Reviewer's report

Title: Early ultrasonographic detection and assessment of the severity of Crohn's disease recurrence after curative ileal resection

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Reviewer: Odd Helge Gilja

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Here comes the details:
The introduction is OK and to the point and refers to previous relevant work, but could be better if it incorporated some of the points that should be cut from the start of the Discussion (See below).

Of the four study questions posed, question 1 is poorly formulated. What does limited and minimal involvement really mean? Furthermore, if one wants to detect the initial/early recurrence, the method described is not appropriate. The patients are examined from 6 months up to 2 years after resection and the author has no way of knowing if the changes seen are early or initial. One would expect that the changes became more severe the further away from the operation date the patients were examined. Actually this is also shown by data in this study as Median time from surgery increases significantly with increasing Rutgeert score (Table 2). The title indicates that this method is used for early detection of recurrence of Crohns disease after ileal resection while the study is not designed for this. It should be more in the line of "Detection of recurrence....and so forth."

The expression "transmural" is introduced in the first paragraph of the introduction is used through the article as synonymous to wall thickening on SICUS. This is not correct as thickening of the gastrointestinal may be detected on ultrasound even though the pathological changes are not transmural. The thickening can be solely caused by edema in the mucosa and submucosa without involvement of the proper muscle and would then not be considered as transmural. The term transmural should therefore not be used.

The patient population in the material and methods (M&M) section is poorly and insufficiently described (Page 3, paragraph 6). There is no explanation as to how and when the patients were recruited, if this was consecutive from a cohort or on a case by case basis. According to M&M (page 4, paragraph 3) all the patients were examined with SICUS and ileocolonoscopy 6 and 12 months after surgery and at regular intervals 6-12 months after. According to Results, however, 19 patients were examined after 6 months, 16 after 12 months, 5 after 18 months and 18 after 24 months (Page 6 paragraph 4). This adds up to 58 patients as described, but only one examination per patient. Furthermore, 111 examinations were included in the study (Page 6, paragraph 5). When were the extra examinations performed, on which patients? How many patients went through 2 examinations? How many patients went through 3 examinations? And so on.
How many patients were excluded and for what reasons?

It is not clear in the M&M what is actually measured in the anastomosis (Page 4, paragraph 5). The author claims to measure wall thickness, but in Figure 1A the cursors actually traverse a fold in the intestine and measure from mucosa to mucosa. In the Discussion (page 10, paragraph 4) the author states that the combined wall thickness of the ileal and colonic limb in the anastomosis is measured. What is actually measured? Between which echo layers are the cursors set? Furthermore, the definition of a bowel stenosis (page 5, paragraph 1) does not make sense and must be rephrased.

The remaining description on how SICUS and ileocolonoscopy was performed and scored is clear, but I wonder why a higher frequency probe was not used? I would argue that it is difficult to properly delineate the GI wall with a 5 Mhz probe and even worse with a 3.5 MHz probe. Since the GI wall can be only 1 mm thick in areas this introduces a selection bias. (Haber, HP, Stern, M. Intestinal ultrasonography in children and young adults: bowel wall thickness is age dependent. J Ultrasound Med. 2000 May;19(5):315-21.)

There is no indication as to why the author would choose to dichotomise the wall thickness data with a cut off of 3.5mm with a reference to previous studies in the text (page 5, paragraph 5). This is especially odd when the definition of pathological wall thickening was set to 3 mm. Again it comes down to what you measure in the anastomosis, but I suspect that this cut off was chosen after the collection of the data. When hypothesis are developed post hoc, this should be mentioned. If this cut off was chosen before the study was performed I would like the author to explain why it was set to 3.5 mm.

It is not clear from the descriptive data when all the 111 different examinations were performed or if some patients were examined more than twice. And I wonder if Fischers exact test be performed on variables which contain a mix of dependent an independent values? Regarding the results from the multiple regression analysis I would leave it to a statistician to evaluate if the criteria for using multiple regression and ordinal logistic regression have been met.

The discussion needs to be shortened. The first three paragraphs are mostly repetition of the introduction and should be removed (Page 9, paragraph 2 and 3. Page 10, paragraph 1 and 2) Content the author feels is essential for the article in these three paragraphs that is currently not in the introduction can be incorporated there.

Previous relevant work is acknowledged, but the author states that MRI does not have resolution to show early recurrence while supporting the claim with a reference on CT enterography. A relevant reference should be provided. (Page 10, paragraph 4) Furthermore, limitations are not discussed properly. Inter-observer variation is mentioned briefly, but the author argues that this may be amended by reducing intra-observer variability, which is not the case. I could think of a number of weaknesses beside this. The patients are for instance examined at different time instances. This means that the author can not be sure if the findings on ultrasound and ileo-colonoscopy represent early or initial
findings. There are 58 patients and 111 examinations which mean that both independent and dependent variables have been pooled. Maybe this can be corrected for, but this must reviewed by a statistician. Finally, the author initially operates with a cut off of 3mm of wall thickness between pathological and healthy intestine in the material and methods. During the analysis of the data, however, the wall thickness data are dichotomised using 3.5mm as cut off and then the Fisher exact test is performed. This hypothesis was probably posed post hoc.

Major compulsory revisions:
Specifically research question 1 should be dropped as the study is not designed to answer this and only the first exam from the 58 patients should be used for data analysis if there is no way of correcting for the pooling of independent and dependent variables. Since these were consistent with the data presented (but not shown) this should not be a problem. The recruitment of the patients must be described better in the M&M section. The definition of what is measured in the anastomosis is unclear and must be defined better. When the author speaks of "transmural lesions" measured on SICUS this should be replaced with wall thickening.

Minor essential revisions:
Figure 1 is of poor quality and offer very little information to the reader. It is difficult to believe that it is possible to measure the intestinal wall thickness at all from these images.

Figure 3: The cut off values that offer the best sensitivity and specificity should be added to the ROC curves. There are some language issues that need to be corrected as some sentences in the manuscript does not seem to make sense.

For specific manuscript editions, also look at the attachment.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

no competing interests with the author