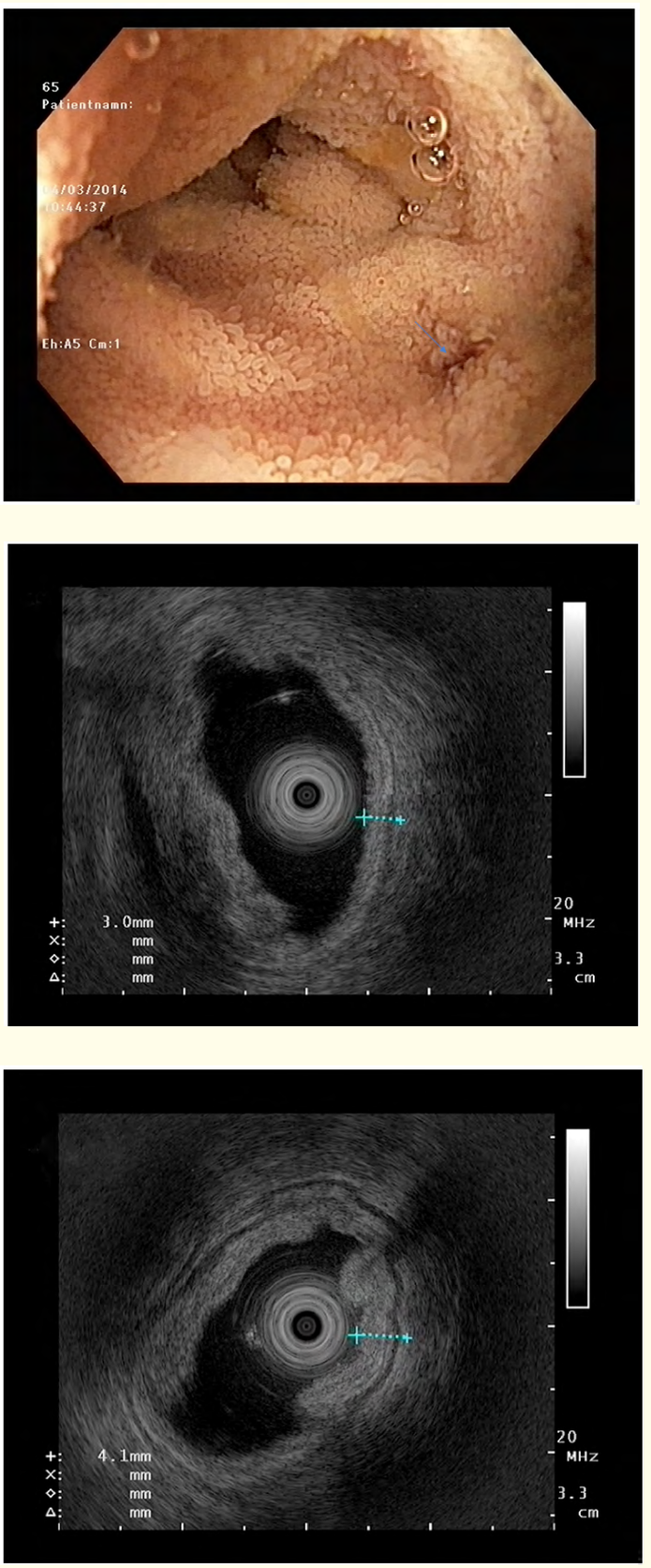

Figure 8: *a. Almost complete endoscopic remission, small erosions still present. b. mEUS shows mostly normal TWT. c slightly increased TWT in areas of erosions and/or blunted shorten villi.*

No effort has been made to explore correlations between clinical and/or endoscopic findings and mEUS features because the limited numbers of patients included precluded meaningful analysis.

The mEUS added about ten additional minutes to the ileocolonoscopy. None of the patients reported any discomfort what so ever during the procedure.

Discussion

Therapeutic objectives in CD are evolving toward control of the inflammatory process aimed at preventing progression of the disease. Indeed, achieving mucosal healing during anti- TNF therapy has been reported to portend favorable clinical outcomes in terms of reduced need for hospitalization, surgery as well as reduced relapse rates [5]. However, to be relevant for the natural course of CD, MH should also be a marker of sustained remission after stopping the treatment. Whilst this has also been shown to be the case in several studies [6-8], mucosal healing did not predict sustained remission after discontinuation of the treatment in other studies [9-11]. This could, at least in part be due to persistent inflammation and continuing structural damage beneath the endoscopically healed mucosa [5]. Hence, cross sectional modalities such as MRE or US may grow increasingly important when defining healing in CD [12,13]. However, both modalities have limitations. In addition, ileocolonoscopy is still regarded as a referent method for establishing the disease activity as well as for evaluation of response to therapy in ileocolic CD [4]. Thus, mEUS might become a useful adjunctive tool providing both endoscopic assessment of intestinal mucosa and mural disease at the same occasion.

Previous experience using mEUS in IBD is scarce and mainly limited to colonic disease [14,15]. Thus, our knowledge of sonographic appearance of CD in terminal ileum stems mainly from transabdominal ultrasonography; CD is characterized by thickening of bowel wall (TWT) as well as loss of layer stratification [16]. The TWT can be objectively quantified, and its clinical relevance as well as excellent reproducibility has been demonstrated in several studies [16,17]; a threshold of > 3 mm of TWT as cut of value offers a sensitivity of 88% and specificity 93% [16]. Moreover, reportedly TWT could be able to predict the risk for surgery in patients who never were operated [18] as well as for symptomatic and/or surgical recurrence after conservative surgery [19-21]. In our study, all patients with active disease showed a TWT exceeding 3.5 mm as well as loss of normal stratification. Three of the patients without CD also showed TWT exceeding 3 mm. It is a well-known that increased TWT is not pathognomonic for CD [22]. Moreover, at times it may be difficult to keep the ultrasonic catheter parallel to the intestinal wall. As a result, the image of the wall structure may become less clear and/or the wall may appear thicker. In addition, because the wall thickness and the luminal diameter are inversely related the acquisition of the mEUS image may be affected by motility. This is clearly illustrated in two of our patients, in whom the TWT during contraction was erroneously estimated as abnormal indicating, that the method needs to be more standardized e.g. by using antispasmodics during the procedure. Nonetheless, none of the patients without CD had a TWT > 4 mm. Increasing the limit of normality to 4 mm increases specificity, but at the expense of sensitivity [16]. Finally, the finding of salient or even thickened m. propria in some patients is intriguing. The relationship between altered bowel wall stratification and TWT is at present not exactly known, but it is tempting to speculate that thickened m. propria may signify deeper layers of the intestinal wall to be afflicted by inflammation and or by structural damage. Clearly, further studies are needed to define the significance of different sonographic alterations to the clinical course of the disease.

The finding of normalization or near normalization of the TWT as well as wall stratification after treatment in two of the patients with CD is worth a comment. In a recent study only four of the 23 patients who showed complete or partial MH achieved TWT < 3 mm [23], and in another study, none of the eight patients who achieved complete MH showed TH [24]. Studies using MRI or US demonstrated improvements of the mural inflammation in response to anti TNF treatment in a proportion of patients, but normalization of the bowel wall occurred only in minority [25,26]. This could be due irreversible structural damage, but also due to healing of mural inflammation lingering behind the mucosal healing e.g. in a recent study normalization of the sonographic wall appearance occurred in 14% after 12 weeks but in almost 30% after a year of treatment [27]. Clearly, even in patients with strong endoscopic improvement active mural activity may still persist which may result in progressive structural bowel damage. Nonetheless, the clinical significance of achieving mural healing remains to be explored.

Result of this study suggest the mEUS is feasible in most cases. It is easily learned, it poses no burden to the patient, and it adds marginally to the procedure time. It is not supposed to compete with other cross sectional studies, but in cases when ileocolonoscopy is indicated it might offer additional useful information. Nonetheless, more work is needed in order to standardize the procedure as well to explore the reproducibility of the method.

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